The Research Council of Norway

Evaluation of the Norwegian Centres of Excellence (SFF) Funding Scheme

Impact cases

RESEARCH FOR INNOVATION AND SUSTAINABILITY

The Research Council of Norway

Evaluation of the Norwegian Centre of Excellence (SFF) Funding Scheme

Impact cases

Evaluation

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Introduction

The Norwegian Centre of Excellence (SFF) scheme's primary objective has been to increase the scientific impact of Norwegian research. Societal impact has not been an aim for the individual SSF. Still, the RCN expects that positive effects on society may spring from the investments in the centres over time. Acknowledging that the path from research results to societal applications may be long and unpredictable, we do not to expect impact to be found in every centre, and certainly not yet. Due to their short time of operation we have also excluded the latest generation (SFF-IV), which started in 2017, from this part of the evaluation exercise.

The RCN invited current and former SFFs to submit case studies that documented some examples of either scientific or societal impact. The invitation was sent in June 2019, and RCN held a workshop in September 2019 to clarify the assignment and to let the SFFs discuss possible cases. RCN has not given feedback on the submitted cases.

Societal impact

The definition of, and model for, societal impact was derived from the upcoming 2021 Research Excellence Framework (REF) in the United Kingdom. In the REF, societal impact is defined as any effect on, change or benefit to the economy, society, culture, public policy or services, health, the environment and quality of life, beyond academia. Impact includes, but is not limited to, an effect on, change or benefit to:

- the activity, attitude, awareness, behaviour, capacity, opportunity, performance, policy, practice, process or understanding
- of an audience, beneficiary, community, constituency, organisation or individuals
- in any geographic location whether locally, regionally, nationally or internationally.

Academic impacts on research or the advancement of academic knowledge is excluded, while impacts on students, teaching or other activities both within and/or beyond the SFF is included.

Scientific impact

The template for scientific impact was developed by the Nordic Institute for Studies in Innovation, Research and Higher Education (NIFU) for this evaluation following the same structure as the template for societal impact. Scientific impact was defined by NIFU as an effect on, change or benefit to the advancement of scholarly knowledge/science. It includes, but is not limited to an effect on, change or benefit to:

- theories/theoretical frameworks,
- scientific methods/approaches to scientific problems
- the research agenda (e.g. by providing unexpected results)

Scientific impact includes opening up new fields of research; enabling new kinds of analyses, and building/developing new research fields or interdisciplinary communities.

The definition of scientific impact was made flexible. If the definition did not fit the field(s) of research of the SFF, the definition could be extended to include the forms of scientific impact that are/were important in the field(s) of the SFF.

Guidelines
The RCN had the following requirements for reporting societal/scientific impact to the evaluation:

- The research underpinning the impact case should be anchored within the SFF, meaning that some of the research should have been performed and reported within the centre period.
- Each SFF (except from SFF IV) is invited to submit up to four impact cases, documenting either societal impact or scientific impact. If the centre chooses to submit more than two impact cases, the centre should submit cases that represent both societal impact and scientific impact.
- The SFF should use the provided templates to report the impact (Appendix A).

Impact cases
The RCN received 62 impact cases from 23 centres of excellence (see appendix B). 32 of the case studies were scientific impact cases, and 26 were societal impact cases. 4 of the submitted cases were a combination of societal and scientific impact. 10 centres from SFF I and -II, and all the centres from SFF-III, submitted one or more case studies to the evaluation. This was an expected result, given the short deadline, and the fact that the SFF-I and - II centres are no longer active. The submission of impact cases was voluntary.

SFF I-III	Scientific impact cases	Societal impact cases	Combination (sci. and soc.)	Number of impact cases	Number of SFFs submitting cases
SFF I	6	6	3	15	5
SFF II	8	5	0	13	5
SFF III	18	15	1	34	13
Total	**30**	**26***	**4**	**62**	**23**

* Three centres sent in the same impact case to the evaluation (CMA, CBC, PGP). The case is counted as a SFF I case in this table.

Amendments made by RCN
The impact cases in this report will be presented in the form submitted by the participating institutions, with two exceptions:

1. Supporting materials of a private character, such as the inclusion of e-mails or personal statements, have been omitted from section 5 in the template. This information has been available to the evaluation committee.
2. Names and contact information for external references have been left out from section 5 in the template. This information has also been available to the evaluation committee.

1 SFF I

1.1 CASTL - Center for the Advanced Study of Theoretical Linguistics

1.1.1 Scientific impact: Formal Framework for Lexical Verb Meaning

Institution: UiT The Arctic University of Norway		
Name of SFF: CASTL (Center for the Advanced Study of Theoretical Linguistics)		
Title of case study: Formal Framework for Lexical Verb Meaning		
Period when the underpinning research was undertaken: 2006-2010		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Prof. Gillian Ramchand	**Role(s) (e.g. job title):** Professor of Linguistics (ISK)	**Period(s) employed by submitting SFF:** 2006-2013
Period when the impact occurred: 2008---> present		

1. Summary of the impact

A new formal theory of verb meaning (First Phase Syntax) designed to account for the typological commonalities and variability across languages in verb class membership. Used as a core research foundation for the next generation of phd and masters students within syntax and semantics.

2. Underpinning research

CASTL's research remit involved a commitment to selective global comparison, meaning that typologically distinct languages were systematically compared in different domains. In the case of Ramchand, her original research profile in the syntax and semantics of verbs produced an intense collaborative theoretical study over the years of CASTL into the scope and flexibilities of verb meaning, semantically and morphosyntactically. Research seminars and collaboration with Svenonius, Taraldsen and Starke provided the theoretical stimulation and discussion which allowed Ramchand to turn her empirical base into a formalized theory of the syntactic and semantic generalizations underpinning verb meaning. This resulted in the research monograph *Verb Meaning and the Lexicon. A First Phase Syntax,* published by Cambridge University Press in 2008 (reported at the end of the SFF). Since then that book has been extensively cited, and has been the basis of many phd and research projects internationally. Based on this work, Ramchand was invited to produce handbook articles on argument structure (Ramchand 2011, 2013, 2019), testifying to the extent to which her model has become the gold standard in this area of theoretical linguistics.

3. References to the research

Research Monograph

2008 *Verb Meaning and the Lexicon* (number of citations: 1626). Cambridge University Press

Relevant Articles in Refereed Journals (research relevant to the impact case)

2008 `Perfectivity as aspectual definiteness: Time and the event in Russian' *Lingua*, volume 118: 1690-1715

2008 `Lexical items in complex predications: selection as underassociation' *Nordlyd. Tromsø Working Papers* 35: 115-141

2008 `Mapping a Parochial Lexicon onto a Universal Semantics' (with Peter Svenonius, CASTL/UiT). in T. Biberauer, ed. *The Limits of Syntactic Variation*. John Benjamins. pp 219-245

2007 `Events in Syntax: Modification and Predication. *Language and Linguistics Compass*. Volume 1: 476-497

2006 `Aspect and Verbal Prepositions' (with Mai Tungseth,UiT. *Nordlyd. Tromsø Working Papers*. 33(2): 149-175

4. Details of the impact

The work on the lexicon within generative grammar has flowed initially from the work on thematic roles which were classified and motivated in the early seventies and eighties of the last century (building on pioneering work by Gruber 65, Fillmore 68). However, later research subsequently uncovered the flaws in that system as a descriptive model (Levin and Rappaport-Hovav 2005). In particular, there was a lack of commensurability and replicability of the classifications because a systematic set of crosslinguistically valid diagnostics was lacking (Dowty 1990). In addition, there was no formally explicit framework that had been articulated as a starting point for other researchers to use, utilizing a common vocabulary and set of primitives. This is what the research monograph *Verb Meaning and the Lexicon* ultimately provided for a whole new generation of researchers. The reason the monograph came into existence was a direct result of bringing together the research expertise of Ramchand in a theoretical environment where she could develop her ideas intensely and freely in close collaboration with experts in syntax and morphology (Svenonius, Taraldsen, Starke). Ramchand was thus able to combine syntactic and morphological generalizations with a formal semantic underpinning, a cross-fertilization between syntax and semantics that is rarely achieved. Her theory makes a claim about the formal semantic primitives of predication that underlie the typological generalizations, and connects the syntax of argument structure to the formal semantics of event structure and aktionsart for the first time. This work has now laid the foundation for subsequent work in the formal syntax and semantics of argument structure. The book produced in 2008 is still being used ten years later to guide beginning research in the field.

5. Sources to corroborate the impact

The google citation claims that the 2008 monograph has already been cited nearly 1700 times and this number is still increasing. It is hard to quantify impact because it does not take into account the phd theses and research articles building from Ramchand 2008, which have also themselves been heavily cited. In a small field, this is nevertheless quite a large citation number for a single highly focused research monograph.

The following handbook articles commissioned by OUP and CUP in the areas of argument structure subsequent to the publication of the 2008 monograph can independently testify to the fact that Ramchand is now considered the major international expert in this field.

2019 Event Structure and Verbal Decomposition in R. Truswell, (ed,). *The Handbook of Event Structure* pp. 314-341. Oxford University Press.

2017 `The Event Domain' in *The Verbal Domain*, Irene Franco and Roberta D'Alessandro (eds).

2013 `Argument Structure and Argument Structure Alternations' in *Cambridge Handbook of Generative Syntax*, M. den Dikken (ed.), CUP

2011 `Minimalist Semantics' in *Handbook of Linguistic Minimalism*, Cedric Boeckx (ed.)

1.1.2 Scientific impact: Microvariation in the Input & Multilingualism

Scientific impact

Impact case: Microvariation in the Input & Multilingualism

Institution: University of Tromsø (currently UiT The Arctic University of Norway)

Name of SFF: Center for Advanced Study in Theoretical Linguistics (CASTL)

Title of case study: Microvariation in the Input & Multilingualism

Period when the underpinning research was undertaken: 2007-2013

Details of staff conducting the underpinning research from the submitting unit:

Name(s): Marit Westergaard (with Merete Anderssen, Kristine Bentzen & Yulia Rodina)	**Role(s) (e.g. job title):** Director / Senior researcher / Professor	**Period(s) employed by submitting SFF:** 2009-2012 (affiliate 2003-2008)

Period when the impact occurred: 2010 -

1. Summary of the impact

The language acquisition group at CASTL produced considerable research on microvariation in the input, mainly using data from Norwegian dialect syntax. This work has contributed to shifting the focus in the field from large-scale generalizations (and setting of innate macro-parameters) to fine-grained details in the input. The findings generally showed that children are sensitive to fine distinctions in syntax and information structure from early on. This led to the development of a new model of L1 acquisition, the Micro-cue Model (Westergaard 2009a, 2014), which has also influenced the field of historical language change. The model is currently expanded to multilingual situations.

2. Underpinning research

While research on *Variation in the Input* in L1 acquisition has to some extent been studied for almost 20 years at UiT, this research focus was defined and officially started with a workshop on this topic in connection with the international conference GLOW XXX in 2007. It was also around this time that the acquisition group was included in the CASTL CoE (through the hiring of Westergaard as director), which gave the language acquisition research group a considerable boost in terms of funding and visibility. This facilitated numerous studies on **microvariation in children's input**, with a focus on **Norwegian dialect syntax**. Much of this work was carried out in connection with another CASTL-based project, the NORMS network (Nordic Center of Excellence in Microcomparative Syntax).

The linguistic phenomena studied were micro-variation related to verb-second word order (e.g. *Kor bor du* vs. *Kor du bor* 'Where live you' vs. 'Where you live'), object shift (*Jeg liker ikke det* vs. *Jeg liker det ikke* 'I like not it' vs. 'I like it not'), double object alternation (*Jeg ga Anne et eple* vs. *Jeg ga et eple til Anne* 'I gave Anne an apple' vs. 'I gave an apple to Anne'), possessive alternation (*Mitt hus* vs. *Huset mitt* 'My house' vs 'House.the my'), etc. Studies on the adult language revealed that the choice of word order was dependent on a variety of **fine distinctions in syntax and information structure**, which also vary across dialects. And crucially, the findings from child language generally showed that, unlike what was often claimed in the literature, children were sensitive to this variation from early on, producing the different options in the same contexts and with similar frequencies as in the adult language.

The child production came from spontaneous corpus data and increasingly from elicitation experiments carried out in the language acquisition lab, which was also established during this period.

The research results were used to develop a new model of L1 acquisition, the **Micro-cue Model** (Westergaard 2009a, 2014); basically claiming that young children do not learn language by making major generalizations (i.e. setting innate macro-parameters), but by paying attention to fine distinctions in the input. The acquisition process is thus **development in small steps**. This means that the innate endowment for language (often referred to as Universal Grammar) is argued to simply provide general principles and constraints for language, not specific linguistic options. The Micro-cue Model was also used to account for step-by-step development in **historical language change**, both for Norwegian and the diachrony of English, in several publications by Westergaard during this time.

The focus of the acquisition research group was soon expanded to the context of the ultimate variation in the input, **bilingualism**. The languages studied were initially English-Norwegian, Saami-Norwegian and Russian-Norwegian, but other language combinations were soon added to the group's profile. In this connection the research group also established a **web-based service for bi- and multilingualism** in 2011, ***Flere språk til flere***, as the first branch of the international network *Bilingualism Matters* (directed by Antonella Sorace, University of Edinburgh, who held an adjunct professorship (20%) at CASTL), which provides research-based information to politicians, administrators, educationalists as well as bilingual families.

3. References to the research

Westergaard, Marit. 2014. 'Linguistic variation and micro-cues in first language acquisition.' *Linguistic Variation*, 14.1, 26-45.

Kemenade, Ans van & Marit Westergaard. 2012. 'Syntax and information structure: Verb-second variation in Middle English.' In Anneli Meurman Solin, María José López-Couso & Bettelou Los (eds.) *Information Structure and Syntactic Change in the History of English [Oxford Studies in the History of English 2]*, 87-118. New York: Oxford University Press.

Anderssen, Merete, Kristine Bentzen & Marit Westergaard (eds.). 2010. *Variation in the Input: Studies in the Acquisition of Word Order*. [*Studies in Theoretical Psycholinguistics* 39], Springer Verlag.

Westergaard, Marit. 2009a. *The Acquisition of Word Order: Micro-cues, Information Structure and Economy.* Amsterdam: John Benjamins.

Westergaard, Marit. 2009b. Usage-based vs. Rule-based Learning: The Acquisition of Word Order in Wh-Questions in English and Norwegian. *Journal of Child Language* 36.5, 1023-1051.

Westergaard, Marit. 2009c. Microvariation as Diachrony: A View from Acquisition. *Journal of Comparative Germanic Linguistics*, 12.1, 49-79.

4. Details of the impact

Our research on microvariation at CASTL, which took place in close collaboration with the Nordic Center of Excellence in Microparametric Syntax (NORMS; see separate impact case by Professor Øystein Vangsnes) has had the following impact nationally and internationally:

- It has contributed to a development away from a view of **L1 acquisition** as large-scale generalizations (setting innate macro-parameters provided by Universal Grammar), which was the dominant theory in the field from the 1980s. Instead the **research focus was shifted to children's sensitivity to fine distinctions in the input**.
- It has contributed to the field of **historical language change** by shifting the focus from considering diachronic development as large-scale phenomena to **development in small steps**.
- It has contributed to putting Norwegian linguistics and **Norwegian dialect variation on the international research scene**.
- The research on microvariation at CASTL has in recent years been **expanded to multilingual situations**, which has resulted in a related model of third language acquisition, the Lingiustic Proximity Model (Westergaard, Mitrofanova, Mykhaylyk & Rodina 2017, Westergaard forthcoming).
- Our numerous publications are widely read and cited, and this has resulted in a number of **invitations** to give plenary lectures at international conferences, teach at summer schools, contribute to important handbooks in the field, be partners in international grant applications, etc.
- Our research findings and publications are used in **teaching** at various levels, e.g. a new international Masters program in English Acquisition and Multilingualism at UiT.
- The web service ***Flere språk til flere*** has been a great success, and members of the research group are regularly invited to give talks all over the country (**Societal impact**). *Flere språk til flere* recently established a branch at NTNU in Trondheim.
- The increased funding and visibility of the acquisition research group during the CASTL period laid the foundation for a **considerable expansion of the group** in the following years: It has attracted a large number of international scholars to UiT, it has massively increased the level of activity of the group in terms of publications, workshops, etc., and it has led to a major increase in external funding (from the RCN, EU commission, etc.). Under Westergaard's leadership, the acquisition group has expanded from a handful of researchers some 7-8 years ago to an exceptionally active and productive group of more than 30 researchers at UiT, currently called LAVA (Language Acquisition, Variation & Attrition). This means that a field that was once a third of CASTL has grown into a large research group of its own, with a corresponding extension of the research focus to new languages and language combinations, new linguistic phenomena, new populations (e.g. heritage speakers and third language learners), and new and more advanced methodologies (e.g. eyetracking or EEG/ERPs (event-related potentials). The group has also joined forces with a similar group at NTNU in Trondheim, establishing the research center **AcqVA (Acquisition, Variation & Attrition),** counting close to 50 researchers in

this research field in Tromsø and Trondheim. This UiT/NTNU joint research group may currently be considered **one of the world's leading research communities on language acquisition and multilingualism**.

5. Sources to corroborate the impact

- The websites of the LAVA / AcqVA research groups, with information about membership, the labs, a number of externally funded sub-projects financed by the RCN, EU commission (MSCA), Centre for Advanced Study at the Norwegian Academy of Science and Letters, etc.
- The website of the multilingualism web service *Flere språk til flere*
- The following publications in high-level journals, showing the **development/extension of the Micro-cue Model to multilingual situations**:

  Westergaard, Marit. Forthcoming. Microvariation in Multilingual Situations: The Importance of Property-by-Property Acquisition. Keynote article in *Second Language Research.*

  Westergaard, Marit, Natalia Mitrofanova, Roksolana Mykhaylyk & Yulia Rodina. 2017. Crosslinguistic influence in the acquisition of a third language: The Linguistic Proximity Model. *International Journal of Bilingualism*.
- A number of **invited contributions**, indicating that Westergaard is considered one of the international experts in this field, e.g. the following:

  Westergaard, Marit & Tanja Kupisch. Submitted. Stable and vulnerable domains in Germanic Heritage Languages. *Blackwell Handbook of Germanic Languages.*

  Westergaard, Marit. In press. Language Acquisition, Microcues, Parameters, and Morphosyntactic Change. In Richard D. Janda, Brian D. Joseph & Barbara S. Vance (eds.), *Handbook of Historical Linguistics*, Volume 2, Ch. 21. Wiley/Blackwell Publishers.

  Westergaard, Marit. 2017. Gradience and gradualness vs. abruptness. In Adam Ledgeway & Ian Roberts (eds.), *Cambridge Handbook of Historical Syntax*, Ch. 21, 446-466. Cambridge: Cambridge University Press.

1.1.3 Scientific impact: The Nordic Center of Excellence in Microcomparative Syntax

Institution: UiT The Arctic University of Norway		
Name of SFF: CASTL (Center for the Advanced Study of Theoretical Linguistics)		
Title of case study: The Nordic Center of Excellence in Microcomparative Syntax (NORMS)		
Period when the underpinning research was undertaken: 2005-2010		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Peter Svenonius Øystein A. Vangsnes	**Role(s) (e.g. job title):** Co-leaders of NORMS	**Period(s) employed by submitting SFF:** Employed **(**Svenonius) and affiliated (Vangsnes) the whole period
Period when the impact occurred: 2005 → present		

1. Summary of the impact

NORMS was a Nordic CoE with partners from seven institutions across five countries, funded by NOS-HS and NordForsk for five years and led from CASTL, UiT. It was part of larger collaboration on mapping and researching syntactic variation across the North Germanic language continuum (ScanDiaSyn), and it specifically allowed deeper and focused investigations of selected dialect areas and selected grammatical topics. The project furthermore contributed to lasting research infrastructure for North Germanic grammatical variation and to revitalization of Nordic dialectology.

2. Underpinning research

The institutions participating in NORMS were University of Iceland, University of Aarhus, University of Oslo, Norwegian University of Science and Technology, University of Tromsø, University of Lund, and University of Helsinki. The participating researchers from these institutions were organized in ten cross-institutional thematic groups with a vertical composition of senior and young researchers which each focused on specific areas of grammar (see below). Each thematic group had between five and ten members and organized on average one scientific meeting per year during the five year period, often with invited international experts. Moreover, NORMS co-organized a larger meeting every year for the greater research collaboration (ScanDiaSyn) with 40-70 participants, including international (non-Nordic) collaborators and guests. Furthermore, fieldwork trips of 5-10 days to seven selected dialect areas were organized during the project period.

The activities in the project allowed many junior researchers both to collect important data for their individual projects and to present their ongoing research in a vibrant and friendly environment which included top researchers in the field. NORMS also contributed valuable data to the lasting research infrastructure represented by the Nordic Dialect Corpus and the Nordic Syntax Database. The project furthermore laid a solid foundation for the Nordic Atlas of Language Structures (NALS) which now lives on as an Open Access journal that continues to disseminate insights on microcomparative variation across the North Germanic language area.

3. References to the research (indicative maximum of six references)

Abels, K. & Ø.A. Vangsnes. 2010. Special issue: Papers from the NORMS Workshop on Exclamatives. *Studia Linguistica* 64:1.

Bentzen, K, H. Rosenkvist & J.B. Johannessen (eds.). 2015. *Studies in Övdalian Morphology and Syntax*. Amsterdam, John Benjamins.

Svenonius, P. 2017. Declension class and the Norwegian definite suffix. In V. Gribonova & S. Shih (eds.) *The Morphosyntax-Phonology Connection: Locality and Directionality at the Interface*. Oxford University Press, 325 - 359. doi: 10.1093/acprof:oso/9780190210304.003.0012.

Thráinsson, H., C. Heycock, H.P. Petersen & Z.S. Hansen (eds.). 2017. Syntactic Variation in Insular Scandinavian. Amsterdam, John Benjamins.

Westergaard, M., Ø.A. Vangsnes & T. Lohndal. 2017. Variation and change in Norwegian wh-questions: The role of the complementizer *som*. *Linguistic variation* 17: (1). ISSN 2211-6834.s 8 - 43.s doi: 10.1075/lv.17.1.02wes.

Wiklund, A.-L., G. Hrafnbjargarson, K. Bentzen & Th. Hróarsdóttir. 2007. Rethinking Scandinavian Verb Movement. *Journal of Comparative Germanic Linguistics* 10: 203. https://doi.org/10.1007/s10828-007-9014-9

4. Details of the impact

The ten thematic groups in NORMS were as follows (group leaders in parentheses)

1. The syntax of noun phrases (Øystein A. Vangsnes, UiT)
2. Verb placement in main and embedded clauses (Höskuldur Thráinsson, Iceland)
3. The syntax of the left periphery (Kristine Bentzen, UiT)
4. Object shift (Sten Vikner, Aarhus)
5. Verb particle constructions (Peter Svenonius, UiT)
6. Argument structure (Christer Platzack, Lund)
7. Subject types (Tor A. Åfarli, NTNU)
8. Auxiliaries and modality (Kristin Eide, NTNU)
9. Pragmatic particles (Jan-Ola Östman, Helsinki)
10. Negation and negative polarity (Janne B. Johannessen, UiO)

As mentioned above, each group organized on average one meeting per year, typically in the form of a two day seminar/workshop where the individual members would present and discuss their ongoing work or alternatively where a more specific topic was put on the agenda. Given the cross-institutional and vertical composition of the groups, with senior scholars collaborating with junior ones (postdocs, PhD students and even sometimes MA students) scientific cross-fertilization along different domains was ensured. This was also formalized insofar that the about ten short term postdoc positions funded by the project came with a mobility requirement: no one could be hired as a NORMS postdoc in their country of origin. These cross-institutional measures ensured the building of networks and contacts across countries and institutions that still in many cases are operative.

The seven dialect areas visited and researched were (in reverse chronological order):

NORMS Fosen 20-23 September 2009
NORMS Indre Skandinavia 4-8 May 2009
NORMS Føroyar 9-16 August 2008
NORMS Vestjylland 7-11 January 2008
NORMS Älvdalen 29 May-1 June 2007

NORMS Senja 30 October-3 November 2006
NORMS Norra Österbotten 3-7 June 2006

The hyperlinks lead to field reports in the form of blogs from each of fieldwork trips. At these excursions, which had between ten and 25 participants, the researchers came with their own research questions and methods and met with local speakers who served as subjects in interviews and recordings. The meetings were well planned in advance and in most cases started with sessions where invited experts gave an introduction to the dialect(s) under investigation. Data from these field trips have made their way into numerous dissertations, scientific papers and in some cases special volumes on the dialect(s), and moreover also into the general and lasting research infrastructure (corpus and database) developed in the greater ScanDiaSyn project.

The research infrastructure represented by the Nordic Dialect Corpus and the Nordic Syntax Database has recently been described in the 2019 paper *The Nordic research infrastructure for syntactic variation: Possibilities, limitations and achievements* by Øystein A. Vangsnes and Janne B. Johannessen, published in *Glossa: A journal of general linguistics* 4:1 (see hyperlink). This infrastructure formed a basis for the roughly 50 entries published in the first edition of *The Nordic Atlas of Language Structures (NALS)*. This online atlas is continued as an Open Access journal where papers detailing various aspect of geographically conditioned linguistic variation across the North Germanic languages will continue to be published, in many cases to a large extent based on data from the existing research infrastructure.

Before the emergence of the ScanDiaSyn collaboration, including NORMS, syntactic variation was a neglected area of research within Nordic dialectology. That is not the case anymore: the collaboration has established a wide range of new empirical discoveries, it has developed new methodologies and trained a new generation of linguists in the research area, and it has raised the general awareness of syntactic variation among both dialectologists and grammarians. The collaboration has furthermore worked on the fundamental understanding that the research object transcends national borders. That understanding has unfortunately too often been neglected in other dialectological projects in the Nordic countries.

5. Sources to corroborate the impact

This section should list:

- NORMS was jointly funded by NOS-HS and NordForsk and evaluations were made at the end of the project.

1.1.4 Societal impact: Mávsulasj Spoken Lule Saami Documentation

Institution: University of Tromsø (currently UiT The Arctic Univerity of Norway)		
Name of SFF: Center for Advanced Study in Theoretical Linguistics		
Title of case study: *Mávsulasj* Spoken Lule Saami Documentation		
Period when the underpinning research was undertaken: 2011-present		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Bruce Morén-Duolljá	**Role(s) (e.g. job title):** Senior Researcher, Project Leader	**Period(s) employed by submitting SFF:** 2003-2013
Period when the impact occurred: 2011-present		

1. Summary of the impact

This project was innovative in describing Lule Saami as a spoken, rather than a written, language. It has increased the awareness and status of this seriously endangered language locally, regionally, nationally and internationally. This includes within the general population and among linguists. It provided jobs/training for non-academics and has improved the understanding of this language among teachers, learners, language planners and speech therapists. The research results of this project form the basis for better educational and language evaluation materials, as well as the core of the world's first BA in Lule Saami and MA in Lule Saami Teacher Education programs.

2. Underpinning research

This was a multi-faceted, multi-year project aimed at a comprehensive description of the Lule Saami language that would meet the needs of researchers, educators, learners and the language community. Data were collected via extensive interviews with several members of the Lule Saami language community who represented diverse age-groups, geographical areas, family affiliations, genders, etc. The data were systematized, analyzed and presented back to native speakers for accuracy verification and to pinpoint individual and dialectal variation.

The key research insight of this project is that much of the Saami language description in the established literature is oversimplified and often wrong and/or misleading. This is because it takes other languages as the starting point in describing Saami languages instead of taking each Saami language as the starting point for its own description. For example, established dictionaries translate many Lule Saami words into colloquial Norwegian/Swedish words that capture the gist but not the nuanced details of the Lule Saami words, and unfortunately those inadequate colloquial Norwegian/Swedish translations are used as the primary source of data for describing Lule Saami words and grammatical phenomena. This results in the omission of vital information needed for understanding, using and analyzing the Lule Saami language. In turn, this leads to problematic language use and educational materials, as well as incomplete language acquisition. Older/traditional research also has a tendency to rely heavily on written norms, which often only reflect particular dialects, social registers and/or literary traditions. This sometimes provides a distorted picture of how the spoken language is used, should be analyzed and should be taught.

As pointed out in several academic and popular science talks and articles (see sections 3 and 4), there are many aspects of Lule Saami grammar that have been seriously misunderstood. The grammatical case system is different than that described, the grammatical number system is different than that described, the inflectional and derivational systems are different, the meaning, distribution and use of many word forms and morphemes (sub-word components) are different, the way vowels and consonants behave is different, etc. The results of the *Mávsulasj* project have shown that noticing and acknowledging the shortcomings of previous research is important for

establishing modern descriptive work on Lule Saami (and other Saami languages). The results also show that an updated understanding of this seriously endangered language has concrete societal impact since it has been (and still is) necessary to develop better resources for language vitalization efforts, language planning, language education, etc.

3. References to the research

Morén-Duolljá, B. (2014) *Lulesamisk grammatikk: den er ikke som du tror* [Lule Saami Grammar: It is not what you think]. Bårjås, pp. 62-72. *Árran – julevsáme guovdásj* [Árran – Lule Saami Center], Ájluokta, Norway.

Fangel-Gustavson, N., R. Ridouane and B. Morén-Duolljá (2014) Quantity contrast in Lule Saami: A three-way system. Proceedings of the 10th International Seminar on Speech Production (ISSP), pp. 106-109. Cologne, Germany.

Morén-Duolljá, B. (2014) *Kartlegging og utredning av (noen) lulesamiske substantiver lånt fra svensk/norsk - med spesiell fokus på vokaler* [Investigating and analyzing some Lule Saami nouns borrowed from Swedish/Norwegian - with special focus on vowels]. Consultation report to *Sámi Giellagáldu* [the Nordic Saami Language Resource Center]. 146 pages.

Morén-Duolljá, B. (2015) *Rapport til Statped nord om hvordan man utvikler en lulesamisk "fonemtest"* [Report to Statped nord about how to develop a Lule Saami "phoneme test"]. Consultation report to Statped nord [the Norwegian National Service for Special Needs Education]. 32 pages.

Morén-Duolljá, B. (2015) *Juler, mager, sander, melker, bukser og bær: den fascinerende verden av grammatiske tall i lulesamisk* [Christmases, stomachs, sands, milks, trousers and berries: The fascinating world of grammatical number in Lule Saami]. Talk presented at the *Lulesamisk språkkonferanse* [Lule Saami Language Conference], Ájluokta, Norway.

Morén-Duolljá, B. (2016) *Kartlegging og utredning av lulesamiske adjektiv som slutter på "lasj" og "lis"* [Investigating and analyzing Lule Saami adjectives that end with "lasj" and "lis"]. Consultation report to *Sámi Giellagáldu* [the Nordic Saami Language Resource Center]. 103 pages.

4. Details of the impact

The *Mávsulasj*: Spoken Lule Saami Documentation Project was a multi-faceted, multi-year project aimed at a comprehensive description of the Lule Saami language that would meet the needs of researchers, educators, learners and the language community. It promoted better contact and understanding between the academic community and the Lule Saami language community, and the resulting data and networking infrastructures are having long-lasting effects on a range of disciplines and on Lule Saami language vitalization efforts.

This project was innovative in describing Lule Saami as a spoken, rather than a written, language. It has increased the awareness and status of this seriously endangered language (and its variations) locally, regionally, nationally and internationally. This includes within the general population and among linguists. It provided jobs/training for non-academic members of the Lule Saami speech community, and it has improved the understanding of this language among teachers, learners, language planners and speech therapists.

While the SFF-initiated *Mávsulasj* project is officially over, it continues to impact the research, teaching and Lule Saami language planning and evaluation activities at Nord University, the Árran Lule Saami Center, Université de la Sorbonne Nouvelle, Statped (Norway's National Service for Special Needs Education) and Sámi Giellagáldu (the Nordic Research Center for Saami Languages).

The project's primary findings have been used in a MA thesis at Université de la Sorbonne Nouvelle, as well as several scientific and popular science presentations and articles. They are currently used in a PhD thesis project (also at Université de la Sorbonne Nouvelle), and they are at the core of Nord University's BA in Lule Saami and MA in Lule Saami Teacher Education course materials. In fact, Lule Saami higher education in Norway is currently dependent on research-based teaching that is a direct result of the *Mávsulasj* project.

The project findings have been the groundwork for a report written to help Statped develop phoneme discrimination tests for Lule Saami, South Saami and North Saami children, as well as two reports to help Sámi Giellagáldu with their time-critical terminology development work. It has also been crucial to the work leading to the official recognition of an orthography for the Pite Saami language.

In concrete terms, the project's discovery of fundamental description errors in the traditional literature has resulted in number of consultation reports, higher education compendia, scientific and popular science talks and articles, and manuscripts nearing their publication phase. Some examples are 1) a three-volume set of books about Lule Saami nouns, 2) a three-volume set of books about Lule Saami verbs and 3) a book teaching the basic grammar of Lule Saami using the description discovered by the *Mávsulasj* project.

The *Mávsulasj* project has also been vital to increasing awareness of the Lule Saami language via the print and broadcast media. This has helped to improve attitudes toward the language, which has also helped to raise its status within the community. Examples are:
Johansen, O. *Amerikansk språkforsker i Tysfjord om lulesamisk: - Svært komplisert språk* [American language researcher in Tysfjord about Lule Saami: "A very complex language"]. Ságat. 11.12.15.

Johansen, K. *Fant hemmelighetene i lulesamenes språk* [Found the secrets in the Lule Saami's language]. Forskning.no [http://forskning.no/sprak/2015/12/fant-hemmelighetene-i-lulesamenes-sprak]. 7.12.15.

Ihlebæk, J.H. *Museum: Lulesamer i Tysfjord* [Museum: Lule Saami in Tysfjord]. NRK Radio P2. 10.01.15.

Boine, L.T. *Samisk er unikt språk* [Saami is a unique language]. Árdna - Samisk kulturmagasin på norsk. NRK Radio. 26.04.13.

Boine, L.T. *Samegiella lea erenoamáš mailmmi gielaid dáfus* [Saami language is special compared to other languages]. Giellamet. NRK Radio. 26.04.13.

Skapalen, K. *Mávsulasj giella/Det edle språket* [The precious language]. Bájkkeavijssa NourttaSállto/Lokalavisa NordSalten. 07.01.11. [This was the newspaper's sixth most read article of 2011.]

To summarize, the *Mávsulasj* project established observations, methodologies and analyses that will have long-term societal impact. It provided insights into the form, meaning, use and distribution of Lule Saami words and grammatical phenomena that have changed our way of viewing the Saami languages in general, and Lule Saami in particular. These insights have already begun to change the way Lule Saami is taught at a variety of levels, and they have begun to change the way Lule Saami is viewed within Norway and Sweden. Those who speak and/or study Lule Saami and have had access to some of the *Mávsulasj* results have claimed that they understand their own language better and use it more confidently. This speaks volumes about the societal impact the project has had, and will continue to have, on the community.

5. Sources to corroborate the impact

Some references to sources that could corroborate key claims made about the societal impact of this case (see also section 3):

Morén-Duolljá, B. (2014) *Kartlegging og utredning av (noen) lulesamiske substantiver lånt fra svensk/norsk - med spesielt fokus på vokaler* [Investigating and analyzing some Lule Saami nouns borrowed from Swedish/Norwegian - with special focus on vowels]. Consultation report to *Sámi Giellagáldu* [the Nordic Saami Language Resource Center]. 146 pages.

Morén-Duolljá, B. (2016) *Kartlegging og utredning av lulesamiske adjektiv som slutter på "lasj" og "lis"* [Investigating and analyzing Lule Saami adjectives that end with "lasj" and "lis"]. Consultation report to *Sámi Giellagáldu* [the Nordic Saami Language Resource Center]. 103 pages.

Morén-Duolljá, B. (2015) *Rapport til Statped nord om hvordan man utvikler en lulesamisk "fonemtest"* [Report to Statped nord about how to develop a Lule Saami "phoneme test"]. Consultation report to Statped nord [the Norwegian National Service for Special Needs Education]. 32 pages.

Andersen, S. *Dette har vi ventet på lenge* [We've waited for this for a long time]. NRK Sápmi. 21.08.19. https://www.nrk.no/sapmi/pitesamisk-skriftsprak-endelig-godkjent-1.14666801

Marakatt, L. Pitesamiskan får godkänt skriftspråk [Pite Saami gets an official written language]. Sameradion & SVT Sápmi. 01.07.2019. https://sverigesradio.se/sida/artikel.aspx?programid=2327&artikel=7255179

Päiviö, A. M. *Elsy Rankvist: Det betyder mycket för utvecklingen av pitesamiskan* [Elsy Rankvist: It means so much for the development of Pite Saami]. Sameradion & SVT Sápmi. 21.08.2019. https://sverigesradio.se/sida/artikel.aspx?programid=2327&artikel=7284028

1.2 CeSOS - Centre for Ships and Ocean Structures

1.2.1 Scientific impact: Analysis of sloshing in tanks by a multi-modal approach

Institution: NTNU		
Name of SFF: CeSOS		
Title of case study: Analysis of sloshing in tanks by a multi-modal approach		
Period when the underpinning research was undertaken: 2003-2013		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
O.M. Faltinsen	Professor	2003-2013
A.N. Timokha	Research Professor	2003-2013
Period when the impact occurred: 2003-2013		

1. Summary of the impact

Multimodal modal approach (method) reduces the original free-surface (sloshing) problem to a (low-dimensional modal) system of ordinary differential equation with respect of a set of dominating hydrodynamic coordinates. Specifically, the modal system keeps sufficient accuracy in quantification of violent resonant (nonlinear) sloshing and, therefore, both provided a breakthrough effect on the modern theory of the liquid sloshing, e.g., by quantifying a series of experimentally-known free-surface phenomena (swirling and diagonal wave modes, secondary resonances, chaotic wave motions, etc.) and enabled an new kind of numerical analyses of the liquid sloshing dynamics that is, especially, important in the three-dimensional case and when the tank is equipped with sharp structures, e.g., perforated screens.

2. Underpinning research

Violent liquid sloshing in ship and storage containers is normally expected for resonant conditions. Specifically, the resonant forcing leads to complex three-dimensional wave motions and causes rather exotic strongly nonlinear phenomena, e.g., swirling and chaotic waves, and, moreover, depending on initial scenarios, these may co-exist in certain frequency ranges. Traditional Computational Fluid Dynamics and analytical (basically, linear) methods are limited in addressing *which, why and when* the phenomena occur and how they affect the hydrodynamic loads. Being proposed by the authors (Professors O.M. Faltinsen and A.N.Timokha) twenty years ago, the multimodal approach (method) is, in fact, a *`third' (alternative) way* in the theoretical and computational liquid sloshing dynamics. Mathematically, its idea consists, by interpreting the original free-surface problem as a dynamic (modal) system with infinite degrees of freedom and by using variational principles of analytical mechanics and asymptotic methods, of reducing the problem to a system of nonlinear ordinary differential equations of a rather low dimension. A forthcoming usage of the modal systems has been providing a breakthrough effect on the liquid sloshing theory and benefits a time-efficient simulation of the nonlinear liquid sloshing.

Theoretical studies on the multimodal approach and related experimental activities were undertaken at CeSOS by Professors O.M.Faltisnen and A.N.Timokha with Drs O.F.Rognebakke and R. Firoozhkoohi and some others. Bearing in mind a series paradoxical and practically dangerous resonant surface wave phenomena, which were not theoretically quantified up to the date, research activities on sloshing by utilizing the multimodal approach basically concentrated on the cases when usage of CFD methods is disputable of even impossible. They are best exemplified, but

not limited to, by strongly three-dimensional steady-state wave flows in rectangular containers [2-5] and free-surface wave motions in tanks with internal structures [6-7]; book [1] presents other case studies employing the multimodal approach. Occurrence of the nonlinear wave phenomena was verified by conducting the corresponding experimental model tests. As for the first case study in [2-5], findings are an explanation of why and for which input parameters chaotic waves are possible, a new theoretical concept of the swirling (rotary) wave mode and estimating its stability range, the concept of secondary resonance for three-dimensional sloshing; a point is the finding `at the tip of the pen' of the so-called square-like waves, which were earlier not detected in experiments but supported by dedicated model tests upon the theoretical finding. The multimodal method also solved another puzzle – the paradoxical multi-peak resonance sloshing response in tanks with perforated screen [7]. Specifically, this needed the secondary resonance concept, which is, in turn of, a `bairn' of the multimodal method.

3. References to the research

1. Faltinsen, O.M., Timokha A.N. (2009) *Sloshing*. Cambridge University Press, 608 pp. (ISBN 9780521881111)
2. Faltinsen O.M., Rognebakke O.F., Timokha A.N. (2003) Resonant three-dimensional nonlinear sloshing in a square base basin. *Journal of Fluid Mechanics*, **487**, 1-42; DOI: 10.1017/S0022112003004816
3. Faltinsen O.M., Rognebakke O.F., Timokha A.N. (2005) Resonant three-dimensional nonlinear sloshing in a square base basin. Part 2. Effect of higher modes. *Journal of Fluid Mechanics*, **523**, 199-218; DOI: 10.1017/S002211200400196X
4. Faltinsen O.M., Rognebakke O.F., Timokha A.N. (2006) Resonant three-dimensional nonlinear sloshing in a square base basin. Part 3. Base ratio perturbations. *Journal of Fluid Mechanics*, **551**, 93-116; DOI:10.1017/S0022112005008281
5. Faltinsen O.M., Rognebakke O.F., Timokha A.N. (2006) Transient and steady-state amplitudes of resonant three-dimensional sloshing in a square base tank with a finite fluid depth. *Physics of Fluids*, 18, Art. No. 012103; DOI: 10.1063/1.2160522
6. Faltinsen O.M., Firoozhkoohi, R., Timokha A.N. (2011) Steady-state liquid sloshing in a rectangular tank with slat-type screen in the middle. Quasilinear modal analysis and experiments. *Physics of Fluids*, 23, Art. No. 04101; DOI: 10.1063/1.3562310
7. Faltinsen O.M., Firoozhkoohi, R., Timokha A.N. (2011) Effect of central slotted screen with a high solidity ratio on the secondary resonance phenomenon for liquid sloshing in a rectangular tank. *Physics of Fluids*, 23, Art. No. 062106; DOI:10.1063/1.3602508

4. Details of the impact

The studies and results on the multimodal approach at CeSOS radically changed landscape of the whole scientific field *"sloshing in tank"* by offering a '*third (alternative) way*' to solving many classes of engineering problems, which are associated with containers carrying a liquid. The book [1], which summarized these results, became the most popular and cited publication (625 citations according to Google Scholar) on sloshing during the last decade. Utilizing citations of the multimodal method to estimate the *timespan* of when the impact done by these studies occurred, outputs *2011*, i.e., this is, definitely, a consequence of the corresponding research activities at CeSOS. Furthermore, searching by Google Scholar for "fluid liquid sloshing" in 2009-2019 and analyzing the first hundred references counts 84 publications citing the authors publications on the multimodal method. Thus, even though the researchers employ another

methods and approaches, they use, implicitly or explicitly, the authors' results in a comparative analysis. This makes *evident* significant effect of these dedicated studies on the research field called "sloshing".

Even though the citing journals are associated with *marine* and *mechanical engineering*, there is serious interest in the `third way' from *applied mathematicians* and *civil engineers*. For example, thanks to works by J.S. Love & M.J. Tait who extended the multimodal methods onto the *tuned liquid damper problem* (mitigation of buildings and huge structure vibrations), the nonlinear modal systems became the main model of liquid dampers and almost postponed publications/studies on equivalent mechanical models of the dampers, which also replaced the original free-surface problem by a low-dimensional systems of ordinary equations but by using phenomenological/empirical arguments.

Another side of the impact done by these studies is how the multimodal approach changed the state-of-the-art on the CFD methods applied to the liquid sloshing dynamics. A main *benefit* of the multimodal approach is that it provided *benchmark* analytical and semi-analytical solutions, e.g., for three-dimensional nonlinear sloshing and, in parallel way, gave a clear theoretical knowledge on the associated sloshing phenomena, expected (stable) steady-state waves and transient regimes. This motivated researchers, which develop the CFD methods, for paying a more attention to the three-dimensional resonant sloshing and other more complicated cases whose simulation requires an extensive validation.

5. Sources to corroborate the impact

1. The State Prizes of Ukraine in Science and Technology (Professor A.N.Timokha, 2012) (in Ukrainian, first in the list http://www.kdpu-nt.gov.ua/en/node/19292).
2. According to Google Scholar, more than 625 citation to the book "Sloshing" by Faltinsen, O.M., Timokha, A.N. (2009) Cambridge University Press, 608 p. (https://scholar.google.no/citations?user=HimAPTsAAAAJ&hl=no&oi=ao#d=gs_md_cita-d&u=%2Fcitations%3Fview_op%3Dview_citation%26hl%3Dno%26user%3DHimAPTsAAAAJ%26citation_for_view%3DHimAPTsAAAAJ%3AgeHnlv5EZngC%26tzom%3D-180).
3. The book [Faltinsen, O.M., Timokha, A.N. (2009) "Sloshing". Cambridge University Press] was translated to Chinese in 2012 (ISBN 987711808608-3).

1.2.2 Scientific and societal impact: Integrated dynamic analysis of floating wind turbines

Institution: NTNU		
Name of SFF: CeSOS		
Title of case study: Integrated dynamic analysis of floating wind turbines		
Period when the underpinning research was undertaken:2007-2012 (2015)		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
T.Moan	Key scientist, Professor, NTNU	2003-2012
Z.Gao	Postdoc,Researcher/Adjunct Assoc.prof./Prof. NTNU	2008-2011 /2010-2015/2015-
M. O. Hansen	Adj.assoc. prof CeSOS/Assoc.prof. DTU	2010-2012 (2015)
Mogens Blanke	Adj.prof. CeSOS/Prof. DTU	2005 – 2012 (contd. in AMOS)
10 PhD candidates & 4 postdocs		2007- 2012 (2015)
Period when the impact occurred: 2007-2012 (2015-)		

1. Summary of the impact

Methods have been developed to account for stochastic wind and wave loads as well as fault conditions in an overall analysis by properly accounting for the properties of the individual sub-systems (rotor, drivetrain, tower, support structure and mooring system) for different types of floating wind turbines to provide relevant responses in the different sub-systems to serve as a basis for design and monitoring during operation of the wind turbines. This information is being considered in the development of proper design standards and guidelines; which are underway, and forms the basis for novel design and innovation.

2. Underpinning research

The research and development of floating wind turbines stated in 2007 and make up a significant activity in the last 5 years of the CeSOS and has continued since then by a team of currently 4 professors at the Department of Marine Technology.

As mentioned above the core of the activity has been the development and application of methods for global dynamic analysis of the complete wind turbine system.

The insight gained partly understanding of features of the dynamic behavior that affect the methodology to be used and is partly the understanding of the features of different systems (helpful for design). Regarding physical insight and development of novel methods, the following selected examples and corresponding references in Section 3, are mentioned herein:

- The observation and modelling of high frequency loads causing transient dynamic effects (ringing or springing) in Tension-leg wind turbines [5]
- The so-called negative damping introduced by the servo system in tension-leg turbines and how it can be ameleriorated by a modified controller gain. [1]
- Developing a time domain analysis method to determine internal forces in floating wind turbines subjected to stochastic wind and wave loads [11]

- The different responses experienced in the drivetrain for wind turbines supported on different fixed versus floating support structures – which has implication on the global control system [2,6]
- The importance of considering the effect on the response caused by internal faults in operating wind turbines – such as blade pitch fault, drivetrain gear or bearing fault and grid short circuit, was documented,e.g. [4] (this research has also lead to pursuing methods for detecting, diagnosing and controlling such faults e.g. [9]).
- The development a method for estimating atmospheric icing on blades and its effect on the aerodynamic loads, e.g. [3]
- The development of a methodology to deal with different wind turbine concepts interacting with wave energy converters. The efforts in this connection are summarized in [8]
- Efficient account of the longterm variability of environmental conditons in integrated response analysis of wind turbines by the countour approach – suitable for facilities with multimodal behavior . [12]
- -Efficient and accurate determination of extreme response by the ACER method developed in CeSOS by professor Næss and coworkers
- Efficient calculation of cyclic stresses for fatigue analysis – which in principle should include all wind and seastate conditions considering several samples to limit the statistical uncertainty [8,19….]

Key results achieved that have implications on design of floating wind turbines relates to floating tension-leg, spar and semisubmersible concepts, e.g. [1]. Moreover, the design of drivetrain – gear and bearings – based on the first principles of mechanics analysis, has lead to a new design of a 5 MW turbine that serve the research and development community as a benchmark case for analysis, e.g. [10]. The modelling of wind turbine drivetrain has taken place in close cooperation with the National Renewable Energy Lab. In Colorado, USA.

3. References to the research

1. Bachynski, E.E. and Moan, T. Design Considerations for Tension Leg Platform Wind Turbines. *Marine Structures.* 2012; 29 (1): 89-114.
2. Xing, Y. and Moan, T. Multi-Body Modelling and Analysis of a Planet Carrier in a Wind Turbine Gearbox. *Wind Energy. 2013. 16(7): 1067-1089*
3. Etemaddar, M. , Hansen, M.O.L. and Moan, T. Wind Turbine Aerodynamic Response Under Atmospheric Icing Conditions. *Wind Energy. 2014. 17(2): 241-265*
4. Jiang, Z., Karimirad, M. and Moan, T: Dynamic response analysis of wind turbines under blade pitch system fault, grid loss, and shutdown events, *Wind Energy* 2014 17(9): 1385-1409.
5. Bachynski, E.E. and Moan, T. Ringing loads on tension leg platform wind turbines Ocean Engineering 84(2014)237–248
6. Xing, Y., Karimirad. M. and Moan, T. Modelling and Analysis of Floating Spar-Type Wind Turbine Drivetrain. *Wind Energy,* 17: 565–587, 2014.
7. Kvittem, Marit Irene; Moan, Torgeir. Time domain analysis procedures for fatigue assessment of a semi-submersible wind turbine. *Marine Structures*. Vol. 40. pp. 38-59
8. Gao, Zhen; Moan, Torgeir; Wan, Ling; Michailidis, Konstantinos. Comparative Numerical and Experimental Study of two Combined Wind and Wave Energy Concepts. *Journal of Ocean Engineering and Science* 2016 ;Vol. 1.(1) pp. 36-51
9. Ghane, Mahdi; Rasekhi Nejad, Amir; Blanke, Mogens; Gao, Zhen; Moan, Torgeir. Statistical fault diagnosis of wind turbine drivetrain applied to a 5MW floating wind turbine. *Journal of Physics, Conference Series* 2016 ;Vol. 753.

10. Rasekhi Nejad, Amir; Guo, Yi; Gao, Zhen; Moan, Torgeir. Development of a 5 MW reference gearbox for offshore wind turbines. *Wind Energy* 2016 ;Vol. 19.(6) pp. 1089-1106
11. Luan, Chenyu; Gao, Zhen; Moan, Torgeir. Development and verification of a time-domain approach for determining forces and moments in structural components of floaters with an application to floating wind turbines. *Marine Structures.* 2017 ; Vol. 51. pp. 87-109
12. Li, Qinyuan; Gao, Zhen; Moan, Torgeir. Modified environmental contour method to determine the long-term extreme responses of a semi-submersible wind turbine. Ocean Engineering 2017 ; Volum 142. pp. 563-576
13. Moan, T., Gao, Z., Bachynski, E.E., Nejad Amir R., Recent Advances in Response Analysis of Floating Wind Turbines in a Reliability Perspective. Submitted for publication.

4. Details of the impact

The starting point of this research (in 2007) was, as always in engineering science , a societal need, namely to meet the challenges associated with providing sufficient and clean energy and, in certain regions, increasing energy security, by exploring renewable energy. However, major research challenges still impede the delivery of a cost-effective and reliable supply of ocean power to end-users. For shallow waters fixed offshore wind turbines are now considered to be a well-established commercial technology. For deep waters, floating wind turbines provide the cheapest solution. Floating wind turbines represent a significant change in technology compared to bottom-supported turbines because of the tight coupling between wind- and wave-induced responses and between the drive train and support structure. The wide range of natural and excitation frequencies represents a challenge for wind turbine design and analysis. To reach the proposed targets of offshore wind power significant developments of novel and users, larger wind turbines, optimised for operation in rough offshore conditions, is needed. The optimal design of wind turbines requires integrated analyses of hydrodynamics, mechanical engineering, structural mechanics, electrical engineering and automatic control. Thus, the multidisciplinary expertise gathered in CeSOS made the subject of research and development of floating wind turbines, the ideal subject area. Moreover, based on our initial efforts in CeSOS on floating wind turbines we became a partner in other programmes, like NOWITECH and the EU projects Marina Platform and MareWint. Only a limited amount of research has been conducted on the coupled aero-hydro-servo-elastic time domain dynamic response of floating wind turbines under harsh environmental conditions when we initiated this research in CeSOS. The dynamic modelling and time domain analysis of various wind turbine concepts, also with faults, and both the extreme operational cases and the survival cases (with an idle rotor), have been considered.

In the period of 2011-2014 (which formally cover the period with journal publications from the wind turbine research in CeSOS) 45 journal publications generally in leading journals like J.Wind Energy, were published by the CeSOS wind group.

Besides documenting novel knowledge generated by publications we have contributed to the development of software, e.g. the SIMA software managed by SINTEF Ocean.

- In the period of 2011-2014 professor Moan has been invited to deliver 7 keynote at international conferences or distinguished lectures on wind turbines. The international recognition of the group is continued to be manifested in this manner, with the last keynote delivered at the Int. Offshore Wind Turbine Conference in San Francisco in Nov. 2018.(to appear as a journal paper[60]
- The quality of our scientific contributions is further manifested by Erin Bachynski receiving the Chorafas research prize in 2012 and the Onsager award in 2015. Nejad et al. got a best paper award at the EERA DeepWind Conference in 2014.

Our research contributes to technology development through contributions to development of standards, advisory services e.g. to Equinor and to novel wind turbine design, e.g. [1,10].

Based on the significant efforts made in the last part of the CeSOS period 2007-2012 (with publications appearing up to 2014), a group of professors consisting of two professors, Torgeir Moan and Zhen Gao, and two associate professors, Erin Bachynski and Amir Nejad in the Department of Marine Technology are currently focusing on offshore wind energy. Moreover, other faculty members in the Department are involved in particular subject areas. In the period of 2007-2018, the wind energy group in the Department has hosted 8 postdocs, 18 PhD graduates. Currently, we have 2 postdoc and 14 PhD candidates. Our involvment in the European Wind Energy Master program, EWEM, together with TUDelft, DTU and Univ. of Oldenburg since 2012 , as well of developing a specialization for wind turbine studies at our NTNU Department, with annually about 15 MSc students, has facilitated dissemination of research results and contributed to educating the needed engineers for the future expansion in this area. In the period of 2011-2018 Prof. Moan delivered 11 keynotes and numerous presentations in research and industry for a on wind turbines.

We have been heavily involved in many national and international research centres, projects and educational programs on offshore wind turbines. This includes the Norwegian offshore wind research centre NOWITECH (2009-2017), the EU projects FP7 MARINA Platform (2010-2014), FP7 Marinet (2011-2014), FP7 MARE-WINT (2012-2016), the EWEM (European Wind Energy Master) Program (2012-), and the international projects IEA OC3-OC6 (2010-), Statoil-MIT-NTNU (2010-). Through these research activities, we have close cooperation with the leading universities, research institutes and companies in the areas of offshore wind, such as DTU, TU Delft, MIT, SINTEF Ocean, NREL, Equinor, DNV-GL and Ørsted.

As mentioned above, 3 previous PhD/postdocs in CeSOS in the wind energy area are now Professor, and Assoc. professors in our NTNU Department. Others are Assoc. professors in other universities, like Shanghai JiaoTong U.and Sun-Yat-Sen University in China, Queen's University Belfast (QUB), as well as University of Stavanger and University of Agder

The core wind energy group is also involved in committees under the auspices of IEC, NEK, DNVGL for developing standards for wind turbines as well as conference committees with dissemination purposes, notably EAWA, OMAE, RENEW, IOWTC and ISSC.

After the CeSOS period the research activities have been expanded to include both horizontal and vertical axis wind turbines as well as planning and execution of transport and installation of offshore wind turbines. The core wind energy group is hence involved in the research based innovation centre SFI MOVE.

5. Sources to corroborate the impact

Awards are mentioned above.

1.2.3 Scientific and societal impact: Ship control in extreme conditions

Institution: NTNU		
Name of SFF: CeSOS - Centre for Ships and Ocean Structures		
Title of case study: Ship control in extreme conditions		
Period when the underpinning research was undertaken: 2003 - 2009		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): **Asgeir J. Sørensen**	**Role(s) (e.g. job title):** **Key scientist/Prof.**	**Period(s) employed by submitting SFF:** **100%**
Period when the impact occurred: 2003 - 2009		

1. Summary of the impact

The motivation to develop improved methods for propulsion and local thruster control was initiated by ABB in the middle of 1990s. The idea was to better utilize the properties of electrical drives and motors to the benefit of improved control and power plant performance as well as reduced mechanical wear and tear of the propulsion components.
The first initial publication on this topic was by Sørensen et al. in 1997. In CeSOS this work was addressed extensively in joint cooperation with industry partners. In particular, thruster control in extreme conditions was studied. Robust thruster control in extreme seas accounting for severe thrust losses due to ventilation and in-and-out-of-water effects was developed, and anti-spin thruster controller and thrust allocation method, motivated by similar effects in wheel slip control on cars, were developed. The new insight was also vital knowledge input in the development of mathematical models for Hardware-In-the-Loop (HIL) simulation testing of dynamic positioning systems on ships. Software testing of computer-controlled systems including HIL-testing of ships has become a new safety standard for the international maritime industry adopted by class societies such as DNV GL, ABS and LRS.

2. Underpinning research

Ships and offshore vessels are controlled by proper action of their propulsion systems. For safe and cost-effective operations, high performance vessel control systems including both high-level dynamic positioning (DP) control and low-level propulsion control as well as power management of the electrical power and distribution system must be addressed as an integrated system. Marine vessels and ships will operate in any conditions from e.g. calm weather to extreme seas with large dynamic ships motions.
Possible consequences of improper ship propulsion control are:

- Decreased closed-loop vessel performance due to inaccurate thrust production.
- Increased vessel down-time and maintenance cost due to unnecessary mechanical wear and tear.
- Increased fuel consumption and risk of blackouts due to unpredictable power consumption.

Two operational regimes are defined: *normal*, and *extreme conditions*. In normal operating conditions, the dynamic loading of the propellers is considered to be moderate, and primarily caused by oscillations in the inflow due to waves. In extreme conditions, the additional dynamic loads due to ventilation and in-and-out-of- water effects can be severe. In order to improve the understanding of these loads and develop a simulation model suitable for control system design and testing, systematic model tests with a ventilating propeller in a cavitation tunnel and a towing tank have been undertaken.

A new method for combined torque/power controller and a combined speed/torque/power controller was developed. When compared to conventional shaft speed control, the proposed method gave improved thrust production, decreased wear and tear, and reduced power oscillations in waves.

Anti-spin thruster controllers and thrust allocation methods that enabled the use of torque and power control also in extreme operating conditions were developed. The idea of anti-spin was motivated from the automotive industry where ventilating propellers can be compared to car wheels losing friction on ice. The proposed method used state estimators to detect ventilation for thereafter compensating the effect by reducing the loading on the ventilation propeller as well as reallocation thrust production to non-ventilating propellers.

3. References to the research

Smogeli, Ø. N. and A. J. Sørensen (2009). Antispin Thruster Control for Ships. IEEE Transaction on Control System Technology Vol. 17, No. 6, pp. 1362-1375, ISSN 1063-6536.

Ruth, E., Ø. N. Smogeli, T. Perez, and A. J. Sørensen (2009). Antispin Thrust Allocation for Marine Vessels. IEEE Transaction on Control System Technology Vol. 17, No. 6, pp. 1257-1269, ISSN 1063-6536.

Sørensen, A. J. and Ø. N. Smogeli (2009). Torque and Power Control of Electrically Driven Marine Propellers. IFAC Journal Control Engineering Practice (CEP), Vol. 17, No. 9, pp. 1053-1064, Elsevier Ltd, ISSN: 0967-0661.

Smogeli, Ø. N., A. J. Sørensen and K. J. Minsaas (2008). The concept of anti-spin thruster control. IFAC Journal Control Engineering Practice (CEP), Vol. 16, No. 4, pp. 465-481, Elsevier Ltd, ISSN: 0967-0661.

Ruth, Eivind (2008). Propulsion Control and Thrust Allocation on Marine Vessels. PhD Thesis 2008:203, Department of Marine Technology, Faculty of Engineering Science & Technology, NTNU.

Smogeli, Øyvind Notland (2006). Control of Marine Propellers From Normal to Extreme Conditions. PhD Thesis 2006:187, Department of Marine Technology, Faculty of Engineering Science & Technology, NTNU.

Sørensen, A. J., A. K. Ådnanes, T. I. Fossen and J. P. Strand (1997). A New Method of Thruster Control in Positioning of Ships Based on Power Control. Proceedings of 4th IFAC Conference on Manoeuvring and Control of Marine Craft (MCMC'97), pp. 172-179, Brijuni, Croatia

4. Details of the impact

Installed power capacity on marine vessels and offshore installations is normally limited. Besides there is an increased focus on environmental aspects motivating technical solutions that reduce the total energy consumption and emission of exhaust gases. The different subsystems/ equipment installed on a vessel or offshore installation can be categorized into two parts, producers and consumers of energy. For dynamically positioned vessels the thruster system normally represents one of the main consumers of energy, and is regarded as a critical system with respect to safety. On the contrary, the dynamic positioning system is only an auxiliary system for the vessel to do a profitable operation of one kind or another, such as drilling, oil production, loading, and so on. Hence, the thruster usage should not cause a load shedding of those productive consumers, or in worst case cause a total power black-out because of unintended
power consumption. The strong requirements to vessel performance, operational availability and overall safety have therefore resulted in increased focus on the total vessel concept and

the interactions between the different equipment and systems installed. Flexibility in operation has enabled electrical power generation and distribution systems for propulsion, positioning, oil production, drilling, and loading, where all equipment and control systems are integrated into a common power plant network and automation network. In fully integrated systems, functional in addition to physical integration of power and automation systems combined with thorough marine process knowledge introduces new and far better opportunities to optimize the overall vessel mission objective at lower life cycle costs. In order to accomplish this, it is essential to properly address the energy control of the consumers and producers of electrical power onboard the vessel. If the various consumers (thrusters, pumps, compressors etc.) of power act separately and uncoordinated from each other, the power generation system must be dimensioned and operated with larger safety margins to account for the corresponding larger mean power demands and unintentional power peaks.
The research on *Ship control in extreme conditions* combined the disciplines control engineering, hydrodynamics and power systems. The research environment in CeSOS made it possible to address the topic with sufficient resources in a multi-disciplinary setting.

5. Sources to corroborate the impact

- Øyvind Notland Smogeli was in January 2007 awarded the TEKNA price for Excellent Young Researcher for the doctoral thesis at NTNU. In May 2007 Smogeli was awarded the ExxonMobile price for best applied doctoral thesis at NTNU.
- The companies Rolls-Royce Marine (Kongsberg Maritime), Kongsberg Maritime, ABB, Siemens, Wärtsila, and Brunvoll did take benefit of the knowledge from this work in their industrial propulsion and DP control systems.
- The work on modelling and control of ship and propulsion systems in extreme weather conditions became important knowledge contribution to the development of Hardware-In-the-Loop (HIL) simulation testing of computer-controlled systems on ships. Software testing including HIL testing has become a new safety standard in the maritime industry originating by researchers at CeSOS and NTNU.
- The NTNU spin-off company Marine Cybernetics was taking benefit of this knowledge in the work of introducing HIL testing as a new test and verification methods in cooperation with class societies, oil companies, ship owners, yards and vendors. Marine Cybernetics was acquired by DNV GL in 2014.

1.2.4 Scientific and societal impact: Vortex Induced Vibrations

Institution: NTNU

Name of SFF: CeSOS

Title of case study: Vortex Induced Vibrations

Period when the underpinning research was undertaken: 2003 - 2013

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period employed by CeSOS**
Carl M. Larsen	Professor	2003-2013
Kristoffer Aronsen	PhD candidate	2003-2006
Jie Wu	PhD candidate	2007-2011
Philippe Maincon	Researcher	2008
Prashant Soni	PhD candidate	2004-2008
Decao Yin	PhD candidate	2009-2013
Ida Aglen	PhD candidate	2009-2013
Hidetaka Sengaats Thorsen	Visiting Post doc	2013
J. Kim Vandiver	PhD candidate	2013-2015
Mike Triantafyllou	Professor, MIT	2004-2013
	Professor, MIT	2006-2013

Period when the impact occurred: 2003 - 2013

1. Summary of the impact

Vortex induced vibrations (VIV) is a complex hydroelastic phenomenon. The only practicle way to calculate VIV for slender marine structures is to apply empirical models for hydrodynamic forces combined with traditional models for structural dynamics. The overall aim for activities at CeSOS has been to improve the quality and generality of VIV analyses, and thereby reduce the uncertainty related to calculation of fatigue damage for slender marine structure. This has been achieved by extending the empirical basis and improve the generality of methods for dynamic analysis of VIV.

2. Underpinning research

Almost all experiments to find hydrodynamic coefficients for VIV analys before 2003 covered pure cross-flow (CF) response only. This was a logical consequence of the fact that CF was considered to be the main contributor to fatigue. However, pure in-line (IL) response is significant for free spanning pipelines, while combined IL and CF will be the normal response pattern for structures like risers and umbilicals. Aronsen /1/ investigated both pure IL and combined IL and CF in his PhD work. His pure IL tests were unique and made it possible to calculate this type of response for free spanning pipelines.

Jie Wu /2/ applied inverse analysis in order to identify the force pattern that was consistent to the measured response of slender elastic beams. The results was used to modify the database for hydrodynamic coefficients in an empirical program for calculation of VIV, and improved the agreement between calculations and observed response.

The first attempt to use inverse analysis for calculation of local forces on flexible beams undergoing VIV, was by a visiting MSc student from University of Stellenbusch, Celeste Barnard /8/. She was supervised by Philippe Mainçon, previously PhD candidate from NTNU.

Soni /3/, Yin /4/ and Aglen /5/ applied a new experimental technique aimed at identifying local forces on flexible beams undergoing VIV. Motions where found from flexible beam experiments,

and later used as forced motions of a rigid cylinder where fores could be measured. This approach gave new information on local forces on beams under combined IL and CF response.

The first attempt to develope a time domain method for calculation of VIV was made by Mainçon/9/. His idea was to define the force at present as a function of the recent history of the local relative velocity between structure and water. He established a data base for force and local relative velocity from the experiments by Soni, Yin and Aglen. The results were promising /9/, but difficult to implement.

Thorsen /6/ developed a new method for time domain analysis of VIV. His key idea was to develope a model for syncronisation of vortex shedding along an oscillating beam, and hence find the forces as function of time, incoming flow and local motion. This approach made it possible to find VIV response for structures with non-linear behavious, such as free spanning pipelines and catenary risers. This method has been implemented in commercial software for calculation of VIV, and is now available to the offshore industry. The approach might also combine forces from current (VIV related) and ordinary wave forces, which will make fatigue analysis of slender marine structures more realistic.

Hidetaka Senga /7/came to CeSOS as a visiting researcher, and made a set of experiments on cylinders with helical strakes. These data are of large interest since designer of strakes often will keep their real performance confidential.

3. References to the research (Priority has been given to PhD thesis)

/1/ Aronsen, Kristoffer: 'An Experimental Investigation of In-line and Combined In-line and Cross-flow Vortex Induced Vibrations', PhD Thesis NTNU 2007

/2/ Wu, Jie: 'Hydrodynamic Force Identification from Stochastic Vortex Induced Vibration Experiments with Slender Beams', PhD Thesis, NTNU 2011

/3/ Sony, Prashant: 'Hydrodynamic coefficients for vortex induced vibrations of flexible beams', PhD thesis, NTNU 2007

/4/ Yin, Decao:'Experimental and Numerical Analysis of Combined In-line and Cross-flow Vortex Induced Vibration', PhD Thesis, NTNU 2013

/5/ Aglen, Ida: 'VIV in Free Spanning Pipelilnes', PhD Thesis, NTNU 2016

/6/ Thorsen, Mats J.: 'Time Domain Analysis of Vortex-Induced Vibrations', PhD Thesis, NTNU 2016

/7/ Senga, Hidetaka and Larsen, Carl M.: 'Forced motion experiments using cylinders with helical strakes', Journal of Fluids and Structures 68:279-294 · January 2017

/8/ Mainçon, P. , C. Barnardo, and C. M. Larsen, "VIV force estimation using inverse FEM", Proceedings of Offshore Mechanics and Arctic Engineering Conference 2008, OMAE 2008-57325.

/9/ Mainçon, P. & Larsen, C., 2011. Towards a time-domain finite element analysis of vortex induced vibrations. s.l., OMAE. Paper No: OMAE2011-49539, pp. 415-425; 11 pages

/10/ Voie, P., Wu, J.,Resvanis, T.,Larsen, C.M., Vandiver, J.K., Triantafyllou, M. and Baarholm, R.: 'Consolidation of Empirics for Calculation of VIV Response', International Conference on Ocean, Offshore and Arctic Engineering, June 25-30 2017, Trondheim, Norway

4. Details of the impact

Calculation of fatigue damage from vortex-induced vibrations has still significant uncertainties. These are consequences of the use of various software, and selection of key parameters like damping and excitation coefficients. Other differences between programs are models for interaction between active frequencies (simultaneously acting, or time sharing), and how fatigue damage is calculated from the response. By defining a set of high quality experiments as a 'consolidated empirical basis', one would expect the disagreements between software to be reduced. This will in turn lead to a reduction of safety factors without increase of probability of failure.

As a consequence of the results from recent research on VIV at CeSOS and others, the need for an updated recommended practice (RP) for engineering type of analyses became obvious. Statoil (Equinor at present) on behalf of The Norwegian Deepwater Programme (NDP) together with DNV-GL, initiated an effort to formulate a new RP. Larsen, Triantafyllou and Vandiver together with researchers from Marintek (Sintef Ocean at present) were invited to contribute to this effort. This work started after the CeSOS period, but should be considered as a direct result of CeSOS activities.

This effort resulted in an internal DNV-GL report 'VIV Best Practice, Guideline on analysis of vortex-induced vibrations in risers and umbilicals' (2016), and also an OMAE paper /10/.

By inviting the two MIT professors Triantafyllou and Vandiver to becone affiliated to CeSOS, cooperation was established between the key persons behind the three most frequently applied softwave for VIV analysis. This in turn made it possible to agree on some fundamental principles and define a 'consolidated empirical basis'.

1.3 CMA - Centre of Mathematics for Applications

1.3.1 Scientific impact:

Institution: University of Oslo, Department of Mathematics		
Name of SFF: Centre of Mathematics for Applications (CMA)		
Title of case study:		
Period when the underpinning research was undertaken: 2003-2013		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Period when the impact occurred:		

1. Summary of the impact

The CMA generated a lot of research activity in the main areas of the center. In total more than 1200 papers in international journals were published. Many of these had major impact in their respective areas. There were more that 1700 international guests, and CMA organised 79 international workshops/conferences. For more details, see the CMA report (Sluttrapport).
A main impact was connected to a high number of research grants. In particular, among these grants, the leading ones were several ERC grants:
(i) 2 ERC advanced grants, (ii) 3 ERC Starting grants and (iii)1 ERC Consolidator grant.
See more on this below.

2. Underpinning research

A main long-term scientific impact of CMA was in connection with the research activity generated by the different ERC grants, briefly mentioned above. There were two ERC Advanced grants to senior member of CMA:

(i) Bernt Øksendal: INNOSTOCH: Innovations in stochastic analysis and applications with emphasis on stochastic control and information (ii) Ragnar Winther: FEEC-A: Finite Element Exterior Calculus and Applications

Moreover, some of the postdocs at CMA have also received ERC grants:

(iii) ERC Starting grant. Researcher Simen Kvaal, Faculty of Mathematics and Natural Sciences, Department of Chemistry. BIVAQUM: Project: Bivariational Approximations in Quantum Mechanics and Applications to Quantum Chemistry (2015-2020) (iv) ERC Starting grant. Professor Snorre H. Christiansen, Faculty of Mathematics and Natural Sciences, Department of Mathematics. Project: STUCCOFIELDS: Structure and scaling in computational field theories (2012-2016). (v) ERC Starting grant, and ERC Consolidator grant. Professor Siddharta Mishra, ETH Zurich. SPARCCLE (Starting grant, 2012-2017). ERC Consolidator grant COMANFLO (2018-2023)

Snorre Christiansen is currently professor at the Department of Mathematics, UiO. He was also granted the EURYI (European Young Investigator) project, NASGWE (Numerical Analysis and Simulation of Geometric Wave Equations), from the European Science Foundation in 2005. This also lead to his appointment as Associate Professor at the Dept. Of Mathematics, UiO. Siddharta Mishra has an adjunct position at the Department of Mathematics, UiO while his main postition is as professor at ETH. Simen Kvaal is involved in another SFF at UiO, in theoretical chemistry: Hylleraas Centre for Quantum Molecular Sciences, headed by Professor

Trygve Helgaker and Professor Kenneth Ruud. These two ERC Advanced grant projects were in stochastic analysis and partial differential equations, respectively. The INNOSTOCH project was in the period of 2009-2014, so with a large overlap with the CMA period, while the FEEC-A project was in the period of 2014-2019 so right after the CMA period. On INNOSTOCH: For almost all kinds of dynamic systems modeling real processes in nature or society, most of the mathematical models we can formulate are - at best - inaccurate, and subject to random fluctuations and other types of "noise". Therefore it is important to be able to deal with such noisy models in a mathematically rigorous way. This rigorous theory is stochastic analysis. Theoretical progress in stochastic analysis will lead to new and improved applications in a wide range of fields. The main purpose of this project is to establish a research environment which enhances the creation of new ideas and methods in the research of stochastic analysis and its applications. The emphasis is more on innovation, new models and challenges in the research frontiers, rather than small variations and minor improvements of already established theories and results. One concentrated on applications in finance and biology, but the theoretical results may as well apply to several other areas. On FEEC-A: The finite element method is one of the most successful techniques for designing numerical methods for systems of partial differential equations (PDEs). It is not only a methodology for developing numerical algorithms, but also a mathematical framework in which to explore their behaviour. The finite element exterior calculus (FEEC) provides a new structure that produces a deeper understanding of the finite element method and its connections to the partial differential equation being approximated. The goal was to develop discretizations which are compatible with the geometric, topological, and algebraic structures which underlie well-posedness of the partial differential equation. The general philosophy of FEEC has led to the design of new algorithms and software developments, also in areas beyond the direct application of the theory. The present project will be devoted to further development of the foundations of FEEC, and to direct or indirect use of FEEC in specific applications. The more application oriented parts of the project includes topics like numerical methods for elasticity, poroelasticity, liquid crystals, and other applications.

1.3.2 Societal impact: Computing and programming is tightly integrated in all science programs at the University of Oslo

Institution: University of Oslo and Simula Research Laboratory

Name of SFF: Center for Biomedical Computing (CBC), Physics of Geological Processes (PGP), Center of Mathematics for Computation (CMA)

Title of case study: Computing and programming is tightly integrated in all science programs at the University of Oslo

Period when the underpinning research was undertaken: 2002-2017

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Periods employed by SFF**
Hans Petter Langtangen	Professor, Center Leader CBC	2007-2016
Joakim Sundnes	Center Leader, CBC	2007-2017
Morten Hjorth-Jensen	Professor, CMA	2003-2013
Knut Mørken	Professor, Deputy leader CMA	2003-2013
Anders Malthe-Sørenssen	Professor, Group leader PGP	2003-2013

Period when the impact occurred:

1. Summary of the impact

The University of Oslo is an international leader in integrating computing and programming in science education. Through a collaborative effort known as *Computing in Science Education,* involving staff of three Centers of Excellence (CBC, PGP, and CMA), computing is now an integral part of all science programs at the University of Oslo, with nearly every single course including components of relevant programming. The result of this effort is a new generation of science graduates that are highly skilled in using computers to solve scientific and engineering problems, and have been trained in solving far more complex and realistic science problems than what is part of a traditional curriculum.

2. Underpinning research

The *Computing in Science Education* initiative is a long-term pioneering effort at the University of Oslo, and its progress was accelerated by the collaborations and research efforts in the Center for Biomedical Computing, Physics of Geological Processes, and Center of Mathematics for Applications. All the three centers have been strongly focused on the use of computational mathematics to solve scientific problems, across a large variety of fields including geology, physics, continuum mechanics, and physiology as well as development of new computational methods.

The long-term research into these areas have led to the observation that successful candidates in science and engineering need deep and broad training in computational methods and programming. Such training needs to be coherently integrated with and not only supplement the traditional analytical techniques of the natural sciences, to make the candidates better prepared for how science problems are solved in the 21st century. A more innovative insight underpinning the initiative is that extensive use of computers will also advance the candidates' understanding of their own scientific field. Being skilled in computational mathematics, the students are able to focus on the underlying scientific questions rather than the advanced algebra often required in

traditional problem solving techniques. At the same time the computational techniques are more general than the traditional techniques, allowing he students to tackle far more complex and realistic scientific problems.

As a result of these efforts, the University of Oslo is at the international forefront in this area, with programming and computational methods tightly integrated into all study programs in the natural sciences. The initiative has been recognized by numerous prizes and awards, and in 2016 received status as a Norwegian Center for Excellence in Education (SFU) as Centre for Computing in Science Education (CCSE), hosted by the Department of Physics, University of Oslo.

3. References to the research

This section should provide references to key outputs from the research described in the previous section, and evidence about the quality of the research. Underpinning research outputs may include, but is not limited to journal articles, book chapters, edited volumes, monographs, patents, prototypes etc.

Hans Petter Langtangen, "Title: A Primer on Scientific Programming with Python", Springer, 2009.

Anders Malthe-Sørenssen, "Elementary Mechanics Using Python"/"Elementary Mechanics Using Matlab", Springer 2015.

Arnt Inge Vistnes, Physics of Oscillation and Waves with use of Matlab and Python, Springer, 2018

Anders Malthe-Sørenssen, Morten Hjorth-Jensen, Hans Petter Langtangen, Knut Mørken, «Integrasjon av beregninger i fysikkundervisningen», *Uniped*, **38**, 4, 2015

Marcos Daniel Caballero, Morten Hjorth-Jensen, "Integrating a computational perspective in physics courses", arXiv, 1802.08871 2018.

4. Details of the impact

Two to three decades ago, the typical curriculum of a physics or mechanics student at the University of Oslo would mainly be focused on traditional, analytical problem-solving methods. A course in programming would be included early on, but then most students would not use programming again as part of their undergraduate studies. About three years later, when starting their Master's studies, many of the students would work on computationally oriented project, which typically would require programming using a new programming language and an entirely different style than what they learnt earlier. Surprisingly, this curriculum remains the standard program in universities all over the world. The approach works in that students get introduced to the basic ideas of programming and get a solid background in their own field, and some students are capable of integrating these two skillsets on their own when needed. However, this is most likely not the best approach for preparing students for an increasingly computer-based work life.

At the University of Oslo, current undergraduate students have a completely different experience. All bachelor programs include an introductory programming course tailored to the needs of the particular field, with examples and applications selected from relevant scientific problems. Students in the most computing-intensive programs, including physics and mathematics, also follow a course in numerical mathematics, which is tightly integrated with the introductory course in programming. Even more importantly, computing-based problem solving is part of many later

undergraduate courses, which maintains and further develops these skills. As a result, students are far better prepared both for graduate school and for the typical tasks they will face in their first job. The Computing in Science Education initiative grew out of a collaboration between three different University departments, as part of the CoEs *Center of Mathematics for Applications, Physics of Geological Processes,* and *Center for Biomedical Computing.* Today, the initiative has turned into a CoE on its own, the *Center for Computing in Science Education (CCSE)*, and plays a central role in further development of the science curriculum in Norwegian Universities.

The CCSE and thereby the original Computing in Science initiative has given many high school teachers new perspectives on how mathematics and science can be taught in school since they attend the basic undergraduate courses in mathematics and physics as part of their training. One of these teachers has developed an elective course for high school based on the CSE ideas. Through the years, scientists involved in CSE have also given presentations to politicians and participated in writing reports about programming in school.

The whole Norwegian school system is currently undergoing a major change in that the content of all disciplines is reformed with a focus on more advanced understanding, so-called «deep learning». One aspect of this is that programming and algorithmic thinking is a skill and way of thinking that all students should learn. This will be hosted by mathematics, but also integrated in other disciplines like science, art and craft, and music. In this process, the CSE-ideas have played a major role, and the CCSE is now offering numerous courses for teachers in preparation for the introduction of the new syllabus in the fall of 2020.

5. Sources to corroborate the impact

The CSE project was featured in the Norwegian white paper on Higher Education, Culture for quality in higher eduction, Meld. St. 16 2016–2017 Kultur for kvalitet i høyere utdanning, p. 42, https://www.regjeringen.no/contentassets/aee30e4b7d3241d5bd89db69fe38f7ba/no/pdfs/stm201620170016000dddpdfs.pdf

The CSE project was awarded a Center for Excellence in Education. The project description and the review of the project can be found on the web-pages of Nokut/Diku. The full review of the external evaluation committee can be found here. The CCSE project received a full score of 6 as the only Center for Excellence funded in 2016: https://www.nokut.no/sentre-for-fremragende-utdanning/sentre/ccse--center-for-computing-in-science-education/

The new curriculum for Mathematics in the Norwegian 1-13 schools system can be found at The Norwegian Directorate for Education and Training's web pages https://www.udir.no/laring-og-trivsel/lareplanverket/fagfornyelsen/hva-er-nytt-fagene-les-vare-korte-oppsummeringer/ . They write that: *«Vi har tatt algoritmisk tenkning og programmering inn i faget. Vi har vektlagt algoritmisk tenkning fordi dette er en viktig problemløsningsstrategi. Når elevene bruker programmering til å utforske og løse problemer, kan det være et godt verktøy for å utvikle matematisk forståelse.»* The CSE project has contributed to this change.

The impact of CSE can be read from the number of invited talks and presentations by key personnel. A full list can be found in the Annual reports from CCSE from 2017 and 2018 found here: https://www.mn.uio.no/ccse/om/rapporter/. Computing is now in the processes of being integrated in science programs at UiB, NTNU, UiT, UiS, at Stockholm University, Uppsala University, , and University of Dublin, Ireland, at Michigan State University, USA, and at the National University of Defense Technology in China.

1.3.3 Societal impact: Education in computational mathematics

Institution: University of Oslo, Department of Mathematics		
Name of SFF: Centre of Mathematics for Applications (CMA)		
Title of case study: Education in computational mathematics		
Period when the underpinning research was undertaken: 2003-2013		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Period when the impact occurred: from 2003 and for decades ahead		

1. Summary of the impact

A basic idea of the CMA was to perform top-level international research in mathematics that was connected to applications and basic society challenges. Therefore the training of PhD candidates, and also postdocs and Master students was a central goal of the center. The center members did their teaching and also arranged seminars, workshops etc. The training of PhD students was highly successful, and during the center period 62 PhDs associated with CMA finished their degrees, with supervisors at CMA. All these candidates learned the "CMA philosophy": combining mathematics and computations in order to work on applications. The candidates have pursued different careers, several to academic jobs, but even more to jobs in industry, consulting and technology development companies. They will have significant impact on society for a long time, based on their unique computational mathematics background.

2. Underpinning research

The CMA training of PhDs in mathematics and computations was linked to another activity. The CMA was strongly involved in "Computing in Science Education" program (CSE) at the Faculty. This was a major education initiative, bringing computational methods into the different study programs and courses in mathematics, physics, chemistry, astrophysics, biology and other areas covered by the faculty.

Thus, this focus strengthened the inter-disciplinary activity and has brought mathematics and computations to a wider community and students. As an extension of the CSE the faculty has a SFU (center of excellence in education) Centre for Computing in Science Education (CCSE). It focuses on the introduction of computing in science, and how it can be integrated into study programs using good educational principles.

This development at the faculty in CSE, and later the CCSE, is a development that largely goes back to the CMA and its members. We believe that this computational focus on various educational programs and courses is very important, and pust UiO in the front internationally on this important development.

1.4 CSCW - Centre for the Study of Civil War

1.4.1 Scientific impact: A platform for theoretical exchange on civil war

Institution: Peace Research Institute Oslo (PRIO)

Name of SFF: Centre for the Study of Civil War (CSCW)

Title of case study: A platform for theoretical exchange on civil war

Period when the underpinning research was undertaken: 2003 and onwards

Details of staff conducting the underpinning research from the submitting unit:

Name(s)/Role(s)[1]/Period(s) employed by submitting SFF

- Scott Gates (Centre Director, R1 2003-)
- Halvard Buhaug (R3 2003-2005, R2 2006-2011, R1 2011-)
- Jon Elster (R1 2002-2012)
- Nils Petter Gleditsch (R1, 2002-)
- Kristian Skrede Gleditsch (R2 2003-2007, R1 2007-)
- Håvard Hegre (R2 2004-2005, R1 2005-2012)
- Joakim Karlsen (Adv 2005-2006, R3 2012)
- Bethany Lacina (RA 2004-2005, R3 2006)
- Halvor Mehlum (R2 2005, R1 2006-2009)
- Karl Ove Moene (R1 2003-2010)
- Kaare Strøm (R1 2003-2013)
- Henrik Urdal (PhD 2003-2006, R2 2007-2012, R1 2013-)
- Nils Weidmann (R2 2011-2012)

Names of SFF Working Group members:

- Lars Erik Cederman (2005-2012)
- Paul Collier (2003-2012)
- James Fearon (2003-2012)
- Diego Gambetta (2003-2012)
- Anke Hoeffler (2003-2012)
- Stathis Kalyvas (2003-2012)
- James Robinson (2003-2012)
- Stergios Skaperdas (2003-2012)
- Elisabeth Wood (2003-2012)

Period when the impact occurred:

1. Summary of the impact

The Centre for the Study of Civil War (CSCW) played a central role in the study of civil war. The world's top civil war scholars were connected to CSCW. CSCW fundamentally altered the way civil war was studied quantitatively. CSCW was instrumental in the development of important datasets that are open, transparent, and free. CSCW also blazed new pathways of research on global trends in conflict, political institutions, inequality, demographics, and shifting public

[1] RA1 (Research Assistant with Masters), PhD/R3 (Doctoral Researcher), R2 (Senior Researcher/Post-docs), R1 (Professor)

opinions about civil armed conflict. Important research on the consequences of war and post-conflict peace.

2. Underpinning research

Summarizing ten years of research in a brief format is challenging. Below we list some research highlights, grouped into several broad themes:

- Global trends in conflict since WWII
    - Collaborative research with Uppsala University. PRIO-Uppsala Conflict Dataset.
    - Declining incidence of civil conflict (peak in 1991/92)
    - Declining severity of civil conflict (peak in early 1950s)
    - Remarkable waning of interstate conflict after the Cold War
        - Lacina and Gleditsch (2005)
- Political institutions and civil conflict
    - Abundant natural resources combined with weak political institutions leads to conflict
    - Political stability is strongly related to the configuration of institutions
        - Mehlum, et al (2006)
- Inequality and civil war
    - Extensive poverty is the most robustly significant factor associated with civil conflict onset
    - Economic growth significantly decreases the risk of civil conflict
    - Inequality between groups (Horizontal Inequality), not between individuals drives conflict
        - Cederman et al (2011)
- Geographical disaggregating the study of civil war
    - Extensive collection and use of geo-referenced conflict data
    - Development of a unique framework for managing and analyzing spatial data
    - Determinants of subnational location and transnational diffusion of civil conflict
    - Two important datasets produced: ACLED and PRIO-Grid
        - Raleigh, et al (2010)
- The demographics of civil conflict
    - Youth bulges (societies with disproportionate shares of youth and young adults) are often associated with higher risks of conflict, but if such societies can avoid armed conflict, they can harness high economic growth rates
        - Urdal (2006)
- Post-conflict stability and conflict recurrence
    - Powersharing arrangements are only peace inducing when human rights and civil liberties are guaranteed. Elite arrangements typically do not last
    - Post-conflict justice mechanisms have differential impact on sustaining peace. Amnesty is particularly problematic. Post-conflict justice dataset.
        - Elster (2004)
- Development consequences of Civil War
    - Civil war unambiguously harms economic development
    - Children suffer the most from civil war, as safe drinking water, infant mortality rates, under five-year mortality rates, maternal health, education and poverty disproportionately affect children
- Shifting political attitudes and conflict
    - Religious differences are not inherently conflictive
    - States' repressive policies are significantly associated with turning social cleavages violent – elites drive hostility between groups
    - Democratic values carry the same meaning across cultures and societies – a survey of 55 countries supports the notion that concepts of human rights and democracy are shared – they are not just culturally universal

- Sexual violence in armed conflict
    - Not all conflict actors engage in sexual violence
    - Most sexual violence is caused by regular uniformed military forces, not the rebels and not pro-government militias
    - Sexual violence patterns do not correspond to death patterns in war. Sexual violence also continues after ceasefire agreements, constituting a "missing peace" in many post-conflict environments

3. References to the research

- Mehlum, H., Moene, K., & Torvik, R. (2006). Institutions and the resource curse. *The economic journal*, *116*(508), 1-20. Web of Science (WoS) cites- 699; Google Scholar (GS) 2648
- Raleigh, C., Linke, A., Hegre, H., & Karlsen, J. (2010). Introducing ACLED: an armed conflict location and event dataset: special data feature. *Journal of peace research*, *47*(5), 651-660. WoS 336; GS 905
- Lacina, B., & Gleditsch, N. P. (2005). Monitoring trends in global combat: A new dataset of battle deaths. *European Journal of Population/Revue Européenne de Démographie*, *21*(2-3), 145-166. WoS 333: GS 912
- Cederman, L. E., Weidmann, N. B., & Gleditsch, K. S. (2011). Horizontal inequalities and ethnonationalist civil war: A global comparison. *American Political Science Review*, *105*(3), 478-495. WoS 291; GS 808
- Urdal, H. (2006). A clash of generations? Youth bulges and political violence. *International studies quarterly*, *50*(3), 607-629. WoS 229; GS 818
- Elster, J. (2004). *Closing the books: Transitional justice in historical perspective*. Cambridge University Press. GS 1116 cites

4. Details of the impact

Of the 100 most cited PRIO articles 2003-2015 (total number of hits was 464), 85 are related to the CSCW. The top 27 cited are all CSCW. Citations for the top 100 range from 699 (Mehlum, Moene, Torvik) to 37. Of a total of six 'highly cited papers' (marked by a trophy by the Web of Science), all are CSCW, which indicates that they are among the 1% most cited of their cohort. The 100th most cited CSCW publication is cited 29 times according to the Web of Science (according to Google Scholar, this article has 70 citations).

Research conducted at the Centre for the Study of Civil War (CSCW) had a profound effect on the research regarding intrastate armed conflict. Before the 2000s the vast majority of scholarship was focused on war between nations – interstate war. CSCW research fundamentally shifted attention to civil wars, their cause, the manners in which they are fought, and how they end. Top scholars writing on civil war were based at PRIO or connected to one of the CSCW Working Groups, including: Paul Collier, Anke Hoeffler, Håvard Hegre, Scott Gates, Jon Elster, James Fearon, Stathis Kalyvas, Ola Listhaug, Kalle Moene, Halvor Mehlum, James Robinson, and Kaare Strøm. Postdocs connected to CSCW became top scholars in their own right, including Halvard Buhaug, Clionadh Raleigh, and Henrik Urdal. Doctoral candidates, Gudrun Østby, Ragnhild Nordås, and Håvard Strand have also established themselves as top scholars.

CSCW research on global trends in armed conflict has profoundly affected one of the biggest debates in conflict research in the 2010s. Steven Pinker (2011), using PRIO-Uppsala conflict data and Lacina and Gleditsch's battle deaths data, argues in his best-selling book, *The Better Angels of Our Nature: The decline of violence in history and its causes*, that among other trends armed conflict is waning. Nils Petter Gleditsch organized a number of panels at the International Studies

Association, which were published as symposium in the *International Studies Review* among other journals. Pinker's thesis has recently been critiqued by Bear Braumoeller (2019) *Only the Dead: The Persistence of War in the Modern Age.* PRIO researcher Håvard Mokleiv Nygård and colleagues at the University of Oslo Applied Mathematics Department drawing on the statistical properties of Power Laws, find a breakpoint following the Korean War whereby war becomes much less likely, supporting the Pinker thesis on the waning of war.

Climate change and armed conflict is another research area that was fundamentally transformed as a result of CSCW research. CSCW and subsequent PRIO research has been instrumental in providing rigorous scientific evidence on security implications of climate change and thereby making human and national security an integral part of the mandate of the UN's Intergovernmental Panel on Climate Change (IPCC) – the agenda setter on climate change adaptation and mitigation policies. Halvard Buhaug and colleagues have continued to examine and explore the connection between climate change and the onset of armed conflict.

Two GIS (geographic information system) datasets, ACLED and PRIO-GRID began at the CSCW. These two datasets serve the academic and policy communities with detailed geographically disaggregated information regarding armed conflict. ACLED (Armed Conflict Location & Event Data Project) records the dates, actors, types of violence, locations, and fatalities of all reported political violence and protest events across Africa, South Asia, Southeast Asia, the Middle East, Europe, and Latin America. ACLED data are regularly used by the Economist and other new sources and international organizations such as the World Bank. PRIO-GRID is a vector grid network with a resolution of 0.5 x 0.5 decimal degrees, covering all terrestrial areas of the world. Each grid cell contains cell-specific information on armed conflicts, socio-economic conditions, ethnic groups, physical attributes, climatic conditions and more. The original version of PRIO-GRID was funded by the Research Council of Norway via the ACDC infrastructure project (grant no. 195400/F50). PRIO-GRID helped foster an explosion of subnational disaggregated analysis of civil war. This focus on disaggregation began and was sustained by CSCW research.

CSCW research contributed heavily to research on the development consequences of war. The initial focus was on a set of development indicators as specified by the Millennium Development Goals. More recent work conducted at PRIO has been on the new Sustainable Development Goals (SDG). Economists such as John Paul Dunne and Ron Smith have examined the economic consequences of war, while PRIO researchers are the only ones engaged in examining the health, economic, and political consequences of civil war.

These areas of research are just a few topics which were indelibly affected by CSCW research.

5. Sources to corroborate the impact

Citations:

Kristian Gleditsch, 2014. Listed in Thomson Reuters Highly Cited Researchers 2014 (http://highlycited.com/) as one of the 3000 researchers with the greatest numbers of Highly Cited Papers, ranking among the top 1% most cited for their subject field (Social Sciences) and year of publication.

Prizes:

2015. International Studies Association Annual Best Book Award, for Lars-Erik Cederman, Kristian Skrede Gleditsch, & Halvard Buhaug. Inequality, Grievances, and Civil War (New York and Cambridge: Cambridge University Press, 2013)

2014. American Pol

itical Science Association, Conflict Processes Section, 2012-3 Best Book Award, for Lars-Erik Cederman, Kristian Skrede Gleditsch, & Halvard Buhaug. Inequality, Grievances, and Civil War (New York and Cambridge: Cambridge University Press, 2013)

2014. Network of European Peace Scientist Medal for the best publication in Peace Science, for Lars-Erik Cederman, Kristian Skrede Gleditsch, & Halvard Buhaug. Inequality, Grievances, and Civil War (New York and Cambridge: Cambridge University Press, 2013)

2012. American Political Science Association's Heinz I. Eulau Award, for the best article published in the American Political Science Review, for Lars-Erik Cederman, Nils B. Weidmann & Kristian Skrede Gleditsch. “Horizontal Inequalities and Ethno-nationalist Civil War: A Global Comparison”, American Political Science Review 105(3): 457-477.

2019. Jon Elster receives the Norwegian Academy of Science and Letters’ Prize for Outstanding Research in the Humanities and Social Sciences. Jon Elster was at PRIO 2003-2012 heading the CSCW working group Microfoundations of Civil War. Jon Elster also gave the first PRIO Annual Peace Address in 2010 on Justice, Truth, Peace.

1.4.2 Societal impact: Conflict is Development in Reverse

Institution: Peace Research Institute Oslo (PRIO)

Name of SFF: Centre for the Study of Civil War (CSCW)

Title of case study: Conflict is Development in Reverse

Period when the underpinning research was undertaken: 2003 onwards

Details of staff conducting the underpinning research from the submitting unit:

Name(s)/Role(s)[2]/Period(s) employed by submitting SFF

- Scott Gates (Centre Director, R1 2003-)
- Håvard Hegre (R2 2004-2005, R1 2005-2012)
- Håvard Nygård (RA 2008-2010, R3 2010-2013, R2 2013-)
- Håvard Strand (R3 2003-2007, R2 2007-)

Period when the impact occurred: 2010 -2019

1. Summary of the impact

War is a major obstacle to development. Long-time PRIO collaborator and former World Bank Director of Research Paul Collier, goes further, stating: conflict is development in reverse. Indeed, in the last UN progress report for the Millennium Development Goals the Secretary General stated: "conflict remains the largest obstacle to development". PRIO has, on behalf of the United Nations and the World Bank, analyzed the effects of conflict on socio-economic development, human rights abuses, and democratization, and this contributed strongly to shaping their analyses and policies. PRIO contributes heavily to research of the development consequences of war. Our focus has been on a set of development indicators of the Millennium Development Goals, and more recently on the new Sustainable Development Goals (SDG).

2. Underpinning research

The consequences of armed conflict are profound and far-reaching, and extend far beyond direct battlefield casualties. Although media attention usually stops soon after a ceasefire has been signed, this is when the most dramatic consequences kick in. PRIO research has examined three types of development consequences: economic, political and health. A great deal of analysis has been carried out in the past decade on the economic consequences of war. A central finding of this literature is that war, especially civil war, is a development issue. War is at once is both a consequence of lacking development, and a cause of it. This has the potential of locking countries in a conflict trap. Wars, the most severe form of conflict, differ from less violent armed conflicts in that the latter usually inflict relatively fewer consequences on their communities. Wars have a lingering effect on growth; conflict both pushes a country off its initial growth path and may slow it down long after the conflict has ended. Wars also have detrimental development effects as evaluated in terms of the United Nation's Millennium Development Goals (MDGs). More concretely, a medium-sized conflict with 2,500 battle deaths is estimated to increase undernourishment by 3.3%, reduce life expectancy by about one year, increase infant mortality by 10%, and deprive an additional 1.8% of the population from access to potable water. The detrimental effects of war on children are especially severe.

[2] RA1 (Research Assistant with Masters), PhD/R3 (Doctoral Researcher), R2 (Senior Researcher/Post-doc), R1 (Professor)

MDG	Label	Indicator	Effect of conflict		Effect of fragility	
			Cross-section	Fixed-effects	Cross-section	Fixed-effects
MDG 1	Ending Poverty and Hunger	Undernourishment	Detrimental	Detrimental	Detrimental	Unclear
MDG 1		Poverty Headcount	Detrimental	Detrimental	Detrimental	No effect
MDG 1		Life expectancy	Detrimental	Detrimental	Detrimental	Detrimental
MDG 1		GDP per capita	Detrimental	Detrimental	Detrimental	Detrimental*
MDG 2	Universal Education	Prim. Sch. Enrollment	Detrimental	Detrimental	Detrimental	Beneficial?
MDG 2		Sec. Sch. Attainment	Detrimental	Unclear	Detrimental	Unclear
MDG 3	Gender Parity	Primary School ratio	Detrimental	Beneficial?	Detrimental	No effect
MDG 3		Life expect. ratio	No effect	Unclear	No effect	No effect
MDG 4	Child Mortality	Infant Mortality	Detrimental	Detrimental	Detrimental	Detrimental
MDG 4		Under-5 Mortality	Detrimental	Detrimental	Detrimental	Detrimental
MDG 5	Maternal Mort.	Birth Attendance	No effect	Unclear	Detrimental	Beneficial?
MDG 6	Combat AIDS	% HIV positive	Beneficial?	Beneficial?	Beneficial?	No effect
MDG 7	Environmental Sustainability	Access to Water	Detrimental	Detrimental	Detrimental	Detrimental
MDG 7		Access to Sanitation	No effect	Unclear	No effect	No effect

*:Estimated on growth in GDP per capita using OLS with panel-corrected standard errors.

The political consequences the effects of conflict are also considerable. Conflict all too often leaves a legacy of repression in its wake. A country which experienced a durable war has a significantly higher probability of being in a situation where "murders, disappearance and torture are a common part of life". The mechanism causing this is state securitization. War induces insecurity for leaders and this causes them to resort to political incarceration, brutal subjugation and torture.

3. References to the research

Gates, Scott; Håvard Hegre, Håvard Nygård, and Håvard Strand.2010. The Consequences of Armed Conflict in the Middle East and North Africa Region. Background Report for the World Bank, Mideast North Africa (MENA) Region.

Gates, Scott; Håvard Hegre, Håvard Nygård, and Håvard Strand. 2011. The Development Consequences of Conflict. Background paper for the World Development Report, World Bank.

Gates, Scott; Håvard Hegre, Håvard Mokleiv Nygård, Håvard Strand. 2012. Development consequences of armed conflict. *World Development* 40(9): 1713-1722.

Håvard Hegre and Håvard Nygård. 2011. The Governance-Conflict Trap in the ESCWA Region, a paper for the UN-ESCWA study on *The Governance Deficit and Conflict Relapse in the ESCWA Regi*on, 2011.

Gates, Scott; Håvard Hegre; Håvard Mokleiv Nygård & Håvard Strand (2014) Development Consequences of Internal Armed Conflict, *Conflict Trends Policy Brief*, 3. Oslo: PRIO.

Hegre, Håvard, Håvard Mokleiv Nygård, & Ranveig Flaten Ræder. 2017. Evaluating the scope and intensity of the conflict trap A dynamic simulation approach. *Journal of Peace Research* 54(2): forthcoming.

4. Details of the impact

PRIO research has contributed fundamentally to World Bank and UN reports. In fact, the 2011 *World Development Report* (WDR) included references to 23 different publications involving PRIO researchers. The 2011 WDR in particular has been referred to as a "game changer". PRIO research as reflected in the 2011 WDR and other reports altered the prioritization of conflict as a development issue. In other words, PRIO's research on the consequences of conflict directly influenced the World Bank's and the United Nation's policies on development and conflict. Indeed, when world leaders reached a consensus

regarding a set of new development goals, the Sustainable Development Goals (SDGs), which replaced the Millennium Development Goals (MDGs), conflict was placed at the center of the agenda. PRIO's research served as the analytical and substantive backbone to the 2011 *World Development Report: Conflict, Security and Development*. This WDR was a watershed in terms of altering World Bank policy. PRIO research also served as the principal background paper for two ESCWA reports. A number of aid agencies, such as UK's DIFID, have also incorporated our analysis into their policymaking. From its beginnings the World Bank has seen violent conflict as a profound development challenge. Much of the world has made rapid progress in building stability and reducing poverty in the past 60 years, but areas characterized by persistent violence and fragile institutions are being left far behind, their economic growth compromised, their citizen security threatened. PRIO researchers have a long history working with the World Bank and the United Nations, especially the Economic and Social Commission for Western Asia (ESCWA). Our research has been instrumental in establishing the relationship between development and conflict. Indeed, the concept of the conflict trap came from our collaboration with Sir Paul Collier during his tenure as World Bank Research Director. Up to this point most research focused on how poverty and underdevelopment was casually linked to the onset of armed conflict. These findings provided an impetus for the inclusion of a specific goal on achieving peaceful societies in the new SDGs. PRIO researchers are now engaged in the international process of developing indicators of the SDGs, a process in which we have, based on our based research, been asked to play an active role in the UN appointed Praia Group on Governance Statistics. These indicators will play a critical role in shaping how development policy is assessed. PRIO research will have served an instrumental role in shaping development policy.

5. Sources to corroborate the impact

MENA Flagship Report 2011. Reducing Conflict Risk: Conflict, Fragility and Development in the Middle East and North Africa. 2011. The World Bank, Sustainable Development Department, Middle East and North Africa Region. December 2011.

Economic and Social Commission for Western Asia (ESCWA*)*. 2011. *The Governance Deficit and Conflict Relapse in the ESCWA Region*, United Nations, New York, 2011. Report no.: 11-0208.

Economic and Social Commission for Western Asia (ESCWA*)*. 2015. Protracted Conflict and Development in the Arab Region, *Trends and Impacts.* Issue No. 4, United Nations, New York, 2015. Report no.: 15-00330.

The Economist. 2011. The Economics of Violence. 14 April 2011.

The Economist. 2013. Defining Conflicts: What Makes it a War? 9 November 2013.

The Economist. 2013. Civil Wars: How to Stop the Fighting, Sometimes. 10 November 2013.

Wolf, Martin. 2011. Remove the scourge of conflict. *Financial Times* April 26, 2011.

Governance and Social Development Resource Centre website.

1.4.3 Societal impact: Debunking Conflict Myths

Institution: Peace Research Institute Oslo (PRIO)

Name of SFF: Centre for the Study of Civil War (CSCW)

Title of case study: Debunking Conflict Myths

Period when the underpinning research was undertaken: 2003 onwards

Details of staff conducting the underpinning research from the submitting unit

Name(s)/Role(s)[3]/Period(s) employed by submitting SFF

- Scott Gates (Centre Director, R1 2003-)
- Halvard Buhaug (R3 2003-2005, R2 2006-2011, R1 2011-)
- Nils Petter Gleditsch (R1, 2002-)
- Håvard Hegre (R2 2004-2005, R1 2005-2012)
- Ragnhild Nordås (PhD 2005-2010, R2 2011-)
- Håvard Nygård (RA 2008-2010, R3 2010-2013, R2 2013-)
- Siri Aas Rustad (RA 2005, PhD 2007-2012, R2 2012-)
- Håvard Strand (R3 2003-2007, R2 2007-)
- Andreas Forø Tollefsen (RA 2008-2010, R3 2010, PhD 2011-2016, R2 2016-)
- Henrik Urdal (PhD 2003-2006, R2 2007-2012, R1 2013-)
- Gudrun Østby (RA 2004-2008, R3 2008-2011, R2 2011-)

Period when the impact occurred: 2003-2013

1. Summary of the impact

Truth and facts are among the first victims of war. The number of people that are affected by an armed conflict is often highly uncertain. Yet, perceptions and numbers about human suffering in conflicts greatly influence public opinion and the willingness of governments to act. Conflict parties often have great incentives to misinform, and third parties working to address humanitarian concerns often have incentives to inflate numbers. PRIO research on conflict data has significantly contributed to shape policy and public debates about conflict developments and has affected how policymakers, media and humanitarian organizations relate to systematic knowledge about conflicts patterns.

2. Underpinning research

PRIO has had a long-term interest in conflict data and was involved in the initial development of both of the leading global conflict datasets, the Correlates of War Project and the Uppsala Conflict Data Project (UCDP). In 1991, discussions started between PRIOs Journal of Peace Research (JPR) and the Department of Peace and Conflict Research (DPCR) at Uppsala University about the publication of the conflict list. The definitions were polished and the threshold for inclusion was set to 25 battle deaths in a calendar year. The first JPR article was published in 1993, and the article has been published annually since. In 2000, PRIO obtained funding from the World Bank and in collaboration with DPCR the armed conflict data were backdated to 1946 and published in JPR in 2002. The idea was to create a standard tool for empirical conflict research, and this proved quite successful. With more than 3600 citations in Google Scholar as of September 2019, the 2002

[3] RA1 (Research Assistant with Masters), PhD/R3 (Doctoral Researcher), R2 (Senior Researcher), R1 (Professor)

article is now the most widely cited article in JPR ever and the most cited article from DPCR and PRIO. The data showed a strong increase in the number of armed conflicts during the Cold War and a marked decrease afterwards. More recently, the number of armed conflicts has fluctuated but with no clear long-term trend. With PRIOs Centre for the Study of Civil War (CSCW), starting in 2002, a project was initiated to assess the annual number of battle deaths (BDs) in the UCDP-PRIO armed conflict dataset, covering the period 1900–2008. Like the UCDP-PRIO armed conflict data, this has become a standard research tool. The data show a jagged curve in annual battle deaths, heavily influenced by individual wars, but with a clear long-term declining trend. UCDP started collecting its own BD data, going back to 1989, with 'low', 'best' and 'high' estimates. The two data series are now often used as equivalent by conflict researchers. Recently, the conflict data research at PRIO has been extended to develop forecasting models describing under what development trajectories and in which geographical areas and countries conflict is becoming more or less likely. The forecasts predict a continued decline in armed conflict globally. PRIO has been instrumental in the geographical disaggregation of conflict analyses. PRIO/CSCW researchers were involved in the development of the Armed Conflict Location and Event Dataset and the PRIO-GRID allowing researchers to study conflict developments in much greater detail.

3. References to the research

Gleditsch NP, E Melander & H Urdal (2016) Introduction – patterns of armed conflict since 1945. Chapter 1 in D Mason & S McLaughlin Mitchell, eds, *What Do We Know About Civil War?* Lanham, MD: Rowman & Littlefield, in press.

Gleditsch, NP, P Wallensteen, M Eriksson, M Sollenberg & H Strand (2002) Armed conflict 1946–2001: A new dataset. *Journal of Peace Research* 39(5): 615–637.

Hegre, H; J Karlsen, H Nygård, H Strand & H Urdal (2013) Predicting armed conflict, 2011–2050. *International Studies Quarterly* 57(2): 250–270.

Lacina B & NP Gleditsch (2005) Monitoring trends in global combat: A new dataset of battle deaths. *European Journal of Population* 21(2–3): 145–166.

Østby, G & H Urdal (2014) Conflict and Educational Inequality: Evidence from 30 Countries in Sub-Saharan Africa. Commissioned report for USAID. http://pdf.usaid.gov/pdf_docs/PA00JW56.pdf

Tollefsen, AF; H Strand & H Buhaug (2012) PRIO-GRID: A unified spatial data structure. *Journal of Peace Research* 49(2): 363–374.

4. Details of the impact

The conflict data research at PRIO has shaped perceptions of the global conflict picture, helped governments and international organizations take an evidenced-based approach to conflict-related issues, and confronted persistent myths. A recent vehicle for this impact has been Conflict Trends, a collaborative project between the Norwegian Ministry of Foreign Affairs and PRIO. Through this work PRIO provides the MFA with information about general trends in armed conflict, their implications, and their resolution and settlement worldwide. Minister of Foreign Affairs, Børge Brende, referred directly to PRIOs work when announcing a forthcoming (2016) government white paper (Stortingsmelding) on major international security challenges. Leading Norwegian newspapers like *VG* and *Aftenposten* regularly use

PRIO data and perspectives in their coverage of global trends in conflict. In two recent cases, PRIO has publically criticized NGOs for knowingly publishing exaggerated estimates of the impact of armed conflict, in part for fund-raising reasons. There is indication that these efforts have had a restraining influence on NGO rhetoric. Popular scholarly work using the conflict data has contributed to shape an international debate about conflict trends. Steven Pinker's book *The Better Angels of our Nature* (2011) relied heavily on data from UCDP and PRIO. It had a wide impact on the public debate about these issues, it was named a *New York Times* Notable Book of 2011 and received massive praise. The *Human Security Report* (2005–13), edited by Andrew Mack, has used our data extensively, and has received very wide publicity in policy circles. Pinker & Mack's op-ed on the global decline in violence was shared more than 110,000 times on Facebook. PRIO research has directly fed into policy processes in the World Bank and UN organizations. The 2011 *World Development Report* on 'Conflict, Security, and Development' included references to 23 different publications involving PRIO researchers. PRIO researchers have authored recent policy documents for organizations like USAID, the World Bank, UNESCO and UN OCHA. PRIO projects on conflict prediction and early warning, drawing both on the global conflict data and the GIS-coded event data (facilitated by PRIO-GRID), have led to the inclusion of PRIO researchers into ongoing conflict forecasting projects with the UN FAO and the EU. PRIO contributed directly to the development of EUs Global Conflict Risk Index (GCRI), which is a global conflict early warning system. The European External Action Service is now using the GCRI directly in their decision making.

5. Sources to corroborate the impact

Beadle, A & S Diesen, FFI Report 15/01452. Globale trender mot 2040 – implikasjoner for Forsvarets rolle og relevans. https://admin.ffi.no/no/Rapporter/15-01452.pdf (p. 4: 'Rapporten benytter blant annet Institutt for fredsforskning (PRIO)s prediksjoner i vurderingene av konfliktpotensialet i geografiske områder av relevans for Norge.')

Human Security Report 2013 (p. 13 'Chapter 1 reports on a remarkable recent statistical study by the Peace Research Institute, Oslo (PRIO) that found that if current trends in key structural variables are sustained, the proportion of the world's countries afflicted by civil wars will halve by 2050.' There are numerous other examples).

World Development Report 2011: * (P. 3 contains a figure showing battle deaths and number of conflicts over time, crediting PRIO. P. 64 contains a graph and reference to PRIO research on the economic consequences of conflict).

Østby, G & H Urdal, 2010. Education and civil conflict: A review of the quantitative, empirical literature. Background report for UNESCOs Education for All: Global Monitoring Report 2011. Oslo: PRIO & UNESCO.

1.4.4 Societal impact: Defining Global Policy on Climate and Conflict

Institution: Peace Research Institute Oslo (PRIO)

Name of SFF: Centre for the Study of Civil War (CSCW)

Title of case study: Defining Global Policy on Climate and Conflict

Period when the underpinning research was undertaken: 2003 onwards

Details of staff conducting the underpinning research from the submitting unit
Name(s)/Role(s)[4]/Period(s) employed by submitting SFF

Within the CSCW period

- Halvard Buhaug (R3 2003-2005, R2 2006-2011, R1 2011-)
- Nils Petter Gleditsch (R1, 2002-)
- Ole Magnus Theisen (RA1 2006, R3 2007, PhD 2007-)
- Ragnhild Nordås (PhD 2005-2010, R2 2011-)
- Henrik Urdal (PhD 2003-2006, R2 2007-2012, R1 2013-)
- Jonas Vestby (RA1 2012-2013, PhD 2013-2017, R2 2017-)

After the CSCW period

- Elisabeth Lio Rosvold (PhD 2015-2019, R2 2019-)
- Todd G. Smith (R2 2018)
- Andrew Linke (R2 2008-2012, 2017, 2018-2020)

Period when the impact occurred: 2008 onward

1. Summary of the impact

Increased conflict, instability, and state collapse are among the gravest foreseeable consequences of climate change. Unfortunately, the early policy debate on the topic suffered from speculative reasoning, selective referencing, and a poor understanding of contemporary climate-conflict connections. Over the past decade, PRIO has become a global hub for rigorous empirical research on climate change and conflict and it has played an instrumental in ensuring that human and national security has become an integral part of the mandate of the UN's Intergovernmental Panel on Climate Change (IPCC) – the agenda setter on climate change adaptation and mitigation policies.

2. Underpinning research

PRIO-based research on security implications of climate change gained momentum with the establishment of the Centre for the Study of Civil War in 2003. With one of the seven working groups dedicated to environmental factors, supplemented by independent research projects, PRIO established itself as the leading provider of empirical research on the environment and armed conflict. Over the past decade, this research portfolio has been strengthened further with financial support from a broad range of funders (see below). This research has resulted in some of the most widely read and cited academic articles in the field as well as a highly influential World Bank-commissioned report that offers important evidence-based recommendations for peers, policy, and practice. This report shaped the World Bank's thinking on this issue. Testimony to PRIO's

[4] RA1 (Research Assistant with Masters), PhD/R3 (Doctoral Researcher), R2 (Senior Researcher), R1 (Professor)

central role in developing the field, PRIO researchers coordinated and guest-edited the first two special issues of scientific journals on climate change and conflict (*Political Geography* 2007; *Journal of Peace Research* 2012), several PRIO scholars have offered critical input to the IPCC's Fifth Assessment Report as contributing author and reviewers, and PRIO is now represented on the lead author team of the Risk chapter for the forthcoming IPCC Sixth Assessment Report (due 2021).

A fundamental component of PRIO's research is rigorous statistical research of the historical association between shifting environmental and climatic conditions and societal response, analyzing as many cases as possible to maximize generalizability and making use of the best available data and advanced methods. Collectively, this research has revealed that climatic changes are not linked to insecurity and conflict in the simple and direct manner that sometimes is assumed. However, more subtle and indirect climate effects that only plays out under certain conditions have been detected. These insights, now shared by the large majority of the scientific community, has accentuated calls to exercise caution when discussing security dimensions of climate change while inspiring a new wave of scientific research on more complex nature-society relations. Central contributors to this work include Tor A. Benjaminsen, Halvard Buhaug, Elisabeth Gilmore, Nils Petter Gleditsch, Ragnhild Nordås, Clionadh Raleigh, Ole Magnus Theisen, Jonas Vestby, and Nina von Uexkull.

Central externally funded projects over the past decade:

* 'Risk Assessment for Natural and Conflict Hazards in Asia', UN OCHA / NGI, 2007-08

* 'Implication of Climate Change for Conflict', The World Bank, 2007-08

* 'Security Implications of Climate Change', RCN NORKLIMA, 2009-12

* 'Climate Change, Hydro-Conflicts, and Human Security, EU 7FP, 2010-12

* 'Forecasting Conflict under Different Climate Change Scenarios', US DoD Minerva, 2013-16

* 'Climate Anomalies and Violent Environments', RCN FRIHUMSAM, 2015-2018

* 'Climate Variability and Security Threats', ERC Consolidator Grant, 2015-20

* 'Quantifying Conflict Risk of Agricultural Productivity Changes', RCN KLIMAFORSK, 2017-20

3. References to the research

Buhaug, H., J. Nordkvelle, T. Bernauer, T. Böhmelt, M. Brzoska, J.W. Busby, A. Ciccone, H. Fjelde, E. Gartzke, N.P. Gleditsch, J.A. Goldstone, H. Hegre, H. Holtermann, V. Koubi, J.S.A. Link, P.M. Link, P. Lujala, J. O'Loughlin, C. Raleigh, J. Scheffran, J. Schilling, T.G. Smith, O.M. Theisen, R.S.J. Tol, H. Urdal, and N. von Uexkull. 2014. 'One Effect to Rule Them All? A Comment on Climate and Conflict.' *Climatic Change* 127: 391–397.

Buhaug, H. 2015. 'Climate-Conflict Research: Some Reflections on the Way Forward.' *WIREs Climate Change* 6(3): 269–275.

Gleditsch, N.P. and R. Nordås. 2014. 'Conflicting Messages? The IPCC on Conflict and Human Security.' *Political Geography* 43: 82–90.

Mach, K.J., C.M. Kraan, W.N. Adger, H. Buhaug, M. Burke, J.D. Fearon, C.B. Field, C.S. Hendrix,

J.-F. Maystadt, J. O'Loughlin, P. Roessler, J. Scheffran, K.A. Schultz, and N. von Uexkull. 2019. Climate as a risk factor for armed conflict. *Nature* 571: 193–197.

Vestby, J. 2019. Climate variability and individual motivations for participating in political violence, *Global Environment Change* 56: 114–123.

von Uexkull, N., M. Croicu, H. Fjelde, and H. Buhaug, 2016. 'Civil Conflict Sensitivity to Growing-Season Drought.' *Proceedings of the National Academy of Sciences of the USA* 113(44): 12391–12396.

4. Details of the impact

PRIO's status as a global leader in peace and conflict studies and the institute's conscious investment in broadening the research portfolio on environmental issues has earned PRIO the reputation as the main hub for quantitative, evidence-based knowledge production on climate and conflict. The fact that the European Research Council in 2015 awarded a prestigious Consolidator Grant to one of PRIO's researchers (Buhaug) for a five-year project on 'Climate Variability and Security Threats' is testimony to the topic's importance, the high quality of PRIO's past research, and PRIO's continued commitment to improving our understanding of nature-society relations.

Publication download and citation statistics reveal that PRIO's investment has been an academic success, and PRIO researchers have published on climate-conflict connections in numerous leading disciplinary and general science journals, including *Environmental Research Letters*, *Global Environmental Change*, *Nature*, and *PNAS*. But our research has reached far beyond our peers and into the field of policy-makers. Perhaps most importantly, we have helped shape the UN's Intergovernmental Panel on Climate Change's (IPCC) and other policy actors' treatment of the security issue in important ways: first by contributing to putting security consequences on the policy agenda; then by ensuring that unfounded alarmist (and denialist) claims were replaced by more careful, evidence-based assessments and advice.

With regard to putting security on the agenda, we believe our 2008 World Bank-commissioned study played a pivotal role. The sixth and final recommendation from that report is unambiguous in recommending that "the IPCC should take the lead in investigating [security implications of climate change] systematically." As the IPCC took this advice onboard, our research continued to contribute to, and form, the IPCC's take on the climate security issue. A 2010 PNAS study on climate change and conflict in Africa generated a lot of attention within international media and beyond. In 2012, Buhaug served as an invited expert at an IPCC-focused workshop in Paris, where he provided extensive guidance on the scope paper underlying the 'Human Security' chapter. Then, Buhaug, Gleditsch, and Theisen served as expert reviewers on three rounds of drafts of various chapters of the AR5 (2014). A systematic comparison of these drafts reveals that our comments, as well as our contributions to the scientific literature more generally, were important in informing and improving the report. Naturally, PRIO research features centrally; the 'Human Security' chapter alone cites 12 PRIO-authored studies as substantiation for its conclusions. As a further contribution to the IPCC AR5, Buhaug served as Contributing Author to the 'Adaptation' chapter. Most recently, Buhaug has been appointed to serve as lead author of the 'Key Risks' chapter of the forthcoming IPCC Sixth Assessment Report (work to be conducted during 2019-21).

PRIO researchers have also been active and visible in engaging with other organizations within policy and practice. For example, we have been invited to hold presentations and briefings on the climate-food-conflict nexus at the Rome headquarters of the UN Food and Agriculture Organization (FAO). PRIO has hosted a seminar with the Executive Director of the World Food Program (WFP) on connections between food insecurity and armed conflict. PRIO researchers have participated and presented research on climate security at high-level international fora, including at the Carnegie Foundation, the Wilson Center, the World Bank, and Oslo Forum; served as invited experts to assist the European Commission's Joint Research Centre in their development of climate-sensitive conflict early warning models; and informed the European Parliament in hearings on desertification and conflict and on climate change-induced migration and conflict.

5. Sources to corroborate the impact

Adelphi. 2017. *Climate Change and Conflict: Reviewing the Statistical Evidence*. Report developed for the German Federal Foreign Office, Berlin.

Adger, W.N., et al. 2014. 'Chapter 12: Human Security.' In *Climate Change 2014: Impacts, Adaptation, and Vulnerability*, Working group II contribution to the IPCC Fifth Assessment Report.

Buhaug, H., N.P. Gleditsch, and O.M. Theisen. 2008. *Implications of Climate Change for Armed Conflict*. Commissioned report, delivered to the workshop on Social Dimensions of Climate Change, The World Bank, Washington, DC, 5–6 March. An updated version of the report was published in 2010 in Mearns and Norton, eds., *Social Dimensions of Climate Change: Equity and Vulnerability in a Warming World*. The World Bank.

Steinbruner, J.D., P.C. Stern, and J.L. Husbands. 2013. *Climate and Social Stress: Implications for Security Analysis.* US National Research Council.

Klein, R.J.T., et al. 2014. 'Chapter 16: Adaptation Opportunities, Constraints, and Limits.' In *Climate Change 2014: Impacts, Adaptation, and Vulnerability*, Working group II contribution to the IPCC Fifth Assessment Report.

1.5 PGP - Physics of Geological Processes

1.5.1 Societal impact: Computing and programming is tightly integrated in all science programs at the University of Oslo

Institution: University of Oslo and Simula Research Laboratory		
Name of SFF: Center for Biomedical Computing (CBC), Physics of Geological Processes (PGP), Center of Mathematics for Computation (CMA)		
Title of case study: Computing and programming is tightly integrated in all science programs at the University of Oslo		
Period when the underpinning research was undertaken: 2002-2017		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Periods employed by SFF**
Hans Petter Langtangen	Professor, Center Leader CBC	2007-2016
Joakim Sundnes	Center Leader, CBC	2007-2017
Morten Hjorth-Jensen	Professor, CMA	2003-2013
Knut Mørken	Professor, Deputy leader CMA	2003-2013
Anders Malthe-Sørenssen	Professor, Group leader PGP	2003-2013
Period when the impact occurred:		

1. Summary of the impact

The University of Oslo is an international leader in integrating computing and programming in science education. Through a collaborative effort known as *Computing in Science Education,* involving staff of three Centers of Excellence (CBC, PGP, and CMA), computing is now an integral part of all science programs at the University of Oslo, with nearly every single course including components of relevant programming. The result of this effort is a new generation of science graduates that are highly skilled in using computers to solve scientific and engineering problems, and have been trained in solving far more complex and realistic science problems than what is part of a traditional curriculum.

2. Underpinning research

The *Computing in Science Education* initiative is a long-term pioneering effort at the University of Oslo, and its progress was accelerated by the collaborations and research efforts in the Center for Biomedical Computing, Physics of Geological Processes, and Center of Mathematics for Applications. All the three centers have been strongly focused on the use of computational mathematics to solve scientific problems, across a large variety of fields including geology, physics, continuum mechanics, and physiology as well as development of new computational methods.

The long-term research into these areas have led to the observation that successful candidates in science and engineering need deep and broad training in computational methods and programming. Such training needs to be coherently integrated with and not only supplement the traditional analytical techniques of the natural sciences, to make the candidates better prepared for how science problems are solved in the 21st century. A more innovative insight underpinning the initiative is that extensive use of

computers will also advance the candidates' understanding of their own scientific field. Being skilled in computational mathematics, the students are able to focus on the underlying scientific questions rather than the advanced algebra often required in traditional problem solving techniques. At the same time the computational techniques are more general than the traditional techniques, allowing he students to tackle far more complex and realistic scientific problems.

As a result of these efforts, the University of Oslo is at the international forefront in this area, with programming and computational methods tightly integrated into all study programs in the natural sciences. The initiative has been recognized by numerous prizes and awards, and in 2016 received status as a Norwegian Center for Excellence in Education (SFU) as Centre for Computing in Science Education (CCSE), hosted by the Department of Physics, University of Oslo.

3. References to the research

This section should provide references to key outputs from the research described in the previous section, and evidence about the quality of the research. Underpinning research outputs may include, but is not limited to journal articles, book chapters, edited volumes, monographs, patents, prototypes etc.

Hans Petter Langtangen, "Title: A Primer on Scientific Programming with Python", Springer, 2009.

Anders Malthe-Sørenssen, "Elementary Mechanics Using Python"/"Elementary Mechanics Using Matlab", Springer 2015.

Arnt Inge Vistnes, Physics of Oscillation and Waves with use of Matlab and Python, Springer, 2018

Anders Malthe-Sørenssen, Morten Hjorth-Jensen, Hans Petter Langtangen, Knut Mørken, «Integrasjon av beregninger i fysikkundervisningen», *Uniped*, **38**, 4, 2015

Marcos Daniel Caballero, Morten Hjorth-Jensen, "Integrating a computational perspective in physics courses", arXiv, 1802.08871 2018.

4. Details of the impact

Two to three decades ago, the typical curriculum of a physics or mechanics student at the University of Oslo would mainly be focused on traditional, analytical problem-solving methods. A course in programming would be included early on, but then most students would not use programming again as part of their undergraduate studies. About three years later, when starting their Master's studies, many of the students would work on computationally oriented project, which typically would require programming using a new programming language and an entirely different style than what they learnt earlier. Surprisingly, this curriculum remains the standard program in universities all over the world. The approach works in that students get introduced to the basic ideas of programming and get a solid background in their own field, and some students are capable of integrating these two skillsets on their own when needed. However, this is most likely not the best approach for preparing students for an increasingly computer-based work life.

At the University of Oslo, current undergraduate students have a completely different experience. All bachelor programs include an introductory programming course tailored to the needs of the particular field, with examples and applications selected from relevant scientific problems. Students in the most computing-intensive programs, including physics and mathematics, also follow a course in numerical mathematics, which is tightly integrated with the introductory course in programming. Even more importantly, computing-based problem solving is part of many later undergraduate courses, which maintains and further develops these skills. As a result, students are far better prepared both for graduate school and for the typical tasks they will face in their first job.
The Computing in Science Education initiative grew out of a collaboration between three different University departments, as part of the CoEs *Center of Mathematics for Applications, Physics of Geological Processes,* and *Center for Biomedical Computing.* Today, the initiative has turned into a CoE on its own, the *Center for Computing in Science Education (CCSE)*, and plays a central role in further development of the science curriculum in Norwegian Universities.
The CCSE and thereby the original Computing in Science initiative has given many high school teachers new perspectives on how mathematics and science can be taught in school since they attend the basic undergraduate courses in mathematics and physics as part of their training. One of these teachers has developed an elective course for high school based on the CSE ideas. Through the years, scientists involved in CSE have also given presentations to politicians and participated in writing reports about programming in school.
The whole Norwegian school system is currently undergoing a major change in that the content of all disciplines is reformed with a focus on more advanced understanding, so-called «deep learning». One aspect of this is that programming and algorithmic thinking is a skill and way of thinking that all students should learn. This will be hosted by mathematics, but also integrated in other disciplines like science, art and craft, and music. In this process, the CSE-ideas have played a major role, and the CCSE is now offering numerous courses for teachers in preparation for the introduction of the new syllabus in the fall of 2020.

5. Sources to corroborate the impact

The CSE project was featured in the Norwegian white paper on Higher Education, Culture for quality in higher eduction, Meld. St. 16 2016–2017 Kultur for kvalitet i høyere utdanning, p. 42,
https://www.regjeringen.no/contentassets/aee30e4b7d3241d5bd89db69fe38f7ba/no/pdfs/stm201620170016000dddpdfs.pdf

The CSE project was awarded a Center for Excellence in Education. The project description and the review of the project can be found on the web-pages of Nokut/Diku. The full review of the external evaluation committee can be found here. The CCSE project received a full score of 6 as the only Center for Excellence funded in 2016: https://www.nokut.no/sentre-for-fremragende-utdanning/sentre/ccse--center-for-computing-in-science-education/

The new curriculum for Mathematics in the Norwegian 1-13 schools system can be found at The Norwegian Directorate for Education and Training's web pages https://www.udir.no/laring-og-trivsel/lareplanverket/fagfornyelsen/hva-er-nytt-fagene-les-vare-korte-oppsummeringer/ . They write that: *«Vi har tatt algoritmisk tenkning og programmering inn i faget. Vi har vektlagt algoritmisk tenkning fordi dette er en viktig problemløsningsstrategi. Når elevene bruker programmering til å utforske og løse problemer, kan det være et godt verktøy for å utvikle matematisk forståelse.»* The CSE project has contributed to this change.

The impact of CSE can be read from the number of invited talks and presentations by key personnel. A full list can be found in the Annual reports from CCSE from 2017 and 2018 found here: https://www.mn.uio.no/ccse/om/rapporter/. Computing is now in the processes of being integrated in science programs at UiB, NTNU, UiT, UiS, at Stockholm University, Uppsala University, , and University of Dublin, Ireland, at Michigan State University, USA, and at the National University of Defense Technology in China.

2 SFF II

2.1 CEES - Centre for Ecological and Evolutionary Synthesis

2.1.1 Scientific impact: Plague

Institution: University of Oslo		
Name of SFF: Centre for Ecological and Evolutionary Synthesis		
Title of case study: Plague		
Period when the underpinning research was undertaken: 2007 – current		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Nils Chr. Stenseth	Prof. and Chair of CEES	2007 – current
Boris Schmid	Postdoc / Researcher	2012 – current
Ryan Easterday	Postdoc / Researcher	2009 – 2018
Barbara Bramanti	Researcher	2013 – 2015
Katharine R. Dean	PhD student	2015 - 2019
Fabienne Krauer	PhD student	2016 – current
Amine Namouchi	Researcher	2016 – 2018
Meriam Guellil	PhD student	2015 - 2018
Oliver Kersten	Researcher ass./PhD student	2016 – current
Stephanie Hänsch	Researcher	2013 – 2017
Claudio Ottoni	Postdoc	2016 - 2018
Period when the impact occurred: 2014-2018		

1. Summary of the impact

Exposing a false assumption that was "known to be true" (plague spread in medieval Europe in the same way as it spread in 20th century Asia and America, namely through wildlife reservoirs and urban rodents). This assumption was blocking effective research into the dynamics of plague in medieval and early-modern Europe. We brought together the fields of history, archeology, genetics and quantitative biology/ecology within the SFF and interacted extensively with those fields outside the SFF to study the newly opened questions and change our idea of what happened historically.

2. Underpinning research

Plague, due to its epidemic past, is an active cross-disciplinary field of investigation. Prior to the SFF, the institute had been mainly involved into the analysis of plague surveillance data (rodents & flea densities, coupled to plague outbreaks within these rodents) in Kazakhstan in the context of climate fluctuations, and had just branched out to using recent historical records from the USA China (see Xu et al, 2014 for the latter) to estimate characteristics of the human pandemics, and how that might relate to what is happening in the wildlife.

In the SFF, the study of this interplay between historic, wildlife and climatic data got expanded towards the second plague pandemic in Europe – during which the plague caused far greater mortalities than before. Ancient DNA research had only recently established beyond doubt that

the agent of the disease was still the same, namely *Yersinia pestis*, between the two pandemics, ruling out the possibility that the higher mortality was due to a different disease.

During the SFF, people employed through the SFF and through ERC grants (ERC Advanced grant MedPlag – PI Barbara Bramanti, and ERC Marie Curie IEF – Boris Schmid), worked on elucidating the location of medieval plague reservoirs that could have sustained the 500 years of plague outbreaks in Europe through computational and genetic sequencing means, but found no evidence for a European reservoir (based on epidemiological studies of outbreak data (Schmid 2015), and on aDNA analysis of plague strains from that time (Namouchi 2018)). Furthermore, using detailed mortality datasets of plague outbreaks (on a daily or weekly resolution) favored a human-human ectoparasite disease transmission dynamcis above a rat-borne disease transmission dynamic (Dean 2018), further weakening the case that medieval plague in Europe followed the classical "rat-borne plague outbreaks spill over into the human population" pattern that was known to be of importance during the Third pandemic in Asia.

At the same time, work continued to understand plague reservoirs in the wild better, by comparative studies of different rodents and different rodent plague reservoirs – both using surveillance data (Xu 2015), and by *de novo* sequencing of one of the most important wildlife plague hosts (great gerbils – Nilsson 2018). In the latter case, we aimed to get a better understanding of the genetic basis of plague reservoir hosts, and found genetic expansion of the immune system (a new MHC class II allele), which may have been a response to selection pressure exerted by *Y. pestis*, or (we cannot exclude this) other pathogens in a semi-desert environment.

3. References to the research

Schmid, Boris V., Ulf Büntgen, W. Ryan Easterday, Christian Ginzler, Lars Walløe, Barbara Bramanti, and Nils Chr Stenseth. 2015. "Climate-Driven Introduction of the Black Death and Successive Plague Reintroductions into Europe." Proceedings of the National Academy of Sciences of the United States of America 112 (10): 3020–25.

Dean, Katharine R., Fabienne Krauer, Lars Walløe, Ole Christian Lingjærde, Barbara Bramanti, Nils Chr Stenseth, and Boris V. Schmid. 2018. "Human Ectoparasites and the Spread of Plague in Europe during the Second Pandemic." Proceedings of the National Academy of Sciences of the United States of America, January.

Namouchi, Amine, Meriam Guellil, Oliver Kersten, Stephanie Hänsch, Claudio Ottoni, Boris V. Schmid, Elsa Pacciani, et al. 2018. "Integrative Approach Using Yersinia Pestis Genomes to Revisit the Historical Landscape of Plague during the Medieval Period." Proceedings of the National Academy of Sciences of the United States of America, November.

Xu, Lei, Leif Chr L. C. Stige, Kyrre Linné Kausrud, Tamara Ben Ari, Shuchun Wang, Xiye Fang, Boris V. Schmid, et al. 2014. "Wet Climate and Transportation Routes Accelerate Spread of Human Plague." Proceedings of the Royal Society B 281 (1780): 20133159.

Xu, Lei, Boris V. Schmid, Jun Liu, Xiaoyan Si, Nils Chr Stenseth, and Zhibin Zhang. 2015. "The Trophic Responses of Two Different Rodent–vector–plague Systems to Climate Change." Proceedings of the Royal Society of London B: Biological Sciences 282 (1800): 20141846.

Nilsson, P., M. H. Solbakken, B. V. Schmid, R. J. S. Orr, and R. Lv. 2018. "The Genome of the Plague-Resistant Great Gerbil Reveals Species-Specific Duplication of an MHCII Gene." bioRxiv. https://www.biorxiv.org/content/early/2018/10/22/449553.abstract.

4. Details of the impact

Academic impact in plague research during the SFF is the exposure of a body of "common knowledge – that is, the rats (or other rodents) as a reservoir species of plague in medieval Europe" as an unfounded assumption. We are not the first to point to problems with that assumption, there have been sporadic historians pointing out to inconsistencies as well, but using data analysis and modeling we were able to make our points very clearly. We pointed to the likely location of the wildlife reservoir of plague of Europe as being located outside Europe (particularly, as being in Central Asia), and to the cause of the high mortality of plague in Europe being related to a new transmission route – that of human ectoparasites, rather than to a severe rat-borne plague.

The effectiveness of our message resulted in producing a 2015 PNAS paper with the highest altmetric score for the UiO in 2015, and a very well picked up 2018 PNAS paper, outranking media attention of 99.99% and 99.9% of other tracked publications respectively. That outreach puts our results in the scientific & public awareness that has resulted into new research lines for archeologists (sieving fleas from plague graves to determine species), our work being part of the well-visited (~7000 times a day) wikipedia pages on Black Death and Yersinia pestis (not by our doing), and ensured the inclusion of our research outputs into museum exhibitions, like the BeastsOfLondon of the Museum of London. Moreover, the exposure has helped in keeping the scientific narrative open to multiple introductions of plague into Europe rather than following an easier-to-conclude narrow interpretation suggested by initial ancient DNA research that presumed local plague reservoirs in Europe.

Developed in tandem with the computational work, the ancient DNA work on plague at the SFF helped support the computational interpretation of historic plague records, by adding a substantial number of new aDNA sequences of the medieval plague bacterium, and providing new theories on the flow of plague across Eurasia (outranking 99% of tracked publications). A final paper from the aDNA group will be the first genetics paper to point to an extra-europe medieval plague reservoir as the source of the plague introductions in Europe.

Where the aDNA work has gone head of the theoretical approach is in drawing the attention of historians in providing them new tools with which to look at the past and resolve historic ambiguities. Plague is (by a large margin) the test case for what can be done by combining ancient DNA and historical and archeological records of past pandemics, with sequences being recovered from human remains from all periods, up to close to the moment of its speciation (with the earliest recovered sequences from about 700 years after its speciation ~5700 years ago). We are actively involved with historians and archeologists (speaking at invited meetings, shared mailing lists) to bridge the gap in methodology to correctly understanding the genetic data, and now also the interpretation of data analysis and modeling efforts. Historians, on their parts, are doing the same in helping us better interpret historic data sources.

While not effortless, this integration of field across the humanities and sciences is a boon to all fields involved. All these developments have led to additional funding (FRIMEDBIO 288551, NCCP PERI, UiO REA:Life) to work on this interplay between the history of plague (or more general diseases) and the life sciences, and continuous invites to present work at various interdisciplinary conferences, or interact with plague or rodent-focused groups from different disciplines (see sources).

Outside the focus on the second plague pandemic, we continued working to ground our understanding of wildlife plague and the genetic basis of plague resistance in a larger variety of plague ecosystems – two papers of which are listed as well (Xu et al, 2015; Nilsson et al, 2018), as well as assessing the third plague pandemic in China (Xu et al, 2014). These studies form the basis from which we inform ourselves and can project potential relevant disease mechanisms further back into the past.

5. Sources to corroborate the impact

Most popular altmetric article from UiO:

- https://www.mn.uio.no/ibv/om/aktuelt/aktuelle-saker/2016/fjorarets-mest-populere-forskningsartikkel.html

Inclusion of our work in the #BeastsOfLondon exposition, at the Museum of London

- https://twitter.com/archaeoRattus/status/1165250584578068481

Altmetric scores of the Schmid 2015 PNAS, and Dean 2018 PNAS papers.

- https://pnas.altmetric.com/details/3721074#score
- https://pnas.altmetric.com/details/31765259#score
- https://pnas.altmetric.com/details/51779404#score

Ongoing dialog with historians

- https://www.dnva.no/detskjer/2014/11/past-plague-pandemics
- https://contagions.wordpress.com/2016/06/27/plague-dialogues-monica-green-and-boris-schmid-on-plague-phylogeny-i/ & https://contagions.wordpress.com/2016/06/29/plague-dialogues-monica-green-and-boris-schmid-on-plague-phylogeny-ii/

New grants

- https://prosjektbanken.forskningsradet.no/#/project/NFR/288551/Sprak=en
- https://cbs.umn.edu/norwegian-centennial-chair/currently-supported-activities
- https://www.uio.no/english/research/strategic-research-areas/life-science/research/convergence-environments/realife/

Interdisciplinary starts of collaborations and presentations

- https://eseh2019.sched.com/event/TYi4/5g-epidemics-history-and-the-environment-crossing-academic-boundaries (Stenseth presenting on Plague)

- https://www.york.ac.uk/medieval-studies/events/archive/2019/long-black-death/ (Part of setting up a project on the role of rats on plague in europe, based on modern quantitative and genetic methods)
- https://www.scotsman.com/news/scottish-scientist-awarded-1m-to-study-how-ratcatchers-fought-plague-1-5004225 (Schmid is on scientific board)
- https://www.radcliffe.harvard.edu/seminars-and-workshops/biraben-black-death-digital-archive (part of setting up a project on Building a better historical plague archive)
- https://guevents.georgetown.edu/event/pathogens_and_climates_in_motion_multidisciplinary_perspectives_on_plague_and_malaria_in_the_late_antique_little_ice_age (part of setting up a project on Plague and Malaria in the late roman period).

2.1.2 Scientific impact: The Atlantic cod genome - discovering a unique immune system

Institution: University of Oslo

Name of SFF: Centre for Ecological and Evolutionary Synthesis (CEES)

Title of case study: The Atlantic cod genome - discovering a unique immune system

Period when the underpinning research was undertaken: 2008 and ongoing

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Kjetill S Jakobsen	Prof, PI	2007 – current
Nils Chr Stenseth	Prof	2007 – current
Bastiaan Star	Postdoc	2008 – current
Alexander J. Nederbragt,	Postdoc	2008 – current
Sissel Jentoft,	Researcher	2007 – current
Unni Grimholt	Postdoc	2007 – 2013
Martin Malmstrom	PhD	2009 – 2017
Trine B. Rounge	Postdoc	2007 – 2012
Monica H. Solbakken	PhD/postdoc	2010 – current
Karin Lagesen	Postdoc	2007 – 2013
Ave Tooming-Klunderud	Engineer	2007 – current
Morten Skage	Engineer	2008 – current
Paul R. Berg	PhD	2010 – 2017
Michael Matschiner	Postdoc	2013 – 2017
Julia MI Barth	Postdoc	2014 – 2017
Marine SO Brieuc	Postdoc	2016 – current
Helle T Baalsrud	PhD/post doc	2012 - current
Siv NK Hoff	PhD	2018 – current
Cecilia Helmerson	PhD	2016 - current

Period when the impact occurred:

1. Summary of the impact

Genome assembly - implications for population differentiation, structural genomic variation and stock management of Atlantic cod. The genome assembly made possible the discovery of the unique immune system and its impact for our understanding of vertebrate immunology. Furthermore, the immune system of Atlantic cod has implications for vaccine development.

2. Underpinning research

Atlantic cod (*Gadus morhua*) is a large, cold-adapted fish that sustains long-standing commercial fisheries. In 2011, we were the first group in Norway to assembly and publish on the genome sequence of this species using next-generation sequencing data only. Automated annotation of this genome assembly identified 22,154 genes, nonetheless, we discovered an unusual immune architecture compared to other sequenced vertebrates. The major histocompatibility complex (MHC) II is a conserved feature of the adaptive immune system of jawed vertebrates, but we show that Atlantic cod has lost the genes for MHC II, CD4 and invariant chain (Ii) that are essential for the function of this pathway. Nevertheless, Atlantic cod is not exceptionally susceptible to disease under natural conditions. We find a highly expanded number of MHC I genes and a unique composition of its Toll-like receptor (TLR) families. This indicates how the Atlantic cod immune system has evolved compensatory mechanisms in both adaptive and innate immunity

in the absence of MHC II. These observations affect fundamental assumptions about the evolution of the adaptive immune system and its components in vertebrates – and it has an impact on how vaccines are developed for a future cod aquaculture.

This discovery has driven the research of the CEES has produced a number of successful grant applications and papers building on this seminal finding. For instance, we discovered the evolutionary origin of this unusual immune strategy by the low-coverage genome sequencing (9–39×), assembly and comparative analyses for 66 teleost species. We found that MHC II is missing in the entire Gadiformes lineage and thus was lost once in their common ancestor. In contrast, we find that MHC I gene expansions have occurred multiple times, both inside and outside this clade. Remarkably, we identify an association between high MHC I copy number and elevated speciation rates using trait-dependent diversification models. These finding greatly extend current understanding of the plasticity of the adaptive immune system and suggest an important role for immune-related genes in animal diversification.

Furthermore, the genome assembly of Atlantic cod (improved in several versions Tørresen et al. 2017 (2.0) and a recent 3.0) has also shown that migratory ecotypes (skrei) and non-migratory (coastal cod) have a different pattern of large inversions on several chromosomes. These inversions are crucial for ecological adaptations of the different stocks, and therefore also crucial for genetic-based management of Atlantic cod.

3. References to the research

Star, Bastiaan, Alexander J. Nederbragt, Sissel Jentoft, Unni Grimholt, Martin Malmstrøm, Tone F. Gregers, Trine B. Rounge et al. The genome sequence of Atlantic cod reveals a unique immune system. *Nature* 477, no. 7363 (2011): 207.

Malmstrøm, Martin, Michael Matschiner, Ole K. Tørresen, Bastiaan Star, Lars G. Snipen, Thomas F. Hansen, Helle T. Baalsrud et al. Evolution of the immune system influences speciation rates in teleost fishes. *Nature Genetics* 48, no. 10 (2016): 1204.

Solbakken MH, Tørresen OK, Nederbragt AJ, Seppola M, Gregers TF, **Jakobsen KS**, Jentoft S (2016) Evolutionary redesign of the Atlantic cod (*Gadus morhua* L) Toll-like receptor repertoire by gene losses and expansions. *Scientific Reports* 6, 25211, doi: 10.1038/srep25211

Berg PR, Star B, Pampoulie C, Sodeland M, Barth JMI, Knudsen H, **Jakobsen KS**, Jentoft S (2016). Three chromosomal rearrangements promote genomic divergence between migratory and stationary ecotypes of Atlantic cod. *Scientific Reports* 6: 23246 doi: 10.1038/srep23246

Barth JMI, Berg PR, Johnsson PR, Bonanomi S, Corell H, Hemmer-Hansen J, **Jakobsen KS**, Johannesson K, Jorde PE, Knudsen H, Moksnes P-O, Star B, Stenseth NC, Svedang H, Jentoft S, Andre C (2017) Genome architecture enables local adaptation of Atlantic cod despite high connectivity. *Mol Ecol* 26:4452-4466

Star B, Boessenkool S, Gondek AT, Nikulina E, Hufthammer AK, Pampoulie C, Knutsen H, André C, Dierking J, Petereit C, Heinrich D, **Jakobsen KS**, Jentoft S, Stenseth NC, Barrett JH (2017) Ancient DNA reveals the arctic origin of Viking age cod from Haithabu, Germany. *PNAS* 114: 9152-9157

4. Details of the impact

The Atlantic cod genome was the first fish genome assembly made with a pure high throughput sequencing approach – and as a consequence it spurred numerous projects on fish (and other vertebrate) genomes.

The finding that cod had a special immune system – and different from all known vertebrates – received large international attention in 2011. It was covered by the leading newspapers (and websites) around the world and commented on in the leading scientific journals such as Nature and Science. The finding that Atlantic cod lacks the MHC II pathway does not only affect immunology concepts in general, but also has impact on vaccine design for future cod aquaculture. It was also noticed in the human/mammalian immunology field through many reviews for example in in Nature Reviews Immunology (Bordon 2011, Flajnik 2018). When we in 2016 showed that all codfishes have a special immune system that has an evolutionary history of perhaps as much as 100 million years, this also got large attention. It was covered by a "News and Views" story in Nature Genetics (Parham 2016) and in different news sites/newspapers around the world. The finding that MHC I copy numbers are associated with speciation rates also received a lot of attention. Now, the special case (not so special anymore since it is seen in all codfishes) has become Textbook curriculum for undergraduate students (Russell, Hertz, McMillan, Biology – the dynamic science (4 ed 2017) Unique immune system of Atlantic cod). Another impact from this finding is that our group at CEES has been approached by medical immunologists, and we have successfully managed to raise funding for a large collaborative project (evolutionary biologists working together with medical scientists affiliated with Rikshospitalet).

The Atlantic cod genome has also had a substantial impact on how we think about stock management. We now know, due to the impact of the large inversions on the local adaptability of Atlantic cod stocks, that there is a need to manage cod stocks on the basis of preserving the inversion pattern for a particular stock or ecotype. This is clearly exemplified by recent reviews in Trends in Ecology and Evolution (Bernatchez et al. 2017, Wellenreuter and Bernatchez 2018). As well as a very recent paper in Science Advances (Kess et al. 2019 : "A migration-associated supergene reveals loss of biocomplexity in Atlantic cod").

5. Sources to corroborate the impact

Turner M (2011) Cod genome reveals stunning gap in immune system. Science August 10
https://www.sciencemag.org/news/2011/08/cod-genome-reveals-stunning-gap-immune-system

Wigmore G (2011) Cod genome reveals an unusual immune system. Nature August 10
https://www.nature.com/news/2011/110810/full/news.2011.470.html

Bordon Y (2011) Cod's wallop? It is first class! Nature Reviews Immunology 11: 571

Parham P (2016) How the codfish changed its immune System (News and Views), Nature Genetics 48: 1103-1104

Russell P, Hertz PE, McMillan B, Biology –The Dynamic Science (4 ed 2017; ISBN-13: 978-1305389892) Unique immune system of Atlantic cod

Bernatchez L, et al. (2017) harnessing the power of genomics to secure the future of seafood. Trends in Ecol Evol 32:665-680

Flajnik MF (2018) A cold-blooded view on adaptive immunity. Nature Reviews Immunology 18: 438-453

Dale G, Johansen T, Westgård J-I, Aglen A, Glover KA (2018) Genetic management of mixed-stock fisheries “real-time”: The case of the largest remaining cod fishery operating in the Atlantic in 2007-2017. Fisheries Research 205: 77-85

Wellenreuter M, Bernatchez L (2018) Eco-evolutionary genomics of chromosomal inversions. Trends in Ecol Evol 33: 427-440

Puncher GN, Rowe S, Rose GA, Leblanc NM, Parent GJ, Wang Y, Pavey SA (2019) Chromosomal inversions in the Atlantic cod genome: Implications for management of Canada's Northern cod stock. Fisheries Research 216 DOI: 10.1016/j.fishres.2019.03.020

2.1.3 Societal impact: Marine population dynamics under anthropogenic induced stress

Institution: University of Oslo

Name of SFF: Centre for Ecological and Evolutionary Synthesis

Title of case study: Marine population dynamics under anthropogenic induced stress

Period when the underpinning research was undertaken: 2007-today

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting SFF:
Joël Durant	Dr. (Researcher)	2007-current
Leif Christian Stige	Dr. (Researcher)	2007-current
Øystein Langangen	Dr. (Researcher)	2009-current
Anne Maria Eikeset	PhD and Dr. (Researcher)	2007-2018
Nils Chr. Stenseth	Prof.	2007-current
Dag Ø. Hjermann	Dr. (Researcher)	2007-2015

Period when the impact occurred: 2007 - today

1. Summary of the impact

The marine work at CEES addresses fundamental knowledge needs for sustainably managing human activities in an era of global change. The interdisciplinary approaches, the international scope, and the strong post-graduate training component makes this work stand out. The research has contributed profoundly towards understanding and quantifying how climate variability and change, harvesting and oil pollution jointly influence marine populations and ecosystems. The research has also incorporated socio-economic consequences and feedback mechanisms. Finally, through a series of PhD and postdoctoral training programmes initiated and led by CEES, a new generation of interdisciplinary skilled researchers has been formed.

2. Underpinning research

The interdisciplinary and international research environment as CEES has fostered a strong marine group that bridges traditional marine fisheries ecology with complementary fields such as statistics, evolutionary biology, socio-economics and eco-toxicology. The interdisciplinary approaches used by the group are essential for understanding how human activities and natural processes interact in influencing marine ecosystems.

One line of marine research, which has gone on throughout the CEES period, has been evaluation of potential effects of oil-spills on marine fish in the Lofoten-Barents Sea region (Hjermann et al. 2007, Langangen et al. 2017). The research has focused on mechanisms that contribute to potential widening of the probability distribution of effects killing a certain fraction of a year-class of fish eggs and larvae, and how such loss of abundance at these early life stages may propagate to the cohort and population level. Awareness and quantification of these sources of uncertainty is essential for ecological impact assessment, as the most likely effect of most oil-spill scenarios tends to be low, but the uncertainty high.

In another line of research, the group has studied combined effects of climate and fishing, and consequences for resources management. The research has for example quantified how loss of old and large fish from heavily fished fish populations may make the fish populations more sensitive to adverse effects of climate (Rouyer et al. 2011, Stige et al. 2017). At longer time scales, fishing may cause genetic changes in the fish populations, which is likely to have economic consequences (Eikeset et al. 2013, 2016). The research has thereby provided quantitative knowledge about combined effects of climate and harvesting on marine resources,

and trained a new generation of interdisciplinary skilled scientists with the knowledge needed to sustainably manage the human influences on marine ecosystems under global change.

The marine group of CEES has developed and led three major international projects funded by Nordforsk and EU. These projects (i.e., *NorMER*, *GreenMAR* and *MARmaED*) lasted seven years, brought together scientists and students from 17 countries and trained over 50 PhD students and Post-docs since 2012. We created these projects carefully with cross-disciplinarity at their core and specifically aimed at educating a new generation of marine scientists with experience in combining physical, biological, social and economic aspects of ecosystem-based management. This objective rose from the fact that anthropogenic impacts on marine systems have important consequences biologically, socially, and economically, and yet approaches to study them are often limited by disciplinary boundaries.

The inter-disciplinary scope and international scale of cooperation was clearly a fruit of the CEES, and placed us in a better position to address global-sized challenges, increase the scope of our impact and influence, and make us more attractive to the international research community.

3. References to the research

Eikeset AM, Richter A, Dunlop ES, Dieckmann U, Stenseth NC (2013) Economic repercussions of fisheries-induced evolution. Proc Natl Acad Sci USA 110:12259-12264. DOI: 10.1073/pnas.1212593110

Eikeset AM, Dunlop ES, Heino M, Storvik G, Stenseth NC, Dieckmann U (2016) Roles of density-dependent growth and life history evolution in accounting for fisheries-induced trait changes. Proc Natl Acad Sci USA 113:15030-15035. DOI: 10.1073/pnas.1525749113

Hjermann, D. Ø. et al. Fish and oil in the Lofoten-Barents Sea system: synoptic review of the effect of oil spills on fish populations. Marine Ecology Progress Series 339, 283–299 (2007). DOI: 10.3354/meps339283

Langangen, Ø. et al. (2017) The effects of oil spills on marine fish: Implications of spatial variation in natural mortality. Marine Pollution Bulletin 119, 102–109. DOI: 10.1016/j.marpolbul.2017.03.037

Rouyer TA, Ottersen G, Durant JM, Hidalgo M, Hjermann DØ, Persson J, Stige LC (2011) Shifting dynamic forces in fish stock fluctuations triggered by age truncation? Glob Chang Biol 17:3046-3057. DOI: 10.1111/j.1365-2486.2011.02443.x

Stige LC, Yaragina NA, Langangen Ø, Bogstad B, Stenseth NC, Ottersen G (2017) Effect of a fish stock's demographic structure on offspring survival and sensitivity to climate. Proc Natl Acad Sci USA 114:1347-1352. DOI: 10.1073/pnas.1621040114

4. Details of the impact

A fundamental challenge for marine science is to deliver scientific impact, global leadership and sustainable blue growth in times of overexploitation, climate change and other anthropogenic stressors. The new generation of researchers emerging from the *NorMER*, *GreenMAR* and *MARmaED* programmes initiated and led by CEES is expected to have a long-lasting impact on the international scientific community as these researchers move through their career and take senior positions. Several have now joined ICES managing groups advocating ideas developed during their time with CEES.

While *NorMER*, *GreenMAR* and *MARmaED* came together as the culmination of a series of strategic decisions, we could not have predicted the strong synergy that would result from bringing together so many different research teams with little history of collaboration. More than just international research programmes, we have created a community. The value of such a community, particularly for small countries such as Norway, though difficult to define, cannot be overstated.

The marine work at CEES has been highly complementary to and often done in close collaboration with the research at the Institute of Marine Research, which is the institution that is primarily responsible for providing advice for marine resources management in Norway. Through these interactions, the results of the work have been incorporated into management advice. We have also communicated with politicians and other stakeholders directly and through various outreach activities (e.g., organization of side event at *Arctic Frontiers*, through newspaper chronicles in *Dagens Næringsliv* and *Aftenposten*, the *Marine Science Blog* of CEES etc.). CEES core member and IMR employee Geir Ottersen is lead author of the IPCC's Special Report on the Ocean and Cryosphere in a Changing Climate, while CEES initiator and leader Prof. Nils Chr. Stenseth is lead author of the introductory chapter in the IPCC report on the vulnerability of socio-economic and natural systems to climate change, negative and positive consequences of climate change, and options for adapting to it.

The scientific work on the potential effects of oil-spills on marine fish has been highly relevant for the political debate regarding opening of potentially vulnerable areas outside the Lofoten area to extraction of oil resources. For example, our work on effects of spatial variability in natural survival of cod eggs and larvae (Langangen et al. 2017) is directly relevant to quantify the potential effects of oil-spills on fish populations in this region. In particular, this research addresses an uncertainty that was highlighted by the government to be of particular interest (stortingsmelding: "Oppdatering av forvaltningsplanen for det marine miljø i Barentshavet og havområdene utenfor Lofoten", Page 110). The marine group at CEES also provided a first estimate of the role of spatial heterogeneity in mortality that was used in the impact assessment of possible oil-spill effects on fish for the revision of the Integrated Management Plan of the Lofoten and Barents Sea (Brude et al. 2010).

Another example of important research contributing directly into the political debate, has been our quantification of effects of mean size of spawners on the spatial distribution of fish eggs (Stige et al. 2018). In this work, we find that fish populations, in particular of cod, will be more vulnerable to oil-spills if the spawning population mostly consists of small fish. These two mechanisms, spatial variations in natural survival and size truncation of spawners, both contribute to increased (but quantified) uncertainty in the potential impact of an oil-spill on fish in the Lofoten area. Given the importance of these results to the political debate, we have been actively participating in it, with, e.g., a newspaper article in *Dagens Næringsliv* on this topic (Stige, Langangen, Stenseth, DN 8. September 2018. Page 32).

5. Sources to corroborate the impact

Brude et al. (2010). Petroleumsvirksomhet. Oppdatering av faglig grunnlag for forvaltningsplanen for Barentshavet og områdene utenfor Lofoten. Konsekvenser av akutt utslipp for fisk. *DNV Rapport* 2010-0527.

Langangen, Ø. et al. (2017). The effects of oil spills on marine fish: Implications of spatial variation in natural mortality. Marine Pollution Bulletin 119, 102–109. DOI: 10.1016/j.marpolbul.2017.03.037

Stige, L. C. et al. (2018). Combined effects of fishing and oil spills on marine fish: Role of stock demographic structure for offspring overlap with oil. Marine Pollution Bulletin 129, 336–342. DOI: 10.1016/j.marpolbul.2018.02.056.

2.1.4 Societal impact: Saxitoxin – a story of innovation

Institution: University of Oslo

Name of SFF: Centre for Ecological and Evolutionary Synthesis

Title of case study: Saxitoxin – a story of innovation

Period when the underpinning research was undertaken: 2007 - 2015

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting SFF:
Kjetill S. Jakobsen	Prof.	2007 – current
Anke Stüken	Postdoc	2007 – 2012
Russell Orr	PhD student/postdoc	2007 - current

Period when the impact occurred:

1. Summary of the impact

Saxitoxin is a potent neurotoxin, known to be produced by certain cyanobacterial species. It is also produced by several dinoflagellate species. The biosynthetic pathway, and the genes involved are known from the cyanobacteria, but the eukaryotic pathway and genes were totally unknown at the time this project was initiated. We wanted to find the responsible genes in dinoflagellates and in particular investigate the hypothesis of horizontal transfer of the genes from bacteria. Using transcriptomics and high throughput sequencing of the dinoflagellate Alexandrium we could identify the gene cluster associated with saxitoxin production. It was also shown that the same genes were present in other dinoflagellate species producing this toxin. Our data showed that the genes indeed had been transferred from a bacterium, but it also showed some dinoflagellate specific features. These features made it possible to design a detection method that discriminated between the bacterial saxitoxin genes and the dinoflagellate ones. We refined this diagnostic method and patented the principle. The patent was sold to the Australian company Diagnostic Technologies, and the test is now commercially available – sold worldwide and is of particular importance for the fish and shellfish aquaculture industry.

2. Underpinning research

3. References to the research

Stüken, A, Riobo P, Franco J, **Jakobsen KS,** Guillou L, Figueroa RI (2015) Paralytic shellfish toxin content is related to genomic *sxtA4* copy number in *Alexandrium minutum* strains. *Front Microbiol* https://doi.org/10.3389/fmicb.2015.00404

Stüken, A. Dittami SM, Eikrem W, McNamee, Campbell, **Jakobsen KS,** Edvardsen B (2013) Novel hydrolysis-probe based qPCR assay to detect saxitoxin transcripts of dinoflagellates in environmental samples. *Harmful Algae* 28: 108-117

Orr RSJ, Stüken A, Murray SA, **Jakobsen KS** (2013) Evolution and distribution of saxitoxin biosynthesis in dinoflagellates. *Marine Drugs* 11:2814-2828

Orr RJS, Stüken, A, Murray SA, **Jakobsen KS** (2013) Evolutionary acquisition and loss of saxitoxin biosynthesis in dinoflagellates: the second core gene sxtG. *Applied and Environmental Microbiology* 79:2128-2136

Stüken, A., Orr, R.J.S., Kellmann, R., Murray, S.A., Neilan, B.A., Jakobsen, K.S. (2011). Discovery of nuclear-encoded genes for the neurotoxin saxitoxin in dinoflagellates. *PLoS ONE 6: e20096*

Kellmann R, Stüken, A, Orr RJS, Svendsen HM, **Jakobsen KS** (2010) Biosynthesis and molecular genetics of polyketides in marine dinoflagellates. *Marine Drugs* 8:1011-1048

4. Details of the impact

We designed a detection method that discriminated between the bacterial saxitoxin genes and the dinoflagellate ones. We refined this diagnostic method and patented the principle. The patent was sold to the Australian company Diagnostic Technologies, and the test is now commercially available – sold worldwide and is of particular importance for the fish and shellfish aquaculture industry.

5. Sources to corroborate the impact

Patents directly connected to the saxitoxin detection:

Australian patent no. 2012255693
Brazilian patent application no. 112013029635-6
Canadian patent application no. 2843618
Chinese patent no. ZL201280023720.9
Germany patent no. 602012043413.9 [
Denmark patent no. 2710153
Spain patent no. 12786407.2
Finland patent no. 2710153
France patent no. 2710153
United Kingdom patent no. 2710153
Ireland patent no. 2710153
Italy patent no. 502018000011791
Netherlands patent no. 2710153
Norway patent no. 2710153
Portugal patent no. 2710153
Sweden patent no. 12786407.2
Singaporean patent no. 194948
South African patent no. 2013/08343
Republic of Korea Patent Application No. 10-2013-7031737
US Patent Application No. 15/370752

Company (Phytoxigene) who owns the patents:
https://www.phytoxigene.com

Company (Diagnostic technology) (https://www.diagnostictechnology.com.au) **who produces the tests kit:**
https://www.diagnostictechnology.com.au/products/phytoxigene-dinodtec-toxin-gene-test?_pos=1&_sid=2b5a10017&_ss=r

Example of industry using the product: Tasmanian shell industry:
https://www.abc.net.au/news/rural/2017-07-06/spring-bay-mussels-shellfish-testing-to-avoid-recall-tasmania/8684884

2.2 CBC - Center for Biomedical Computing

2.2.1 Scientific impact: CSF flow

Institution: Simula Research Laboratory		
Name of SFF: Center for Biomedical Computing (CBC)		
Title of case study: CSF flow		
Period when the underpinning research was undertaken:2010 til now (CBC was 207-2017)		
Details of staff conducting the underpinning research from the submitting unit:		
Name: **Kent-Andre Mardal** **Marie Rognes**	**Role(s) (e.g. job title):** **Group leader for group "biomedical flows"** **Senior Research Scientist**	**Period employed by SFF:** **2007-2017** **2010-2017**
Period when the impact occurred: may impact towards the end of the center and onwards		

1. Summary of the impact

The research conducted in the Center for Biomedical Computing (CBC) has led to an outstanding and long-lasting research collaboration involving Simula Research Laboratory, University of Oslo, and Oslo University Hospital, in addition to several international institutions. Recent results are published in high-profile journals like PNAS, JCI, and also top field-specific journals like NeuroImage, Journal of Cerebral blood flow and Metabolism, SIAM Journal of Scientific computing etc., as well as multiple reports in public media in Norway (VG, NRK, forskning.no etc) and grants from ERC and NFR.

2. Underpinning research

In CBC, we decided to investigate the flow of cerebrospinal fluid in the context of the Chiari malformation, a congenital disease in which the lower parts of the brain (cerebral tonsils) are displaced into the spinal column. Children born with this disease often suffers from daily pain and the condition often worsen with developing cysts in the spinal cord that may eventually cause paralysis. The condition is rare, but has received significant attention from the biomedical community because it is clearly biomechanical and that the forces are related to pain and symptoms.

3. References to the research

[1] Iliff, Jeffrey J., et al. "A paravascular pathway facilitates CSF flow through the brain parenchyma and the clearance of interstitial solutes, including amyloid β." *Science translational medicine* 4.147 (2012): 147ra111-147ra111.

[2] Holter, Karl Erik, et al. "Interstitial solute transport in 3D reconstructed neuropil occurs by diffusion rather than bulk flow." *Proceedings of the National Academy of Sciences*114.37 (2017): 9894-9899.

[3] Ringstad, Geir, et al. "Brain-wide glymphatic enhancement and clearance in humans assessed with MRI." *JCI insight* 3.13 (2018).

[4] Vinje, Vegard, et al. "Respiratory influence on cerebrospinal fluid flow–a computational study based on long-term intracranial pressure measurements." *Scientific reports* 9.1 (2019): 9732.

Public media:

[5] VG:
https://www.vg.no/forbruker/helse/i/VRwBK4/norske-forskere-soevn-kan-bremse-demens

[6] NRK:

https://www.nrk.no/norge/norsk-studie-pusterytmen-din-kan-ha-en-relevans-til-alzheimer-1.14629499

[7] Forskning.no:

https://forskning.no/hjernen-menneskekroppen-sovn/ny-studie-pusten-kan-pavirke-rensing-av-hjernen/1357964

4. Details of the impact

Recent breakthroughs have related the development of Alzheimer and other types of dementia to a malfunctioning clearance system in diseased brains. As the diseases progress over decades it is crucial to understand the process in order to intervene. Furthermore, increased clearance has been linked to a good night´s sleep as well as deep breathing such as in the case of yoga. These new concepts have obtained widespread attention, are currently under scrutinous investigation and are lively debated. With the expertise developed in the CBC, we are currently at the forefront of computational modeling of the clearance process, with numerous profiled results.

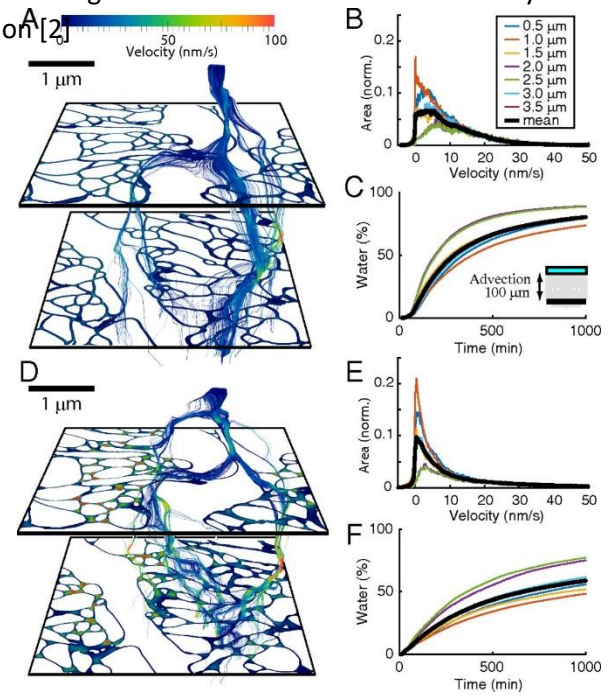

Fig. 1. Velocity profiles in the extracellular space of the illustrating that the convection is dominated by diffusion [2].

The breakthroughs leading to the new and prevailing framework of brain clearance started in 2012 [1], which demonstrated that the cerebrospinal fluid (CSF) that bathes the brain and spinal cord has an important role for waste clearance. In establishing these results, the CSF, which earlier only has been thought of as a cushion for the brain, all of a sudden became a fluid which function is fundamental for healthy aging. As CSF was one focus area within CBC, although in congential conditions, we started to model the clearance system. In our first study in PNAS [2], see Fig. 2, showed that the hydrostatic pressure which was proposed to be a main driver of the clearance is not of sufficient magnitude. Later, in a study in JCI [3] which even made it to public media such as VG, we demonstrated brain-wide circulation originating from the CSF within less than 24 hours, much faster than previously anticipated, see Fig. 2. The wide-spread distribution is from a modeling point of view challenging to explain by diffusion alone, which has been the paradigm of solute transport for several decades. However, breathing – deep and shallow – may have profound effect on the CSF dynamics, a fact that may perhaps explain the benefits of eastern techniques such yoga and medication [4].

Alongside the scientific publications, CBC has strengthened the quality of scientific work as evident by prestigous grants for the development of mathematical models for brain clearance such as Marie Rognes´ NFR and ERC grants: Waterscape and Waterscales. Simula also hosted the 5th international CSF symposium, with international researchers from all around the worlds at the forefront CSF investigations.

[1] Iliff, Jeffrey J., et al. "A paravascular pathway facilitates CSF flow through the brain parenchyma and the clearance of interstitial solutes, including amyloid β." *Science translational medicine* 4.147 (2012): 147ra111-147ra111.

[2] Holter, Karl Erik, et al. "Interstitial solute transport in 3D reconstructed neuropil occurs by diffusion rather than bulk flow." *Proceedings of the National Academy of Sciences*114.37 (2017): 9894-9899.

[3] Ringstad, Geir, et al. "Brain-wide glymphatic enhancement and clearance in humans assessed with MRI." *JCI insight* 3.13 (2018).

[4] Vinje, Vegard, et al. "Respiratory influence on cerebrospinal fluid flow–a computational study based on long-term intracranial pressure measurements." *Scientific reports* 9.1 (2019): 9732.

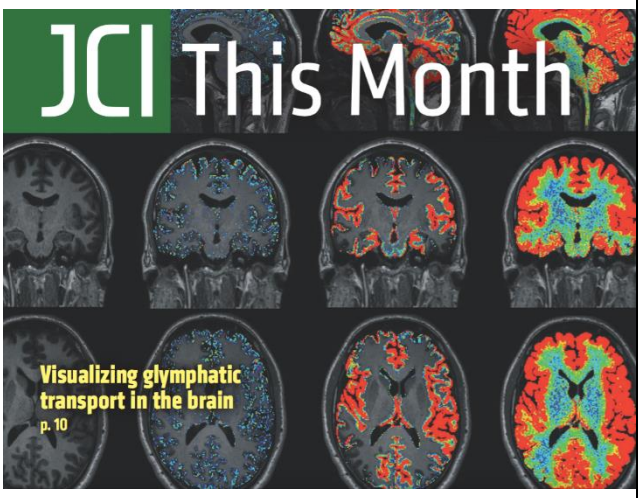

Fig. 2. Brainwide distribution of CSF contrasts within 24 hours

Målinger av spinalvæskens gjennomstrømming i hjernen, viser at pusten påvirker vel så mye som hjerteslag, ifølge ny, norsk hjernestudie. [Foto: Shutterstock]

Ny studie:

Pusten kan påvirke rensing av hjernen

Pusterytmen vår kan påvirke hvor godt spinalvæsken flyter i og rundt hjernen. Spinalvæsken skyller blant annet bort avfallsstoffer i hjernen. Funnet kan ha betydning for sykdommer som Alzheimers.

5. Sources to corroborate the impact

Our works are frequently cited in discussions of the glymphatic system. See, e.g. the recent discussion in Physiology where our works [2,3] are frequently mentioned. Illiff and Verkman are distinguished researchers in basic medical science.

https://physoc.onlinelibrary.wiley.com/doi/full/10.1113/JP277635
https://physoc.onlinelibrary.wiley.com/doi/full/10.1113/JP277636
https://physoc.onlinelibrary.wiley.com/doi/full/10.1113/JP278460
https://physoc.onlinelibrary.wiley.com/doi/abs/10.1113/JP278461

2.2.2 Societal impact: Computing and programming is tightly integrated in all science programs at the University of Oslo

Institution: University of Oslo and Simula Research Laboratory

Name of SFF: Center for Biomedical Computing (CBC), Physics of Geological Processes (PGP), Center of Mathematics for Computation (CMA)

Title of case study: Computing and programming is tightly integrated in all science programs at the University of Oslo

Period when the underpinning research was undertaken: 2002-2017

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Periods employed by SFF**
Hans Petter Langtangen	Professor, Center Leader CBC	2007-2016
Joakim Sundnes	Center Leader, CBC	2007-2017
Morten Hjorth-Jensen	Professor, CMA	2003-2013
Knut Mørken	Professor, Deputy leader CMA	2003-2013
Anders Malthe-Sørenssen	Professor, Group leader PGP	2003-2013

Period when the impact occurred:

1. Summary of the impact

The University of Oslo is an international leader in integrating computing and programming in science education. Through a collaborative effort known as *Computing in Science Education,* involving staff of three Centers of Excellence (CBC, PGP, and CMA), computing is now an integral part of all science programs at the University of Oslo, with nearly every single course including components of relevant programming. The result of this effort is a new generation of science graduates that are highly skilled in using computers to solve scientific and engineering problems, and have been trained in solving far more complex and realistic science problems than what is part of a traditional curriculum.

2. Underpinning research

The *Computing in Science Education* initiative is a long-term pioneering effort at the University of Oslo, and its progress was accelerated by the collaborations and research efforts in the Center for Biomedical Computing, Physics of Geological Processes, and Center of Mathematics for Applications. All the three centers have been strongly focused on the use of computational mathematics to solve scientific problems, across a large

variety of fields including geology, physics, continuum mechanics, and physiology as well as development of new computational methods.

The long-term research into these areas have led to the observation that successful candidates in science and engineering need deep and broad training in computational methods and programming. Such training needs to be coherently integrated with and not only supplement the traditional analytical techniques of the natural sciences, to make the candidates better prepared for how science problems are solved in the 21st century. A more innovative insight underpinning the initiative is that extensive use of computers will also advance the candidates' understanding of their own scientific field. Being skilled in computational mathematics, the students are able to focus on the underlying scientific questions rather than the advanced algebra often required in traditional problem solving techniques. At the same time the computational techniques are more general than the traditional techniques, allowing he students to tackle far more complex and realistic scientific problems.

As a result of these efforts, the University of Oslo is at the international forefront in this area, with programming and computational methods tightly integrated into all study programs in the natural sciences. The initiative has been recognized by numerous prizes and awards, and in 2016 received status as a Norwegian Center for Excellence in Education (SFU) as Centre for Computing in Science Education (CCSE), hosted by the Department of Physics, University of Oslo.

3. References to the research

This section should provide references to key outputs from the research described in the previous section, and evidence about the quality of the research. Underpinning research outputs may include, but is not limited to journal articles, book chapters, edited volumes, monographs, patents, prototypes etc.

Hans Petter Langtangen, "Title: A Primer on Scientific Programming with Python", Springer, 2009.

Anders Malthe-Sørenssen, "Elementary Mechanics Using Python"/"Elementary Mechanics Using Matlab", Springer 2015.

Arnt Inge Vistnes, Physics of Oscillation and Waves with use of Matlab and Python, Springer, 2018

Anders Malthe-Sørenssen, Morten Hjorth-Jensen, Hans Petter Langtangen, Knut Mørken, «Integrasjon av beregninger i fysikkundervisningen», *Uniped*, **38**, 4, 2015

Marcos Daniel Caballero, Morten Hjorth-Jensen, "Integrating a computational perspective in physics courses", arXiv, 1802.08871 2018.

4. Details of the impact

Two to three decades ago, the typical curriculum of a physics or mechanics student at the University of Oslo would mainly be focused on traditional, analytical problem-solving methods. A course in programming would be included early on, but then most students would not use programming again as part of their undergraduate studies. About three years later, when starting their Master's studies, many of the students would work on computationally oriented project, which typically would require programming using a new programming language and an entirely different style than what they learnt earlier. Surprisingly, this curriculum remains the standard program in universities all over the world. The approach works in that students get introduced to the basic ideas of programming and get a solid background in their own field, and some students are capable of integrating these two skillsets on their own when needed. However, this is most likely not the best approach for preparing students for an increasingly computer-based work life.

At the University of Oslo, current undergraduate students have a completely different experience. All bachelor programs include an introductory programming course tailored to the needs of the particular field, with examples and applications selected from relevant scientific problems. Students in the most computing-intensive programs, including physics and mathematics, also follow a course in numerical mathematics, which is tightly integrated with the introductory course in programming. Even more importantly, computing-based problem solving is part of many later undergraduate courses, which maintains and further develops these skills. As a result, students are far better prepared both for graduate school and for the typical tasks they will face in their first job.

The Computing in Science Education initiative grew out of a collaboration between three different University departments, as part of the CoEs *Center of Mathematics for Applications, Physics of Geological Processes,* and *Center for Biomedical Computing.* Today, the initiative has turned into a CoE on its own, the *Center for Computing in Science Education (CCSE)*, and plays a central role in further development of the science curriculum in Norwegian Universities.

The CCSE and thereby the original Computing in Science initiative has given many high school teachers new perspectives on how mathematics and science can be taught in school since they attend the basic undergraduate courses in mathematics and physics as part of their training. One of these teachers has developed an elective course for high school based on the CSE ideas. Through the years, scientists involved in CSE have also given presentations to politicians and participated in writing reports about programming in school.

The whole Norwegian school system is currently undergoing a major change in that the content of all disciplines is reformed with a focus on more advanced understanding, so-called «deep learning». One aspect of this is that programming and algorithmic thinking is a skill and way of thinking that all students should learn. This will be hosted by mathematics, but also integrated in other disciplines like science, art and craft, and music. In this process, the CSE-ideas have played a major role, and the CCSE is now offering numerous courses for teachers in preparation for the introduction of the new syllabus in the fall of 2020.

5. Sources to corroborate the impact

The CSE project was featured in the Norwegian white paper on Higher Education, Culture for quality in higher eduction, Meld. St. 16 2016–2017 Kultur for kvalitet i høyere utdanning, p. 42,

https://www.regjeringen.no/contentassets/aee30e4b7d3241d5bd89db69fe38f7ba/no/pdfs/stm201620170016000dddpdfs.pdf

The CSE project was awarded a Center for Excellence in Education. The project description and the review of the project can be found on the web-pages of Nokut/Diku. The full review of the external evaluation committee can be found here. The CCSE project received a full score of 6 as the only Center for Excellence funded in 2016: https://www.nokut.no/sentre-for-fremragende-utdanning/sentre/ccse--center-for-computing-in-science-education/

The new curriculum for Mathematics in the Norwegian 1-13 schools system can be found at The Norwegian Directorate for Education and Training's web pages https://www.udir.no/laring-og-trivsel/lareplanverket/fagfornyelsen/hva-er-nytt-fagene-les-vare-korte-oppsummeringer/ . They write that: *«Vi har tatt algoritmisk tenkning og programmering inn i faget. Vi har vektlagt algoritmisk tenkning fordi dette er en viktig problemløsningsstrategi. Når elevene bruker programmering til å utforske og løse problemer, kan det være et godt verktøy for å utvikle matematisk forståelse.»* The CSE project has contributed to this change.

The impact of CSE can be read from the number of invited talks and presentations by key personnel. A full list can be found in the Annual reports from CCSE from 2017 and 2018 found here: https://www.mn.uio.no/ccse/om/rapporter/. Computing is now in the processes of being integrated in science programs at UiB, NTNU, UiT, UiS, at Stockholm University, Uppsala University, , and University of Dublin, Ireland, at Michigan State University, USA, and at the National University of Defense Technology in China. Contact points to corroborate that computing is being integrated in science education are: Stian Anfinsen at UiT, Harald Walderhaug at UiB, Magnus Lilledahl at NTNU, Aksel Hiorth at UiS, Marcos Danny Caballero at Michigan State University.

2.3 CGB - Centre for geobiology

2.3.1 Scientific impact: Discovery and characterization of a new group of microbes - Lokiarchaeota

Institution: University of Bergen

Name of SFF: Centre for Geobiology (CGB, 2007-2017)

Title of case study: Discovery and characterization of a new group of microbes - Lokiarchaeota.

Period when the underpinning research was undertaken: 2008-2015

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period employed by submitting SFF:
Steffen Leth Jørgensen	PhD/Post doc, microbiology	2008-2017
Andres Lanzén	PhD, microbiology	2008-2013
Christa Schleper	Adjunct Prof, microbiology	2007-2015
Lise Øvreås	Ass.Prof/Prof, microbiology	2007-2017
Ida H. Steen	Researcher/Prof, microbiology	2007-2017
Rolf Birger Pedersen	Professor, geology	2007-2017
Ingunn H. Thorseth	Ass.Prof/Prof, geology	2007-2017
Bjarte Hannisdal	Post doc/researcher, geology	2007-2017
Kristin Flesland	PhD, geology	2009-2017

Period when the impact occurred: 2015-2017

1. Summary of the impact

The discovery lead to a paradigm shift in evolutionary biology and to the reconstruction of the fundamental structure of the tree of life.

2. Underpinning research

The study identified, named and described a specific group of Archaea as being the closest prokaryotic relative to the complex eukaryotic cell. It provided evidence that the domain Archaea is a direct ancestor to all eukaryotic life and thus re-arranging the previous topography of the tree of life. Further, the genomic inventory of this archaeal group profoundly alters our perception of the nature of the last common ancestor to the Eukaryotic domain of life and hold clues about the timing of events leading to eukarygenesis.

A strong focus on the deep biosphere from the beginning of the CGB period was pivotal in providing the critical background information finally leading to our discovery. This included identification and abundance estimates of the Lokiarchaeota (at that time known as Deep Sea Archaeal Group) in sample material obtained during several CGB cruises to the Arctic Mid-Ocean Ridge (AMOR). The main results from these studies were published in PNAS (2012) and Frontiers in Microbiology (2013). Based on these studies a number of samples were selected by CGB staff for further investigation. A close collaboration with Dr. Thijs Ettema at Uppsala University was then established to investigate the genomic information from this group of organisms in more details. DNA extracted by Centre staff was subsequently sequenced and the genome of Lokiarchaeota was reconstructed in Uppsala. In close collaboration with our Swedish collogues we annotated and analyzed the genome.

3. References to the research

- Jørgensen SL, Hannisdal B, Lanzèn A, Baumberger T, Flesland K, Fonseca R, Øvreås L, Steen IH,

Thorseth IH, Pedersen RB, Schleper C (2012). Correlating microbial community profiles with geochemical data in highly stratified sediments from the Arctic Mid-Ocean Ridge. *PNAS* (doi710.1073/pnas.1207574109).

- SL Jørgensen, IH Thorseth, RB Pedersen, T Baumberger, C Schleper (2013). Quantitative and phylogenetic study of the Deep Sea Archaeal Group in sediments of the Arctic mid-ocean spreading ridge. *Frontiers in microbiology* 4, 299.
- Spang A, Saw JH, Jørgensen SL, et al (2015). Complex archaea that bridge the gap between prokaryotes and eukaryotes. *Nature* 521.

4. Details of the impact

Samples collected by Centre staff during a CGB cruise in 2008 were essential in the study. After careful investigation and analyses of the microbial content at the CGB, specific samples were selected for further in-depth metagenomic evaluation. Without this foundation we would not have been successful.

Our findings are two-folded. 1) we find and describe a new archaeal group, Lokiarchaeota which represent the closest living relative to all complex life (Eukaryotes). It represents a transition form that evolutionist has been searching for a long time, which genomic inventory profoundly alters our perception of the nature of the last common ancestor to the Eukaryotic domain of life and hold clues about the timing of events leading to eukarygenesis. 2) We prove beyond doubt that the ancestor to the Eukaryotic domain was an archaeal cell, and by doing so the tree-domain tree of life has to be redrawn into a two-domain tree where Eukarya branches off within the archaeal domain.

Our findings are greatly influencing the current direction of evolutionary biology and prove that metagenomics is a suitable tool to access the evolutionary relationship between ancient uncultured microbial lineages. This way of pursuing research questions is now used by a high number of research groups, worldwide.

While the study was done in collaboration with colleagues from Uppsala, CGB was essential in providing the sample material, and in performing the initial molecular analyses of the Lokiarchaeota. Hereafter, CGB initiated and established collaboration with Thijs Ettema who along with his group in Uppsala did all the subsequent genomic sequencing. CGB staff were highly involved in the entire planning of the project, in the subsequent discussions/analysis and in the writing.

The impact of our study is at the base of all biological sciences and thus ramifies all of the sub-disciplines, but with a specific impact on evolutionary biology.

This impact is still ongoing as can be seen by the steady number of citations (130-140/year) and as new textbooks are written it includes the new view of the evolutionary history.

5. Sources to corroborate the impact

The paper describing our findings is in the top 99 percentile of all publications from that year in Natures tracked journal (> 220.000 publications) Ranked 59th. The below list of references testifies to its profound scientific impact.

- Brock Biology of microorganisms 15th edition. Testify how this discovery has led to a paradigm shift in evolutionary biology and is now incorporated into key textbooks.
- Embley and Williams (2015) Evolution: Steps on the road to eukaryotes. Nature 521(7551).

Comment to our paper highlighting the significance of the finding by calling it a "*technically outstanding paper with far reaching implication for how we view our own deep ancestry"* .

- - L Eme et al (2017), Archaea and the origin of eukaryotes, Nature Reviews Microbiology 15 (12), 711. Testify how our finding have impacted the field.
- - A Spang and TJG Ettema, (2016) Microbial diversity: the tree of life comes of age. Nature microbiology 1 (5), 16056. Another example of the significance and how it progressed our understanding.
- Koonin (2015) "Archaeal ancestors of eukaryotes: not so elusive any more" BMC Biology. Comment to our paper highlighting the significance of the finding by leaders in the field of evolutionary biology, such as its "*spectacular results*" argued to call for the "*reassessment of some of the most general concepts in biology*".

2.3.2 Societal impact: Deep-sea mineral resources, unique ecosystems and bioprospecting potential within Norwegian territorial waters - hydrothermal vent fields at the Arctic Mid-Ocean Ridges (AMOR) in the Norwegian-Greenland Sea.

Institution: University of Bergen

Name of SFF: Centre for geobiology (CGB, 2007-2017)

Title of case study: Deep-sea mineral resources, unique ecosystems and bioprospecting potential within Norwegian territorial waters - hydrothermal vent fields at the Arctic Mid-Ocean Ridges (AMOR) in the Norwegian-Greenland Sea.

Period when the underpinning research was undertaken: 1999-2017

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting SFI
Rolf Birger Pedersen	Professor, geology	2007-2017
Ingunn H. Thorseth	Ass.Prof/Prof, geology	2007-2017
Deborah Kelley	Adjunct Prof, geology	2010-2012
Ingeborg Økland	PhD/Post Doc, geology	2007-2016
Benjamin Eickmann	Post Doc, geology	2009-2012
Tamara Baumberger	Post Doc, geology	2012-2015
Cedric Hamelin	Post Doc/Ass.Prof, geology	2012-2017
Desiree Roerdink	Post Doc/Ass.Prof, geology	2013-2017
Anna Filipa Marques	Researcher, geology	2013-2017
Kristin Flesland	PhD, geology	2009-2017
Anne Stensland	PhD, geology	2013-2017
Alden Denny	PhD, geology	2013-2016
Christoffer Schandler	Professor, marine biology	2007-2011
Hans Tore Rapp	Researcher/Prof, marine biology	2008-2017
Bernt Rydland Olsen	PhD/Post Doc, marine biology	2009-2016
Joana Xavier	Post Doc, marine biology	2013-2017
Jon Hestetun	PhD, marine biology	2013-2016
Mari Heggernes Eilertsen	PhD, marine biology	2013-2017
Christa Schleper	Adjunct Prof, microbiology	2007-2015
Lise Øvreås	Ass.Prof/Prof, microbiology	2007-2017
Ida H. Steen	Researcher/Prof, microbiology	2007-2017
Håkon Dahle	Post Doc/researcher, microbiolgy	2007-2017
Runar Stokke	Post doc/researcher, microbiology	2007-2017
William Hocking	PhD, microbiology	2007-2015
Bjørn Olav Steinsbu	PhD, microbiology	2007-2012
Tim Urich	Researcher, microbiology	2008-2010
Anders Lanzen	PhD, microbiology	2008-2013
Steffen Leth Jørgensen	PhD/Post Doc, microbiology	2008-2017
Anders Schouw	PhD, microbiology	2012-2017

Period when the impact occurred:

The societal interest in the deep-sea mineral resources and bioprospecting potential in Norway increased significantly from 2009, when Norway's claim in regard to the limits of the extended continental shelf was adopted by the United Nations. As part of the preparation of the

Norwegian claim, CGB contributed with data and interpretations, including an oral presentation to the UN commission on the nature of the seafloor in key areas.

1. Summary of the impact

As the global population continues to increase, and green technologies are being developed, the interest in deep-sea mineral resources is increasing. Norway has large deep-sea areas that contain mineral resources, but also unique ecosystems with bioprospecting and biotechnological potential. The mineral resources that currently are known in Norwegian waters have all been discovered as a result of the research that has been carried out by CGB. The Norwegian government has recently delegated the management of marine mineral resources to the Norwegian Petroleum Directorate. The know-how and competence developed at CGB will be critical for the exploration of these resources, and the associated ecosystems and environmental issues.

2. Underpinning research

Extending over 66 000 km through all the Earth's oceans, mid-ocean spreading ridges are the largest geological feature on the planet. The most vigorous and extensive interaction between warm, juvenile submarine rocks and water takes place at these ridges. Seawater constantly circulates through faults and fractures in the oceanic crust and upper mantle. This hydrothermal circulation alters the seafloor, forms massive mineral deposits and influences the chemical composition of the oceans. The up-flow portion of this circulation ranges from vigorous hot black smoker venting, to more diffuse, cooler venting, to cold seeps of fluid and gases from methane-rich sediment deposits at continental margins. The first discovery of deep-sea hydrothermal venting in the 1970's was revolutionary in terms of the geology and the biology. Researchers discovered previously unknown, thriving ecosystems around these deep vent locations. The ecosystems were based on chemosynthesis (energy derived from geochemical reactions) instead of photosynthesis (energy derived from light). Existing in isolated stepping stones in all the world's oceans, chemosynthetic deep-sea ecosystems have now been identified in many locations around vents.

A major goal for CGB was to study and document the largely unexplored deep-sea spreading system along the Arctic Mid-Ocean Ridge (AMOR) in the Norwegian-Greenland Sea, and to attain insights into the interactions between the geo- and biospheres. Centre researchers already started initial studies in this region in 1999 and had obtained the first evidence for the existence of both ancient (1999, 2000, 2002) and active (2005, Troll Wall and Soria Moria) hydrothermal vent fields[1].

One of the first CGB breakthroughs was the discovery of the Loki´s Castle vent field in 2008. In the resulting *Nature Communications* article[2], CGB researchers described the novelty of this field, including: the first hydrothermal black smoker vent field discovered at the AMOR; an unusually large hydrothermal mineral deposit (first evidence for extensive and long-lived hydrothermal systems at ultra-slow spreading ridges); the presence of a distinct vent fauna that differs from the fauna to the south along the Mid-Atlantic Ridge; and an unusual vent fluid composition suggesting a sedimentary influence to a volcanic-hosted hydrothermal system.

Since this discovery, CGB has located several new vent fields (Seven Sisters, Perle & Bruse, Ægir´s vent field) and chemical water column anomalies indicating additional active venting sites, during annual cruises to the AMOR[3].

During the Centre period all these vent fields have been subjected to more detailed studies of fluid and mineral composition, and unique ecosystems, and the bioprospecting and biotechnological potentials are currently evaluated[4-6].

3. References to the research

1. Pedersen RB, Thorseth IH, Nygård TE, Lilley MD, Kelley D **(2010)**. Hydrothermal activity at the Arctic Mid-Ocean Ridges. In (Eds. P. Rona, C. Devey, J. Dyment, B. Murton) Diversity of Hydrothermal Systems on Slow Spreading Ocean Ridges. Geophysical Monograph Series 188. 2010. American Geophysical Union; 10.1029/2008GM000783, pages 67-89.
2. Pedersen RB, Rapp HT, Thorseth IH, Lilley MD, Barriga FJAS, Baumberger T, Flesland K, Fonseca R, Früh-Green GL, Jørgensen SL **(2010)**. Discovery of a black smoker vent field and novel vent fauna at the Arctic Mid-Ocean Ridges. *Nature Commun.* 1:126; doi: 10.1038/ncomms1124(2010).
3. Stensland A, Baumberger T, Mork AK, Lilley M, Thorseth IH, Pedersen RB **(2019)**. ^{3}He along the ultraslow spreading AMOR in the Norwegian-Greenland Seas. *Deep-Sea Research Part I –* Oceanographic research papers 147: 1-11.
4. Eilertsen MH, Kongsrud JA, Alvestad T, Stiller J, Rouse GW, Rapp HT **(2017)**. Do ampharetids take sedimented steps between vents and seeps? Phylogeny and habitat-use of Ampharetidae (Polychaeta, Terebelliformia) in chemosynthesis-based ecosystems. *BMC Evolutionary Biology* 17: 222 https://doi.org/10.1186/s12862–017-1065–1
5. Dahle H, Økland I, Thorseth IH, Pedersen RB, Steen IH (**2015**). Energy landscapes shape microbial communities in hydrothermal systems on the Arctic Mid-Ocean Ridge. *ISME Journal,* 9:1593-1606.
6. Vuoristo KS, Fredriksen L, Oftebro M, Arntzen MO, Aarstad OA, Stokke R, Steen IH, Hansen LD, Schuller RB, Aachmann FL, Horn SJ, Eijsink VGH **(2019)**. Production, characterization, and application of an Alginate Lyase, AMOR _ PL7A, from Hot Vents in the Arctic Mid-Ocean Ridge. *Journal of Agriculture and Food Chemistry* 67: 2936-2945.

4. Details of the impact

Seafloor mineral resources

Minerals and metals are of fundamental importance for society. As the global population continues to increase, on-land resources are being exploited more heavily than ever before. Access to minerals and rare earth elements is also becoming increasingly important as modern technologies become widespread and green technologies are being developed. As a result, the interest in deep-sea mineral resources is increasing.

The societal interest in the deep-sea mineral resources and bioprospecting potential in Norway increased particularly from 2009, when Norway's claim in regard to the limits of the extended continental shelf was adopted by the United Nations. As part of the preparation of the Norwegian claim, CGB contributed with data and interpretations, including an oral presentation to the UN commission on the nature of the seafloor in key areas.

Norway has large deep-sea areas that contain mineral resources. The mineral resources that currently are known in Norwegian waters have all been discovered as a result of the deep-sea expeditions and the basic research that has been carried out by CGB. The Norwegian government has recently been delegated the management of marine mineral resources to the Norwegian

Petroleum Directorate. The know-how and competence developed as part of CGB, will be critical as the pioneering phase now transitions into an exploration phase, and the NPD collaborate therefore closely with UiB and the former CGB researhers[1].

CGB contributions also include a written report to the Norwegian Environmental Agency (Miljødirektoratet) entitled "Environmental challenges related to offshore mining and gas hydrate extraction"[2], and numerous presentations to the involved ministries and stakeholders on the nature of the mineral resources and associated environmental issues [3-6], and interviews on national Radio, TV programmes and various newspapers.

Biotechnology

Enzymes play important roles in our daily lives, being used in processing of food, in the pharmaceutical and chemical industries, in bioremediation and in the production of energy. A major challenge for the use of enzymes is their limited temperature stability. Finding new enzymes with new and improved catalytic activities at high temperatures (thermozymes) is important to bring the modern society forward.

Deep-sea hydrothermal vents provide a broad range of diverse and extreme habitats, with steep temperature and pH gradients, hence they are an interesting potential source of new thermozymes. Due to the unique technological and scientific competence generated at CGB, the researchers have been attractive partners in several national and international biotechnology projects. Being part of these projects has in turn enabled the researchers to gain an overview of the bioprospecting and biotechnological potentials of the deep-sea hydrothermal vent microbiome. The results thus have implications for how we assess this microbiome as a future marine resource, and how this resource should be managed and exploited in the future[7-10].

5. Sources to corroborate the impact

1. Oljedirektoratet (NPD) –news. Ressurser for framtiden: Havbunnsmineraler og gasshydrater. 11.Sept. 2018. https://www.npd.no/fakta/publikasjoner/rapporter/ressursrapporter/ressursrapport-2018/kapittel-8/
2. Olsen, Bernt Rydland; Økland, Ingeborg Elisabeth; Thorseth, Ingunn Hindenes; Pedersen, Rolf B.; Rapp, Hans Tore (2016). Environmental challenges related to offshore mining and gas hydrate extraction. *Miljødirektoratet*, rapport (14080454), 28 pages.
3. Bergstad, Odd Aksel; Pedersen, Rolf B.; Buhl-Mortensen, Lene; Kutti, Tina. Mineralutvinning i dyphavet. Potensiell næring som utfordrer rådgivningen. *Havforskningsrapporten* 2016, s122-124.
4. Marques, Ana Filipa Alfaia; Pedersen, Rolf B. Contrasting hydrothermal systems and seafloor mineralization at the Arctic Mid-Ocean Ridge. *On- and Offshore Exploration and Prospecting in Extreme Nordic Environments Changes and Benefits of Finding Exploitable Raw Materials*; Reykjavik, conference 20-24 May, 2015 (abstract & oral pres.).
5. Marques, Ana Filipa Alfaia; Pedersen, Rolf B. Quantifying resources and the discovery of deep-sea hydrothermal systems of the Arctic Mid-Ocean Ridge. *Workshop on Marine Minerals*, IMPA, Portugal, 27-28 Oct. 2015 (oral pres.).
6. Pedersen, Rolf B. Contrasting hydrothermal systems and seafloor mineralizations at the Arctic Mid-Ocean Ridge. International workshop on deep-sea mineral resources; Bergen, 11-13 May 2015 (oral pres.).

7. Tvedt, Morten Walløe; Eijsink, Vincentius Gerardus Henricus; Steen, Ida Helene; Strand, Roger; Rosendal, Guri Kristin (2016). The missing link in ABS: The relationship between resource and product. *Environmental Policy and Law* 46: 227-237.
8. Steen, Ida Helene. Exploitation of genetic resources from the Arctic mid-ocean ridge vent fields in the norwegian industry. International workshop on deep sea mineral resources; Bergen, 11-13 May 2015 (oral pres.)
9. Steen, Ida Helene; Stokke, Runar. Bakteriar frå Norskehavet kan gjere fiskeslo om til mat. NRK Hordaland [Internett] 2015-07-09.
10. Steen, Ida Helene. Jakter superenzymer på havbunnen. Teknisk Ukeblad [Avis] 2013-05-12

2.4 CIR - Centre for Immune Regulation

2.4.1 Scientific impact: Cell surface IgA and IgM expression in plasma cells

Institution: University of Oslo/Oslo University Hospital

Name of SFF: Centre for Immune Regulation

Title of case study: Cell surface IgA and IgM expression in plasma cells

Period when the underpinning research was undertaken: 2007-2017

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting SFF:
Roberto Di Niro	Postdoc	01.01.08 - 31.12.09
Luka Mesin	PhD student	01.12.07 - 28.02.10
Øyvind Steinsbø	PhD student	15.02.10 - 27.03.15
Rasmus Iversen	PhD student/Postdoc	01.01.09 - 31.12.16
Omri Snir	Postdoc	29.08.14 - 28.08.17
Bishnuedo Roy	Postdoc	15.01.14 - 14.01.17
Knut E.A. Lundin	Professor	01.12.07 - 30.11.17
Ludvig M. Sollid	Professor	01.12.07 - 30.11.17

Period when the impact occurred:

1. Summary of the impact

Naïve and memory B cells express cell surface immunoglobulin as their antigen receptor. Textbook immunology commonly states that effector B cells – the plasma cells – do not express cell surface immunoglobulin. Work at CIR demonstrated that this notion is not correct. We discovered that IgA and IgM expressing gut plasma cells (in contrast to IgG expressing plasma cells) display cell surface immunoglobulin. We harnessed this feature to invent a method to isolate and to characterize antigen specific plasma cells.

2. Underpinning research

In 2010 in work resulting from work done at CIR we published a paper reporting that gut plasma cells express cell surface IgA or IgM (1). In the abstract of the paper we state: "*We found that CD138-positive plasma cells from the duodenum expressed surface IgA or IgM*." The first author of this paper is Roberto Di Niro, and the work was done as a collaborative effort between the groups of Ludvig Sollid at CIR and Patrick Wilson at the University of Chicago. In more or less parallel work, we further work discovered that gut effector B cells can live in culture without signs of proliferation for weeks and such cells retain their cell surface expression of IgA or IgM suggesting that the cells in question indeed are mature plasma cells (2). We exploited the feature of cell surface expression of Ig and IgM to establish a method to isolate and characterize antigen specific plasma cells (1). This method we first used to isolate rotavirus specific plasma cells. A DOFI made and a patent application was submitted with Di Niro, Sollid and Wilson as inventors. Inven2, the tech office University of Oslo/Oslo University Hospital sponsored the patent application, but decided to drop the patenting process as it was judged that an immediate licensing partners of a patent would be hard to find.

In the few next years, we used the method to isolate transglutaminase 2 and deamidated gliadin peptide specific plasma cells from gut biopsies of celiac disease patients (3-6). This work has greatly impacted on the understanding of the pathogenesis of celiac disease.

3. References to the research

Key publications presenting and harnessing the impact:

1. Di Niro R, Mesin L, Ráki M, Zheng NY, Lund-Johansen F, Lundin KE, Charpilienne A, Poncet D,

Wilson PC, Sollid LM. Rapid generation of rotavirus-specific human monoclonal antibodies from small-intestinal mucosa. J Immunol. 2010 Nov 1;185(9):5377-83. PubMed PMID: 20935207.
2. Mesin L, Di Niro R, Thompson KM, Lundin KE, Sollid LM. Long-lived plasma cells from human small intestine biopsies secrete immunoglobulins for many weeks in vitro. J Immunol. 2011 Sep 15;187(6):2867-74. PubMed PMID: 21841131.
3. Di Niro R, Mesin L, Zheng NY, Stamnaes J, Morrissey M, Lee JH, Huang M, Iversen R, du Pré MF, Qiao SW, Lundin KE, Wilson PC, Sollid LM. High abundance of plasma cells secreting transglutaminase 2-specific IgA autoantibodies with limited somatic hypermutation in celiac disease intestinal lesions. Nat Med. 2012 Feb 26;18(3):441-5. PubMed PMID: 22366952
4. Steinsbø Ø, Henry Dunand CJ, Huang M, Mesin L, Salgado-Ferrer M, Lundin KE, Jahnsen J, Wilson PC, Sollid LM. Restricted VH/VL usage and limited mutations in gluten-specific IgA of coeliac disease lesion plasma cells. Nat Commun. 2014 Jun 9;5:4041. PubMed PMID: 24909383
5. Roy B, Neumann RS, Snir O, Iversen R, Sandve GK, Lundin KEA, Sollid LM. High-throughput single-cell analysis of B cell receptor usage among autoantigen-specific plasma cells in celiac disease. J Immunol. 2017 Jul 15;199(2):782-791. PubMed PMID: 28600290.
6. Snir O, Chen X, Gidoni M, du Pré MF, Zhao Y, Steinsbø Ø, Lundin KE, Yaari G, Sollid LM. Stereotyped antibody responses target posttranslationally modified gluten in celiac disease. JCI Insight. 2017 Sep 7;2(17). pii: 93961. PubMed PMID: 28878138.

4. Details of the impact

Immunology textbooks mostly still state that plasma cells are devoid of surface immunoglobulin. This is true for IgG plasma cells but not IgA/IgM plasma cells. An observation that many effector B cells in the gut have expression of IgA and IgM was made before by other researchers (Farstad et al., Immunology 2000. PMID:11106939), but the authors concluded that these cells were likely short-lived plasma blasts and not plasma cells. Our experience being able to keep gut effector B cells in culture for weeks without sign of proliferation and with cells keeping their cell surface immunoglobulin property contradicted that the cells should be short-lived plasma blast (2). Our other effort to phenotype the cells also led us to conclude that they are mature plasma cells (3). Still we are faced with skepticism from other researchers on this conclusion, but the field is on the move to accept that IgA and IgM plasma cells as a normal feature have cell surface immunoglobulin.

Influence on research outside of CIR by the impact:
Subsequent to our discovery, other researchers have demonstrated that plasma cell surface IgA and IgM are functional as B-cell receptors (Pinto et al., Blood 2013. PMID: 23550036). There is now an increased attention to the role of plasma cells that express B-cell receptors, and for instance as worded by Hans-Martin Jäck, a leader in the field, that these cells are special entity of “unconventional plasma cells” at a European B cell network meeting in July 2019. Likely, the IgA/IgM B-cell receptor’s function is to sense presence of antigen, and that this in turn will regulate presence/persistence of the given plasma cells in the mucosal tissues. Teleologically, this make sense as mucosal surfaces predominantly populated by IgA and IgM plasma cells, in contrast to the bone marrow mainly populated by IgG plasma cells, are constantly flooded by antigen exposure. More work on B-cell receptor expressing plasma cells can be expected to appear in the coming years, including identifying the exact by which mechanism IgA/IgM plasma cells sense antigen.

Several researchers have used our method to isolate gut plasma cells specific for both viral (Nair et al., Sci Trans Med 2017, PMID: 28637924) and bacterial antigens (Linder et al., Nat Immunol 2015. PMID: 26147688). It is to be expected that industry that is currently gearing up to produce therapeutic antibodies against pathogens will harness the method to generate monoclonal antibodies from plasma cells of subjects who are naturally protected against severe infectious diseases.

Involvement of other researchers to the making of the impact:
The group of Patrick Wilson at the University of Chicago was contributing to the work by cloning and producing recombinant monoclonal antibodies from single antigen specific plasma cells.

Which fields/research groups/scholarly communities are impacted:
Many fields are likely to be impacted ranging from industry to make therapeutic antibodies against mucosal pathogens, public health organizations testing and monitoring vaccines against gut pathogens like rotavirus and Vibrio cholera to basic scientists studying mucosal immunity.

5. Sources to corroborate the impact

In 2012 the excellent research paper award of Oslo University Hospital given to Roberto Di Niro for his Nature Medicine paper.

ERC Advanced Grant awarded to LM Sollid in 2010 for the project AUTO-CD, ERC-2010-AdG_20100317. An essential part of the grant proposal entitled: “Coeliac disease: Understanding how a foreign protein drives autoantibody production” was the endeavor to isolate and characterize transglutaminase 2 specific plasma cells with antigen as bait for cell surface B-cell receptors.

The Oslo University Hospital’s Excellent Researcher Award given to LM Sollid in 2014 for his outstanding research on the pathogenesis of celiac disease.

Anders Jahre’s Senior Award for Medical Research given to LM Sollid in 2015 for his groundbreaking research on coeliac disease.

2.4.2 Scientific impact: Long lived gut plasma cells

Institution: University of Oslo/Oslo University Hospital

Name of SFF: Centre for Immune Regulation

Title of case study: Long lived gut plasma cells

Period when the underpinning research was undertaken: 2007-2017

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting SFF:
Ole Landsverk	Postdoc	15.08.13 - 30.11.17
Omri Snir	Postdoc	29.08.14 - 30.11.17
Raquel Casado	PhD student	13.04.15 - 30.11.17
Espen Bækkevold	Researcher	01.02.13 - 30.11.17
Lisa Richter	Postdoc	15.10.15 - 15.06.16
Ludvig M. Sollid	Professor	01.12.07 - 30.11.17
Frode L. Jahnsen	Professor	01.12.07 - 30.11.17
Luka Mesin	PhD student/postdoc	01.12.07 - 31.12.13
Roberto Di Niro	Postdoc	01.01.08 - 31.12.09

Period when the impact occurred:

1. Summary of the impact

Plasma cells in the gut produce grams of antibodies every day that play an important role in immune defense of the gut. It was previously thought that gut plasma cells only lived for days. However, we demonstrate that gut plasma cells live for decades. This is a paradigm shift in our understanding of mucosal immunity and our finding will have important implications for vaccination strategies against intestinal pathogens and for how we can exploit the immune system to treat dysbiosis-associated disorders.

2. Underpinning research

In 2011, Mesin et al published a paper demonstrating that gut plasma cells survive for weeks when intestinal biopsies are cultured ex vivo (1). This finding opened up for the possibility that gut plasma cells could survive for a longer time than previously thought. To determine the life span of gut plasma cells the Jahnsen group initiated, in 2014, a collaboration with transplantation surgeons at Oslo University Hospital (OUH) in which we studied the longevity of gut plasma cells in transplanted duodenum (2). We applied two methods: 1) Immunohistochemistry of tissue sections combined with fluorescence in situ hybridization with XY probes in recipients with a donor of different gender, and 2) Flow cytometry of single cells from enzyme-digested transplanted duodenum where donors and recipients expressed different HLA class I molecules. We were able to show that the majority of plasma cells survived for more than a year in the transplanted tissue. To follow up on this finding we established, in 2015, a collaboration with gastrointestinal surgeons at OUH and the group of Jonas Frisén, Karolinska Institute. Because of a dramatic change in atmospheric carbon 14 after over-ground test bombing in the late 50ties, that later has dropped exponentially, Jonas Frisén has developed a method to retrospectively determine the age of cells by measuring their DNA content of carbon 14. Using this method, we demonstrated that plasma cells sorted from normal intestinal mucosa could be divided into three equally large populations. Those that were short-lived (< 2 years), intermediate (median of 11 years), and long-lived (median of 22 years). Taking into account that these measurements were average levels of millions of cells it is very likely that some of the long-lived plasma cells in the gut live for a lifetime. The implications of the findings are many, some are discussed here (3).

3. References to the research

1. Mesin L, Di Niro R, Thompson KM, Lundin KE, Sollid LM. Long-lived plasma cells from human small intestine biopsies secrete immunoglobulins for many weeks in vitro. J Immunol. 2011 Sep 15;187(6):2867-74. PubMed PMID: 21841131.
2. Landsverk OJ, Snir O, Casado RB, Richter L, Mold JE, Réu P, Horneland R, Paulsen V, Yaqub S, Aandahl EM, Øyen OM, Thorarensen HS, Salehpour M, Possnert G, Frisén J, Sollid LM, Baekkevold ES, Jahnsen FL. Antibody-secreting plasma cells persist for decades in human intestine. J Exp Med. 2017 Feb;214(2):309-317. PubMed PMID: 28104812.
3. Jahnsen FL, Baekkevold ES, Hov JR, Landsverk OJ. Do long-lived plasma cells maintain a healthy microbiota in the gut? *Trends Immunol* **2018, 39;**196-208 PMID: 29162322
4.

4. Details of the impact

The existence of long-lived plasma cells in the bone marrow explains why systemic vaccination (e.g. against measles and mumps) provides long-lasting protective antibody responses. However, whether mucosal plasma cells are long-lived has been an open question for many years. In fact, several studies have shown that gut plasma cells are short-lived and dynamically reconstituted to adjust to a constantly changing environment in the gut. Our result clearly demonstrates the gut contains subsets of plasma cells with different life span. Most plasma cells are very long-lived whereas a smaller population shows high turnover.

Influence on research outside of CIR by the impact:
The finding that gut plasma cells can be long-lived will most likely have great impact on the design of oral vaccines in the future, and mainly for this reason the paper have received a lot of attention. At day present it has been cited 37 times and been discussed in several reviews by internationally leading researchers, e.g. Albert Bendelac (Chicago) and William Agace (Copenhagen); both in the journal *Immunity* (PMID:30134201 and PMID: 28423335). It has been recommended three times in F1000Prime by leading researchers in the field, e.g. Stephen Nutt, Melbourne, Australia.

Involvement of other researchers to the making of the impact:
We collaborated with transplant surgeons at our hospital (OUH) to perform studies on transplanted small intestinal tissue (Ole Øyen, Rune Horneland and Ole Martin Aandahl) and gastrointestinal surgeon Sheraz Yacub to study plasma cells in normal intestine. In collaboration with the group of Jonas Frisén at Karolinska we measured the levels of carbon 14 in the DNA isolated from gut-derived plasma cells.

Which fields/research groups/scholarly communities are impacted:
Our findings will have broad implications for continued research mainly along two avenues of research. There are currently few effective oral vaccines. To make an efficient vaccine it is important that it initiates long-lasting immune responses. Now that we know that plasma cells in the gut can survive for many years, efforts will be made to design oral vaccines that will generate vaccine-specific long-lasting neutralizing antibody responses in the gut.

The other research area is the treatment of dysbiosis-associated disorders. Over the last years there has been a tremendous interest in how the composition of gut microbiota affects health and disease. A number of scientific reports show how a dysregulated microbiota is associated with neurological diseases, chronic inflammatory diseases, obesity and cancer. Locally produced secretory antibodies in the gut bind to the microbiota and it likely that long-lived plasma cells play an important role in regulating the microbiota composition. It is therefore likely that manipulation of gut plasma cells may be a target to treat dysbiosis-related disorders.

5. Sources to corroborate the impact

In 2017 the excellent research paper award of Oslo University Hospital given to Ole Landsverk for his J Exp Med paper.

In 2018 Frode Jahnsen received research funding from the Research Council of Norway NOK 9,7 mill for the project “Human gut plasma cells live for decades: implications for vaccination and treatment of chronic inflammation”

2.4.3 Scientific impact: Idiotypes and T cells in autoimmunity and B cell malignancies

Institution: University of Oslo/Oslo University Hospital

Name of SFF: Centre for Immune Regulation

Title of case study: Idiotypes and T cells in autoimmunity and B cell malignancies

Period when the underpinning research was undertaken: 2007-2017

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by
Bjarne Bogen	Professor	01.12.07 - 30.11.17
Ludvig Munthe	Professor	01.12.07 - 30.11.17
Ole Audun Haabeth	PhD candidate/Postdoc	01.01.10 - 30.11.17
Anders Tveita	Postdoc	01.03.12 - 30.11.17
Johanne Jacobsen	PhD candidate/Postdoc	01.10.09 - 30.11.17
Kristin Aas-Hanssen	PhD candidate	01.01.10 - 31.12.15

Period when the impact occurred: 2007-2019

1. Summary of the impact

B cells make antibodies that protect us from disease, and receive help from T cells partners in immune reactions. Antibodies have unique sequences called Idiotypes. Our research results have demonstrated that T cell immune responses directed towards Idiotypes presented on the surface of B cells can induce B cell cancer as well as autoimmunity. Other types of T cell immune responses directed towards Idiotypes can combat established B cell cancer. There is now increased focus on these immune responses, both pathogenic and as part of developing new therapies, in the search for new therapies and research driven innovation and in precision medicine.

2. Underpinning research

Using genetically engineered mice, CIR scientists demonstrated that B cell cancer could be induced by B cell interaction with T cells. The T cells recognized B cell Idiotypes presented as antigen on MHC II molecules by B cells (J Exp Med, 2007, PMID: 17485509). The cancers arose in a setting of autoimmune disease. CIR scientists visualized disease development in whole body optical imaging of mice engineered to emit photons after activation of cellular inflammation responses by NF-kB signaling (Am.J Pathol, 2009). The work inspired CIR scientists to investigate if similar support could be found in human patients where we found that Th cells supported the proliferation of B cell cancers called CLL, chronic lymphocytic leukemia. Th cells stimulated CLL cells as described above in vitro and after transfer of human cells into mouse hosts (Cell Reports, 2013, PMID: 23933259; J Immunol 2014, PMID: 25505279; and Haematologica. 2015, PMID: 26589914). This was extended to a B cell cancer of bone and bone marrow, multiple myeloma (Leukemia, 2017, PMID: 28232741) as well as childhood leukemia B-ALL (Oncogene. 2019 PMID: 30532071) where CIR scientist demonstrated that T cells supported the growth of antigen presenting cancer B cells. In all these mouse and human studies, autoimmune phenomenon where T cells responded to self peptides (Idiotypes) and where B cell autoimmune responses (autoantibodies) were common. CIR scientists followed up these observations and demonstrated: 1) T cells that that recognized B cell Idiotypes could support Anti-dsDNA B Cells in mice with lupus (J Immunol. 2014. PMID: 25127856), 2) immune cross reactions could play a role (Frontiers in immunology 2015; PMCID: 4517057), 3) this type of interaction could occur in the absence of other antigen presenting cells and when responding cells were of low frequency (Immunol Cell Biol. 2010; PMID:20066000; J Immunol. 2014 PMID: 24706724) and 4) described Idiotype driven T-B Cell Collaboration in human Multiple Sclerosis patients (Front Immunol, 2017 PMID: 29038659).

T cells are capable of many types of immune responses. In addition to the supportive role described above, CIR scientists have been central in defining the role of Idiotype specific T cells in killing cancer cells. They found that inflammatory (type 1) cytokines were required (Nat Commun. 2011, PMID: 21407206; Oncoimmunology. 2015; PMID: 26942052), presentation of Idiotype and cell contact was necessary, but killing of cancer cells could be indirect and required Nitrous Oxides (Cancer Res. 2009 ; PMID:19567679; Eur J Immunol. 2014; PMID: 24846412; Oncotarget. 2016; PMID: 27626487; Cancer Res. 2018 PMID: 29752262; Front Immunol. 2018 PMID:30083157). In light of such results, CIR scientists have been on the forefront of developing vaccination strategies, including DNA vaccines (Mol Ther. 2006, PMID:16414309; J Transl Med. 2014, PMID:25059102; Haematologica. 2006, PMID:16818282).

In extension of this work, a CIR researcher co-authored a paper that demonstrated that Idiotypes were the most important cancer antigen for T cells in a common B cell cancer (Nature. 2017, PMID: 28329770). Others have recently found that Idiotypes may play a role in the pathogenesis of Type 1 diabetes in patients (Cell, 2019, PMID: 31150624) and T cells have been implicated in the induction of multiple myeloma (CANCER-CELL-D-19-00505, at SSRN: https://ssrn.com/abstract=3409453).

Scientists from CIR have followed up the work by demonstrating Th cell and Idiotype-dependent autoimmunity and induction of B cell cancer in physiological mouse models (Ms submitted) and are defining T cell specificity and function as well as new molecular targets in human B cell cancer.

3. References to the research

- Zangani MM, Frøyland M., Qui, GY, Meza-Zepeda, LA, Kutok, JL, Thompson, KM, Munthe LA, Bogen, B. Lymphomas can develop from B cells chronically helped by idiotype-specific T cells. J.Exp.Med. 2007, 204:1189-91. PMID: 17485509
- Os,A., Burgler,S., Ribes,A.P., Funderud,A., Wang,D., Thompson,K.M., Tjonnfjord,G.E., Bogen,B., Munthe, L.A. Chronic lymphocytic leukemia cells are activated and proliferate in response to specific T helper cells. Cell Reports. 4, 566-577. 2013. PMID: 23933259
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- Haabeth OA, Lorvik KB, Hammarström C, Donaldson IM, Haraldsen G, Bogen B, Corthay A. Inflammation driven by tumour-specific Th1 cells protects against B-cell cancer. Nat Commun. 2011;2:240. doi: 10.1038/ncomms1239. PMID: 21407206
- Corthay A, Lundin KU, Lorvik KB, Hofgaard PO, Bogen B. Secretion of tumor-specific antigen by myeloma cells is required for cancer immunosurveillance by CD4+ T cells. Cancer Res. 2009 Jul 15;69(14):5901-7. doi: 10.1158/0008-5472.CAN-08-4816. Epub 2009 Jun 30. PMID: 19567679

4. Details of the impact

The CIR scientists have been pioneers in the work to demonstrate that T cells can regulate B cells by recognizing idiotype and thereby either helping B cells (autoimmunity or induction of B cell malignancy) or by the direct opposite, by killing cancer B cells. The induction of

autoimmunity has recently culminated in a discovery of Idiotype driven disease in human diabetes type 1 patients (Cell, 2019, PMID: 31150624). This article refers to the work of CIR scientists (Aas-Hanssen K et al), the first demonstration linking Id-specific T cells to systemic autoimmunity (lupus). There currently is a revitalization of the field that extends seminal work from CIR scientists, and involves advanced informatics and new technology.

The presentation of Idiotypes and the impact on T cells and the immune system is very complex as the plethora of different antibody expressing B cells, each with distinct Idiotypes. Others have concluded that Idiotypes are the dominant antigen in the body in terms of shaping the T cell repertoire (Front Immunol. 2014, PMID: 25389426; Front Immunol. 2015, PMID: 26557118). This has consequences for prediction of T cell epitopes and vaccine design (Front Immunol, 2018, PMID: 30108588). Thus, T cell repertoire and potential responsiveness to pathogens and vaccines is dependent upon selection pressures of idiotypes that are presented to T cells in primary or secondary lymphoid organs. Most idiotype-specific T cells are therefore deleted or are regulated by regulatory T cells.

In B cell cancer, a CIR scientist and the group of Ron Levy demonstrated that idiotypes was the dominant mutated peptide that is presented by B cell cancers (Nature. 2017, PMID: 28329770) and that this is a general feature of B cell cancers (Blood. 2019 PMID: 30545830). Immunotherapy was the topic of the 2018 Nobel Prize. Immunotherapy has shown great promise for solid tumors, but not for B cell cancers (except Hodgkin lymphoma). Similarly, idiotype vaccine trials have previously failed for the incurable type of B cell cancer follicular lymphoma (J Clin Oncol. 2014, PMID: 24799467). This may be due to the duality of T cell induction/help of B cell cancer or T cell killing of B cell cancers as presented by CIR scientists. This important topic was discussed recently (Blood. 2019 PMID: 30545830) and authors heavily cite the work of CIR scientists (9 of 30 references). Others are also pursuing idiotypes as target for B cell therapy (e.g. Oncoimmunology, 2016. PMID: 27999743) and new vaccine formats or adjuvants may be necessary.

5. Sources to corroborate the impact

- Ahmed R, Omidian Z, Giwa A, Cornwell B, Majety N, Bell DR, Lee S, Zhang H, Michels A, Desiderio S, Sadegh-Nasseri S, Rabb H, Gritsch S, Suva ML, Cahan P, Zhou R, Jie C, Donner T, Hamad ARA. A public BCR present in a unique dual-receptor-expressing lymphocyte from type 1 diabetes patients encodes a potent T cell autoantigen. Cell. 2019 May 30;177(6):1583-1599.e16. PubMed PMID: 31150624.
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2.4.4 Societal impact: Extending in vivo half-life of IgG therapeutics and albumin fused biologics

Institution: University of Oslo/Oslo University Hospital

Name of SFF: Centre for Immune Regulation

Title of case study: Extending *in vivo* half-life of IgG therapeutics and albumin fused biologics

Period when the underpinning research was undertaken: 2007-2017

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting SFF:
Jan Terje Andersen (PhD 2008)	Postdoc	08.09.08 - 30.11.17
Stian Foss (PhD 2016)	PhD student	01.01.11 - 30.11.17
Algirdas Grevys (PhD 2019)	PhD student	16.08.12 - 30.11.17
Kine MK Sand (PhD 2017)	PhD student	16.08.12 - 30.11.17
Malin Bern (PhD 2017)	PhD student	01.09.13 - 30.11.17
Jeannette Nilsen (PhD 2019)	PhD student	01.01.13 - 30.11.17
Muluneh Daba (PhD 2012)	PhD student	01.01.08 - 01.09.12
Kristin S Gunnarsen (PhD 2012)	PhD Student/Postdoc	29.03.12 - 31.03.15

Period when the impact occurred: 2012-present

1. Summary of the impact

We have revealed the biological mechanism responsible for the long serum half-life of albumin, which is 3-weeks. It is due to binding of albumin to the neonatal Fc receptor (FcRn) which also binds the antibody IgG. FcRn binding rescues both molecules from degradation, while all other serum proteins degrade within hours or a few days. The new knowledge opens new avenues for therapeutic applications of albumin, albumin derivatives and IgG variants. Their long serum half-life allows one to reduce dose size and dosing frequency of biologics, which increase patient compliance and reduce cost.

2. Underpinning research

Most proteins in blood degrade within a few hours or days, but the two most abundant - IgG and albumin - are rescued from degradation and have half-lives of three weeks. The long half-lifes of these proteins come from their binding to FcRn. In our laboratory, we have revealed how binding of these proteins to FcRn regulates their serum half-life and biodistribution via cellular recycling and transcytosis. We have thus obtained fundamental new insight that has tremendous implications for the understanding of the biology of IgG and albumin. As both albumin and IgG are increasingly utilized for medical treatments, this new basic knowledge has paved the way for design of antibody and albumin molecules with tailored FcRn binding and transport properties.

We designed an IgG variant with increased FcRn binding and half-life (*PCT/IB2017/000327*). We found that such engineered IgGs may bind other effector molecules less well, ultimately leading to less induction of effector functions (*Grevys, J Immunol 2015*). Importantly, the variant engineered by us induces effector functions on a level on par with or better than natural, nonengineered IgG molecules.

We have dissected the interaction between FcRn and albumin (*Andersen, Nat Commun 2012*). Studies of the interaction with albumin fused to other protein sequences have then given information on how long half-life can be conferred upon albumin-fused therapeutics *(Andersen, J Biol Chem 2013)*. We have also designed albumin variants with increased binding to FcRn at acidic pH that have increased half-life *(Anderen, J Biol Chem 2014).*

FcRn is expressed intracellularly, and binds IgG taken up by fluid-phase endocytosis. The molecule can then direct monomeric IgG to the surface of the opposite side of the cell (transcytosis) or to the side of entry (recycling). We studied both processes using the natural ligands as well as engineered variants. A new *in vitro* recycling assay designed by us allows us to predict the behavior of designed FcRn-binding molecules *in vivo* in animal models *(Grevys, Nat Commun 2017).* Furthermore, we recently found that albumin is transcytosed efficiently from the apical to the basolateral side (from the outside and into the body). This observation holds great promise for needle free mucosal delivery of albumin-based vaccines and therapeutics *(Bern, J Control Release 2015).* We demonstrate that transport correlates with FcRn binding, and that engineered albumin with improved FcRn binding is transported more efficiently.

FcRn is the only Fc receptor required for transport of IgG across cellular barriers and placenta *(Mathiesen, Blood 2013).* We also have unpublished data demonstrating that IgG is transported in an FcRn-dependent manner across the human placenta, whereas albumin is not, which is in line with a study in humans from 1964 using radioactive ligands.

3. References to the research

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- Bern M, Sand KM, Nilsen J, Sandlie I, Andersen JT (2015). The role of albumin receptors in regulation of albumin homeostasis: Implications for drug delivery. J Control Release. 2015 Aug 10;211:144-62. PubMed PMID: 26055641.
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4. Details of the impact and 5. sources to corroborate the impact

Long serum half-life is important for the therapeutic success of IgG antibodies, and thus, there is an intense interest in increasing the half-life even further. We have designed an IgG variant with increased FcRn binding and extended half-life. It is described in a patent (*PCT/IB2017/000327)* that was recently licensed nonexclusively by *Tillotts Pharma*, a large international drug

development company, for use in therapy against inflammatory bowel disease. Other companies may well sign license agreements with *Inven2*.

Potent broadly neutralizing antibodies (bnAb) can be isolated from individuals chronically infected with HIV. This finding has made the idea of using bnAbs for prevention of infection realistic. Compared to existing prevention products, antibodies are naturally long-acting and the half-life can be extended even longer with FcRn half-life extension mutations such as those designed by us, which can prolong efficacy for up to 3 to 6 months. This combination of higher potency and extended half-life *in vivo* greatly improves the likelihood that bnAbs for prophylaxis can become affordable for global access, particularly in low and middle income countries where HIV infection risk is higher. Specifically, we have obtained *Research Council GlobVac funding* to engineer bnAbs with enhanced breadth and potency and extended half-life. We will also transfer technologies and capabilities to partners to support international collaboration between Norwegian, US, Indian, and sub-Saharan African scientists (Project title: Developing HIV broadly neutralizing antibodies as a prevention product for global access through antibody half-life engineering).

The therapeutic efficacy of small proteins, peptides, and chemical drug candidates is hampered by short serum half-life, which is the main reason why they fail *in vivo*. Thus, strategies to tailor their serum persistence and biodistribution are highly needed. An attractive approach is to link them to albumin, genetically or chemically, and thereby take advantage of the exceptionally long half-life of albumin. Our research has resulted in launching of the Veltis® technology by *Novozymes Biopharma A/S*, where any drug of interest is genetically fused or conjugated to wild type or engineered albumin variants designed by us, that have extended half-life. In 2016, Novozymes separated its albumin activity to form *Albumedix A/S* as an independent pharma company based on our results (*granted patent US 8822417 B2*). Recently, *Novartis* initiated a program to explore our technology across multiple therapeutic areas and against multiple targets.

We also have unpublished data demonstrating that IgG is transported in an FcRn-dependent manner across the human placenta, while albumin is not, which is in line with a study in humans from 1964 using radioactive ligands. This is important, since monoclonal IgGs are increasingly used in therapy, and the fetus may well be exposed when the patient is a pregnant woman. The use of albumin as a fusion partner for antibody fragments and other biologics may be a safer treatment option.

We have found that albumin is transcytosed efficiently from the apical to the basolateral side (from the outside and into the body). This observation holds great promise for needle free mucosal delivery of albumin-based vaccines and therapeutics. The transport efficiency is greatly increased when albumin is engineered for enhanced FcRn binding. We have obtained very encouraging results from studies in mice, where mouse albumin fused to hemagglutinin from Influenza A given intranasally gives complete protection from a deadly dose of the virus (manuscript in revision for Nature Comm).

2.5 CSMN - Centre for the Study of Mind in Nature

2.5.1 Scientific impact: Philosophy without Intuitions

Institution: University of Oslo		
Name of SFF: CSMN		
Title of case study: Philosophy without Intuitions		
Period when the underpinning research was undertaken: from 2009-2012		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): **Herman W. Cappelen**	**Role(s) (e.g. job title): Professor and Research Director, CSMN**	**Period(s) employed by submitting SFF:** **Throughout 2007-2017**
Period when the impact occurred: From 2012 to date		

1. Summary of the impact

This book has established a very specific position in philosophical methodology that revises and criticizes almost all standard positions, and also exhibits the data of philosophical theorizing as nothing special and as continuous with the theoretical parts of science. It generated a lot of international discussion and also through this exhibited new ways in which philosophy is continuous with the scientific enterprise and intellectual pursuit in general.

2. Underpinning research

The standard view of philosophical methodology is that philosophers rely on intuitions as evidence. Herman Cappelen argues and establishes that this claim is false: it is not true that philosophers rely extensively on intuitions as evidence. At worst, analytic philosophers are guilty of engaging in somewhat irresponsible use of 'intuition'-vocabulary. While this irresponsibility has had little effect on first order philosophy, it has fundamentally misled meta-philosophers: it has encouraged meta-philosophical pseudo-problems and misleading pictures of what philosophy is. A correct conception brings meta-philosophy in tune with actual theorizing and opens for easy interaction the epistemology of philosophy and the rest of epistemology.

This book was thus a contribution of great importance for how to conduct philosophical research, and it also reflects the interdisciplinarity of CSMN itself in that it counteracts all thoughts to the effect that there is a kind of evidence for philosophical theories that sets them apart from all other disciplines, and thus stand in the way for intellectual work of the sort CSMN pursued throughout its existence.

The book was as a matter of produced by the CSMN centre of excellence, primarily by Cappelen's own research and his intense interaction with the international community, but also through two different graduate classes taught jointly by Cappelen and Olav Gjelsvik at CSMN, with attendance from several countries, seminars where all the major topics of the book were pursued. There were also several presentations for the centre as a whole, and much interaction and feedback.

3. References to the research

Herman Cappelen,
Philosophy Without Intuitions
Oxford University Press UK
(2012)

Samples of articles with references to this work in major journals:

The Intellectual Given. John Bengson - 2015 - *Mind* 124 (495):707-760.

Gettier Across Cultures. Edouard Machery, Stephen Stich, David Rose, Amita Chatterjee, Kaori Karasawa, Noel Struchiner, Smita Sirker, Naoki Usui& Takaaki Hashimoto - 2015 - *Noûs*:645-664.

Recent Attempts to Defend the Philosophical Method of Cases and the Linguistic Turn. Avner Baz - 2016 - *Philosophy and Phenomenological Research* 92 (1):105-130.

Intuition in Contemporary Philosophy. Jonathan Jenkins Ichikawa - 2016 - In Lisa M. Osbeck & Barbara S. Held (eds.), *Rational Intuition*. Cambridge university Press. pp. 192-210.

Intuitions in Philosophy: A Minimal Defense. David J. Chalmers - 2014 - *Philosophical Studies* 171 (3):535-544.

4. Details of the impact

Cappelen's book identified a major position in a sharp and distinct way. It led to many reviews, meetings, book symposia in major journals in the field of philosophy, among others a symposium at American Philosophical Association's meetings, and a full day seminar at the University of London, at the Institute of Philosophy at the School of Advanced Study in 2013, where more than a hundred philosophers from all over the UK participated.

The research behind the book included major discussions at the centre, two graduate classes, and considerable interaction between centre director Gjelsvik and Cappelen. All graduate students engaged intensely with the claims, and thus almost the whole community of CSMN took part in two years.

The contribution generated much new interest in philosophical methodology, loads of discussions about that, ways of breaking down barriers between philosophy and related disciplines, and also led to a major handbook in Philosophical Methodology published by Oxford University Press in 2016. (The Oxford Handbook of Philosophical Methodology , Edited by Herman Cappelen, Tamar Gendler and John Hawthorne, Oxford University Press, 2016) This handbook is now a major influence in philosophical research, as Philosophy without Intuitions also is.

Philosophy without Intuitions generated symposia in important journals and engaged many major contributors. It has a large number of citations for a philosophy work (philosophy has traditionally few cirations, about the same level as mathematics) . Here are some major book symposia in journals

- The *Philosophical Studies* Symposium, 2014:
    - John Bengson ('How Philosophers use Intuition and 'Intuition'')
    - David Chalmers ('Intuitions in Philosophy: A Minimal Defense')
    - Jonathan Weinberg ('Cappelen between a Rock and a Hard Place')
    - Brian Weatherson ('Centrality and Marginalisation')

- Replies to Weatherson, Chalmers, Weinberg and Bengson:
    - Precis of Philosophy without Intuitions
    - Socratic Knowledge and its Role in Philosophy: Reply to Weatherson
    - Philosophy without Minimal Intuitions: Reply to Chalmers
    - An Enormous Mistake: Experimental Philosophy: Reply to Weinberg
    - On the interpretation of 'Intuition'-talk in Naming and Necessity: Reply to Bengson
- The *Analytic Philosophy* Symposium, 2014:
    - Paul Boghossian ('Cappelen on Intuitions')
    - Brit Brogaard ('Intuitions and Intellectual Seemings')
    - Mark Richard ('Analysis and Intuitions')
- Replies to Boghossian, Brogaard and Richard:
    - Twin Earth and Intuitions: Reply to Boghossian
    - Intuitions and Intellectual Seemings: Reply to Brogaard
    - Conceptual Structure, Indeterminacy, and Intuitions: Reply to Richard

This shows that the impact can be seen in major journals in the field, and that the direct impact in print was especially strong a couple of years after the publication, when this was a focus of many centrally placed researchers. The long-term impact is also seen in many kinds of ways, and can be measured through the increasing number of citations.

5. Sources to corroborate the impact

'This is an engaging and exciting book ... Whether one is convinced by its conclusion or not, Philosophy Without Intutions represents a clear jolt to contemporary metaphilosophical orthodoxy. It is a vivid and powerful call for philosophers to examine their assumptions about philosophy. Anyone interested in the role of intuitions in philosophy or the proper description of contemporary philosophical practice will benefit from studying it.'

— Jonathan Ichikawa in *International Journal for Philosophical Studies*

'If you're interested in the role of intuitions in philosophy, you need to read this book. Even if you're not particularly concerned by this metaphilosophical issue you would probably still benefit from reading this book, for it may well convince you to change the way in which you articulate your arguments and interpret other authors. Cappelen has made an excellent contribution to the ongoing debate over the importance of intuitions in philosophy.'

— Stephen Ingram in *Metaphilosophy*

'Experimental results on the variability and intra-personal instability of philosophical intuitions have recently sparked a lively methodological debate about the reliability of the philosophical method. In his new book, Herman Cappelen argues that this entire debate is

misguided. The reason is simple: philosophers don’t rely on intuitions, so there is no reason for philosophers to worry about their reliability. Cappelen’s case for this claim amounts to one of the most original and well-argued contributions to recent discussions about philosophical methodology. His book should be essential reading for anyone interested in the debate.'

— Kristoffer Ahlstorm-Vij in *Philosophical Quarterly*

 'wonderfully clear ... this is a well-argued, interesting book, challenging contemporary metaphilosophy fundamentally; I highly recommend it.'

— Daniel Cohnitz in *Disputatio*

2.5.2 Societal impact: Health Impact Fund

Institution: University of Oslo		
Name of SFF: CSMN		
Title of case study: Health Impact Fund		
Period when the underpinning research was undertaken: whole duration of CSMN		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): **Thomas Pogge**	**Role(s) (e.g. job title):** **Research Director**	**Period(s) employed by submitting SFF: 2007-17**
Period when the impact occurred:		

1. Summary of the impact

The Health Impact Fund was launched by CSMN at a broadly attended meeting in Oslo 2008 (see annual report 2008). It developed a research-based meta-innovation regarding how innovations are rewarded and incentivized. The conventional method grants innovators a temporary monopoly that enables them to collect licensing fees or larger markups. The proposed alternative allows innovators to register particular innovations for participation in publicly funded reward distributions, based on the assessed impact of their registered innovations, provided they agree to forego said licensing fees and markup, i.e. supply their product at the cost of manufacture and distribution. This model has been developed in detail for the area of pharmaceuticals and has been quite influential there. Pogge obtained a follow-on grant of €2 billion from the European Research Council and is currently negotiating with potential funders (states and foundations) over a much larger pilot project.

2. Underpinning research

The task was to conceive and specify in detail a new international agency – called the Health Impact Fund – that would receive funds form states and other donors as well as product registrations from pharmaceutical innovators. The Health Impact Fund would track the impact of registered products and, each year, distribute a fixed pool of reward money among the registered products according to the health gains each of them achieved. Each product would participate in 10 consecutive reward distributions before going generic.

The Centre research consisted in a thorough sighting of the relevant literature on innovation, pharmaceutical markets, health technology assessment and institutional design. The proposed Health Impact Fund was then conceived and specified on this basis, as part of CSMN's Moral Agency project.

Formulated in the TRIPS Agreement, current rules entitle pharmaceutical innovators to apply for 20-year product patents on their new medicines. Such patents encourage R&D by enabling innovators to charge very large markups on new products during their first few years on the market. But they also have important drawbacks, including:

(1) In a context of high economic inequality, the profit-maximizing price for patented medicines tends to exclude most of the world's poor.

(2) R&D motivated by large patent-protected markups neglects the diseases of the poor and unreasonably encourages the development of me-too products and maintenance drugs.

(3) The present system causes massive waste through patenting, litigation and competitive promotion expenses as well as through deadweight losses and counterfeiting.

(4) Existing patent rewards focus patent holders on promoting sales of their products without regard to whether their use is in the patient's best interest.

While the TRIPS Agreement is all but impossible to replace, we can greatly improve the status quo by creating a complementary reward track. Jointly financed by many countries, the *Health Impact Fund* (HIF) would distribute each year a fixed sum of money among new pharmaceutical products according to their measured health impact that year. Innovators would have the option to register any of their new products with the HIF and would then participate in ten consecutive annual pay-outs. Receiving such payments would be conditional on the innovator's forgoing its ordinary patent-protected markup opportunities by agreeing to sell its product at the lowest feasible cost of manufacture and distribution. The innovator would also agree to its product going generic after expiry of its 10-year reward period. Some main benefits of the HIF would be:

(1) HIF-registered new medicines would be affordable even to poor patients from day 1.

(2) Research into diseases concentrated among the poor would become far more profitable and intensive. Me-too drugs would be rewarded only for incremental health gains; and there would be no premium for maintenance drugs and greatly strengthened incentives for developing new vaccines.

(3) Participating innovators would take care to market registered medicines only to patients who stand to benefit from using them.

(4) Waste and corruption due to patenting, litigation, competitive advertising, deadweight losses, counterfeiting etc. would be massively reduced.

(5) The HIF would collect and analyze great amounts of valuable treatment data that would not merely inform the reward distribution but also greatly improve how well we use our pharmaceutical arsenal.

The HIF would complement existing organizations such as the Global Fund and GAVI by providing to them, at very low prices, the novel medicines and vaccines they need to fight the diseases of the poor most cost effectively.

3. References to the research

Pogge, Thomas and Hollis, Aiden (eds.)
'The Health Impact Fund: Making New Medicines Accessible for All' Report, CSMN, University of Oslo, 2008

"The Health Impact Fund" in Julio Frenk and Steven Hoffman, eds.: **"To Save Humanity": What Matters Most for a Healthy Future** (Oxford: Oxford University Press 2015).
"The Health Impact Fund: Enhancing Justice and Efficiency in Global Health," (the 2011 Mahbub ul Haq Memorial Lecture of the Human Development and Capability Association) in **Journal of Human Development and Capabilities**, 13/4 (November 2012), 537–559 (published online July 16, 2012); reprinted as "The Health Impact Fund: Aligning Incentives" in Jeroen van den Hoven, Seumas Miller and Thomas Pogge, eds.: **Designing in Ethics** (Cambridge: Cambridge University

Press 2017), 95–118; and in Abraar Karan and Geeta Sodhi, eds.: **Protecting the Health of the Poor: Social Movements in the South** (London: ZED Books 2015), 249–276.
"Combating Antibiotic Resistance Through the Health Impact Fund," authored with Kevin Outterson and Aidan Hollis, in Boston University School of Law, **Law & Economics Research** Paper No. 11-30, June 21, 2011; and in I. Glenn Cohen ed.: **The Globalization of Health Care: Legal and Ethical Issues** (Oxford: Oxford University Press 2013), 318–338.
"The Health Impact Fund: How to Make New Medicines Accessible to All" in Solomon Benatar and Gillian Brock, eds.: **Global Health and Global Health Ethics**(Cambridge: Cambridge University Press 2011; new edition 2019), 241–250. Spanish Korean
"New drug development," authored with Steven J Hoffman and Aidan Hollis, in the **Lancet**, Volume 377, No. 9769, p901–902, 12 March 2011.
"The Health Impact Fund: Better Pharmaceutical Innovations at Much Lower Prices" in Thomas Pogge, Matt Rimmer, and Kim Rubenstein, eds.: **Incentives for Global Public Health: Patent Law and Access to Essential Medicines** (Cambridge: Cambridge University Press 2010), 135–154. Spanish
"Incentives for Pharmaceutical Research: Must They Exclude the Poor from Advanced Medicines?" in Roland Pierik and Wouter Werner, eds.: **Cosmopolitanism in Context: Perspectives from International Law and Political Theory** (Cambridge: Cambridge University Press 2010), 106–126.
"The Health Impact Fund and Its Justification by Appeal to Human Rights" in **Human Rights: Normative Requirements and Institutional Constraints**, special issue edited by Andreas Follesdal, Thomas Pogge, and Carol C. Gould of **Journal of Social Philosophy** 40/4 (2009), 542–569. German Chinese Portuguese

4. Details of the impact

Both the research and the impact are ongoing, and the largest impact will or would come if and when we will get up a major pilot of the Health Impact Fund idea. This is currently being discussed with several states and other funders. Past impact – for example on platforms of political parties and on the deliberations of World Health Organisation expert committees was largely mediated through project publications as well as personal appearances at WHO, parliamentary committees, international conferences and so on. Pogge has given well over 100 lectures on the Health Impact Fund idea in just the last 8 years.

The Health Impact Fund proposal is widely known among relevant policy makers, stakeholders and experts and has helped various more limited and typically disease-specific "pay-for-performance" schemes to be tried. The Health Impact Fund proposal is the leading candidate for implementing **delinkage** of the price of pharmaceutical from the fixed cost of R&D. Unlike other proposed schemes, the Health Impact Fund achieves such delinkage though **pull** rather than push funding: innovators do not get money up front in the hope that they will deliver but are rewarded ex post according to the health gains they deliver. We are hoping for vastly greater impact through the currently considered pilot.

German Social Democratic Party, Motion (16 June 2010) "The German Bundestag calls on the Federal Government … to actively support the pilot phase of the HIF under the auspices of the Global Fund, and to financially and actively support and promote the establishment of a HIF, tested through evidenced efficacy." Renewed with Bilateral Support in the Bundestag, 19 May 2015

Liberal (Venstre) Party of Norway (June 2015) "An international Health Impact Fund (HIF) should be established as a supplement to the current patent system. Through HIF pharmaceutical companies can voluntarily register their drugs and commit to making them available at the lowest price against payment of support over ten years from the Fund on the basis of major health impact their drugs have. This gives companies incentives to develop medicines for those with the greatest health needs and not only those with the greatest purchasing power."

Janssen Pharmaceuticals (part of Johnson & Johnson) (letter, Aug 12 2015) "The purpose of this letter is to express the support of Janssen, the Pharmaceutical Companies of Johnson & Johnson, for the proposed Health Impact Fund and miniHIF. … "With sufficient funding, the HIF could be an effective way of stimulating investment from small and large bio-pharmaceutical companies to address the needs of low-income populations. It would align commercial incentives with social goals of reducing excess morbidity and mortality. It could support companies, including Janssen, in their efforts to develop innovative products within a competitive, market-based framework that rewards outcomes. "It would be sensible to test the viability of the HIF approach at a smaller scale. A timelimited 'miniHIF' could demonstrate the responsiveness of firms to competitive performance-based rewards, and could provide a live example of measuring performance in challenging environments. … "We hope to see the miniHIF funded, and would certainly make an effort to participate. We will also be pleased to provide our views on the structure and design details of the miniHIF and to help propagate the project among our peers within industry associations and beyond."

Timespan when these impacts occurred: 2009-19.

5. Sources to corroborate the impact

A google scholar search produces 1008 English publications discussing the Health Impact Fund idea, many of them highly detailed and critical. For instance:

Amisano F, Cassone A, 2011. Economic sustainability of an alternative form of incentives to pharmaceutical innovation. POLIS Working Papers n. 181.

Grootendorst P, 2009. How Should We Support Pharmaceutical Innovation? Expert. Rev. Pharmacoeconomics Outcomes Res. 9(4): 313-320.

Lexchin J, 2010. One step forward, one step sideways? Expanding research capacity for neglected diseases. BMC International Health and Human Rights 10:20.

Longo, CJ, 2011. Encouraging pharmaceutical innovation to meet the needs of both developed and developing countries. International Journal of Development Issues, 10(1): 92- 101.

Pekarsky B, 2010. Should Financial Incentives be Used to Differentially Reward 'Me-Too' and Innovative Drugs? Pharmacoeconomics 28(1): 1-17.

Rubio JC, 2015. Ebola, R&D on Neglected Diseases and the Health Impact Fund. http://ssrn.com/abstract=2663616.

Sakiko Fukuda-Parr and Proochista Ariana "Health Impact Fund – Raising Issues Of Distribution, IP Rights And Alliances" in **Intellectual Property Watch**, September 26, 2011; "A Response

From The Authors Of The Health Impact Fund" in **Intellectual Property Watch**, October 3, 2011.

Timmermann C. 2012. "The Health Impact Fund and the right to participate in the advancement of science." European journal of applied ethics 1, no. 1 (2012).

3 SFF III

3.1 AMOS - Centre for Autonomous Marine Operations and Systems

3.1.1 Scientific impact: An efficient numerical hydrodynamic method for fully-nonlinear analyses in marine technology

Institution: NTNU		
Name of SFF: Centre for Autonomous Marine Operations and Systems – NTNU AMOS		
Title of case study: An efficient numerical hydrodynamic method for fully-nonlinear analyses in marine technology		
Period when the underpinning research was undertaken: 2011-ongoing		
Details of staff conducting the underpinning research from the submitting unit: ??		
Name(s): **Odd Magnus Faltinsen** **Claudio Lugni** **Marilena Greco**	**Role(s) (e.g. job title):** **Professor** **Adjunct Professor** **Professor**	**Period(s) employed by submitting SFF:** **2013-**
Period when the impact occurred: 2014-ongoing		

1. Summary of the impact

Computational Fluid Dynamics (CFD) is becoming popular for simulating marine scenarios with steep waves and violent wave-body interactions (involving e.g. large motions, slamming). However, accurate and feasible fully-nonlinear seakeeping analyses are beyond the state-of-the-art. Without viscous-flow effects, the problem can be solved through a velocity potential satisfying the Laplace equation (LE). With viscous-flow effects, the Projection approach involves a pressure's Poisson equation (PE). The *Harmonic Polynomial Cell* (HPC) and *Generalized HPC* methods provide innovative, efficient and accurate, solutions for LE and PE, respectively. Their combination paves the way for realistic simulations of wave-structure interactions including nonlinear and viscous-flow effects.

2. Underpinning research

The *Harmonic Polynomial Cell* (HPC) method was proposed by Shao and Faltinsen [1]. The fluid domain is divided in overlapped cells, where the velocity potential is expressed as linear combination of Harmonic Polynomials, known solutions of the Laplace equation, leading to a spatial accuracy higher than third order; the global equation system has a sparse matrix and can be solved efficiently. They successfully applied the HPC to relevant 3D fully-nonlinear marine-hydrodynamic problems involving wave-propagation, wave-focusing and wave-fixed body interaction phenomena.

Compared against traditional panel methods, the HPC is i) able to solve large-scale problems, ii) more accurate than and as stable as the low-order panel methods and more stable than high-order panel methods. Therefore, the HPC (combined with a proper time-stepping

scheme) can solve both linear and nonlinear unsteady problems in an efficient, accurate and stable manner. Its key feature of a local analytical representation of the solution is kept in the Generalized HPC method proposed by Bardazzi, Lugni, Faltinsen and co-authors [2], documenting high accuracy and efficiency also for the solution of the Poisson equation and envisaging disruptive solution strategies for the Navier-Stokes (NS) equations of viscous-flow problems.

Ma, Hanssen, Siddiqui, Greco and Faltinsen [3] carried out an in-depth analysis of the HPC's local and global properties in 2D to provide guidance for a rational implementation of the method. Strategies for cell selection and boundary treatment were suggested to minimize error, including concepts like immersed-boundary and overlapping grids not used previously with the HPC. Such concepts are especially useful for modelling complex geometries or deforming boundaries and were compared by Hanssen, Bardazzi, Lugni and Greco [4] to track the free surface, documenting similar performances. The 2D potential-flow HPC method can simulate steep waves even up to the limit of breaking and accurately predict the flow features and local-induced pressures during water-entry of solid objects. In this framework, Wang and Faltinsen showed the importance of dynamic local-grid refinement for accurate and stable solutions (IWWWFB conference, 2018).

Strand and Faltinsen [5] used the HPC in the analysis of closed flexible fish cages (CFFC), which represent an alternative to the net-based fish-farms for limiting fish lice and escapes. A linear mathematical model of a freely-floating 2D CFFC in waves was developed involving HPC solution of the sloshing water inside the cage.

Fredriksen, Kristiansen and Faltinsen [6] coupled an HPC method with a NS solver within a domain-decomposition (DD) strategy to investigate hydrodynamic challenges in moonpool operations. The problem was simplified assuming regular waves interacting with a 2D floating body with a moonpool. In this DD, the two solvers exchange information along a common boundary immersed in water. At IWWWFB conference, 2019, Hanssen, Colicchio and Greco proposed a 2D DD coupling of an HPC method and a NS solver with information exchange through a boundary crossing the free surface.

From these research steps: 1) a fully-nonlinear sea-state analysis with real-time speed and without wave breaking is not a dream anymore and 2) even more realistic scenarios are envisaged through the Generalized HPC method.

3. References to the research

1. Shao, Y.L., Faltinsen, O.M., 2014, A Harmonic Polynomial Cell (HPC) method for 3D Laplace equation with application in marine Hydrodynamics, Journal of Computational Physics, 274, 312-332. DOI: 10.1016/j.jcp.2014.06.021.
2. Bardazzi, A., Lugni, C., Antuono, M., Graziani, G., Faltinsen, O. M., 2015, Generalized HPC method for the Poisson equation, Journal of Computational Physics, 299, 630-648. DOI: 10.1016/j.jcp.2015.07.026.

3. Ma S., Hanssen F-C. W., Siddiqui M.A., Greco M., Faltinsen O.M., 2018, Local and Global Properties of the Harmonic Polynomial Cell Method: In-depth Analysis in Two Dimensions, International Journal for Numerical Methods in Engineering, 113 (4). DOI: 10.1002/nme.5631
4. Hanssen F-C. W., Bardazzi A., Lugni C., Greco M., 2018, Free-Surface Tracking in 2D with the Harmonic Polynomial Cell Method: Two Alternative Strategies, International Journal for Numerical Methods in Engineering, 113 (2). DOI: 10.1002/nme.5615
5. Strand, I.M., Faltinsen, O.M., 2019, Linear wave response of a 2D closed flexible fish cage. Journal of Fluids and Structures. vol. 87. DOI: 10.1016/j.jfluidstructs.2019.03.005.
6. Fredriksen A.G., Kristiansen T., Faltinsen O. M., 2015, Wave-induced response of a floating 2D body with moonpool, Phil. Trans. R. Soc. A, 373, 20140109.

4. Details of the impact

The development on the *Harmonic Polynomial Cell* (HPC) method was initiated at the Marine Technology department within the Centre of Excellence (CoE) for Ships and Ocean Structures (CeSOS) and is continued at NTNU AMOS. The systematic and in-depth fundamental research undertaken at NTNU AMOS has been crucial for 1) the understanding of the HPC properties and of the required cell features for minimizing locally the solution error, for 2) the extension of the method from its standard formulation with boundary-fitted grids to boundary-immersed and multi-grid set-ups, including local dynamic mesh refinement, for 3) the assessment of the method in a great variety of scenarios relevant for marine-hydrodynamic applications, and last but not least for 4) giving visibility of the method in Norway and abroad, maximizing its scientific impact.

Prof. Faltinsen has been and is a crucial actor in the studies carried out and ongoing, and his involvement has accelerated the curiosity and interest on the HPC method worldwide. In addition, the NTNU-AMOS HPC team involves professors affiliated with the CoE, PhD students and post-docs at NTNU AMOS or connected with the CoE through internships, and other national and international collaborators coming from Universities and Research Institutes.

Researchers affiliated with NTNU AMOS have communicated the novelties of the HPC method at the International Workshop for Water Waves and Floating Bodies (IWWWFB), gathering worldwide recognized marine-hydrodynamic researchers and talented PhD students, as well as at the International Conference on Ocean, Offshore and Arctic Engineering (OMAE). NTNU-AMOS researchers also documented many publications in acknowledged journals, such as Journal of Computational Physics (Impact Factor: 2.845, Quartile: Q1), International Journal for Numerical Methods in Engineering (Impact Factor: 2.746, Quartile: Q1), Journal of Fluids and Structures (Impact Factor: 3.070, Quartile: Q1). Thanks to this great effort, the use of the method is spreading in the NTNU AMOS network, in Norway, in Europe and in Asia and its scientific impact is expected to grow along the years. Examples of recent and ongoing HPC investigations in and out NTNU AMOS are given in the following.

At NTNU AMOS, Siddiqui, Greco, Colicchio and Faltinsen weakly coupled the HPC with a Navier-Stokes solver to investigate the hydrodynamics of a damaged ship section with

preliminary results presented at the IWWWFB in 2018. The successful use of HPC for the sloshing of water inside a 2D model of a flexible cage in waves has inspired the ongoing post-doc investigation by Dr. Yugao Shen, with supervision of Greco and Faltinsen, on cylindrical, closed and rigid fish farms in waves. Such fish-farms represent an attractive concept for aquaculture platforms when moving to more exposed sea areas with severe waves and strong current. In his PhD under the supervision of Greco, Lugni and Faltinsen, Ma is using the HPC within a strip-theory plus a lifting-surface theory to investigate fish hydrodynamics.

The new method is also making international waves. Shao, presently associate professor at the University DTU, Denmark, continues his use of HPC method with his students as documented by a publication on the journal *Wave Motion* in 2019, in collaboration with Hanssen from NTNU AMOS. Graziani, professor at the University "Sapienza", Italy, valued the HPC potentialities and supported the development of the Generalized HPC by his PhD student Bardazzi (presently graduated) in collaboration with NTNU AMOS. Robaux and Benoit at the research institute IRPHE and Ecole Central Marseille, France, initiated their own HPC development with preliminary presentation at the IWWWFB in 2018.

The method is also being put to good use in Asia. During his PhD internship at NTNU AMOS, Liang (from Dalian University of Technology) studied the application of a 2D HPC method to singular flows and lifting problems, with supervision of Faltinsen and Shao. Now, he cultivates his interests in the code and in its use at the Technology Centre for Offshore and Marine, Singapore. Wang, presently professor at Harbin Engineering University, China, is still deeply involved in HPC development and its use for complex hydrodynamic problems, as external collaborator of NTNU AMOS affiliated researchers.

Aside from the impact that this method has on research in the university sector, private industry is starting to take note. The classification society DNV GL, partner of NTNU AMOS, has been using HPC in projects supporting industry in obtaining better design loads on marine structures, and they see a great potential for further developing HPC to be an important part of design load methodology in combination with other tools.

5. Sources to corroborate the impact

The novelties and scientific impact of the method are witnessed by the following two prizes and researchers working in institutions outside NTNU AMOS:

1. In 2015, **Arnt Fredriksen** won the prize as "Årets Unge Rådgiver", awarded by the Association of Consulting Engineers (RIF) in Norway. Excerpt from the statement of the jury (translated): "Fredriksen develops things that haven't been there before. He is innovative and has contributed to the development of new tools and standards, among others within current and waveloads" (https://www.ntnu.edu/imt/news2015).
2. In 2017, **Finn-Christian Hanssen** won the Best Paper Award on Marine Hydrodynamics for his paper, Free-surface Tracking in 2D with the Harmonic Polynomial Cell Method: Two Alternative Strategies, which was published in the International Journal of Numerical Methods in Engineering and was co-authored by Hanssen, Bardazzi, Lugni and Greco (https://www.ntnu.edu/amos/newsandevents2017).

3.1.2 Scientific impact: Development of analysis methods for design against accidental ship and iceberg collisions

Institution: NTNU		
Name of SFF: Centre for Autonomous Marine Operations and Systems – NTNU AMOS		
Title of case study: Development of analysis methods for design against accidental ship and iceberg collisions		
Period when the underpinning research was undertaken: 2010-ongoing		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed**
Jørgen Amdahhl	**Professor**	**2010-**
Torgeir Moan	**Professor**	**2010 -**
Martin Storheim	**PhD**	**2011-2015**
Ekaterina Kim	**PhD/Postdoc**	**2011-14/2015-**
Zhaolong Yu	**PhD/Postdoc**	**20114-17/2018 -**
Yanyan Sha	**Postdoc (associated)**	**2015-2019**
Period when the impact occurred: 2013-ongoing		

1. Summary of the impact

Accidental actions like ship collision, fires, explosions, ice impact may have catastrophic consequences in terms of fatalities, pollution or economic damage. It is vital to have safe design of marine and coastal against accidental actions. An important task of AMOS has been to contribute to the development of improved analysis methods ship collisions and iceberg impacts, The forthcoming updated recommended practice for design against accidental actions DNVGL RP-C204 is based on largely based on the results form this activity.

2. Underpinning research

Ship collision with offshore structures has been acknowledged for a long time to be a potentially hazardous event. Present guidelines and methods for design against collision have were basically developed two decades ago and have become partially out-dated due to rapid increase of ship size , the introduction of a variety of bow shapes and ice strengthening. Hence, the requirements in the NORSOK N-003 guidelines: Actions and action effects were significantly enforced, by increasing the standard bow impact energy by a factor of four, refer Moan et. al. [1]

The development of efficient computer algorithms and increase in CPU capacity has enabled enhanced modelling of both the hit structure and the impacting ship, so as to allow for better understanding of the interaction between the ship and the structure, Yu and Amdahl [2]. New impact design curves for various ship bow configurations (including ice strengthened), ship side - and stern structures were generated. A crucial factor in nonlinear finite element analysis is prediction of ductile fracture, which depends on stresses and strains in a localized region: For large-scale analysis of accidental events a coarse shell finite elements mesh must be used to avoid excessive CPU consumption. In collaboration with Prof. Hopperstad in SFI CASA an efficient model coarse elements was developed by Storheim et. al [3].

The structural response to collisions comprises two aspects, local deformation in the contact area as described above and “rigid” body motion of the hull girder. The latter is heavily influence by fluid structure-interaction. It has been difficult to include both effects in one simulation.

Based on linear potential theory a nee model was implemented in the LS-DYNA BY YU ET. AL [4] that takes into account for the frequency dependence of the fluid forces.

Ship collision has also been recognized as a major threat to ultra-long bridges or submerged tunnels (ferry free E39). Collisions with suspension bridges supported by tension-leg towers and pontoon supported floating bridges have been especially addressed. Local damage analysis of bridge girder subjected to forecastle collision was analysed with LS-DYNA by Sha et. al [5]. The predicted local damage was combined with global response analysis with USFOS suing beam elements. The residual strength of deck girder with collision damage has ben assessed for a monotonous single load or cyclic loads during an extreme storm.

Bergybits and growler impacts are of concern for ships and offshore structures navigating or operating in Arctic waters. The work has especially focused on development of continuum mechanics models for ice to so as to allow for studies of ice- structure interaction with LS-DYNA and ABAQUS. A during accidental ice impacts. A laboratory tests test where an ice block was towed into a steel panel of barge type floater was carried out and analysed numerically modelling the fluid as well, refer Song et. al. . [3]. This been done in collaboration with SFI SAMCoT, which partially funded Postdoc E. Kim.

3. References to the research

7. Moan,T., Amdahl,J. and Errsdal, G., Assessment of ship impact risk to offshore structures – New NORSOK N-003 Guidelines, Journal of Marine Structures, 63 (2019) 484-494. DOI: 10.1016/j.marstruc.2017.05.003
8. Yu, Z. and Amdahl, J., 2017, Analysis and design of offshore tubular members against ship impacts. Marine Structures58 (2018), 109-135, DOI:10.1016/j.marstruc.2017.11.004
9. Storheim, M., Alsos, H. S., Hopperstad, O. S. and Amdahl, J., A damage-based failure model for coarsely meshed shell structures, Int. Journal of Impact Engineering 83, (2015) , 59-75 DOI: 10.1016/j.ijimpeng.2015.04.009
10. Yu, Z., Shen, Y., Amdahl, Jørgen. and Greco, M., Implementation of Linear Potential-Flow Theory in the 6DOF Coupled Simulation of Ship Collision and Grounding Accidents. Journal of Ship *Research 60.*(3), *(2016),* 1-26 DOI:10.5957/JOSR.60.3.160012
11. Sha, Y., Amdahl, J. and Liu, K., Design of steel bridge girders against ship forecastle collisions. Engineering structures 196, (2019) 1-14, DOI: 10.1016/j.engstruct.2019.109277
12. Song,M., Kim,E., Amdahl, J., Ma, J. and Huang Y., A comparative analysis of the fluid-structure interaction method and the constant added mass method for ice-structure collisions. Marine Stru*ctures 49 (2016)* 58-75, DOI:10.1016/j.marstruc.2016.05.005

4. Details of the impact

The work on accidental load analysis form ship and iceberg collisions is a continuation of activities prior to the CoE but was substantially enforced in AMOS. Prof. Amdahl is a one of the key persons behind the development of the computer program USFOS, which is a nonlinear software used world wide in the design offshore structures against accidental loads. It is a nonlinear extension of DNVGL's software package SESAM. The results and methods developed by AMOS research staff are continuously being implemented in the software. In the period 2012-2015 Amdahl gave several courses organized by DNVGL Software on accident load analysis and use of USFOS to engineering companies in Europe, Middle East and Far-East Asia.

The design methods adopted for offshore structures has been adapted to and further developed for ultra-long bridges subjected to ship collision. The concept of representing

local force deformation curves, obtained with a detailed ship bow/deck girder model in LS-DYNA ANALYSIS, as nonlinear spring in global response analysis with USFOS based on beam modelling is new, which has substantially increased the realism of the collision simulations.

The research work has been presented in numerous papers in recognized journals as *Marine Structures* (Impact factor 2.87), *Offshore Engineering* (Impact factor 2.73) , *Impact Engineering* (Impact factor 3.12), *Engineering Structures* (Impact factor 3.08).

Amdahl was the official discusser for the report of Committee V.1 Accidental Limit States on 20th Int. Ship and Offshore Structures Congress (ISSC 2018) in Belgium/Amsterdam

Analysis methods for ship collisions are now being extended to fish farms in exposed waters (in collaboration with SFI Exposed) and to floating and bottom supported wind farms. Amdahl and Prof Herve Le Sourne, ICAM, Nantes have initiated a collaboration on *Development of a rapid simulation tool for the analysis of ship / floating offshore wind turbine collisions.* An application for research funds is under evaluation at WEAMEC – West Atlantic Marine Energy Community in France. Postdoc Z. Yu will be involved and 2 students will study the behavior of different floating support structures subjected to collisions in their master thesis in 2020.

Within NTNU AMOS:

In the period 2016-2019 Prof. Amdahl supervised 17 Master students working on ship and iceberg collision problems, thereof 9 theses dealing with ship-bridge collisions and 4 theses on iceberg impacts.

Following the COSL innovator accident wave slamming has become of concern. Most analysis have studied the effect form hydro-elastic point of view, which implies ULS design. In the case of ALS loads, finite deformations should be taken into account. Y. Lu had developed a resistance model for stiffened plating to predict platting damage during collision and explosions. He observed that this model would also be useful for ALS slamming loads. Applying the principles adopted for a hydro-elastic response, a simple closed form solution hydro-plastic behaviour was proposed, which showed good agreement with nonlinear finite element analysis based on ALE method. This work has been published in two-companion papers in *Marine Structures* in 2019.

Inspired by the fracture model developed for collision analysis, PhD Woongshik Nam in collaboration with Hopperstad (SFI CASA) extended the model to account for the ductile to brittle farcture transition, which is essential to control for structures in extremely low Arctic temperatures or exposed to cryogenic spills (LNG). A paper was published in Marine Structures in 2019. Laboratory tests have been conducted to verify the model.

From NTNU AMOS to National Public Road Administrasjon (Statens Vegvesen) NPRA financed the associated postdoc position of Y. Sha. Y. Sha analysed tension leg suspension bridges and floating bridges subjected to ship impact on tower, pontoon and deck girder including residual strength of damaged deck girder subjected to wind and wave forces during storms. Papers were published jointly with NPRA.

From NTNU AMOS to Classification Society DNVGL: DNVGL is a partner of NTNU AMOS. The recommended practice for design against accidental loads, DNVGL-RP-C204, is largely based on the results form the research staff at AMOS and mainly prepared by J. Amdahl. M. Storheim took active part in the DNVGL project for updating the recommended practiseDNVGL-

RP-C208 determination of structural capacity by of nonlinear finite element analysis methods. In 2019 a master student implemented the ice material model developed by AMOS researchers in ABAQUS for DNVGL

5. Sources to corroborate the impact

The novelties and scientific impact of the method are witnessed by the following two prizes and researchers working in institutions outside NTNU AMOS:

1. In 2016, **Ming Song** a visiting PhD student from Dalian University in China won the Moan-Faltinsen Best Paper Award on Marine Structures for award for her paper: A comparative analysis of the fluid-structure interaction method and the constant added mass method for ice-structure collision (https://www.ntnu.edu/imt/news2016). It was co-authored by E. Kim and J Amdahl from NTNU/AMOS

2.In 2018, Postdoc **Zhaolong Yu** won the Moan-Faltinsen Best Paper Award on Marine Structures for award for his paper: Large Inelastic Deformation Resistance of Stiffened Panels Subjected to Lateral Loading (https://www.ntnu.edu/imt/newsandevents) It was co-authored by J Amdahl and Y. Sha from NTNU/AMOS

3.1.3 Scientific impact: Marine robotic platforms – Underwater Snake Robots

Institution: NTNU		
Name of SFF: NTNU AMOS – Centre for Autonomous Marine Operations and Systems		
Title of case study: Marine robotic platforms – Underwater Snake Robots		
Period when the underpinning research was undertaken: 2013 - now		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): **Kristin Y. Pettersen** **Marilena Greco**	**Role(s) (e.g. job title):** **Key scientist/project manager/Prof.** **Key scientist/Prof.**	**Period(s) employed by submitting SFF:** **100% 2013 - 2022**
Period when the impact occurred: 2015 - now		

1. Summary of the impact

The research on underwater snake robots performed in NTNU AMOS has had a considerable impact on science in this area, as it has led to a high number of publications in high-impact international journals and international recognition including a high demand for keynotes and plenary talks at distinguished international conferences. It has also opened up new avenues of research within areas as diverse as ROVs, aerial manipulators, space robots and even underwater computer vision. In the process, NTNU have developed expertise that is leading the international field in underwater robotics research.

2. Underpinning research

To fully understand how to design and control snake robots, we build a mathematical model of the robot. The reason why we need a mathematical model, in addition to building physical snake robots, is that the mathematical model can describe features of all the snake robots in the world, regardless of their size, shape, or whether they move on land or swim in water. By analyzing this mathematical model, we have found inherent properties of snake robots – and biological snakes – and in this way we use mathematics to decode the secrets of nature.

Our first research question: How do we make the snake robot move forward? We could, for instance, observe the terrestrial robot Anna Konda, which was the first water hydraulic snake robot in the world. We made it move using the same undulations that biological snakes use, but despite any undulation the robot would not move forward. Using our mathematical model to analyze this problem, we found that the reason is the smooth surface of Anna Konda. In order for undulations to make the snake robot move forward, the robot needs to have a certain friction property. Specifically, the friction in the sideways direction needs to be much larger than the friction in the lengthwise direction. Biological snakes have this friction property due to their scaled skin, and in water, the hydrodynamic drag forces provide this property also without this kind of scales, because of the long, slender body of the snake. Our analysis of the mathematical model thus told us that in water, undulations *would* make our snake robots move forward.

Knowing then how to make our snake robots move forward, our next research question was: How to make the robots move forward as fast as we would like. How would for instance the choice of amplitude affects the forward speed at of the robot? Would increasing the amplitude make the robot move faster, since it pushes away more water, propelling it forward, or would it make the robot move slower, as it has to move a longer distance from side to side in order to move forward? Again, our mathematical model provided the answer: Our analysis found that

increasing the amplitude will make the robot move *faster*. In fact, doubling the amplitude not only doubles the forward speed, but the speed actually becomes 4 times as fast. Furthermore, we also found a linear relationship between the frequency of the undulations and the forward speed. We also found how the phase shift of the undulations affects the forward speed, making it possible to find the optimal phase shift for any given snake robot, which was seen to depend significantly on the length of the snake. Our analysis furthermore showed that there will be a trade-off between the forward speed and energy consumption of the robot, as was expected, and by analyzing Pareto curves we can find the best set of amplitude, frequency and phase shift, optimizing both the desired forward speed and energy consumption.

Having understood how to make the robot move forward, and with the speed and energy consumption that we wanted, our next research question was: How do we make the robot, not only move forward, but go exactly *where* we want it to be – in other words, how do we make the snake robot follow a given path. To achieve this, we developed a model-based line-of-sight guidance a control law which we could show guaranteed that the path was followed under the condition that the look-ahead-distance is chosen sufficiently large, or else the system becomes unstable. An additional challenge that the snake robot faces when moving in water is the ocean current, which will make the robot drift away from its path if the current has a component in the traverse direction of the path. To address this, we showed that we could extend the line-of-sight control law to autonomously adapt to and handle ocean currents of unknown magnitude and directions, through integral line-of-sight guidance control. This was validated experimentally using our snake robot Mamba. The robot does not need to know which direction the current comes from, or how strong it is, and yet the algorithms that we have built into Mamba notice that something is pushing the robot away from the desired path, and the algorithms automatically adapt the swimming motion to compensate for this, such that the robot still follows the path.

3. References to the research

E. Kelasidi, A.M. Kohl, K.Y. Pettersen, B.H. Hoffmann and J.T. Gravdahl, "Experimental Investigation of Locomotion Efficiency and Path Following for Underwater Snake Robots with and without a Caudal Fin", *Annual Reviews in Control*, Vol. 46, 2018, pp. 281-294. DOI: 10.1016/j.arcontrol.2018.10.001

J. Sverdrup-Thygeson, E. Kelasidi, K.Y. Pettersen and J.T. Gravdahl, "The Underwater Swimming Manipulator - A Bio-Inspired Solution for Subsea Operations", *IEEE Journal of Oceanic Engineering*, Vol. 43, No. 2, 2018, pp. 402-417. DOI: 10.1109/JOE.2017.2768108

E. Kelasidi, P. Liljebäck, K.Y. Pettersen and J.T. Gravdahl, "Integral Line-of-Sight Guidance for Path Following Control of Underwater Snake Robots: Theory and Experiments", *IEEE Transactions on Robotics*, Vol. 33, No. 3, 2017, pp. 610-628. DOI: 10.1109/TRO.2017.2651119

K.Y. Pettersen, "Snake Robots", *Annual Reviews in Control*, Vol. 44, 2017, pp. 19-44. DOI: 10.1016/j.arcontrol.2017.09.006

A. Mohammadi, E. Rezapour, M. Maggiore and K.Y. Pettersen, "Maneuvering Control of Planar

Snake Robots Using Virtual Holonomic Constraints", *IEEE Transactions on Control Systems Technology*, Vol. 24, No. 3, 2016, pp. 884-899. DOI: 10.1109/TCST.2015.2467208

Underwater Manipulator Arm Robot, Kristin Y. Pettersen, Pål Liljebäck, Asgeir Sørensen, Øyvind Stavdahl, Fredrik Lund, J. Tommy Gravdahl and Aksel Transeth, International (PCT) Patent Application, PCT/EP2016/050569

The NTNU AMOS spin-off company Eelume: www.eelume.com

4. Details of the impact

Our research on snake robots is motivated by the nature, and specifically by the mobility of biological snakes. Snakes can move in virtually any terrain; they can traverse highly cluttered environments, slither through narrow spaces, they can climb, and they are excellent swimmers. This mobility is what we want to achieve in our autonomous robots, as it generally supersedes that of legged and wheeled robots. In addition, a snake robot is a manipulator arm that can transport itself, which adds tremendously to its applicability.

Analysis of and control design for snake robots is challenging since these mechanisms are underactuated. Research on snake robots had been conducted for several decades before Pettersen and her group started working on this. The research was, however, for the most part focusing on the mechatronics and empirical studies of biological snakes, and simulations or experiments were the main tools for system analysis and development, and verification of control methods. Pettersen and her group targeted these limitations of the existing literature on snake robots by providing a model-based approach to analysis and control of snake robot locomotion. Using methods from nonlinear analysis and control design, fundamental properties of snake robots´ stability and controllability were analyzed, and control methods achieving control system performance that largely exceeded those of existing literature were developed. The research on snake robots has thus brought the research field of snake robots a significant step forward, by increasing the understanding of the inherent properties of the system and developing new models and control methods that other research groups now base their research on, both for terrestrial and swimming snake robots.

The establishment in 2013 of the CoE Autonomous Marine Operations and Systems (AMOS) was an important factor in shifting the focus of our research to become mainly on underwater snake robots. The underwater environment poses additional challenges both for modelling, analysis and control compared to the land-based case, as the hydrodynamics and ocean current disturbances increase the complexity. Another research problem that arose from this was that snake robots like Mamba cannot stand still in water; they cannot hover. If they stop undulating, the ocean currents will make the robot drift away. Another research question we wanted to pursue was thus: Why not combine the best from biology and nature with the best from technology. Combining the slender and flexible body of snakes with thrusters - giving the robot the ability to hover. This makes the robot able to stand still in water to, for instance, inspect objects and, since it is a manipulator arm, pick something up. Our (still ongoing) research is thus to develop a framework for analysis and control design for this new class of swimming snake robots: The underwater swimming manipulator - aka articulated intervention-AUVs (AIAUVs).

This new class of robots required new mathematical models, and new analysis and control design. Specifically, the addition of thrusters along the body makes the robot-arm redundant, as the many joints and thrusters provide more degrees of freedom than the mission task requires. The motion planning algorithm must thus include redundancy resolution. The methods for motion planning and control of redundant robots in existing literature were developed for fixed-base robots or for floating-base robots with a large base, and because of this they do not work satisfactorily for AIAUVs. This is an active new field of research, which is expected to have a significant impact on the robotics literature on motion planning with redundancy resolution in general. Specifically, the results that we get here are advancing the state of the art of motion planning of floating-base robots, not just for snake robots, but also for ROVs, aerial manipulators, and space robots.

The research also opened up other new research directions, for instance within underwater computer vision: The articulation of the robot, with active joint control, makes it possible to tilt both cameras and lighting. This high-degree-of-freedom motion capability of the flexible body, where the light and cameras can be positioned at different places along the body and can be actively controlled through link motion, makes the AIAUV a unique robotic platform providing a novel tool for active illumination and scene reconstruction. This has the the potential of achieving improved situational awareness for efficient motion planning and subsea exploration, and constitutes a new line of research which is currently being pursued.

By focusing on this area of research, NTNU has taken the field of underwater robotics in a new and promising direction, and in the process, we have become a world leader within research on underwater vehicles.

5. Sources to corroborate the impact

- Quotes from Kongsberg and Equinor press release 2016-04-16 (https://www.kongsberg.com/maritime/about-us/news-and-media/news-archive/2016/collaboration-on-swimming-robots-for-subsea-maintenance):
  - "This partnership offers the chance to bring radical technology to the market, not just in what the Eelume robot can do, but how it does it," says Bjørn Jalving, Executive Vice President Subsea Division at Kongsberg Maritime. "It is a new tool that will enable operators to realise large scale cost savings by introducing new ways of conducting routine tasks and helping prevent unscheduled shutdowns by reacting instantly when required."
  - "Eelume is a good example of how new technology and innovation contributes to cost reduction. Instead of using large and expensive vessels for small jobs, we now introduce a flexible robot acting as a self going janitor on the seabed. To support smaller companies in bringing new technology to the market is an important part of our research portfolio», says Statoil's Chief technology officer Elisabeth Birkeland Kvalheim.
- Quotes from "Revolutionary New Underwater Robot Makes first UK Appearance at Ocean Business": https://www.kongsberg.com/maritime/about-us/news-and-media/news-archive/2017/revolutionary-new-underwater-robot-makes-first-uk-appearance-at-ocean-business

- "In addition to its superior manoeuvrability, Eelume is a highly stable sensor and actuator platform offering unmatched access to underwater structures for diverse operations. The Eelume solution will dramatically reduce costs and the environmental impact associated with having a ship overhead a traditional ROV operation."

- Eelume reshaping underwater operations (video): https://www.kongsberg.com/maritime/products/marine-robotics/autonomous-underwater-vehicles/AUV-eelume/
- Video, made by the oil and gas company Equinor in 2018 shows how the Eelume robot will be used at their subsea oil and gas installations: https://www.equinor.com/en/how-and-why/etv-news/eelume-to-be-piloted-at-aasgard.html Quote: "As autonomous robots enter our subsea operations, they are expected to radically change the way we operate – and potentially also build – our subsea equipment. The Eelume underwater autonomous robot is a NTNU-originated technology supported by Kongsberg Maritime and Equinor, and has been a LOOP project in ETV since 2016. The tests performed at Åsgard will be significant step towards showing the capabilities of a resident underwater drone. In parallel the technology is being further developed to continuously increase capabilities and level of autonomy.
- Video, made by NRK, showing how the Eelume robot was used to find and inspect the Norwegian submarine "Uredd" which disappeared without trace in 1945 and constituted one of the largest Norwegian losses during World War II https://tv.nrk.no/serie/operasjon-muskedunder/sesong/1/episode/3/avspiller -t=52m25s
- This research has gained international recognition, which amongst other is demonstrated by invitations to give keynotes and plenary lectures at key international conferences:

2019 Snake robot control. Plenary lecture at Indian Control Conference (ICC), Hyderabad, India, December 18-20, 2019.

2019 Snake robots moving on land and exploring the oceans. Keynote lecture at IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS), Macau, China, November 4-8, 2019.

2019 Snake robot control. Plenary lecture at the joint IFAC Conference on Control Applications in Marine Systems, Robotics, and vehicles (CAMS) and IFAC Workshop on robot control (WROCO), Daejeon, Korea, September 18-20, 2019.

2018 Underwater Swimming Manipulators. Keynote lecture at the 5th Workshop on EU-funded Marine Robotics and Applications (EMRA'18), Limerick, Ireland, June 12-13, 2018.

2017 Snake Robots: from Biology, through University, towards Industry. Plenary lecture at IFAC World Congress, Toulouse, France, July 9-14, 2017.

2016 Snake Robots – Swimming snake robots – a bio-inspired solution for subsea inspection and intervention. Plenary lecture at IEEE International Symposium on

	Safety, Security, and Rescue Robotics (SSRR), Lausanne, Switzerland, October 23-27, 2016.
2015	Snake Robots – A solution for firefighting, search and rescue, and subsea IMR operations. Distinguished Lectures Speaker at University of Toronto, Canada, October 22, 2015. http://www.ece.utoronto.ca/about/distinguished-lectures/
2014	Swimming manipulators – a bio-inspired underwater robotic solution. Plenary lecture at 10th IFAC Conference on Manoeuvring and Control of Marine Craft (MCMC), Copenhagen, Denmark, August 24-26, 2015.
2013	Snake Robots - From Biology to Nonlinear Control. Semi-Plenary lecture at IFAC Symposium on Nonlinear Control, Toulouse, France, September 4-6, 2013.

3.1.4 Scientific and societal impact: Icing Protection for Unmanned Aerial Vehicles

Institution: NTNU		
Name of SFF: NTNU AMOS – Centre for Autonomous Marine Operations and Systems		
Title of case study: Icing Protection for Unmanned Aerial Vehicles		
Period when the underpinning research was undertaken: Since 2013		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): **Tor Arne Johansen**	**Role(s) (e.g. job title):** **Key scientist/project manager/Professor**	**Period(s) employed by submitting SFF:** **Since 2013**
Period when the impact occurred: Since 2017		

1. Summary of the impact

There was no commercially available technology that could enable unmanned aerial vehicles (UAVs) to operate in icing conditions, which are typical for harsh climate regions throughout significant parts of the world. Icing leads to reduced lift, increased drag, increased weight, and reduced control and propulsion efficiency, where all these factors may compromise the UAV's ability to fly and maneuver. Consequently, UAV operators must either accept the risk of loss of control due to the icing impact, or to keep their UAVs on the ground. Motivated by the need for a solution, AMOS researchers developed the technology needed to make an autonomous electro-thermal control system that can prevent icing, or remove ice inflight by automatically detecting icing and optimizing the operation of the system to minimize energy consumption. This has led to successful proofs of concept in icing wind tunnel experiments, the world's first flights of small UAVs with an icing prevention system, and establishing a spin-off company that is making the technology commercially available. One key impact is increased safety and all-weather capability of UAV operations.

2. Underpinning research

A basic research question that was answered was how does icing impact UAV flight performance, i.e. how stability, lift and drag characteristics are modified by icing. Due to the low air speed of UAVs, the impact of atmospheric conditions and characteristics of the UAV cannot be learned from manned aviation where this problem has been extensively studied. The next research question that was answered was related to the combined thermodynamics of icing and electro-thermal heating together with the aerodynamics that implies significant heat losses. This led to an understanding of how an electro-thermal heating system needs to be designed, considering the physical layout of thin layers of electrically conductive carbon materials on exposed airfoils, the control system and optimization of the electric power and energy consumption. An autonomous control system that can detect icing conditions and actual icing is instrumental to invoke anti- and de-icing control modes to maintain flight safety. Several methods for icing detection have been studied, based on real-time analysis of the electro-thermal control system power and temperature measurements, as well as aerodynamic flight performance data such as angle-of-attack estimation and flight dynamics models. These elements have been combined into a total icing protection system that was proven in several steps in icing wind tunnel tests and flight tests in the field. Another branch of the research was related to flight planning in potential icing conditions, and how to autonomously execute UAV missions while maximizing performance while keeping risk due to icing at an

acceptable level. This research has used AI search methods together with mathematical models of aerodynamics, icing, electro-thermal heating, terrain and atmospheric conditions such as liquid water contents, droplet size, temperature, terrain and wind speed.

3. References to the research

A. Winter, R. Hann, A. Wenz, K. Gryte, T. A. Johansen, Stability of a Flying Wing UAV in Icing Conditions, 8th European Conference for Aeronautics and Space Sciences (EUCASS), Madrid, 2019

R. Hann, K. Borup, A. Zolich, K. Sørensen, H. Vestad, M. Steinert, T. A. Johansen, Experimental Investigations of an Icing Protection System for UAVs, International Conference on Icing of Aircraft, Engines, and Structures, Minneapolis, 2019

R. Hann, A. W. Wenz, K. Gryte, T. A. Johansen, Impact of Atmospheric Icing on UAV Aerodynamic Performance, Workshop on Research, Education and Development of Unmanned Aerial Systems (RED-UAS), Linköping, 2017

K. L. Sørensen, T. A. Johansen, Flight Test Results for Autonomous Icing Protection Solution for Small Unmanned Aircraft, Int. Conf. Unmanned Aircraft Systems, Miami, 2017

K. L. Sørensen, M. Blanke, T. A. Johansen, Diagnosis of Wing Icing Through Lift and Drag Coefficient Change Detection for Small Unmanned Aircraft, Proc. 9th IFAC Symposium on Fault Detection, Supervision and Safety of Technical Processes, Paris, 2015

K. L. Sørensen, A. S. Helland, T. A. Johansen, Carbon Nanotube Based Airfoil Heating System for In-Flight Anti-Icing and De-Icing of UAVs, IEEE Aerospace Conference, Big Sky, 2015

4. Details of the impact

The research leading to the novel UAV icing protection technology involved several elements:

- Fundamental research on icing accretion and active heating thermo- and aerodynamics on airfoils operating at low airspeed; primary researcher has been doctoral candidate Richard Hann at NTNU AMOS.
- Research on inflight icing detection was conducted since 2013 by numerous doctoral and postdoctoral candidates at NTNU AMOS (Andreas Wenz, Kasper Borup, Kim Sørensen, Damiano Rotondo, Andrea Cristofaro) and international collaborators.
- Research on electro-thermal anti- and de-icing was conducted since 2013; primary researcher has been doctoral candidate and later postdoc Kim Sørensen, now CEO of spin-off UBIQ Aerospace AS, but also others such as Richard Hann, Kasper Borup and Artur Zolich has been instrumental in this research.
- Wind tunnel experiments has been conducted to validate the results at LeClerk (New York), Cranfield (UK), VTT (Finland) and NTNU, Trondheim since 2015.
- Flight tests have been conducted in Alaska and Norway, in collaboration between NTNU, University of Alaska Fairbanks, NASA Ames Research Center and NORCE/NORUT Tromsø since 2015.
- Research on route planning for UAVs in icing conditions; primary researchers were doctoral candidates Anthony Hovenburg and Fabio Andrade.

The research activity was directed by Prof. Tor Arne Johansen, one of the key scientists in SFF AMOS. A part of the research was funded by associated projects.

A key step towards commercialization was a FORNY grant given by the Research Council of Norway to NTNU's Technology Transfer Office that has been important to take the technology from TRL 4 or 5 to solutions that can be offered commercially, to establish the spin-off company UBIQ Aerospace, and its business development.

The impact is primarily on the industry and end users. The first commercial pilot project is currently being finalized with a Norwegian UAV manufacturer Maritime Robotics AS. Active collaboration and interaction with industry and end users (such as US Coast Guard, NOAA, NORUT/NORCE, Andøya Space Center, Norwegian Defense, and others) was an important driver for initiating this research, and necessary to validate requirements, ideas and results.

5. Sources to corroborate the impact

https://www.ubiqaerospace.com/

https://www.bloomberg.com/news/articles/2019-06-28/james-murdoch-ventures-into-drone-technology-with-new-investment

https://insideunmannedsystems.com/new-technologies-aid-arctic-operations/

https://robotrabbi.com/2018/08/06/ice/

https://www.tu.no/artikler/da-den-amerikanske-kystvakten-fortalte-at-nedising-av-forerlose-fly-koster-dem-millioner-fikk-kim-en-forretningside/448391

3.2 BCSS - Birkeland Centre for Space Science

3.2.1 Scientific impact: Understanding the Asymmetry of Geospace

Institution: Department of Physics and Technology		
Name of SFF: Birkeland Centre for Space Science (BCSS)		
Title of case study: Understanding the Asymmetry of Geospace		
Period when the underpinning research was undertaken: 2013 - 2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Anders Ohma	**PhD**	**2015- 2018**
Nikolai Østgaard	**Professor**	**2013 ---**
Paul Tenfjord	**PhD/postdoc**	**2013 –**
Jone Reistad	**PhD/postdoc**	**2013 ---**
Karl Magnus Laundal	**Researcher**	**2013 ----**
Period when the impact occurred: January 2019		

1. Summary of the impact

We have presented a paradigm-shift in understanding how auroral asymmetries between the hemispheres are produced (Tenfjord et al., 2015, 2016 and 2018) and also how they are removed (Reistad et al., 2018, Ohma et al., 2018, Østgaard et al. 2018). An AGU press release in January 2019 presented this as a paradigm-shift and was picked up by more than 120 news media all over the world, including the New York Times.

2. Underpinning research

Characterizing and understanding how and why the auroas in the northern and southern hemispheres are not similar has been the focus of researchers from University of Bergen since 2004. It started with a couple of papers describing that auroras were indeed displaced in the two hemispheres (Østgaard et al., 2004, 2005). Another milestone in this research was a paper by Laundal and Østgaard (Nature 2009) that found that the auroras could be not only displaced but completely different in the north and south. This result made it to the front page of Nature July 2009.

A break-through in understanding how the asymmetries is created was presented in three papers by Tenfjord et al.(2015, 2016 and 2018). Here it was shown that it is the asymmetric loading of magnetic pressure and not tail reconnection that is the source of asymmetries. Several features that this new understanding predicts, like asymmetric plasma flows in the ionosphere was shown by Reistad et al., (2016, 2018). The asymmetric current patterns in the two hemsipheres were presented by Laundal et al., 2018.

The two last papers (Ohma et al., 2018 and Østgaard et al. 2018) have applied this understanding and also explained how the asymmetries are removed by tail reconnection, contrary to what many have thought.

Since 2004 this research has led to 4 PhDs, 11 Master´s og 22 publications.

This research has been a truly group effort at BCSS and represents a paradigm-shift in understanding the asymmetric geospace.

3. References to the research

K. M. Laundal and N. Østgaard Asymmetric auroral intensities in the Earth's Northern and Southern hemispheres. **Highlight and Cover in Nature Letters**, Vol. 460, pg. 491-493, doi:10.1038/nature08154, 2009.

A. Ohma, N. Østgaard, J.P. Reistad, P. Tenfjord, K. M. Laundal, K. Snekvik, S. E. Haaland, M. O. Fillingim. Evolution of asymmetrically displaced footpoints during substorms. J. Geophys. Res., doi: 10.1029/2018JA025869, 2018.

N. Østgaard, S. B. Mende , H. U. Frey , T. J. Immel, L. A. Frank, J. B. Sigwarth, T. J. Stubbs. Interplanetary magnetic field control of the location of substorm onset and auroral features in the conjugate hemispheres.
J. Geophys. Res., Vol. 109, No. A7, A07204, 10.1029/2003JA010370, 2004

P. Tenfjord, N. Østgaard, K. Snekvik, K. M. Laundal, J. P. Reistad, S. E. Haaland, S. E. Milan. How the IMF By induces a By component in the closed magnetosphere and how it leads to asymmetric currents and convection patterns in the two hemispheres. J. Geophys. Res, 120, doi: 10.1002/2015JA021579, 2015.

P. Tenfjord, N. Østgaard, R. Strangeway, S. E. Haaland, K. Snekvik, K. M. Laundal, J. P. Reistad, S. E. Milan. Magnetospheric response and reconfiguration times following IMF By reversals. J. Geophys. Res, doi: 10.1002/2016JA023018, 2016.

P. Tenfjord, N. Østgaard, S. Haaland, K. Snekvik, K. M. Laundal,J.P. Reistad, R. Strangeway, S. E. Milan, M. Hesse, A. Ohma. How the IMF By induces a local By component during northward IMF Bz and characteristic timescales. J. Geophys. Res., 123, doi: 10.1002/2018JA025186, 2018.

4. Details of the impact

The results presented by BCSS will impact all research that focuses on understanding how solar disturbances affect the Earth´s near space (geospace). These disturbances are carried by the solar wind, which then affect the geospace. The impact of the research is two-fold: 1) We explain why and how the two hemispheres (north and south) respond differently to solar wind disturbances, and 2) This asymmetric behavior of geospace is the most common state of the system. Any realistic predictions about how solar disturbance affect Earth (also known as Space Weather) must consider the results presented by BCSS, so this affect the entire international Space Science community.

The research was mainly carried out by one of the BCSS research group, which also includes international collaborators (Prof. Steve Milan from the University of Leicester and Dr. Stein Haaland, Max Plank Institute, Germany). The main contributors were: Paul Tenfjord, Nikolai Østgaard, Jone Reistad, Anders Ohma and Karl Magnus Laundal.

Although the research started as early as 2004, the main progress was made from 2015 and onwards. Both observations and modelling have been essential to reach these results.

5. Sources to corroborate the impact

The press release from AGU (January 2019)
https://news.agu.org/press-release/new-study-presents-surprising-explanation-for-differences-in-southern-and-northern-lights/
was picked up by news media all over the world:
https://birkeland.uib.no/media-news-about-the-asymmetric-geospace/

This fall BCSS will give three invited talks on this topic at international meetings (AGU 2019, San Francisco, US, the 14th International Conference on Substorms, 2019, Tromsø, Norway and the 29th Cluster workshop**, 2019, Lanzarote, Canary Islands, Spain).**

To study the asymmetries between hemispheres is a field that myself and our group has raised as a new direction in space physics. This has now led several other groups around the world to also go in this direction. A spacecraft mission concept to study conjugate aurora (with BCSS as Co-Investigators) will be submitted as a NASA MIDEX proposal this fall, and a large collaboration (7 year funding) also with BCSS as Co-Investigators, was submitted to the NASA's DRIVE Center opportunity.

3.2.2 Scientific impact: Building Space Instrumentation to Understanding Hard Radiation from Thunderstorms

Institution: Department of Physics and Technology		
Name of SFF: Birkeland Centre for Space Science (BCSS)		
Title of case study: Building Space Instrumentation to Understanding Hard Radiation from Thunderstorms		
Period when the underpinning research was undertaken: 2013 - 2019		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Nikolai Østgaard	**Professor**	**2013 ---**
Kjetil Ullaland	**Professor**	**2013 –**
Georgi Genov	**Engineer**	**2013 ---**
Shiming Yang	**Engineer**	**2013 ----**
Martino Marisaldi	**Professor**	
Period when the impact occurred: January 2019		

1. Summary of the impact

We have launched the most sophisticated instrument payload, Atmosphere Space Interaction Monitor (ASIM) to date to the International Space Station to study hard radiation from thunderclouds. Based on ASIM data we have shown, for the first time, that the lightning stroke that produces a TGF also produces an Elve (Neubert et al., Science, 2019). Another game-changer was to solve the temporal sequence of lightning leader and TGFs (Østgaard et al. 2019b). This result gives a clear guidance in which direction future TGF research should go. We conducted the first gamma-ray detection from aircraft altitude of 20 km (Østgaard et al., 2019a).

2. Underpinning research

After 14 years (BCSS: since 2013) of design, building, testing and finally integrating the large Modular X- and Gamma-ray Sensor (MXGS) on to the Atmosphere Space Interaction Monitor (ASIM) the successful launch took place on April 2, 2018. This has been the largest space instrumentation project that the Norwegian Academy has taken on. The Norwegian part of the project was approximately 50 MNOK and has given BCSS the expertise to handle future ESA projects as well, bith on the technical part as well as the management part.

After a successful commissioning phase (April – June, 2018), where we figured out how to optimize the performance, ASIM has delivered unprecedented data. ASIM is the first payload specifically designed to measure both optical lightning and Terrestrial Gamma-ray flashes. First results from ASIM were presented as invited talks at AGU 2018 meeting and EGU 2019 meeting, and the first three papers will appear soon (Neubert et al. 2019, Østgaard et al., 2019, Sarria et al., 2019). There are many “first” observations by ASIM, but two of the most significant are: 1) We observe Elves and TGF from same lightning flash about 15% of the TGF events. 3) WE have resolved the sequence of TGF and large current pulse in the lightning leader. This was something we suggested in 2013 (Østgaard et al., 2013), but realized that the temporal resolution of the LIS data, we used then, was not good enough. With the relative timing of the optical instruments and gamma-ray instrument on ASIM (+/- 80 microsecond) we have resolved this. These results have been received by the community with great excitement, and will definitely give a clear direction for current and future TGF research.

3. References to the research

Neubert, T., N. Østgaard, V. Reglero, O. Chanrion, M. Heumesser, K. Dimitriaduo, F. Christiansen, C. Budtz-Jørgensen, I. Kuvvetli, I. Lundgaard Rasmussen, A. Mezentsev, M. Marisaldi, K. Ullaland, G. Genov, S. Yang, P. Kochkin, J. Navarro-Gonzalez, P. H. Connell, and C. J. Eyles. (2019) A Terrestrial Gamma-ray Flash and Ionospheric UV Emissions Powered by a Lightning Discharge, Science, in revision.

Østgaard N., T. Neubert, V. Reglero, K. Ullaland, S. Yang, G. Genov, M. Marisaldi, A. Mezentsev, P. Kochkin, N. Lehtinen, D. Sarria, B. H. Qureshi, A. Solberg, C. Maiorana, C. Budtz-Jørgensen, I. Kuvvetli, F. Christiansen, O. Chanrion, M. Heumesser, J. Navarro-Gonzales, P. Connell, C. Eyles, H. Christian, S. Al Nussirat. (2019b) First ten months of TGF observations by ASIM. J. Geophys. Res., doi: 10.1029/2019JD031214, in revision.

Sarria D., P. Kochkin, N. Østgaard, N. Lehtinen, A. Mezentsev, M. Marisaldi, B. E. Carlson, C. Maiorana, K. Albrechtsen, T. Neubert, V. Reglero, K. Ullaland, S. Yang, G. Genov, B. Hasan Qureshi, C. Budtz-Jørgensen, I. Kuvvetli, F. Christiansen, O. Chanrion, M. Heumesser, K. Dimitriadou, J. Navarro-Gonzales, P. Connell, C. Eyles. (2019) The First Terrestrial Electron Beam Observed by The Atmosphere-Space Interactions Monitor J. Geophys. Res., doi: 10.1029/2019JA027071, in revision.

4. Details of the impact

For TGF research it has been a long-standing question whether TGFs are produced either by the large ambient electric field between two main charge structures in a thundercloud, or in the electric field ahead of a an extended leader channel. Our results definitely show that the electric field ahead of a leader channel plays an essential role in producing TGFs. Consequently, we have given further research a clear direction.

5. Sources to corroborate the impact

The launch of ASIM were covered by more than 400 news media
https://birkeland.uib.no/asim-news/
and the first results from ASIM was featured in a news article in Nature
https://www.nature.com/articles/d41586-019-02181-8

The ASIM team gave three invited talks at the AGU meeting 2018 (Washington DC, US), one at EGU 2019 meeting and press coference (Vienna, Austria), two at the IUGG meeting 2019 (Montreal, Canada) and will give two invited talks at AGU meeting 2019 (San Francisco, US). Five of these invited talks were/will be given by BCSS members.

3.2.3 Societal impact: Space Weather, Climate and Lightning Protection

Institution: Department of Physics and Technology		
Name of SFF: Birkeland Centre for Space Science (BCSS)		
Title of case study: Space Weather, Climate and Lightning Protection		
Period when the underpinning research was undertaken: 2013 - 2019		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Nikolai Østgaard	**Professor**	**2013 ---**
Hilde Nesse Tyssøy	**Researcher**	**2013 –**
Pavlo Kochkin	**PostDoc/Researcher**	**2014 --**
Period when the impact occurred:		

1. Summary of the impact

Although BCSS is a research centre for fundamental science, and the value of the outcome will first and foremost be to move frontiers in our civilization´s understanding of nature and our environment. However, the results we have published will also have societal impact. Our understanding of the asymmetric geospace will have impact on any Space Weather predictions. Our collaboration with climate researchers to address the effects of energetic particle precipitation will have impact on how we understand Climate changes. And finally, our laboratory experiments with aircrafts in high electroc fields will have impact on lightning protection.

2. Underpinning research

As described in more detail in Impact_science_BCSS_1, the paradigm-shift we have presented in understanding how the two hemispheres as well as the entire geospace respond asymmetrically to solar wind forcing is fundamental for making any realistic Space Weather prediction. Space Weather has become an applied physics activity driven mostly by the fact that our civilization is surrounded by sophisticated infra-structure, that can be damaged by solar disturbances that reaches the Earth. This applies to power plants, power grids, spacecraft etc.

Energetic particles can penetrate deep into the atmosphere and deposit their energy down to 60-70 km. It is not well established how this energy deposition is transported by neutral winds to even lower altitudes and affect both temperature and chemistry in the mesosphere. Our collaboration with Bjerknes Centre for Climate Research will resolve this question, and is important for how our Society understand Climate changes in general.

In our research on terrestrial gamma-ray flashes and gamma-ray glows we have initiated and been involved in several aircraft campaigns. As a spin-off from these campaigns we have realized that most of the lightning “hitting” aircraft are indeed initiated by the aircraft itself. In the laboratory we have built an experiment that mimic airacft behavior in thundercloud electric field. The target is to address: How can damage to smaller aircraft from thunderstorms and lightning be minimized? Our research focuses on identifying risk factors and finding ways to prevent damage to both the exterior surfaces of planes and to sensitive on-board electronics.

3. References to the research

Space Weather (see also Impact_science_BCSS_1):

P. Tenfjord, N. Østgaard, K. Snekvik, K. M. Laundal, J. P. Reistad, S. E. Haaland, S. E. Milan. How the IMF By induces a By component in the closed magnetosphere and how it leads to asymmetric currents and convection patterns in the two hemispheres. J. Geophys. Res, 120, doi: 10.1002/2015JA021579, 2015.

A. Ohma, N. Østgaard, J.P. Reistad, P. Tenfjord, K. M. Laundal, K. Snekvik, S. E. Haaland, M. O. Fillingim. Evolution of asymmetrically displaced footpoints during substorms. J. Geophys. Res., doi: 10.1029/2018JA025869, 2018.

Climate:

https://birkeland.uib.no/research/particle-precipitation/

Lightning Protection:

https://birkeland.uib.no/electric-aircraft-lightning-protection-initiative-at-bcss/

4. Details of the impact

The three societal impact cases we have described here are all recent findings, and it is too early to assess in detail the how these results will affect society.

For Space Weather prediction the beneficiaries will be power grid, power plants, space craft etc.

For Climate it is our entire understanding about how Climate changes and what are the importance of various sources that affect climate.

Lightning protection is aircraft industry and operation.

5. Sources to corroborate the impact

Space Weather:

The press release from AGU (January 2019)

https://news.agu.org/press-release/new-study-presents-surprising-explanation-for-differences-in-southern-and-northern-lights/

Climate:

https://birkeland.uib.no/research/particle-precipitation/

Lightning Protection:

https://birkeland.uib.no/electric-aircraft-lightning-protection-initiative-at-bcss/

3.3 CAGE - Centre for Arctic Gas Hydrate, Environment and Climate

3.3.1 Scientific impact: Ice sheet - methane hydrate interactions

Institution: UiT - The Arctic University of Norway in Tromsø

Name of SFF: Centre for Arctic Gas Hydrate, Environment and Climate (CAGE)

Title of case study: Ice sheet - methane hydrate interactions

Period when the underpinning research was undertaken: 2015-present

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by SFF:**
Prof. Karin Andreassen,	Professor, WP leader/SFF Director	2013 – present
Dr Henry Patton,	Researcher	2015 - present
Dr Monica Winsborrow,	Researcher, WP leader	2015 – present
Prof Alun Hubbard	Professor II	2015 – present
Andreia Plaza Faverola	Researcher	2013 - present
Alexey Portnov	PhD student	2012 - 2018
Pavel Serov	PhD student	2015- present
Prof. Jürgen Mienert	Professor/SFF Director	2013 - 2019

Period when the impact occurred: 2015- present

1. Summary of the impact

CAGE ice sheet-methane interaction work has changed understanding of the importance of ice sheets for methane storage and release. Demonstrating that the waxing and waning of ice sheets over glacial cycles fundamentally influences the release of the powerful greenhouse gas methane, the research has highlighted the threat posed by Arctic and Antarctic subglacial methane reservoirs under predicted climatic warming. Publication of multiple articles in high-ranking academic journals has have attracted exceptional interest; as have a series of invited presentations on the topic at national and international conferences. Furthermore, over 33 million NOK has been generated in externally funded projects related to this research.

2. Underpinning research

The powerful greenhouse gas methane can exist as ice-like structures known as gas (methane) hydrates under high-pressure, low temperature conditions. The subglacial environment beneath an ice sheet provides ideal conditions for the formation of extensive and thick reservoirs of hydrate, however their role and significance for global carbon budgets remains as yet undetermined. Since 2015, CAGE has been pioneering research into the storage and release of methane from Arctic subglacial reservoirs over glacial to interglacial timescales. CAGE has the first research group to specifically focus on glaciated regions with thermogenic sources of methane (petroleum systems). This setting has been largely ignored in previous considerations of subglacial gas hydrate, but represents a potentially vast store and source of carbon. Through combined empirical and numerical modelling approaches, this work has for the first time demonstrated the fundamental role that ice sheet advance and retreat plays in modulating methane storage and release from glaciated petroleum systems.

CAGE researchers presented the first study to show the potential for significant gas hydrate storage and release capacity during past glacial/inter-glacial conditions (Portnov et al. 2016).

Key breakthroughs in our understanding of ice sheet-methane interactions relate to understanding the processes and drivers of catastrophic (Andreassen et al. 2017) versus steady (Serov et al. 2017) methane release in response to ice sheet retreat, which are of vital importance for predicting the climatic impact of ice sheet-driven methane release. Further, this research has demonstrated that the regulating impact of ice sheets on methane hydrate storage and release also extends far beyond the glaciated margins in cold water depths > 1000 m (Plaza-Faverola et al. 2015).
In addition to ice sheets influencing methane hydrate, CAGE research has for the first time indicated that the presence of methane hydrate beneath ice sheets exerts a primary control on how this ice mass flows and therefore its stability (Winsborrow et al. 2016). This has important implications for work to predict the flow evolution of the widespread contemporary Antarctic and Arctic ice masses that overlie methane hydrate reservoirs.
Key to CAGE's ice sheet-methane hydrate research has been the development of a high-resolution numerical model reconstruction of the Eurasian ice sheet during the last ice age. The geologically constrained ice model experiments run by Patton and Hubbard, represent a game-changer in our understanding of the glacial history of Eurasia, providing a unique quantitative framework against which to examine the evolution of methane storage and release within the Arctic cryosphere.

3. References to the research

Bold highlight CAGE affiliated co-authors.

Andreassen, K., Hubbard, A., Winsborrow, M., Patton, H., Vadakkepuliyambatta, S., Plaza-Faverola, A., Gudlaugsson, E., Serov, P., Deryabin, A., Mattingsdal, R., **Mienert, J., Bünz, S.**, 2017. Massive blow-out craters formed by hydrate-controlled methane expulsion from the Arctic seafloor. Science 356, 948–953. https://doi.org/10.1126/science.aal4500. Citations (Scopus): 42; Online attention: in the 99th percentile (ranked 1,059th) of the 267,817 tracked articles of a similar age in all journals. Altmetric score 433

Patton, H., Hubbard, A., Andreassen, K., Auriac, A., Whitehouse, P., Stroeven, A.P., **Shackleton, C., Winsborrow, M.C.M.**, Heyman, J., Hall, A.M., 2017. Deglaciation of the Eurasian ice sheet complex. Quaternary Science Reviews 169, 148–172. https://doi.org/10.1016/j.quascirev.2017.05.019. Citations (Scopus): 47; 11th most cited article from QSR since 2016 (buildup paper 10th); peaked 2nd most downloaded article in QSR (now 9th in September 2019)

Serov, P., Vadakkepuliyambatta, S., Mienert, J., Patton, H., Portnov, A., Silyakova, A., Panieri, G., Carroll, M.L., Carroll, J., Andreassen, K., Hubbard, A., 2017. Postglacial response of Arctic Ocean gas hydrates to climatic amelioration. Proceedings of the National Academy of Sciences 114, 6215–6220. https://doi.org/10.1073/pnas.1619288114. Citations (Scopus): 17; Online attention: in the 98th percentile (ranked 4,464th) of the 267,501 tracked articles of a similar age in all journals. Altmetric score 146

Portnov, A., Vadakkepuliyambatta, S., Mienert, J., Hubbard, A., 2016. Ice-sheet-driven methane storage and release in the Arctic. Nature Communications 7, 10314. https://doi.org/10.1038/ncomms10314. Citations (Scopus): 41; Online attention: in the 97th percentile (ranked 4,625th) of the 359,214 tracked articles of a similar age in all journals. Altmetric score 117

Winsborrow, M., Andreassen, K., Hubbard, A., Plaza-Faverola, A., Gudlaugsson, E., Patton, H., 2016. Regulation of ice stream flow through subglacial formation of gas hydrates. Nature Geoscience 9, 370–374. https://doi.org/10.1038/ngeo2696. Citations (Scopus): 15; Online

attention: in the 97th percentile (ranked 6,478th) of the 264,818 tracked articles of a similar age in all journals. Altmetric score 93

Plaza-Faverola, A., Bünz, S., Johnson, J.E., Chand, S., Knies, J., Mienert, J., Franek, P., 2015. Role of tectonic stress in seepage evolution along the gas hydrate-charged Vestnesa Ridge, Fram Strait. Geophysical Research Letters 42, 733–742. https://doi.org/10.1002/2014GL062474. Citations (Scopus): 45; Online attention: in the 96th percentile (ranked 8,137th) of the 268,982 tracked articles of a similar age in all journals. Altmetric score 48

4. Details of the impact

The ice sheet-methane hydrate research of CAGE has generated considerable scientific attention. This is demonstrated by 17 invited presentations on the theme at national and international research conferences since 2015.

CAGE has published a wide body of research relating to this topic in a range of high-ranking international journals including Science, Nature Geoscience, Nature Communications and Proceedings of the National Academy of Sciences of the United States of America (PNAS), since 2015 (see section 3 for a selection of 6 such publications). Despite only being recently published, these articles have already been highly cited. Furthermore, the high media-attention scores (Altmetric) associated with the papers published (section 3) highlight the interest that this topic has generated with the scientific community, with scores between 96th - 99th percentile of similarly aged publications. The conceptual model for km-scale craters on the Barents Sea floor (Andreassen et al., 2017) generated the most significant media coverage, with reports found across 100+ media outlets globally, including interviews with BBC and "America in the Morning – Science Update", and features in the Washington Post, New Scientist and Newsweek

The geophysically constrained ice-sheet modelling has played a key role in helping determine the role of ice sheets in regulating methane release from Arctic marine sectors. This work has attracted wide attention, with articles relating to this being among the most widely downloaded and widely cited from Quaternary Science Reviews. In addition, model results have been adopted by institutions, including GEOMAR to untangle the role of postglacial uplift versus anthropogenic warming for hydrate dissociation during the Late Holocene (Wallmann et al., 2018). This modelling work has also had considerable cross-disciplinary impact outside Norway, with the reconstructed glacial and environmental evolution being utilised in a range of studies in the fields of archaeology, fisheries, oceanography, terrestrial hydrology, geohazards, and climatology.

5. Sources to corroborate the impact

The scientific impact of ice sheet-methane hydrate research carried out by CAGE is corroborated by the numerous externally funded research projects within this field that have been funded. Since 2015, this represents over 33 million NOK.

3.3.2 Societal impact: Ice sheet - methane hydrate interactions

Institution: University of Tromsø – The Arctic University of Norway / Institute of Geosciences		
Name of SFF: Centre for Arctic Gas Hydrate, Environment and Climate - CAGE		
Title of case study: Ice sheet - methane hydrate interactions		
Period when the underpinning research was undertaken: 2015 - present		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Prof. Karin Andreassen, Dr Henry Patton, Dr Monica Winsborrow, Prof Alun Hubbard Andreia Plaza Faverola Alexey Portnov Pavel Serov Prof. Jürgen Mienert	**Role(s) (e.g. job title):** Professor, WP leader/SFF Director Researcher Researcher, WP leader Professor II Researcher PhD student PhD student Professor/SFF Director	**Period(s) employed by submitting SFF:** From 2013
Period when the impact occurred: 2013-2019 and onward		

1. Summary of the impact

CAGE ice sheet-methane interaction work has changed understanding of the importance of ice sheets for methane storage and release. Demonstrating that the waxing and waning of ice sheets over glacial cycles fundamentally influences the release of the powerful greenhouse gas methane, the research has highlighted the threat posed by Arctic and Antarctic subglacial methane reservoirs under predicted climatic warming. Its high relevance for the global community has been communicated to the general public, contributing to the discussion at large regarding climate change and society. These **scientific results have been garnering immense public attention - as has a novel outreach project aimed for school children - creating synergies beyond science.**

2. Underpinning research

CAGE focuses on narrating our results to the general public, industry, stake holders, and media. Communication strategies play an important role in our overall strategy. The research outlined below has been widely communicated to diverse groups, through several projects, in an attempt to contribute scientific input into general discourse on climate change.

The powerful greenhouse gas methane can exist as ice-like structures known as gas (methane) hydrates under high-pressure, low temperature conditions. The environment beneath an ice sheet provides ideal conditions for the formation of extensive and thick reservoirs of hydrate, however their role and significance for global carbon budgets remains undetermined. Since 2015, CAGE has been pioneering research into the storage and release of methane from Arctic subglacial reservoirs over glacial to interglacial timescales. CAGE has the first research group to specifically focus on glaciated regions with thermogenic sources of methane (petroleum systems). This setting has been largely ignored in previous considerations of subglacial gas hydrate, but represents a potentially vast store and source of carbon. Through combined empirical and numerical modelling

approaches, this work has for the first time demonstrated the fundamental role that ice sheet advance and retreat plays in modulating methane storage and release from glaciated petroleum systems.
CAGE researchers presented the first study to show the potential for significant gas hydrate storage and release capacity during past glacial/inter-glacial conditions (Portnov et al. 2016).
Key breakthroughs in our understanding of ice sheet-methane interactions relate to understanding the processes and drivers of catastrophic (Andreassen et al. 2017) vs. steady (Serov et al. 2017) methane release in response to ice sheet retreat, which are of vital importance for predicting the climatic impact of ice sheet-driven methane release. Further, this research has demonstrated that the regulating impact of ice sheets on methane hydrate storage and release also extends far beyond the glaciated margins in cold water depths > 1000 m (Plaza-Faverola et al. 2015).
In addition to ice sheets influencing methane hydrate, CAGE research has for the first time indicated that the presence of methane hydrate beneath ice sheets exerts a primary control on how this ice mass flows and therefore its stability (Winsborrow et al. 2016). This has important implications for work to predict the flow evolution of the widespread contemporary Antarctic and Arctic ice masses that overlie methane hydrate reservoirs.
Key to CAGE's ice sheet-methane hydrate research has been the development of a high-resolution numerical model reconstruction of the Eurasian ice sheet during the last ice age. The geologically constrained ice model experiments represent a game-changer in our understanding of the glacial history of Eurasia, providing a unique quantitative framework against which to examine the evolution of methane storage and release within the Arctic cryosphere.

3. References to the research

Bold highlight CAGE affiliated co-authors.

Andreassen, K., Hubbard, A., Winsborrow, M., Patton, H., Vadakkepuliyambatta, S., Plaza-Faverola, A., Gudlaugsson, E., Serov, P., Deryabin, A., Mattingsdal, R., **Mienert, J., Bünz, S.**, 2017. Massive blow-out craters formed by hydrate-controlled methane expulsion from the Arctic seafloor. Science 356, 948–953. https://doi.org/10.1126/science.aal4500. Citations (scopus): 41; Online attention: in the 99th percentile (ranked 1,059th) of the 267,817 tracked articles of a similar age in all journals. Altmetric score 433

Patton, H., Hubbard, A., Andreassen, K., Auriac, A., Whitehouse, P., Stroeven, A.P., **Shackleton, C., Winsborrow, M.C.M.**, Heyman, J., Hall, A.M., 2017. Deglaciation of the Eurasian ice sheet complex. Quaternary Science Reviews 169, 148–172. https://doi.org/10.1016/j.quascirev.2017.05.019. Citations (scopus): 46; 11th most cited article from QSR since 2016 (buildup paper 10th); peaked 2nd most downloaded article in QSR (today 9th September 2019)

Serov, P., Vadakkepuliyambatta, S., Mienert, J., Patton, H., Portnov, A., Silyakova, A., Panieri, G., Carroll, M.L., Carroll, J., Andreassen, K., Hubbard, A., 2017. Postglacial response of Arctic Ocean gas hydrates to climatic amelioration. Proceedings of the National Academy of Sciences 114, 6215–6220. https://doi.org/10.1073/pnas.1619288114. Citations (scopus): 16; Online attention: in the 98th percentile (ranked 4,464th) of the 267,501 tracked articles of a similar age in all journals. Altmetric score 146

Portnov, A., Vadakkepuliyambatta, S., Mienert, J., Hubbard, A., 2016. Ice-sheet-driven methane storage and release in the Arctic. Nature Communications 7, 10314. https://doi.org/10.1038/ncomms10314. Citations (scopus): 41; Online attention: in the 97th

percentile (ranked 4,625th) of the 359,214 tracked articles of a similar age in all journals. Altmetric score 117

Winsborrow, M., Andreassen, K., Hubbard, A., Plaza-Faverola, A., Gudlaugsson, E., Patton, H., 2016. Regulation of ice stream flow through subglacial formation of gas hydrates. Nature Geoscience 9, 370–374. https://doi.org/10.1038/ngeo2696. Citations (scopus): 15; Online attention: in the 97th percentile (ranked 6,478th) of the 264,818 tracked articles of a similar age in all journals. Altmetric score 93

Plaza-Faverola, A., Bünz, S., Johnson, J.E., Chand, S., Knies, J., Mienert, J., Franek, P., 2015. Role of tectonic stress in seepage evolution along the gas hydrate-charged Vestnesa Ridge, Fram Strait. Geophysical Research Letters 42, 733–742. https://doi.org/10.1002/2014GL062474. Citations (scopus): 16; Citations (scopus): 44; Online attention: in the 96th percentile (ranked 8,137th) of the 268,982 tracked articles of a similar age in all journals. Altmetric score 48

4. Details of the impact

CAGE communications strategy has so far been fruitful - in 2017 alone we have had over 450 media mentions, the majority of them shining a light on our published scientific results. We also moved into the realm of data visualisation for children in 2018 - developing an interactive installation and web page about the Eurasian ice sheet and methane release together with Nordnorsk vitensenter, the science centre in Tromsø. In 2019 CAGE scientists appeared in the new climate change documentary produced and narrated by Leonardo DiCaprio – further extending our involvement in the global discourse on climate and environmental issues.

CAGE aims for high exposure of our results by distributing them through press releases to the general public. This was also the case with the Science paper on massive methane craters in the Barents Sea that was published in May 2017. We provided a content package to the press office at Science - a press release with quotes and several stunning images. All content was developed in-house by our communications advisor and scientists involved in the publication.

Close cooperation with the press office at Science enabled the content to be distributed widely. In turn, this resulted in massive attention, which first author Karin Andreassen was willing to take head on.

Throughout the following year she was interviewed on numerous occasions, and made herself available for journalists and inquisitive peers alike. The effort resulted in over 100 unique news articles published world-wide on abrupt methane release in the Arctic. News outlets as diverse as The Washington Post, The Atlantic and Mashable covered this story.

As far as wider communication of fundamental research goes, the Science paper proved that given the results are of global interest, scientific publications are sound, and scientists are willing to engage with the media, a lot can be gained.

ICEMAP - an innovative take on data visualization for kids

Our second example is something completely different: development of an interactive installation, together with Nordnorsk vitensenter, a science activity centre in Tromsø.

CAGE received funding from the Research Council of Norway's KLIMAFORSK programme in autumn 2016 to develop an interactive map-based story, ICEMAP. ICEMAP is an innovative take on data visualisation, combining a cutting-edge numerical ice-sheet reconstruction with narrative illustrations to convey knowledge about how the complex natural world around us functions, changes and leaves a lasting geological legacy.

It was based on recently published model reconstructions of the last ice age, and two CAGE scientists, Henry Patton and Alun Hubbard, were instrumental in development of the map visualizations.

Throughout 2017 a multi-layered interactive web page - icemap.no - as well as a physical installation at the Science Centre in Tromsø, was developed, together with illustrators, communicators, exhibition and graphic designers, engineers and web developers.

From February 2018, children, teachers and tourists alike could interact with the ice age simulation to explore how the ice sheet grew and melted, and experience how the changing environment around Europe affected our narrator Lenny Lemming, a cartoon avatar that travels through thousands of years of climate change.

ICEMAP has received significant amount of attention, and elements of the exhibition are now being used in a new permanent exhibition at Ulster Museum in Belfast, Northern Ireland. The project was also presented at European Geosciences Union in 2018.

ICEMAP project and overall communication strategy work at CAGE is managed by CAGE senior communications advisor Maja Sojtaric.

The scientific achievements, as well as the focused work towards their visibility in the popular realm, has led to CAGE scientists being contacted to participate in the latest climate change documentary produced and narrated by Leonardo DiCaprio. "*ICE ON FIRE" is a documentary about climate change,* Arctic methane release, and newly developed technologies that could reverse global warming. Scientists from CAGE, among others Pavel Serov, appear in the HBO documentary, which premiered to a standing ovation at Cannes Film Festival in May 2019. The film is aimed at stakeholders, industry and policymakers as well as the general public.

5. Sources to corroborate the impact

Here is a short selection of media impact of the communications strategy at CAGE, specifically targeting the ice sheet and methane hydrate interaction research. The selection has been made from among hundreds of mentions, aimed at demonstrating the wide range of impact, both geographically but also in terms of outlets, that have been including our science in their reporting:

https://www.theatlantic.com/science/archive/2017/06/methane-burps/528654/

https://weather.com/science/environment/news/crater-arctic-ocean-methane-blowout

https://www.nature.com/news/methane-exploded-from-arctic-sea-floor-as-ice-age-ended-1.22095

https://www.washingtonpost.com/news/energy-environment/wp/2017/06/01/like-champagne-bottles-being-opened-scientists-document-an-ancient-arctic-methane-explosion/

https://www.newscientist.com/article/2133397-huge-ice-age-methane-blowout-is-ill-omen-for-glacier-retreat/
https://www.geomar.de/en/news/article/methanhydrataufloesung-vor-spitzbergen-nicht-durch-klimawandel-bedingt/

http://physicstoday.scitation.org/do/10.1063/PT.6.1.20170706a/full/

http://www.vesti.ru/doc.html?id=2895653

https://www.thesun.co.uk/tech/3737295/huge-frozen-domes-hidden-at-the-bottom-of-arctic-sea-could-soon-explode-and-spew-toxic-gas/

https://www.dailymail.co.uk/sciencetech/article-4133888/Stunning-images-reveal-Eurasian-ice-sheet-started.html

https://www.nordlys.no/skole/var/kultur/fredag-apnet-en-ny-attraksjon-pa-et-av-tromsos-mest-populare-aktivitetssentre/s/5-34-786490

https://www.nrk.no/finnmark/ny-forskning_-isstrommene-kan-bremse-opp-1.12907568

3.3.3 Societal impact: Innovation in Monitoring of Marine Methane Release

Institution: University of Tromsø – The Arctic University of Norway / Institute of Geosciences		
Name of SFF: Centre for Arctic Gas Hydrate, Environment and Climate - CAGE		
Title of case study: Innovation in Monitoring of Marine Methane Release		
Period when the underpinning research was undertaken: 2015 - present		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Bénédicte Ferré; Anna Silyakova; Pär Jansson; Knut Ola Dølven; Manuel Moser; Jürgen Mienert	**Role(s) (e.g. job title):** BF: WP leader; AS and PJ: researchers; KOD and MM: PhD students; JM: ex-director and creator of CAGE	**Period(s) employed by submitting** SFF: From 2013
Period when the impact occurred: 2013-2019 and onward		

1. Summary of the impact

Release of greenhouse gas methane from shallow areas of the Arctic Ocean is poorly understood. For the benefit of the society, scientists and innovators need to join forces to provide research-driven innovation and development of monitoring tools. CAGE scientists have contributed to development of world-class sea-floor observatories in collaboration with Kongsberg Maritime ("K-Landers"), as well as development of a new mobile, **high-resolution underwater laser spectrometer in collaboration with the University of Grenoble.** The landers have proven to be of industrial and commercial value, in addition to providing crucial data of scientific significance.

2. Underpinning research

The K-landers seafloor observatories were produced in 2015 after a collaboration between CAGE and Kongsberg Maritime (Frietzek et al., 2016). They were deployed in two intense methane seepage areas offshore Svalbard at 90 and 250m depth, and in the Barents Sea inside a methane-seeping crater (~360m depth). The K-landers record any variation in methane and carbon dioxide emission, along with other parameters such as temperature, salinity, pressure, oxygen, pH and chlorophyll. In addition, a hydrophone records the sounds emitted by the bubbles as they escape the seafloor, and a multibeam echosounder looks at the bubbles and records variation in their frequency and size distribution. It is the first time that such complete observatories have been deployed for one-year of continuous measurement in the Arctic and in the Barents Sea. Deployed three times already offshore Svalbard and in the Barents Sea, these K-Landers provide invaluable information on methane release in relation to surrounding ocean parameters.

The landers themselves are of crucial importance in the development of climate and environmental models that can provide the scientific and technology community with better understanding of gas release. Such models have been used to test the performance of a mobile, high-resolution spectrometer newly developed at University of Grenoble (Jansson et al., 2019b). Most spectrometers that perform these measurements are bulky and usually tested in laboratories. The team in Grenoble has developed a compact laser spectrometer and gas extraction system, which, linked together, can do very fast and precise measurements of methane seeps, emission from which are known to highly variable.

Numerical 1 and 2-dimensional models (Jansson et al., 2019a and b) predicting the fate of free and dissolved gasses help us understand the mechanisms behind their transport from the seabed to atmosphere in order to estimate their impact on the environment. While the 2-

dimensional model (Jansson et al., 2019a) resolves the evolution of dissolved methane in the water column resulting from methane bubble emissions, advection with water currents and diffusion; the 1-dimensional model (Jansson et al., 2019b) resolves interaction between the free and dissolved gas phases and gas propagation toward the atmosphere in aquatic environments. The scientific input from CAGE, provided a strong foundation for the technological development.

3. References to the research

Fietzek, B.P., Sobin J., Kapricheski P., Meyer M., Eftedal T., Nilsen T., Themann S. A modular approach to subsea monitoring. *International Ocean Systems*. 2016. 20(2):6-9.

Jansson, P., Triest, J., Grilli, R., Ferré, B., Silyakova, A., Mienert, J., and Chappellaz, J. High-resolution underwater laser spectrometer sensing provides new insights into methane distribution at an Arctic seepage site. 2019a. Ocean Science, 10.5194/os-15-1055-2019, 15, 4, (1055-1069).

Jansson, P., Ferré, B., Silyakova, A., Dølven, K. O. and Omstedt, A. A new numerical model for understanding free and dissolved gas progression toward the atmosphere in aquatic methane seepage systems. 2019b. Limnol Oceanogr Methods, 17: 223-239. doi:10.1002/lom3.10307

Ferré, B., Dølven, K.O., Silyakova, A., Frank, C., Meyer, M., Themann, S., Mienert, J. A new method for long-term monitoring of Arctic methane release systems – Application offshore NW Svalbard. 2017, Oral presentation at EGU General Assembly 2017-04-23 - 2017-04-28.

Dølven, K.O., Ferré, B. Long-term multi-variable time series of seep sites offshore West Spitsbergen. 2019, Poster presentation at EGU General Assembly 2019-04-07 - 2019-04-12

Moser, M., Bergès, B., Ferré, B. Long-term multibeam monitoring of natural methane seepage offshore Prins Karls Foreland, Svalbard. 2019, Poster presentation at EGU General Assembly 2019-04-07 - 2019-04-12.

4. Details of the impact

The main goal of CAGE is “to study methane release from gas hydrates beneath the Arctic Ocean in order to unveil potential impacts on marine environments and global climate systems”. The scientific community at CAGE has, through research and development efforts, contributed to innovation of high-tech monitoring tools that have multiple uses for both science and industry. The K-Lander seabed observatory is currently the core of the Kongsberg Modular Subsea Monitoring-Network (MSM). With a unique building block concept, the K-Lander mk2 can be customized for a variety of long-term deployments. The modular design, coupled with a self-floating buoyancy based recovery system, allows for easy integration and recovery of various sensors suited for diverse subsea monitoring applications. Trawl proof design, and the fact that the landers have been extensively tested by CAGE in extremely harsh conditions, made these landers commercially viable for Kongsberg Maritime and industry that needs better understanding of subsea gas leaks.

In addition, the modelling efforts related to work with the landers has been instrumental in the development of another high tech, ground breaking monitoring device that will be

commercially available. A collaboration with IGE (Institut des Géosciences de l'Environnement, France) using the 2-dimensional model led to a publication in Ocean Science (see section 3).

Both K-landers and the modelling effort help unravel the conundrum about variations of methane release and provide insights into how much methane can potentially reach the atmosphere. The collaboration with Kongsberg Maritime was successful and led the company to sell the K-lander to international markets in, among others, Japan and Germany. Sören Themann, Vice President of Subsea Monitoring at Kongsberg Maritime, stated that "CAGE has provided the required expertise and guidance for Kongsberg Maritime to make this a success. The K-Lander has collected a complete annual cycle of multi-sensor data from the Arctic Ocean, which sets a new standard for long-term ocean observatories worldwide". Our efforts related to this technology and research are used in large monitoring projects, with external funding providing the opportunity for scientists to further develop landers for multiple uses such as: SIOS-InfraNor - the first major investment in research infrastructure coordinated by SIOS-KC - funded the third K-lander deployment offshore Svalbard on the 90m depth site. This will provide a 3-year long time series, informing us on the inter-annual variation of methane release in the area. Another project, NorEMSO (The Norwegian node for the European Multidisciplinary Seafloor and water column Observatory) has just received funding, with B.Ferré co-leading the project. In this project, a Norwegian node will upgrade, operate and maintain five observation buoys in the Norwegian Sea and the Baltic Sea. One of the goals of this project is to improve models and notification of changes such as methane release, and our expertise will greatly benefit the project. In addition, our experience from the K-landers will be valuable to interpret the data from the newly deployed cabled observatory in the Lofoten-Vesterålen area, within the Infrastruktur-funded project LoVe which we are also part of.
The fields and research groups that benefit this case study are in air and marine research, in particular in geology, biology, oceanography and chemistry. The industry that may benefit from this infrastructure and technology includes technology development. But most importantly, the monitoring will provides us with crucial observational data that will inform environmental models that are of enormous significance for the development of policies to meet climate challenges in the society at large.

The topic is presented at Tromsø University Museum, and results were presented at the international EGU general assembly in Vienna in 2017 and 2019.

Press releases and coverage in relation to CAGE's deployments and recovery:
https://www.huffpost.com/entry/methane-gas-norway_n_56f55632e4b0143a9b4800d9?guccounter=1

https://vimeo.com/136431421
https://www.kongsberg.com/maritime/about-us/news-and-media/news-archive/2015/k-lander-observatories-successfully-deployed-in-the-arctic/
https://www.kongsberg.com/maritime/products/mapping-systems/subsea-monitoring/K-Lander/
https://www.kongsberg.com/maritime/about-us/news-and-media/news-archive/2017/uit-k-lander-recovered/

https://phys.org/news/2016-06-observatories-long-term-greenhouse-gas-arctic.html
https://aliciapatterson.org/stories/methane-arctic-promise-and-peril
https://www.newsdeeply.com/arctic/articles/2016/03/25/the-icy-fire-beneath-norways-seabed

Other press release related to the K-lander:
https://www.marineinsight.com/shipping-news/innovation-meets-new-modular-design-kongsberg-k-lander-mk2-seabed-observatory/
https://www.spe.org/en/jpt/jpt-article-detail/?art=766
https://www.simrad.no/www/01/nokbg0238.nsf/NewsPrintKM?ReadForm&cat=2C98EFDFF0EF4960C1257E13004BC2BB
https://www.offshorewind.biz/2014/09/24/kongsberg-maritime-awarded-for-its-contribution-in-field-of-subsea-monitoring/
http://www.intoceansys.co.uk/articles-detail.php?iss=0000000053&acl=0000000476

3.4 CBD - Centre for Biodiversity Dynamics

3.4.1 Societal impact: Generic ecological impact assessments of alien species

Institution: Norwegian University of Science and Technology		
Name of SFF: Centre for Biodiversity Dynamics		
Title of case study: Generic ecological impact assessments of alien species		
Period when the underpinning research was undertaken: 2010–2017		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Hanno Sandvik	**Role(s) (e.g. job title): Researcher**	**Period(s) employed by submitting SFF: 2010–2017**
Period when the impact occurred: 2012 and onwards		

1. Summary of the impact

This project has developed the methodology for ecological impact assessments of alien species. The method has been applied to alien species in Norway (twice, in 2012 and 2018) and in Sweden (2018). The resulting listings have had a huge impact on the management of alien species in Norway, as the impact assessment are used as an important tool for the prioritisation of management efforts.

2. Underpinning research

The project consisted of several phases. During the first phase (2010–2012), a framework for the ecological impact assessment of alien species was developed. The guiding principles were that the assessment should be testable and generic (i.e. equally applicable to animals, fungi and plants; terrestrial, freshwater and marine species; established species as well as door-knockers). The result was a set of criteria that quantified the ecological effect of species using six criteria, and the invasion potential of alien species using an additional three criteria. During this phase of the project, Tomas Holmern, Bernt-Erik Sæther, Jarle Tufto and Steinar Engen of CBD were involved. Somewhat later, Hanno Sandvik succeeded Tomas Holmern in leading this research, and the results were published in 2013 [1].

The second phase of project started after the first large-scale application of the method (see section 4 below), and lasted from 2014 to 2017. It consisted, first, of a revision the set of criteria based on the experience collected [5]. Most criteria underwent only minor changes, whereas expansion speed was developed as a novel indicator of the speed with which an alien species increases its area of occupancy [7]. Second, two **R** applications were developed as a tool for experts carrying out impact assessments. One of these estimates the population lifetime of a species, based on demographic parameters [3]; the other one estimates expansion speed based on spatiotemporal data on observations of a species [4]. Third, CBD was more heavily involved in defining the delimitations of assessments, so as to ensure a coherent set of guidelines for which species to assess [2,5,6].

3. References to the research

[1] **Sandvik H**, **Sæther B-E**, **Holmern T**, **Tufto J**, **Engen S**, Roy HE (2013) Generic ecological impact assessments of alien species in Norway: a semi-quantitative set of criteria. *Biodiversity and Conservation* **22**:37–62. DOI: 10.1007/s10531-012-0394-z

[2] **Sandvik H**, Gederaas L, Hilmo O (2017) *Guidelines for the generic ecological impact assessment of alien species*. Trondheim: Norwegian Biodiversity Information Centre. URL: https://artsdatabanken.no/Files/21160

[3] **Sandvik H** (2017a) LIFETIME (R program, version 1.6). Trondheim: CBD. URL: http://r.evol.no/liti

[4] **Sandvik H** (2017b) EXPANSION (R program, version 2.5). Trondheim: CBD. URL: http://r.evol.no/expa

[5] **Sandvik H**, Hilmo O, **Finstad AG**, Hegre H, Moen TL, Rafoss T, Skarpaas O, Elven R, Sandmark H, Gederaas L (2019a) Generic Ecological Impact Assessment of Alien Species (GEIAA): the third generation of assessments in Norway. *Biological Invasions* **21**:2803–2810. DOI: 10.1007/s10530-019-02033-6

[6] **Sandvik H** et al. (2019b) Alien plants, animals, fungi and algae in Norway: an inventory of neobiota. *Biological Invasions* **21**:2997–3012. DOI: 10.1007/s10530-019-02058-x

[7] **Sandvik H** (2020) Expansion speed as a generic measure of spread for alien species. *Acta Biotheoretica* **68±1**:in press. DOI: 10.1007/s10441-019-09366-8

4. Details of the impact

The research at CBD was done in close co-operation with the Norwegian Biodiversity Information Centre (*Artsdatabanken*; hereafter NBIC), a governmental body that serves as a national source of information on species and ecosystems in Norway, and aims at making information on biodiversity widely available and easily accessible to the society. Among other activities, NBIC is responsible for carrying out impact assessments of alien species. CBD has not been directly involved in assessing specific species, but has provided the entire theoretical background for these impact assessments. The first milestone was thus the application of the set of criteria to 1383 alien species in Norway, which resulted in a "Black List" published in 2012 [8].

This Black List was used by Norwegian management authorities (especially the Norwegian Enviroment Agency [*Miljødirektoratet*] and the county governors [*fylkesmenn*]) as one of the main information sources when prioritising management efforts. Feedback from these end-users was also incorporated when CBD revised the set of criteria and the method. The revised method was applied to 1532 alien species in Norway, and resulted in an updated "Alien Species List" [9]. During the intervening years, alien species had experienced an explosive increase in interest by the public, due, among other factors, to the NBIC assessments. When the revised list was launched early in 2018, interest was enormous (see section 5 for some examples [10–14]). There is now a broad understanding in the Norwegian public that alien species pose a problem, and NBICs assessments are widely accepted as the best available source of knowledge about the ecological risks attached to the specific species. Of course, most of the coverage was concerned with the results of the assessments rather than its methodology (i.e. they did not mention CBD, but rather quoted NBIC's Alien Species List, which of course acknowledges CBD [15]).

In parallel with these developments in Norway, CBD's method also received some international interest. Swedish management authorities (the Swedish Environmental Protection Agency [*Naturvårdsverket*] and the Swedish Agency for Marine and Water

Management [*Havs- och vattenmyndigheten*]) decided to use "the Norwegian method", and in 2018 the Swedish Species Information Centre (*ArtDatabanken*) published an impact assessment of 1033 alien species in Sweden [16], which was based on CBD' set of criteria. Furthermore, in a comparative investigation of different alien species assessment schemes [17], CBD's method turned out to be the method with highest repeatability (lowest variance across investigators).

5. Sources to corroborate the impact

[8] The first application of CBD's method to alien species in Norway:
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Fylkesmannen i Nordland (2018) Den nye Fremmedartslista 2018. URL: https://www.fylkesmannen.no/nn/Nordland/Miljo-og-klima/Naturmangfald/Fremmede-arter/Fremmedartslista-2018/

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[13] Example of coverage by Norway's public broadcasting company:
Hansen ET (2018) Advarer mot hagerømlinger. NRK: 16. juli 2018. URL: https://www.nrk.no/vestfold/advarer-mot-hageromlinger-1.14114074

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Strand M, Aronsson M, Svensson M (2018). Klassificering av främmande arters effekter på biologisk mångfald i Sverige – ArtDatabankens risklista. *ArtDatabanken rapporterar* **21**:1–45. URL: https://www.artdatabanken.se/publikationer/artdatabanken-rapporterar/frammande-invasiva-arter/

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3.5 CCBIO - Centre for Cancer Biomarkers

3.5.1 Scientific impact: Repurposing identified new molecular target and mechanism of old drug

Institution: University of Bergen

Name of SFF: Centre for Cancer Biomarkers (CCBIO)

Title of case study: Repurposing identified new molecular target and mechanism of old drug.
(Qu Y, Olsen JR, Yuan X, Cheng PF, Levesque MP, Brokstad KA, Hoffman PS, Oyan AM, Zhang W, Kalland KH, Ke X. Small molecule promotes β-catenin citrullination and inhibits Wnt signaling in cancer. Nat Chem Biol., 2018; 14:94-101.)

Period when the underpinning research was undertaken: *2014 - 2017*

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Yi Qu	Postdoc	01.07.16-31.12.16
Xisong Ke	Senior Researcher	01.05.13 – 31.03.17
Karl-Henning Kalland	Professor, PI	2013-Present
Jan Roger Olsen	PhD Student	01.08.14 – 31.08.16
Weidong Zhang	Researcher	

Period when the impact occurred: *2018 – 2019*

1. Summary of the impact

A screening strategy to examine if drugs already in use for different disease conditions can be identified and developed to new cancer therapy. A compound previously used to treat parasitic infections was shown to attack mechanisms that promote cancer cells. A series of experiments identified the molecular target of the compound in cells and the molecular mechanisms. The work consequently was published in a high impact international journal and received considerable attention in publications by others and in the scientific news media. Follow-up work examines the potential use in cancer immunotherapy and combination therapy.

2. Underpinning research

Repurposing represents a drug discovery strategy where an already approved drug, *e.g.* by the US Food and Drug Administration (FDA), is developed for new indications through discovery of new therapeutic targets. The idea is that drugs already in use for a certain disease conditions could have additional unknown attributes that could be exploited for different diseases, *e.g.* cancer. FDA-approved drugs have the advantage that much information is available regarding their absorption and distribution in the body and they have been thoroughly tested for adverse effects. It is a very common problem that newly discovered compounds that show promising effects when tested in cell culture, fail during subsequent testing due to toxic effects in the body or because it turns out to be difficult to achieve therapeutic concentrations in cancer cells within the body. Most FDA-approved drugs have already performed well regarding general toxicity and distribution and consequently have advantageous starting points in drug development.

The repurposing drug screening strategy was used to test around 600 hundred different FDA-approved drugs for their ability to inhibit a cellular protein called beta-catenin. Over-activation of beta-catenin happens in subgroups of many cancers and increasingly as cancer progresses. Beta-catenin is important in cancer stem cells, a small subpopulation among the bulk of cancer cells. Cancer stem cells have specific resistant abilities against chemotherapy and radiation therapy, and

although they may contribute to only a minute portion of any tumor, cancer stem cells are the ones that re-generate the tumor following apparently efficient therapy. For these reasons there is broad interest in beta-catenin inhibitors as new cancer drugs.

Several candidate compounds were identified in the high throughput strategy using a luciferase reporter system in multiwell format. Researchers Yi Qu and Xisong Ke in Professor Karl-Henning Kalland's research group, showed that a drug known as *nitazoxanide*, previous used against parasitic infections, inhibited tumor formation in mice. Beta-catenin was inhibited in tumors of treated animals. In a series of experiments that have been referred to as "an elegant study" in a review paper of the field, Ke and Qu went on to identify the enzyme PAD2 as molecular target of nitazoxanide in cancer cells. A method that stabilizes the molecular target when it binds to a drug was used to identify cellular proteins that bind nitazoxanide. Additional experiments by Ke and Qu showed that nitazoxanide stabilized the enzyme PAD2 and this enzyme next modified beta-catenin by a process called citrullination that next led to proteasome-mediated degradation of beta-catenin.

In summary, the discoveries comprise the new drug action of nitazoxanide, the identification of a novel molecular target and novel beta-catenin regulatory mechanisms. The current status is that nitazoxanide represents a leading compound for further development. The new mechanisms are pursued for dual cancer treatment strategies that take into consideration both the cancer cells and the immune responses in the tumor microenvironment that seeks to destroy cancer cells. This is due to the observation that aberrant beta-catenin activation both stimulates cancer cells and inhibits the immune system's key antigen-presenting dendritic cells.

3. References to the research

1. Qu Y, Olsen JR, Yuan X, Cheng PF, Levesque MP, Brokstad KA, Hoffman PS, Oyan AM, Zhang W, Kalland KH, Ke X. Small molecule promotes β-catenin citrullination and inhibits Wnt signaling in cancer. Nat Chem Biol., 2018; 14:94-101.

2. Yuzhalin AE. Citrullination in Cancer. Cancer Res. 201979(7):1274-1284.
3. Grainger S, Willert K. Mechanisms of Wnt signaling and control. Wiley Interdiscip Rev Syst Biol Med.; 2018:e1422.
4. Goldsberry WN, Londono A, Randall, TD, Norian La, Arend RC. A Review of the Role of Wnt in Cancer Immunomodulation. CANCERS, 2019;11:771 – 790.
5. Wang B, Tian T, Kalland KH, Ke X, Qu Y. Targeting Wnt/β-Catenin Signaling for Cancer Immunotherapy. Trends Pharmacol Sci., 2018; 39:648-658.
6. Albuquerque C, Pereira LP. Wnt Signalling-Targeted Therapy in the CMS2 Tumour Subtype: A New Paradigm in CRC Treatment? TARGETED THERAPY OF COLORECTAL CANCER SUBTYPES, 2018 Book Series: Advances in Experimental Medicine and Biology, 2018; 1110: 75-100.

4. Details of the impact

Several hundred drugs that are approved for different disease conditions were screened in order to find inhibitors of a signal pathway that is often aberrantly over-activated in cancer cells. The screening identified the drug nitazoxanide. This is a drug that has been used for a long time to treat infections with parasites in humans and animals. It has not been known previously that this drug could inhibit a protein called beta-catenin. If beta-catenin becomes too active, it may go into the nucleus of cancer cells and activate their genome to produce components that promote cancer progression. Tests in a mouse strain that spontaneously develops tumours, showed that nitazoxanide could reduce tumor development and that beta-catenin activity was reduced in the tumors of treated animals. Researchers Yi Qu and Xisong Ke consequently undertook experiments to find out how nitazoxanide worked. After a series

of experiments, the result was that nitazoxanide led to reduced levels of beta-catenin in the tested cancer cell type. Qu and Yi and the PhD student, Jan Roger Olsen managed to find the mechanisms for this effect. Nitazoxanide binds to several proteins in the cell and one of those proteins was an enzyme that modifies proteins by a process called citrullination. Nitazoxanide strengthened that enzyme, PAD2. PAD2 modified beta-catenin by citrullination. Citrullination made beta-catenin susceptible to degradation in the cell with consequent reduced beta-catenin activity.

These discoveries on nitazoxanide and the identification of its molecular target and its mechanism to inhibit cancer cells were published in the "high impact journal" *Nature Chemical Biology* in 2018 following several rounds of evaluation by 4 different experts or "peer reviewers". The requests to perform additional experiments before publication improved the work.

Most scientists want to have their work published in "high impact journals". The grading of "impact" is based upon the extent to which publications in that journal have been cited by other scientists in previous years. The impact factor reflects the potential visibility of the publication to the scientific community and consequently new publications in high impact journals represent a recognition of the value of the work according to peers.

The attention and interest of a publication may be at different levels. At the time of this writing the paper in Nature Chemical Biology by Yi Qu, Jan Roger Olsen and collaborators has been cited 18 times by other peer reviewed journals registered in the database PubMed that features only scientific and peer reviewed journals. In addition to focused research articles, PubMed also lists review articles that regularly are published to summarize the history and recent progress of a field. The Nature Chemical Biology paper has been cited in review publications, *e.g.* by Yuzhalin AE: "…..Further, colony growth assays suggested that PAD2-mediated citrullination of beta-catenin could limit the proliferation of colon cancer cells by inhibiting the Wnt pathway. As a result, this elegant study uncovered a hitherto unrecognized mechanism of Wnt signaling inhibition via PAD2."

A different type of recognition of a scientific publication is that key findings and anticipated impact are commented on by the editors of a journal in "editorial comments". This is exemplified by the journal Cancer Discovery, an international scientific commentary journal with a high "impact factor". According to the editorial of Cancer Discovery the significance of the present work is the following: "**Major finding:** The antiparasitic drug NTZ inhibits WNT signaling and *APC*-mutant colorectal cancer cell growth. **Mechanism:** NTZ stabilizes PAD2, which promotes β-catenin citrullination and turnover, to block WNT signalling. **Impact:** NTZ may effectively inhibit WNT signaling to treat patients with WNT pathway–mutant tumors."

A next line of attention is that popular science news media feature the findings and often present their interpretation and anticipation. The present work was broadly covered by multiple international sources, *e.g.* in the USA, Europe and China, in addition to Norway. One result of this attention is that we have been contacted by patients worldwide as a reflection of unmet needs in cancer therapy. We have been very clear that nitazoxanide is not yet any

therapeutic alternative, and it has been clearly communicated to all patients that they follow the advice of their doctors and oncologists regarding documented and available therapy.
The findings are currently followed up with examination of panels of chemically modified compounds of nitazoxanide in order to increase potency and specificity as we found that nitazoxanide bound to different molecular targets in the same cell. We also test the effect of nitazoxanide and the discovered mechanisms on cells of the immune system. Our group conducts clinical trials based on immunotherapy and currently investigates if nitazoxanide and the uncovered mechanisms can be used to enhance cancer immunotherapy and combination therapy.

5. Sources to corroborate the impact

1. NTZ Increases β-catenin Citrullination to Suppress WNT Signaling. **Research Watch Cancer Discovery**
2. Nelson, B. The Curious Case of Repurposed Remedies CANCER CYTOPATHOLOGY Volume: 126 Issue: 8 Pages: 509-510
3. Yuzhalin AE. Citrullination in Cancer. Cancer Res. 201979(7):1274-1284.
4. Huang, P, Yan, R, Zhang, X et al.PHARMACOLOGY & THERAPEUTICS, 2019; 196: 79-90.
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6. https://forskning.no/2017/11/bendelorm-kur-bekjemper-prostatakreft/produsert-og-finansiert-av/universitetet-i-bergen
7. https://www.medicalnewstoday.com/articles/320085.php

3.5.2 Scientific impact: Targeting AXL receptor tyrosine kinase to improve cancer therapy

Institution: University of Bergen

Name of SFF: Centre for Cancer Biomarkers, CCBIO

Title of case study: Targeting AXL receptor tyrosine kinase to improve cancer therapy

Period when the underpinning research was undertaken: 2013-2019

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
James Lorens, PhD	Professor, PI	2013-19
Agnete Engelsen, PhD	Postdoc	2014-19
Sebastian Bougnaud, PhD	Postdoc	2014-17
Bjørn Tore Gjertsen, MD PhD	Professor, PI	2013-19
Oddbjørn Straume, MD PhD	Professor, PI	2013-19
Lars A. Akslen MD PhD	Professor, Director of CCBIO	2013-19
Rolf Brekken, PhD	Professor, adjunct	2014-19
Mark LaBarge, PhD	Professor, adjunct	2014-19
Jean Paul Thiery, PhD	Professor, adjunct	2016-19

Period when the impact occurred: 2017-2019

1. Summary of the impact

In spite of the advances in cancer treatment most patients will fail current therapies and will not experience lasting benefit. A key driver of treatment failure is resistance factors in the tumor microenvironment that mediate acquired drug resistance. Deeper understanding of the underlying molecular mechanisms of acquired therapy resistance and new precision medicine concepts that target these mechanisms are required to meet this major health challenge. Translational research at CCBIO identified the AXL receptor as a key mediator of acquired resistance in cancer. By uncovering the molecular mechanism of AXL regulation of the tumor microenvironment, in concert with combination clinical trials with AXL targeting agents, a new paradigm to improve cancer treatment has emerged.

2. Underpinning research

The confounding reality for cancer treatment is the astonishing heterogeneity of tumors; the result of physiological forces acting on genetically unstable tumor cells during cancer progression. The breakdown of normal tissue architecture by a growing tumor exposes cancer cells to numerous biophysical and metabolic challenges such as oxygen and nutritional deprivation and an altered microenvironment. Gene mutations are manifested as neo-antigens that can elicit an adaptive immune response and the extent of T-cell infiltration into the tumor microenvironment correlates with patient responses to all classes of anti-cancer therapy. The recent advent of immunotherapies target immune checkpoint proteins (e.g. programmed death-1 (PD-1) receptor and its ligand PD-L1) that restrain pre-existing T-cell-mediated immunity in tumors. In response, tumor cells trigger tissue damage repair (wound healing) processes that recruit protective anti-inflammatory stromal and immune cells that block immune editing and promote tumor cell survival. In particular, tumor epithelial-to-mesenchymal transition (EMT), a phenotypic plasticity program associated with wound healing, is a critical driver of acquired drug resistance and is a strong predictor of poor clinical outcome.

We discovered that the AXL receptor tyrosine kinase (RTK) is an essential regulator of tumor EMT, acquired drug resistance, and the anti-tumor immune response. Although seldom mutated, AXL expression in tumors is a remarkably universal poor prognostic factor for patient outcomes. Targeting AXL blocks EMT, reverses drug resistance and prevents metastasis in several different tumor models (e.g. myeloid leukemia, breast, lung, kidney, pancreatic cancer). AXL is also a critical negative regulator of innate immune cell responses and is expressed by suppressive myeloid (M2 macrophages, MDSC) and tolerogenic dendritic cells in the tumors. Our recent results show that small molecule AXL inhibition improves chemo- and immunotherapy efficacy by blocking both tumor EMT and immune suppressive cell mechanisms in the tumor microenvironment. These results are translated into 8 phase II clinical trials worldwide that are evaluating new cancer treatment paradigms with the small molecule AXL kinase inhibitor (bemcentinib/BGB324, BerGenBio ASA) in combination with chemo-, targeted- and immunotherapies in leukemia, melanoma, breast, pancreas and lung cancer.

3. References to the research

Peer-reviewed publications

1. Terry S, Abdou A, Engelsen AST, Buart S, Dessen P, Corgnac S, Collares D, Meurice G, Gausdal G, Baud V, Saintigny P, Lorens JB, Thiery JP, Mami-Chouaib F, Chouaib S. AXL targeting overcomes human lung cancer cell resistance to NK and CTL-mediated cytotoxicity. Cancer Immunol Res. 2019 Sep 5.
2. Ludwig KF, Du W, Sorrelle NB, Wnuk-Lipinska K, Topalovski M, Toombs JE, Cruz VH, Yabuuchi S, Rajeshkumar NV, Maitra A, Lorens JB, Brekken RA. Small-Molecule Inhibition of Axl Targets Tumor Immune Suppression and Enhances Chemotherapy in Pancreatic Cancer. *Cancer Res*. 2018 Jan 1;78(1):246-255
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4. Jokela TA., Engelsen AST., Rybicka, A., Pelissier Vatter, FA., Garbe,J., Akslen L., Stampfer M., Lorens JB*, LaBarge MA*. Microenvironment-induced non-sporadic expression of the AXL and cKIT receptors are related to epithelial plasticity and drug resistance. *Front. Cell Dev. Biol.,* 2018
5. Kirane A, Ludwig KF, Sorrelle N, Haaland G, Sandal T, et al. Warfarin Blocks Gas6-Mediated Axl Activation Required for Pancreatic Cancer Epithelial Plasticity and Metastasis. Cancer Res. 2015 Sep 15;75(18):3699-705.
6. Gjerdrum C, Tiron C, Høiby T, Stefansson I, Haugen H, et al. ..Lorens, J.B Axl is an essential epithelial-to-mesenchymal transition- induced regulator of breast cancer metastasis and patient survival. Proc Natl Acad Sci U S A. 2010 Jan 19;107(3):1124-9.

Selected presentations

Davidsen, KT et al., (2019). *AXL inhibition improves immunotherapy by targeting local and systemic tumor myeloid cross-talk.* CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference Paris, France, September 2019

Clinical trial participation (*presentations***): NCT02488408***:Multicenter Open-label Study of BGB324 as a Single Agent and in Combination With Cytarabine in Patients With AML (ASCO, 2016,2017,2018; ESMO, 2018, ASCO, 2019);* **NCT02424617***: A Study of BGB324 in Combination With Erlotinib in*

Patients With Non-Small Cell Lung Cancer (EORTC, 2016, WCLC 2018); **NCT029227**: *Trial of Dose Escalated BGB324 in Previously Treated Non-small Cell Lung Cancer (Docetaxel) (WCLC 2018)*; **NCT02872259**: *BGB324 in Combination With Pembrolizumab or Dabrafenib/Trametinib in Metastatic Melanoma (AACR 2017, ASCO, 2018; ESMO, 2018,2019)*; **NCT03184558** *BGB324 in Combination With Pembrolizumab in Patients With TNBC (SABCS, 2017; ASCO-SITC ,2018)*; **NCT03184571** *BGB324 in Combination With Pembrolizumab in Patients With Advanced NSCLC (ASCO-SITC, 2018, ASCO 2018, WCLC 2018; ESMO, 2018; ASCO, 2019, WCLC 2019)*; **NCT03649321** *A randomized clinical trial of chemotherapy with gemcitabine/cisplatin/nab-paclitaxel with or without the AXL inhibitor bemcentinib (BGB324) for patients with advanced pancreatic cancer (ASCO GI Cancer Symposium 2018).*

ASCO: American Society for Clinical Oncology; ESMO: European Society for Clinical Oncology; EORTC: European Organization for Research and Treatment of Cancer; AACR: American Association for Cancer Research; SABCS: San Antonio Breast Cancer Symposium

4. Details of the impact

Cancer is now the leading cause of death in Western countries. As our population ages and cancer incidence increases, greater strain is placed on public health resources. Hence, improving the efficacy and durability of cancer treatments is a key objective for health authorities.

How cancers become resistant to cancer treatment is the essence of this health challenge. During the past decade our research has addressed this fundamental question. We discovered that cancer cells exploit normal protective physiological mechanisms to evade anti-cancer treatments. This important insight came at a time when the cancer research community remained focused on characterizing the landscape of gene mutations harbored by malignant cells. Although undeniably important, this obscured a more general underlying cause of treatment failure: the ability of cancer cells to change in response to hostile conditions. The “phenotypic plasticity” is a feature of normal stem cells and important for wound healing. Further, the dramatic success of cancer immunotherapy, harnessing the immune system to treat cancer, fueled a reorientation to understand cancer as a dysfunctional organ comprised of tumor, stromal and immune cells. This appreciation for the complexity of the tumor microenvironment fueled a push to treat cancer with combinations of agents that target different strategic points within the tumor. Clinical trials are increasingly comprised of combinations of novel and established (eg chemotherapy) drugs.

Our discovery of the AXL receptor as both a driver of tumor phenotypic plasticity and innate immune suppression underpinning acquired resistance to multiple anti-cancer agents represents a fundamental insight into how tumors exploit normal protective processes. Interestingly AXL is also a target of pathogenic viruses during infection, leading to anti-viral suppression that is related to the immune evasion characteristic of malignancy. Importantly, AXL is a drug target with selective compounds in development. Our alliance with industry facilitated rapid clinical translation of treatment concepts revealed by our basic research.

5. Sources to corroborate the impact

Scientific Articles from outside of Centre for Cancer Biomarkers:

1. Approaches to treat immune hot, altered and cold tumours with combination immunotherapies. Galon J1, Bruni D2. Nat Rev Drug Discov (2019) 18 (3): 197-218. PMID: 30610226
2. Kinase inhibitors: the road ahead. Ferguson FM, Gray NS. Nature Review Drug Discovery (2018) 17 (5): 353-377. PMID: 29545548
3. First Axl inhibitor enters clinical trials. Sheridan C. Nature Biotechnology (2013) 31(9):775-6.
4. ASCO Daily News Posters Highlight Emerging Therapies for AML. June 2, 2019
5. eCancer.org AXL inhibitor bemcentinib in combination with chemotherapy exerts anti-leukaemic activity in AML patients. ASCO 2019
6. OncLive Bemcentinib/Pembrolizumab Combo Active in Chemo-Refractory NSCLC. Sept 8, 2019

Press releases from BerGenBio ASA https://www.bergenbio.com/company/

7. BERGENBIO PRESENTS PHASE II TRIAL UPDATES WITH SELECTIVE AXL INHIBITOR BEMCENTINIB AT THE EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY (ESMO) 2019 CONGRESS https://www.bergenbio.com/bergenbio-presents-phase-ii-trial-updates-with-selective-axl-inhibitor-bemcentinib-at-the-european-society-for-medical-oncology-esmo-2019-congress/
8. BERGENBIO PRESENTS NEW PHASE II CLINICAL DATA THAT BEMCENTINIB IN COMBINATION WITH LOW DOSE CHEMOTHERAPY IMPROVES EFFICACY AND DURATION OF SURVIVAL IN ELDERLY AML PATIENTS AT ASCO 2019 https://www.bergenbio.com/bergenbio-presents-new-phase-ii-clinical-data-that-bemcentinib-in-combination-with-low-dose-chemotherapy-improves-efficacy-and-duration-of-survival-in-elderly-aml-patients-at-asco-2019/
9. BERGENBIO PRESENTS NEW PRELIMINARY CLINICAL AND BIOMARKER DATA SHOWING DURABLE RESPONSE AND MEDIAN SURVIVAL RATES IN PHASE II TRIAL WITH BEMCENTINIB AND KEYTRUDA IN PATIENTS WITH ADVANCED NSCLC AT ASCO 2019 https://www.bergenbio.com/bergenbio-presents-new-preliminary-clinical-and-biomarker-data-showing-durable-response-median-survival-rates-in-phase-ii-trial-with-bemcentinib-and-keytruda-in-patients-with-advanced-nsclc-at-asco/

3.5.3 Societal impact: Co-Creation of Reflexive Cancer Research

Institution: University of Bergen		
Name of SFF: Centre for Cancer Biomarkers (CCBIO)		
Title of case study: Co-Creation of Reflexive Cancer Research		
Period when the underpinning research was undertaken: 2013 and onwards		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period employed at SFF**
Roger Strand	Professor, PI	2013-present
Anne Bremer (formerly Blanchard)	Post-Doc / Researcher	2015—present (excl mat. leaves)
Period when the impact occurred[5]: Gradually from 2016 and onwards		

1. Summary of the impact

CCBIO includes Responsible Research and Innovation (RRI) action research directed towards awareness and clarity with regard to ethical and societal aspects of cancer research itself. The impact we aim at, is *changing the biomedical research culture* towards increased societal responsibility. After years of continuous effort, we see a variety of signs that we have achieved this impact in terms of increased reflexivity in the biomedical research culture. While it is too early (and perhaps too difficult) to identify how this changes biomedical research results, we also see signs of this impact at the interface between CCBIO and local civil society.

2. Underpinning research

Prior to, and alongside with, the existence of CCBIO, Strand, Blanchard and other colleagues at the *Senter for vitenskapsteori* have worked for years to develop methods and approaches to normative interventions to increase reflexivity within STEM[6] research environments. These approaches have gone under various labels: normative *vitenskapsteori;* ELSI/ELSA[7], integrated ELSA; integrated research; RRI; co-creation, etc. A large part of this research was developed in FP7 Science-in-Society and H2020 Science-with-and-for-Society projects.

Such approaches must, however, be grounded in the specific normative issues at stake within the particular research field. Accordingly, in the years 2013-15, we mapped relevant issues and aspects, before gradually introducing them in an action research-oriented fashion. Such important issues include the (problem of) clinical effectiveness of biomarkers, and the (speculative character of) imaginaries of precision medicine. While it is a commonplace in STS (science and technology studies) that such imaginaries play an important role in the co-production of research policies and research agendas, and ultimately the co-production of future science, technology and society, the research task was to identify the imaginaries at play and the normative issues related to them. When such work is performed in an action-research type of approach, there is no absolute distinction between "research" and "impact", as little as there is an absolute distinction between "researcher" and "research subject". Hence, within CCBIO, the biomedical researchers were simultaneously our interlocutors, research subjects and co-researchers. A major achievement in this regard was the edited volume from 2017 (see reference below) that included not only scholars in our field but also several authors and co-authors from the

[6] Science, Technology, Engineering & Medicine
[7] Ethical, Legal & Societal Issues/Aspects

biomedical realm, engaging in the normative social issues. (Work on the 2. edition is ongoing).

At the same time, we continued to develop the theoretical and methodological framework underlying our approach by participation in EU (and RCN-funded) research projects and policy processes. An important milestone in that regard was the EU expert group report on RRI indicators that was chaired by Strand, and which delineated the principles of how to promote and monitor such efforts for reflexivity and social responsibility in science by an embedded, network-oriented approach.

3. References to the research

- R. Strand, J. Spaapen, M. W. Bauer, E. Hogan, G. Revuelta, S. Stagl, L. Paula & Â. Guimarães Pereira (2015): *Indicators for promoting and monitoring Responsible Research and Innovation. Report from the Expert Group on Policy Indicators for Responsible Research and Innovation.* European Commission. Directorate-General for Research and Innovation.
- A Blanchard (2016) "Mapping ethical and social aspects of cancer biomarkers." New Biotechnology 25;33(6):763-772. doi: 10.1016/j.nbt.2016.06.1458.
- A Blanchard & R Strand, editors (2017). Cancer Biomarkers: Ethics, Economics and Society. Bergen: Megaloceros Press, 148pp. doi: 10.24994/2018/b.biomarkers

4. Details of the impact

Strictly speaking "impact" means collision; it is the result of pressing something hard onto something else. We interpret the wider meaning of the term "impact" to also encompass our focus on increased reflexivity in a community of practitioners (of cancer research).

One such narrative begins with dissemination of our research to research students of CCBIO, through a designated PhD course called CCBIO903. We first gave this course in 2015, then in 2016 and 2018, to be repeated in 2019/2020. In this course, we invited PhD students (and some postdocs) to enter into the problematic ethical and societal issues of cancer research and cancer care together with us, and also develop them further through their own writing. Seeing this as a spawning bed for co-creation, we continued to follow individual young biomedical scientists and research students to develop their own reflexive understandings of these issues. A narrative should have a hero, and one such hero would be Caroline Engen, who developed her course essay into a lecture, then conference presentations, a book chapter in the mentioned edited volume, and hopefully, independent research papers. In her book chapter she asks the fundamental question: "If we are fighting a war on cancer because we do not want to die from cancer, but rather from something else, we must be frank and ask ourselves why this is so." She repeated this question in the international conference on Anticipation in London 2017 (an event that gathered a variety of researchers, practitioners and citizens devoted to the creation of good futures), and in public meetings on issues of medical philosophy and health policy in Bergen in 2018 and 2019. Similar stories can be told about other medical students and PhD fellows; and senior researchers in CCBIO, who have been involved in the course CCBIO903 or through other co-creation processes and events, including our Director Lars A. Akslen (see reference below) and the Leader of the CCBIO Research School, Elisabeth Wik, who co-authored a chapter in the mentioned edited volume, with a critical discussion of the concept of "good biomarkers" as such. At the time of writing, CCBIO recently hosted a research meeting with cancer investigators and students from Harvard University (based on an INTPART project), in which these and related ideas – of the ethical

and societal aspects of cancer research – were given ample space, and we are currently working to expand our efforts also to that group. The big question is if these changes in research culture will also translate into changes in research practice. This question cannot be answered yet, and more fundamentally there are problems of attribution that may render the question very difficult to answer. We are currently involved, however, in two H2020 projects that work specifically on this methodological question: SuperMoRRI (2019-2023) and TRANSFORM (2020-2022).

5. Sources to corroborate the impact

- The main sources to corroborate the impact are the annual reports of CCBIO, see https://www.uib.no/en/ccbio/73609/ccbio-annual-report The reports provide documentation of events such as courses, public meetings, etc; however, more importantly, the impact is *displayed* through various commentary pieces, often co-authored by a biomedical researcher and Strand/Blanchard.
- Another instance of this type of display is the following commentary piece in the Norwegian medical journal, see: https://tidsskriftet.no/en/2017/02/perspectives/what-responsible-cancer-research

3.6 CEED - Center for Earth Evolution and Dynamics

3.6.1 Scientific impact: Linking Surface Processes to the Deep Earth

Institution: University of Oslo		
Name of SFF: Center for Earth Evolution and Dynamics		
Title of case study: Linking Surface Processes to the Deep Earth		
Period when the underpinning research was undertaken: 2004-2019 and on-going		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Trond. H. Torsvik (THT), Bernhard Steinberger (BS), Pavel Doubrovine (PD), Reidar Trønnes (RT), Matthew Domeier (MD), Clinton Conrad (CC), Grace Shephard (GS)	**Role(s) (e.g. job title):** Professors (THT, RT, CC), Prof II (BS), Postdoctoral Researcher (PV, MD, GS)	**Period(s) employed by submitting SFF:** THT, BS, PV, RT, MD (2013→), GS (2014→), CC (2016→)
Period when the impact occurred: From about 2011		

1. Summary of the impact

CEED scientists have proposed that two large thermochemical piles in the lowermost mantle are stable for hundreds of million, perhaps billions of years, and their margins played an important role in generating plumes that sourced large volcanic eruptions at the surface, directly perturbing the climate system but also punctuating plate tectonics by creating and modifying plate boundaries. Many geological observations, global models of plate tectonics and sophisticated global numerical models corroborate to the new paradigm that explains how plate tectonics and mantle plumes interact. This has opened new research fields, which have been probed by hundreds of new studies in the last decade.

2. Underpinning research

The underpinning research started in 2004 (Torsvik and the *late* Kevin Burke) and our prime motivation was to explore possible links between reconstructed large igneous provinces (LIPs) at the Earth's surface and two prominent low-velocity regions in the lowermost mantle beneath Africa and the Pacific, commonly dubbed Large Low Shear-wave Velocity Provinces (LLSVPs; Garnero *et al.* 2016). Global shear-wave-velocity models provide broadly similar characteristics of the LLSVPs, and originally we used published shear-wave-velocity models or seismic voting maps (e.g., Torsvik *et al.* 2010, 2014), but from 2016 we have used our own tomographic model (*s10mean:* an average of ten global shear-wave-velocity models) and seismic voting maps (Doubrovine *et al.* 2016 and work of Shephard). Oxford and CEED (Shephard, Domeier) researchers have also created a set of open, interactive, user-friendly web-based tools to explore seismic tomography models of the Earth's interior (submachine.earth.ox.ac.uk).

An imminent challenge in exploring links between surface processes and the deep Earth was to develop ways to derive ancient longitudes from paleomagnetic data (the only data that can be used to quantify reconstructions before the Cretaceous) but also methods to quantify true polar wander (TPW, i.e. the changing orientation of the spin-axis relative the Earth's crust and mantle) from paleomagnetic reconstructions. The first method that we developed in 2004 (work of Torsvik) made use of the fact that longitudinal uncertainty of continents that were assembled in the Supercontinent Pangea (at around 320 Ma) can, for subsequent times, be eliminated, if longitude motion is known for at least one of these continents. The best assumption is zero-longitude motion for Africa and with this assumption we demonstrated that most hotspot lavas, LIPs and kimberlites (Torsvik *et al.* 2010), almost exclusively erupted above the margins of the two LLSVPs. This remarkable observation, ***perhaps the most important discovery since the Plate Tectonic***

Revolution of the 1960's, also considering the effect of TPW (work of Steinberger), led to a second method, the plume generation zone reconstruction method (Torsvik *et al.* 2014), unlocking a way forward in modelling absolute plate motions before Pangea, and exploring links between plate tectonics, intra-plate volcanism and Deep Earth dynamics. Conceptually, that link can be viewed as a simple mass-balance: subducted lithosphere slabs restore mass to the mantle and trigger the return flow toward the surface, including mantle plumes, rising from the margins of the LLSVPs (Steinberger & Torsvik 2012; Conrad *et al.* 2013; Torsvik *et al.* 2014).

Quantifying longitudes with the plume generation zone method also resulted in the first "*full-plate"* tectonic model for the Paleozoic which included the entire lithospheric plate system — i.e. both the continental and oceanic components of plates and their boundaries (Domeier & Torsvik 2014).

3. References to the research (CEED authors in bold)

1. Diamonds sampled by plumes from the core-mantle boundary, 2010**, T.H. Torsvik**, K. Burke, **B. Steinberger**, S.J. Webb & L.A. Ashwal. *Nature* 466 (7304), 352 (Google/Scopus Citations:301/238).
2. A geodynamic model of plumes from the margins of Large Low Shear Velocity Provinces, 2012, **B. Steinberger & T.H. Torsvik**. *Geochemistry, Geophysics, Geosystems*, 13 (G/S: 122/100)
3. Stability of active mantle upwelling revealed by net characteristics of plate tectonics, 2013**, C.P. Conrad, B. Steinberger, T.H. Torsvik.** *Nature* 498 (7455), 479 (G/S:40/32).
4. Deep mantle structure as a reference frame for movements in and on the Earth, 2014**, T.H. Torsvik**, R. van der Voo**, P.V. Doubrovine**, K. Burke, **B. Steinberger**, L.D. Ashwal**, R. Trønnes**, S.J. Webb, A.L. Bull. *Proceedings of the National Academy of Sciences* 111 (24), 8735-8740 (G/S:98/80)
5. Plate tectonics in the late Paleozoic, 2014, **M. Domeier, T.H. Torsvik**. *Geoscience Frontiers* 5 (3), 303-350 (G/S:237/207).
6. A failure to reject: Testing the correlation between large igneous provinces and deep mantle structures with EDF statistics, 2016. **P.V. Doubrovine, B. Steinberger, T.H. Torsvik**. *Geochem. Geophys. Geosyst.* 17, doi:10.1002/2015GC006044 (G/S: 28/24).

4. Details of the impact

The description of the movement and deformation of the Earth's outer layer has evolved from Continental Drift (1912) into Sea-Floor Spreading (1962) and then to the paradigm of Plate Tectonics in the mid- to late-1960s. Plate tectonics is as fundamentally unifying to the Earth Sciences as Darwin's Theory of Evolution is to Life Sciences, but it is an incomplete theory without an understanding of how plate tectonics and mantle dynamics interact. The CEED vision was therefore to develop an Earth model (the *fourth* revolution in the Earth Sciences) that explains not only how mantle processes and plate tectonics interacts, but also how mantle processes trigger massive volcanism and associated environmental and climate changes throughout Earth history.

The connections between the Earth's interior and its surface are defined by processes of material transfer: from the deep Earth to lithosphere, through the crust and into the interconnected systems of the atmosphere-hydrosphere-biosphere, and back again. Conceptually, subduction - a key driving force behind plate tectonics - restore mass (lithosphere slabs) to the mantle and trigger the return flow toward the surface, including mantle plumes. Our extraordinary findings that (*i*)

plumes mainly form at the margins of LLSVPs, and that (*ii*) these margins are approximately stable through time promoted a number of numerical modelling experiments (from about 2011 and onwards) to reproduce and explain these features, and the impact of our work was elaborated in a *Science* news report during the opening year of CEED (Kerr 2013).

Tan *et al.* (2011), inspired by our work, were the first to show that plumes tend to form preferentially along the steep margins (and not on the top) of thermochemical piles (LLSVPs). In a complementary approach, Steinberger & Torsvik (2012) prescribed subduction zone locations for the past 300 Myrs, and in their model, plumes almost exclusively form at the margins of thermochemical piles, as slabs push both the basal chemical layer and hot material from the thermal boundary layer. In this way, hot piles of chemically distinct material are formed, and, as more hot material is pushed against their margins, it is forced to rise, forming mantle plumes. Numerical models of mantle convection made to investigate the stability of the LLSVPs have shown that it is possible to maintain stability for hundreds of millions years (e.g., Bower *et al.* 2013 and *in-house* CEED work) and their continued existence for billions of years (Mulyukova *et al.* 2015). The LLSVPs, sourcing hotspot lavas, large igneous provinces (LIPs) and kimberlites, could be *primordial* thermochemical piles (Garnero *et al.* 2016; Ballmer *et al.* 2017; Jackson *et al.* 2018; McNamara 2019; Timmerman *et al.* 2019) possibly formed during early magma ocean crystallization (or shortly afterward), but it is still unclear why lower-mantle structures similar to today could have existed in deep time. Long-term stability of the LLSVP's with plumes sourced from their margins is therefore debated by some modellers (e.g., Austermann *et al.* 2014; Hassan *et al.* 2016), and some question the very existence of mantle plumes (www.mantleplumes.org).

Scientific papers by CEED scientists and collaborators that have underpinned and elaborated how the Earth's interior can be linked to its surface in deep geological time (including the development of new plate motion reference frames and paleogeography at large), has been cited ~6000 times since 2004 (Google Scholar). That witnesses a considerable international impact, not only in the fields of geodynamics, isotope geochemistry, seismology and paleogeography, but also within paleoclimatology and planetology at large. We have also shown that the two antipodal LLSVPs largely control the Earth's moment of inertia, and without subduction on Earth, causing TPW that shifts slabs in the upper part of the mantle towards the equator, the north-pole would have been located in northern Siberia. Torsvik received the EGU Arthur Holmes Medal 2016 and an ERC Advanced Grant (2010-2015) for the fundamental work of linking Deep Earth and Surface Processes, whilst Domeier was awarded the 2018 EGU Arne Richter Award for Outstanding Early Career Scientists for the ***application*** of the plume generation zone method (Torsvik *et al.* 2014) to make the first full-plate tectonic reconstructions for the Paleozoic.

One of the most spectacular surface expressions of mantle plumes is the catastrophic emplacement of LIPs, which have led to rapid climate changes and mass extinctions, but also to moments of transformation with respect to Earth's evolving paleogeography. But equally critical are those process which involve material fluxes going the other way—as best exemplified by subduction, a key driving force behind plate tectonics, but also a key driver for long-term climate evolution through arc volcanism and degassing of CO_2. First generation global full-plate Earth models based on our work are available back to 410 Ma, but many groups (including us) are now developing full-plate models for the past one billion years; this would allow us to quantify global

tectonic degassing (CO_2 sourcing; e.g. Mills *et al.* 2017) and use those estimates as input for long-term carbon-cycle modelling to constrain the variations of atmospheric CO_2 in deep time.

5. Sources to corroborate the impact

- **Examples of references that describe/illustrate the impact:**

1. Tan, E. *et al.* **2011**. On the location of plumes and lateral movement of thermochemical structures with high bulk modulus in the 3-D compressible mantle. Geochemistry Geophysics Geosystems, **12**: Q07005. doi:10.1029/2011GC003665.
2. Kerr, R.A. **2013**. The Deep Earth machine is coming together. *Science*, 340, 22-24.
3. Bower, D.J., Gurnis, M., Seton, M. **2013**. Lower mantle structure from paleogeographically constrained dynamic Earth models. Geochemistry, Geophysics, Geosystems, **14**: 44–63.
4. Austermann, J. *et al.* **2014**. A statistical analysis of the correlation between Large Igneous Provinces and lower mantle seismic structure. *Geophysical Journal International* 197**,** 1-9.
5. Mulyukova, E. *et al.* **2015**. Survival of LLSVPs for billions of years in a vigorously convecting mantle: replenishment and destruction of chemical anomaly. Journal of Geophysical Research: *Solid Earth*, 120, 3824–3847.
6. Garnero, E.J., McNamara, A.K. & Shim, S.H. **2016**. **Continent-sized anomalous zones with low seismic velocity at the base of Earth's mantle.** *Nature Geoscience*, 9, 481-489.
7. Hassan, R. *et al.* **2016**. A rapid burst in hotspot motion through the interaction of tectonics and deep mantle flow. *Nature* 533, 239–241.
8. Ballmer *et al.* **2017**. Persistence of strong silica-enriched domains in the Earth's lower mantle. *Nature Geoscience* 10, 236-240.
9. Mills, B.J.W. *et al.* **2017**. Elevated CO_2 degassing rates prevented the return of Snowball Earth during the Phanerozoic. *Nature Communications.* DOI:10.1038/s41467-017-01456-w
10. Jackson, M.G., Becker, T.W., & Konter, J.G. **2018**. Geochemistry and distribution of recycled domains in the mantle inferred from Nd and Pb isotopes in oceanic hot spots: Implications for storage in the large low shear wave velocity provinces. *Geochemistry, Geophysics, Geosystems*, 19, 3496–3519.
11. McNamara, A.K. **2019**. A review of large low shear velocity provinces and ultra low velocity zones. *Tectonophysics* 760, 199-220.
12. Timmerman, S. *et al.* **2019**. Primordial and recycled helium isotope signatures in the mantle transition zone. *Science* 365, 692-694.

- **Awards/prizes which illustrate the impact**

T.H. Torsvik:

2017: FRIDTJOF NANSEN MEDAL: Norwegian Academy of Science and Letters
https://www.dnva.no/detskjer/2017/03/fridtjof-nansens-belonning-2017?tid=69594

2016: THE UNIVERSITY OF OSLO RESEARCH PRIZE
https://www.mn.uio.no/geo/om/aktuelt/aktuelle-saker/2016/prisutdeling-uios-aarsfest.html

2016: ARTHUR HOLMES MEDAL: European Union of Geosciences
https://www.egu.eu/awards-medals/arthur-holmes/2016/trond-h-torsvik/

B. Steinberger:

2015: Elected as foreign member of the Norwegian Academy of Scince and Letters

https://www.gfz-potsdam.de/en/events/detail/article/bernhard-steinberger-elected-as-member-of-the-norwegian-academy-of-science-and-letters/
2014: GFZ Science Award
https://www.mn.uio.no/ceed/om/aktuelt/i-media/2014/bernhard-steinberger-got-the-highest-gfz-award-.html

M. Domeier
2018: EGU Arne Richter Award for Outstanding Early Career Scientists
https://www.egu.eu/awards-medals/arne-richter/2019/mathew-domeier/
2018: Reusch Medal (Norwegain Geological Society)
https://www.mn.uio.no/ceed/om/aktuelt/i-media/2019/reusch-medal-2018-to-mathew-domeier.html

G.E. Shephard:
2016: EGU Arne Richter Award for Outstanding Early Career Scientists
https://www.egu.eu/awards-medals/arne-richter/2016/grace-e-shephard/

3.6.2 Scientific impact: Understanding ARCTIC's geodynamics and paleoenvironment

Institution: University of Oslo		
Name of SFF: Center for Earth Evolution and Dynamics		
Title of case study: Understanding ARCTIC's geodynamics and paleoenvironment		
Period when the underpinning research was undertaken: 2008-2019 and on-going		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Carmen Gaina (CG), Jan Inge Faleide (JIF), Grace Shephard (GS), Alexander Minakov (AM), Morgan Jones (MJ), Sergei Medvedev (SM), Sverre Planke (SP), Fernando Corfu (FC), Henrik H. Svensen (HHS)	**Role(s) (e.g. job title):** Professors (CG, JIF, FC), Prof II (SP), Postdoctoral Researcher (GS, AM), Researcher (SM, MJ, HHS)	**Period(s) employed by submitting SFF:** CG (2011→), JIF, SM, SP, HHS (2005→), GS (2014→), AM, MJ (2015→)
Period when the impact occurred: From about 2015		

1. Summary of the impact

We pioneered 4D geodynamics studies of the Arctic region for understanding large-scale tectonic and volcanic events. A remote and complex region like the Arctic can reveal its structure only if large remote sensing data is concurrently analysed. CEED researchers have constructed for the first time models for the High Arctic where deep structures (like lost oceans and ascending mantle plumes) imaged by data from satellites and earthquakes can be directly correlated with volcanic and mountain building episodes. As Arctic region is a hot topic not only for science, but also for economy and society, our models are routinely used or modified/improved by many international groups.

2. Underpinning research

The underpinning research started around 2008 (Gaina while employed at NGU), and earlier (Faleide at UiO) motivated by new collaboration with Arctic countries and the lack of comprehensive models to explore the links between the complex history of volcanism in the Arctic region and Earth's interior. State-of-the-art geology and geophysics of the Barents Sea and Norwegian margins has been summarised in a review paper by Faleide et al. (2008, Episodes, cited more than 400 times) and was the starting point for Arctic margins modern concepts. A study of continental margins of the Eurasia Basin (Minakov et al., 2012), which used a wealth of geophysical data, proposed a novel scenario for this rifted margin, invoking an early strike-slip motion that challenged the conventional models of continental break-up.

CEED scientists (Minakov, Gaina) and collaborators used novel methods to infer useful knowledge about the large-structure of the Arctic lithosphere, in particular they have used gravity data from satellites to map the crustal thickness and derive the age of oceanic basins which otherwise are hardly accessible (Alvey et al., 2008; Minakov et al., 2012). These methods are continuously improved (Minakov, Gaina) and used with updated geophysical data to provide the community with state-of-the-art models of Arctic's crust and lithospheric structure (e.g. Lebedeva-Ivanova, Gaina et al., ArcCRUST, G3, 2019).

Volcanic activity has impacted the Arctic region for many million of years and numerous studies attempted to decipher the causes, timing and magnitude of volcanism through time. New geophysical data interpretation (Faleide, Minakov) and geochronological results (Corfu) contributed substantially to narrow down the timing of major magmatic activity in the European Arctic, to

quantify its volume, and explain its regional distribution by employing new modelling techniques (Minakov et al., 2018, doi:10.1144/SP460.4).

Tracing volcanic eruptions through time and studying their effect on paleoclimate is also central to CEED's activities, and we were able to identify northern Greenland as the source for the 55 million years old tephra layers in Svalbard (Jones et al., 2017). These results stemed from a multi-disciplinary study that combined many years of research into volcanism-paleoclimate direction (Svensen, Planke), with state-of-the-art plate tectonic reconstructions (Shephard).

The new approach of combining knowledge about the deep Earth with data from surface beared many fruits, and in the Arctic region CEED researchers were the first to identify alternative causes from punctuated, long-term magmatism. They showed that subducted oceans that were closer to the Pacific realm are now buried deep under Greenland and their journey through the mantle trigerred part of the magmatic activity north of the Canadian Islands and Greenland (Shephard et al., 2016).

Modern digital maps of circum-Arctic region that gathered geophysical data collected by airplanes, submarines and satellites (Gaina et al., 2011, Geol. Soc. London, https://doi.org/10.1144/M35.3), and an analysis of tomographic models of the Arctic mantle (Gaina et al., 2014) set the scene for a series of studies that opened the door for new Arctic research directions or challenged some of the established paradigms as shown in the next section.

3. Selected references to the research (CEED authors in bold)

7. Alvey, A, **Gaina, C.,** Kuznir, N. and **T. H. Torsvik**, 2008, Integrated crustal thickness mapping and plate tectonic reconstructions for the High Arctic, *Earth and Planetary Science Letters*, 274, 310-321. (Google/Scopus Citations:147/105).
8. **Gaina, C., S. Medvedev, T. H. Torsvik,** I. Koulakov and **S. C. Werner**, 2014, 4D Arctic: A Glimpse into the structure and evolution of the Arctic in the light of new geophysical maps, plate tectonics and tomographic models, *Surveys in Geophysics,* DOI:10.1007/s10712-013-9254-y. (G/S: 45/32)
9. **Minakov, A., Faleide, JI,** VY Glebovsky, R Mjelde, 2012, Structure and evolution of the northern Barents-Kara Sea continental margin from integrated analysis of potential fields, bathymetry and sparse seismic data, *Geophysical Journal International* 188 (1), 79-102 (G/S:48/32)
10. **Jones, MT**, **Augland, LE, Shephard, GE**, Burgess, SD, Eliassen, GT, Jochmann, MM, Friis, B., **Jerram, DA, Planke, S, Svensen, HH,** 2017, Constraining shifts in North Atlantic plate motions during the Palaeocene by U-Pb dating of Svalbard tephra layers, *Scientific Reports* 7 (1), 6822 (G/S:11/9)
11. S Polteau, BWH Hendriks, **S Planke**, M Ganerød, **F Corfu**, **JI Faleide** et al, 2016, The Early Cretaceous Barents Sea sill complex: distribution, 40Ar/39Ar geochronology, and implications for carbon gas formation, *Palaeogeography, Palaeoclimatology, Palaeoecology* 441, 83-95, (G/S:60/48).
12. **Shephard, G., R. Trønnes, W. Spakman**, I. Panet, and **C. Gaina**, 2016, Evidence for a distinct slab under Greenland and links to North Atlantic and Arctic magmatism. *Geophysical Research Letters,* 43, doi:10.1002/2016GL068424. (G/S: 4/4).

4. Details of the impact

The Arctic region is one of the last frontiers for human exploration, mainly because its remote position and inhospitable environment. Yet in the last couple of decades the circum-Arctic

countries and not only, became more and more interested in the Arctic ocean and its margins due to economical, political and societal reasons. The structure of the unique extended continental margins, the ocean between them, and the type of rocks and possible natural resources to be found in this region was imperative to know.
CEED scientists participated and led international projects that assembled the first modern Atlas of the Arctic that gathered remote data from satellites, airplanes and submarines to illustrate the structure and distribution of various types of rocks based on their physical (magnetic and density) properties (Gaina et al., 2011). This information was used to derive the crustal thickness of the Arctic (ArcCRUST model, Lebedeva-Ivanova et al., 2019) – a model freely shared with the community and which is already used by other international groups for better understanding the geological history of this region, for example how basins and mountains were formed in the Arctic region (e.g. Schiffer at al., 2018).

The circum-Arctic geophysical maps were extensively used by the circum-Arctic countries (Canada, Russia, USA and Denmark) for identifying data gaps and for planning new data acquisition that served national and international programmes like the Law of the Sea or natural resources mapping (Døssing et al. 2013, 2017, Berglar et al., 2016). In addition, CEED scientists (Faleide) advised on regular basis the Law of the Sea comission.

The unique geophysical dataset over the wider Barents Sea area in the European Arctic allowed CEED researchers and collaborators to build detailed models for Arctic sedimentary basins and continental margins (Klitzke et al., 2015, Solid Earth, 6) which in turn were used by the wider scientific community and by a large number of state and private companies. Large-scale models that illustrate how the Arctic region evolved for millions of years have been useful and adopted by other regional and global models (Shephard et al., 2013; Golonka et al., 2011). A recent scientific initiative that aimed to gather state-of-the-art lithospheric-scale regional transects through the Arctic lithosphere (Circum-Arctic Lithosphere -CALE, Pease & Coakly, 2018) built on previous CEED expertise in the Barents Sea (e.g. Faleide et al., 2018, Geol.Soc.London, 460) and adopted the four-dimensional space-time approach pioneered by CEED in the 4D-Arctic project (Gaina et al., 2014).

CEED research on the evolution of Arctic oceanic basins also constitutes the basis for studying the inception of major oceanic currents (like the North Atlantic Deep Water current) and their effects on glaciations and climate in general (e.g. Knies et al (including Gaina)., Effect of early Pliocene uplift on late Pliocene cooling in the Arctic–Atlantic gateway, 2014, EPSL 387). This study contributed to better understanding of the effect of Northern and Southern hemisphere climate and ocean interactions on sea-level fluctuations (Woodart et al., 2014, Science, 346).

CEED researchers are leaders in disseminating their Arctic scientific results in Europe and elsewhere. They have run an Arctic session at the largest geoscientific meeting in Europe (EGU) since 2012, are organising an international conference on Arctic Tectonics and Volcanism in October 2019 (https://connect.agu.org/aguchapmanconference/upcoming-chapmans/arctic-volcanism/general-info), and had special sessions and key note talks at other international meetings, including AGU (the largest geoscientific meeting in USA). The Arctic-related knowledge was disseminated not only among scientific peers, but also to the new generation. Tens of PhD students and postdoctoral researchers have been trained in Arctic research; during CEED time they were especially exposed to multi-disciplinary data and approaches. Many of them are now working for industry and some continue to collaborate with CEED and to diseminate our Arctic knowledge to the industrial sector. CEED proposed and run for 5 years a cross-disciplinary summer school course at UiO (course ISSMN4030, A Changing Arctic, https://www.uio.no/studier/emner/iss/sommerskolen/ISSMN4030) which combined for the first time natural sciences with political and social sciences related to the Arctic region. Our state-of-

the-art models of the Arctic are also used by new courses established in collaboration with the University Center in Svalbard (UNIS) https://www.unis.no/course/ag-851-arctic-tectonics-and-volcanism/.

5. Sources to corroborate the impact

- **Examples of references that describe/illustrate the impact:**

Models made by groups outside CEED that used CEED Arctic models:

Paleogeography of Arctic:

1. GE Shephard, RD Müller, M Seton , 2013, The tectonic evolution of the Arctic since Pangea breakup: Integrating constraints from surface geology and geophysics with mantle structure, Earth-Science Reviews,124, 148-183. 88 citations (Scopus)

2. J. Golonka, 2011, **Phanerozoic palaeoenvironment and palaeolithofacies maps of the Arctic region,** Jan Golonka**,** Geological Society, London, Memoirs, 35, 79-129, 2011, https://doi.org/10.1144/M35.6 (S: 50 cits)

Arctic Structure and geodynamics:

3. Circum-Arctic Lithosphere Evolution, 2018, Geological Society Special Volume 460, edited by Pease, V and B. Coakley

4. C Schiffer, C Tegner, AJ Schaeffer et al., 2018, High Arctic geopotential stress field and implications for geodynamic evolution,

Local Arctic studies using the methods developed by Alvey et al. (2008) and Minakov et al. (2012)

5. A Døssing, TM Hansen, AV Olesen, JR Hopper, 2014, Gravity inversion predicts the nature of the Amundsen Basin and its continental borderlands near Greenland, Earth and Planetary Science Letters (S: 30 cits)

Data gaps identified by CEED models (eg. Gaina et al., 2011) filled in by international groups

6. K. Berglar, D. Franke, R. Lutz, B. Schreckenberger and V. Damm, Initial Opening of the Eurasian Basin, Arctic Ocean, 2016, Front. Earth Sci., https://doi.org/10.3389/feart.2016.00091

CEED Arctic models used as case-examples by Industry:

7. E.R. Lundin and A.G. Dore, 2017, The Gulf of Mexico and Canada Basin: Genetic Siblings on Either Side of North America, GSA Today, 27, 4-11

New CEED models highlighted by American Geophysical Union outreach magazine EOS:

8. EOS article about ArcCRUST, https://eos.org/editor-highlights/revealing-the-arctic-crust

- **Awards/prizes which illustrate the impact**

2017: NANSEN AWARD: **Jan Inge Faleide**
https://www.mn.uio.no/geo/om/aktuelt/aktuelle-saker/2017/framkomiteens-belonning-jan-inge-faleide.html
https://arcex.no/professor-jan-inge-faleide-receives-the-nansen-award-2017/
2017: Elected member of the Norwegian Academy of Science and Letters: **Carmen Gaina**

https://www.mn.uio.no/ceed/om/aktuelt/i-media/2017/carmen-gaina-is-elected-as-a-member-of-the-norwegi.html
2017: Reusch Medal (Norwegain Geological Society): **Alexander Minakov**
https://www.geologi.no/organsisasjon/om-ngf/hedersbevisninger/reuschmedaljen/reuschmedaljen-prisvinnere
2016: EGU Arne Richter Award for Outstanding Early Career Scientists: **Grace E. Shephard**
https://www.egu.eu/awards-medals/arne-richter/2016/grace-e-shephard/

3.6.3 Societal impact: Improving the Public's Understanding of today's Climate Crisis

Institution: University of Oslo, Department of Geosciences		
Name of SFF: Centre for Earth Evolution and Dynamics (CEED)		
Title of case study: Improving the Public's Understanding of today's Climate Crisis		
Period when the underpinning research was undertaken: 2004-today		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Henrik H. Svensen (HHS) Sverre Planke (SP) Adriano Mazzini (AM) Kirsten Kruger (KK) Dougal Jerram (DJ) Anne Hope Jahren (AHJ)	**Role(s) (e.g. job title):** Researcher CEED Adjunct Professor, CEED Researcher CEED Prof. CEED and Dept. of Geosciences Prof. II, CEED Professor, CEED	**Period(s) employed by submitting SFF:** HHS, SP, AM, DJ: 2013-today, KK: 1.11.18 – today, AHJ: 2016-today
Period when the impact occurred: 2013 - today		

1. Summary of the impact

For understanding today's Climate Crisis and describing its importance to the public, we study Earth's geological history, with a focus on mass extinctions and rapid global climate change. At CEED, we have contributed to the understanding of the complex Earth system changes in several ways and ensured that this knowledge is transferred and communicated to the scientific community and society at large. The societal impact of our research is achieved by a wide range of outreach platforms, written and oral communication, on national and international level.

2. Underpinning research

The core scientific ideas were developed around 2004 (HHS, SP) and continued at CEED since 2013. They are related to the understanding and quantifying gas release from the Earth's crust, in particular during time-periods when large scale volcanism coincided in time with climate changes and mass extinctions. We study so-called Large igneous provinces (LIPs) and discovered that the geology of the magma plumbing system and the host sedimentary basin holds the key to understand the types and volumes of gases released to the atmosphere. One example is the Siberian Traps LIP, which coincided in time with the end-Permian extinction 252 million years ago. In LIPs, the gases travel through explosive conduits without any modern analogues. The closest we get is a mud and water-rich hydrothermal pipe in Indonesia called LUSI. AM had led a ERC Starting grant project at CEED devoted to LUSI, following initial research published in 2007. In addition, we study sedimentary sequences where traces of the volcanism and environmental changes co-exist. Our research is also targeted at a rapid climate change 56 million years ago, and the end-Triassic mass extinction, but additionally to more recent events such as the extinction of large mammals during the Pleistocene.

The presented cases represent a continuum of activities spanning the entire lifetime of the SFF. We would like to stress that the outreach has not been motivated by branding or the desire to attract funding, but by taking seriously our role as scientists. We have to share and discuss our key findings with those outside academia – and we have to spread our knowledge to a wide group of audiences, across different ages and fields of interest.

Finally, we would like to emphasize that our outreach feeds back into the research we do as part of a continuum. A striking example is how a popular science book about natural disasters (The End is Nigh; 2006/9; HHS) initiated a small CEED project about the relationship between volcanism in the mid 500's AD and the societal crises and social unrest that unfolded the same time. The scientific results were published in 2016 (Toohey et al.; downloaded 13 000 times) together with a popular science article in Aftenposten (HHS; among the most read science stories in Aftenposten that year), forming the starting point for a large Toppforsk proposal (NFR) about Viking age climate and the role of volcanic eruptions. The proposal was funded in 2018 (led by KK and involving HHS and AHJ) and the project will provide the first detailed climatic and environmental reconstruction (natural and made-made) of the Viking age based on Eastern Norway cases – a topic of great interest both in Norway and abroad.

3. References to the research (CEED researchers **in bold)**

Svensen, H., Planke, S., Malthe-Sørenssen, A., Jamtveit, B., Myklebust, R., Rasmussen Eidem, T., Rey, S.S. (2004). Release of methane from a volcanic basin as a mechanism for initial Eocene global warming. Nature, 429(6991):542-5.

Svensen, H.H., Frolov, S., Akhmanov, G.G., Polozov, A.G., **Jerram, D.A**., Shiganova, O.V., Melnikov, N.V., Iyer, K., **Planke, S**. (2018) Sills and gas generation in the Siberian Traps. Phil. Trans. R. Soc. A 2018 376 20170080

Heimdal, T.H., Svensen, H., Ramezani, J., Iyer, K., Pereira, E., Rodrigues, R., Jones, M.T., & Callegaro, S. (2018) Large-scale sill emplacement in Brazil as a trigger for the end-Triassic crisis. Scientific Reports. ISSN 2045-2322. 8 .

Mazzini, A., Svensen, H., Akhmanov, G.G., Aloisi, G., **Planke, S.,** Malthe-Sørenssen. A., and Istadi, B. (2007) Triggering and dynamic evolution of the LUSI mud volcano, Indonesia.Earth and Planetary Science Letters 261, 375-388.

Toohey, M., **Krüger, K**., Sigl, M., Stordal, F., and **Svensen, H.** (2016) Climatic and societal impacts of a volcanic double event at the dawn of the Middle Ages, Climate Change, 136, 3-4, 401-412, DOI: 10.1007/s10584-016-1648-7

M.T. Rabanus-Wallace, M.J. Wooller, G.D. Zazula, E. Shute, **A.H. Jahren**, P. Kosintsev, J.A. Burns, J. Breen, B. Llamas and A. Cooper (2017) Megafaunal isotopes reveal role of increased moisture on rangeland during Late Pleistocene extinctions. *Nature Ecology & Evolution*, 1, 0125, DOI: 10.1038/s41559-017-0215.

4.Details of the impact

An increasing number of young people are concerned about climatic changes and the need for humans to respond to this, and this creates a momentum for learning. There is also a large group of people arguing that all climate changes can be attributed to natural variations only. The scientific society needs to respond to this with updated and relevant insight, which incorporate the "state of the art" understanding of the interplay between natural climate variation, deep time lessons, and human-induced changes, and how these may be distinguished.

- The importance of the history of the Earth for understanding our role on the planet. We (HHS, AHJ, DJ) have given numerous presentations and lectures at schools, libraries, literary

events, at special events in for instance Telenor Arena (1300 kids age 10-11 present), and at science festivals.

- The role of degassing of CO2 and methane from the Earth in triggering changes and crises. We use deep time cases (HHS, SP, DJ) and the LUSI system in Indonesia (AM) to show people Earth analogies to the anthropogenic carbon degassing today. The common ground is how sedimentary deposits store carbon underground and emit carbon to the atmosphere. The research has received media coverage internationally and is of importance for those living near LUSI, as >40 000 people have lost their homes.
- We have communicated to wide audiences via newspaper columns in Norway and abroad. HHS has written in Morgenbladet since 2012 and AHJ in New York Times.
- Popular science books by AHJ, HHS, and DJ that present personal approaches to science. The book Stein på stein (HHS; 2018) focused on mass extinctions and the research process, and was distributed to all Norwegian libraries by the Arts Council of Norway (innkjøpsordningen, Kulturrådet). Lab girl (AHJ; translated to Norwegian) was an international best-seller sharing knowledge about the Earth. The book The Centre of the Earth: The Traveller's Guide (DJ) presented the central aspects of the Earth in a very accessible way.
- HHS was awarded the outreach price from the Norwegian Research Council in 2017 for his work. AHJ was awarded the 2016 National Book Critics Circle award in Autobiography.
- Introducing these research themes in a textbook. HHS is co-writing a textbook in geography for High-school, where geography is compulsory for about 100 000 students per year. The textbook (“Kompass”) will be out in 2020 as part of the new curriculum (Fagfornyelsen) from The Norwegian Directorate for Education and Training. This is a great opportunity to share knowledge from the research front about the Earth System, potentially shaping the attitudes of the coming generation the next ten years.

3.6.4 Societal impact: Planetary Sciences - A new research and education direction in Norway

Institution: University of Oslo, Department for Geosciences		
Name of SFF: Centre for Earth Evolution and Dynamics (CEED)		
Title of case study: Planetary Sciences - A new research and education direction in Norway		
Period when the underpinning research was undertaken: 2009-today		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): **Stephanie C. Werner (SCW)** **Reidar G. Trønnes (RGT)** **Carmen Gaina (CG)** **Bernhard Steinberger (BS)** **Tobias Rolf (TR)**	**Role(s) (e.g. job title):** **Prof. + Director, Research School** **Prof.** **Prof.** **Prof. II** **Postdoctoral Researcher**	**Period(s) employed by submitting SFF:** **SCW, RGT, CG, BS, RT:** **2013-today**
Period when the impact occurred: 2013-today		

1. Summary of the impact

CEED has cultivated an environment for research in Planetary Sciences that has fostered collaboration between Norwegian universities, working together with the *National* Research School: Dynamics and Evolution of the Earth and Planets (DEEP). This effort has established comparative planetology within the Norwegian academic landscape and strengthened national and cross-departmental interaction (e.g., between the Departments of Theoretical Astrophysics and Geosciences at the University of Oslo). This has led to additional educational opportunities (GEO-AST3410/4410 Planetary Sciences) and new interactions between industry and academia in hardware contributions to space missions. The latter is complementary to traditional oil and energy industry, with positive implications for Norway's "geo-return" from the European Space Agency.

2. Underpinning research

CEED's fundamental goal is to link the surface record of plate tectonics and volcanism through time with the Earth's interior dynamics. Plate tectonics with recycling of oceanic crust into the interior, triggering plumes and large-scale volcanism is unique for Earth, although volcanism occurs on many planetary bodies. Massive volcanism and its environmental consequences are inferred by unravelling the geological history. For Earth, this requires plate tectonic reconstruction, whereas other planets, such as Mars, have long geological records preserved on their surfaces. Research at CEED has developed new methods and calibrated temporal frames for other solid surface objects in the Solar System. These activities are based on crater statistics, dating planetary surfaces using the density of impact craters as a measure of surface exposure to the bombardment of small bodies from space [1, 2]. Such impact bombardment can influence the thermal interior evolution of for example the Earth's Moon [3]. By comparing the Earth to other Earth-like planets, we derive new insights in the interior structure from gravity data [4]. This allows an evaluation of the cause and effect of mantle convection, and we can rule out or support process suggestions for Earth and other planets. Experimentally derived phase relations and mineral properties, coupled with the chemical compositions of the Sun and meteorites, and planetary accretion and differentiation models, enhance our understanding of the similarities and differences between Earth-like planets [5]. Our insights into Earth's and the terrestrial planets' interiors are largely based on meteorites and samples from the Moon, as well as the recent

robotic missions to Mars, Vesta and other planetary objects. With the imminent European space missions to study exoplanets, our expertise from Earth and the terrestrial planets is valuable to the PLATO and ARIEL mission teams [e.g. 6]. We support these studies of exoplanets by providing models for planetary structure and evolution and the effects of volcanic degassing on atmospheres, climate evolution and habitability potential.

CEED promotes several aspects of new and groundbreaking research, which requires educational means that were missing before CEED, or poorly covered in the curricula of the Norwegian universities. Besides local additions of Planetary Sciences in the study plan, we also successfully applied for the National Research School "Dynamics and Evolution of the Earth and Planets". This school is a national facility educating Earth and planetary scientists in a holistic way by placing the Earth in a comparative planetology perspective.

3. References to the research (CEED authors in bold)

1. **Werner, S.C.,** A. Ody, F. Poulet (2014) The Source Crater of Martian Shergottite Meteorites, ***Science***, 343 (6177) 1343-1346.
2. **Werner, S.C.,** B. A. Ivanov (2015) Exogenic Dynamics, Cratering and Surface Ages, In: ***Treatise on Geophysics***, 2nd Edition, Elsevier, 10, 327-365. (Invited Book Chapter)
3. **Rolf, T.,** M.-H. Zhu, K. Wünnemann, **S.C. Werner** (2017) The role of impact bombardment history in lunar evolution. ***Icarus***, 286, 138-152.
4. **Steinberger, B., S.C. Werner, T. H. Torsvik** (2010) Deep versus shallow origin of gravity anomalies, topography and volcanism on Earth, Venus and Mars, ***Icarus***, 207 (2), 564-577.
5. **Trønnes, R.G., M.A. Baron, K.R. Eigenmann, M.G. Guren, B.H. Heyn, A. Løken, C.E. Mohn** (2019) Core formation, mantle differentiation and core-mantle interaction within Earth and the terrestrial planets, ***Tectonophysics***, 760, 165-198. (Review paper)
6. Rauer, H., C. Catala, and 160 co-authors including **S.C. Werner** (2014) The PLATO2.0 Mission, ***Experimental Astronomy***, 1-82. (ESA Mission)

4. Details of the impact

Prior to the development of CEED in 2013, the Norwegian research community held strengths in both Earth science and astrophysics, but held minimal international-level expertise in planetary science. Yet, curiosity about planetary science has always held the public's interest, and much of Norwegian expertise in Earth science and astrophysics holds relevance for developing advances in planetary science. Furthermore, Norwegian technology companies, especially those that serve the petroleum industry, have expertise that can be applied to developing equipment for planetary science missions, such as those being proposed by the European Space Agency (ESA). Thus, a "niche" for planetary science has been present in Norway for some time, but had remained unfilled.

Although a "niche" for planetary science has existed for some time, it has been difficult to develop this area because Norway lacked individuals with the critical expertise and connections to compete in planetary science at an international level. Norway also lacked an educational program in planetary science that could serve as a pipeline for developing this expertise. This has left Norwegian students and technology companies, and Norwegian society generally, without a voice in the international planetary science community.

At UiO, CEED has established an internationally recognized planetary science program that is engaged in high-level research in planetary science. This planetary science focus was part of the original plan of CEED, and it has steadily grown both in size and in scope due to the past 6 years of effort. For the first time, a Norwegian University (UiO) has now established a research and educational direction in Planetary Sciences. This was possible only because CEED started and promoted this new topic, and which the host GEO-UiO supported by opening a new professorship and engaging in a successful collaboration with the astrophysics ITA-UiO. The establishment of the new "Planetary Sciences" course (GEO-AST3410/4410), has marked Oslo and Norway as an interesting exciting destination for studying this topic and therefore it attracts Norwegian as well as exchange students. We have also helped to build and lead a national research school (DEEP,

https://www.mn.uio.no/ceed/english/research/doctoral-degree/national-phd-school/) which is funded independently of CEED now can train the next generation of planetary scientists in Norway.

Our efforts have already produced 2 PhD and 2 Master's degrees, all based on high-level scientific research in planetary science. These are the first such degrees ever awarded in Norway. In the first year 2018, 12 students successfully finished the course GEO-AST3410/4410, this year 2019 possibly even more. Our program also has several postdocs, PhD and masters students currently working at an international level in planetary science. Students from other Norwegian universities can now attend specialized courses coordinated by the DEEP school, which is filling a niche in the higher education curriculum in Norway. The school offers yearly three to four PhD level short courses in which on average 8 PhD students finish successfully. These early career scientists will eventually contribute to Norwegian excellence in planetary science, helping to build a new academic discipline with industry contacts within the Norwegian technology sector. Already our scientific expertise provided opportunities for Norwegian industrial involvement in ESA-led space telescopes designed to search for and characterize exoplanets (PLATO and ARIEL projects).

To meet the public's curiosity for astronomy, planetary sciences and promote natural sciences at large, we currently consult and contribute to the content development of the new permanent exhibitions at the Natural History Museum in Oslo

5. Sources to corroborate the impact

https://www.romsenter.no/no/Aktuelt/Siste-nytt/Europeisk-rover-til-flodslette-paa-Mars

https://www.uniforum.uio.no/nyheter/2015/12/far-nasjonal-forskarskule-om-jorda-og-planetane.html

https://www.uniforum.uio.no/nyheter/2018/03/han-er-norges-forste-med-doktorgrad-i-planetologi.html

3.7 CEMIR - Centre of Molecular Inflammation Research

3.7.1 Scientific impact: Cell biological studies of host-pathogen interactions for identifying new therapeutic targets to treat infections

Institution: Norwegian University of Science and Technology, NTNU

Name of SFF: CEMIR - Centre of Molecular Inflammation Research

Title of case study:
Cell biological studies of host-pathogen interactions for identifying new therapeutic targets to treat infections

Period when the underpinning research was undertaken: 2010-2019

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting SFF:
Trude Helen Flo	Professor, PI, Co-Director CEMIR	2013-2019
Terje Espevik	Professor, PI, Director CEMIR	
Egil Lien	Adjunct Professor CEMIR	

Period when the impact occurred: 2014-2019

1. Summary of the impact

According to WHO, infectious diseases underlie six out of ten major threats to global health (1). Antimicrobial resistance, vaccine scepticism, emerging pathogens and diseases with no cure, call for new drugs and treatment strategies. CEMIR researchers have contributed significantly to the understanding of sepsis and patented peptide drugs purposed for sepsis treatment. Research from CEMIR and Univ. Massachusetts revealed virulence strategies of pathogens like *Yersinia pestis* and *Mycobacterium tuberculosis*, with the prospect of developing host-directed therapeutic strategies (HDTs). The development of advanced imaging approaches for spatiotemporal studies of host-pathogen relations has been essential for these findings and constitute a resource for the scientific community as well as pharmaceutical industry.

2. Underpinning research

Pathogen recognition and inflammatory responses has been a long-term research focus of Terje Espevik, starting with the discovery of TNF and its detrimental role in sepsis (*Waage, Halstensen, Espevik. Lancet 1987*). A key initiating factor is recognition of bacterial products by host cell sensors, and research from Espevik's group revealed that the key sensor of LPS from Gram-negative bacteria, TLR4, elicits different inflammatory responses depending on its sub-cellular location within host macrophages (ref.1, 2010). The small GTPase Rab11a controlled the recruitment of TLR4 from the endocytic recycling compartment to phagosomes where, together with the adaptor TRAM, it elicited a robust IFNβ induction in response to *E. coli*. A follow-up study demonstrated how a co-receptor, SLAMF1, interacts with TRAM and is required for TLR4- induced IFNβ and killing of Gram-negative bacteria (ref.2, 2018). The interaction is human-specific and has therapeutic potential: mapping of the interaction domains has led to the development and patenting of peptide drugs purposed for curbing inflammation.

A cell biological approach using confocal microscopy was employed in these studies and has since been central in CEMIR research to resolve the spatiotemporal trafficking and interaction

of innate receptors and pathogens. In contrast to *E. coli*, pathogenic mycobacteria survive within host macrophages by manipulating intracellular trafficking, thus avoiding degradation. Flo's group discovered that *Mycobacterium avium* are targeted to phagolysosomes where they are recognised by TLR7/8, but some of the bacteria escape and re-establish in a compartment supporting survival (ref.3, 2017). Surprisingly, no inflammatory signalling was elicited from this compartment, making it a perfect hiding place and explaining how *M. avium* can cause chronic infections. This discovery was only possible by imaging of single infected cells. To obtain ultrastructural insight, Flo's group developed a platform for live-cell fluorescent imaging combined with high-resolution 3D electron microscopy (CLEM) and used this to reveal a novel mechanism for pyroptosis and spread of infection acting through plasma membrane damage both during and after phagocytosis of *M. tuberculosis* (ref. 4, 2019). Plasma membrane damage allowed K+ efflux, NLRP3 inflammasome activation and pyroptosis, and was a common mechanism utilized by other canonical NLRP3 activators, like silica crystals, that have previously been reported to act through lysosomal damage. Preservation of membrane integrity is thus key to contain *M. tuberculosis* infection, which makes cell necrosis an attractive target for HDTs.

Y. pestis, the causative agent of plague, has several strategies for inducing cytotoxicity through its effector protein, YopJ. Interestingly, rapid death is induced as *Y. pestis* is temperature-shifted from 26°C to 37°C, a condition that mimics the temperature change associated with infection via a fleabite. Research by Egil Lien (Univ. Massachusetts, prof II at CEMIR) identified a RIP1-caspase-8/RIP3-dependent caspase-1 activation pathway induced by YopJ that regulates macrophage cell death, NF-κB and inflammasome activation, and host resistance after *Y. pestis* infection (ref.5, 2010). In a follow-up study, they showed that YopJ inhibits TAK1–IκB kinase signalling (ref.6, 2018). This, in turn, results in caspase-8–directed cleavage of GSDMD, pyroptosis, and the release of IL-1β and IL-18. Thus, YopJ may induce both protective and harmful effects for the host since death of immune cells can eliminate the replication niche of pathogens, or conversely, elimination of key immune cells can diminish the ability to respond to infection.

3. References to the research

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3. Gidon A, Åsberg SE, Louet C, Ryan L, Haug M, **Flo TH**. Persistent mycobacteria evade an antibacterial program mediated by phagolysosomal TLR7/8/MyD88 in human primary macrophages. PLoS Pathog. 2017 Aug 14;13(8):e1006551. doi: 10.1371/journal.ppat.1006551.

4. Kai S. Beckwith, Marianne S. Beckwith, Sindre Ullmann, Ragnhild Sætra, Haelin Kim, Anne Marstad, Signe E. Åsberg, Trine A. Strand, Harald A. Stenmark, **Trude H. Flo.** Plasma membrane damage causes NLRP3 activation and pyroptosis during *Mycobacterium tuberculosis* infection. 2019 In revision in Nature Communications and deposited: bioRxiv 747014; doi: https://doi.org/10.1101/747014

5. Weng D, Marty-Roix R, Ganesan S, Proulx MK, Vladimer GI, Kaiser WJ, Mocarski ES, Pouliot K, Chan FK, Kelliher MA, Harris PA, Bertin J, Gough PJ, Shayakhmetov DM, Goguen JD, Fitzgerald KA, Silverman N, **Lien E**. Caspase-8 and RIP kinases regulate bacteria-induced innate immune responses and cell death. Proc Natl Acad Sci U S A. 2014 May 20;111(20):7391-6. doi: 10.1073/pnas.1403477111.

6. Orning P, Weng D, Starheim K, Ratner D, Best Z, Lee B, Brooks A, Xia S, Wu H, Kelliher MA, Berger SB, Gough PJ, Bertin J, Proulx MM, Goguen JD, Kayagaki N, Fitzgerald KA, **Lien E**. Pathogen blockade of TAK1 triggers caspase-8-dependent cleavage of gasdermin D and cell death. Science. 2018 Nov 30;362(6418):1064-1069. doi: 10.1126/science.aau2818.

4. Details of the impact

Impacts include:

1. New knowledge on mechanisms underlying sepsis and tissue pathologies in tuberculosis and Yersinia infections resulting from bacteria-induced host-cell responses and host-cell killing
2. New methodologies for live-cell and high-resolution imaging applicable for research and industry (drug screening)
3. Identification of drug targets and host-directed therapeutic strategies to treat infections

Main beneficiaries include:

The scientific community, biotech industry, health workers, policy makers, the public

WHO recently listed **ten threats to global health in 2019** (1). Six out of these concern infectious diseases directly: influenza pandemic, antimicrobial resistance, high-threat pathogens, vaccine hesitancy, dengue, HIV. Research at CEMIR is addressing five of them, and this is also where CEMIR research has made the most impact. In addition, climate change can cause emergence of new or re-emergence of old threats like *Yersinia pestis* (plague) from natural reservoirs. Researchers at CEMIR and Univ. Massachusetts have made important discoveries on why *Y. pestis* cause deadly disease in humans, which can be used in vaccine development. Research on inflammation since the early 80's together with **development of advanced imaging approaches** for studies of host-pathogen interactions are underlying CEMIRs impact on the understanding of sepsis and virulence strategies of pathogens like Yersiniae and *Mycobacterium tuberculosis*, with the prospect of developing new **host-directed therapeutic (HDT) strategies** to increase the efficacy of existing treatment, reduce tissue pathology and curb antimicrobial resistance (2).

Pathogen recognition and inflammatory responses have been a long-term research focus of Terje Espevik, starting with the discovery of TNF and its detrimental role in sepsis (3). Sepsis arises when the body mounts an overwhelming inflammatory response to an infection that injures its own tissues and organs (https://www.worldsepsisday.org/). A key initiating factor is recognition of bacterial products by host cell sensors, and underpinning research from Espevik's group revealed that the most central sensor, TLR4, elicits different inflammatory responses depending on its sub-cellular location within host macrophages. Findings were highlighted by Harvard professor Jonathan Kagan (4) and paved the way for seminal discoveries from CEMIR and internationally on **trafficking of immune receptors and compartmentalized signalling** (5). A follow-up study revealed how the TLR4 adaptor TRAM together with SLAMF1 regulates phagocytosis of bacteria and interferon signalling. Underpinning research in this study resulted in new innovation grants (6) and peptide drugs that are currently being patented for possible sepsis treatment (DOFI at TTO, NTNU). The impact can be substantial since sepsis treatment needs to happen instantly and before the causative bacterial agent is known. Pathogenic mycobacteria survive within host macrophages by manipulating intracellular trafficking, thus avoiding degradation. CEMIR scientists discovered that *Mycobacterium avium* targeted to phagolysosomes elicit inflammatory responses, but some manage to escape and establish in a compartment where they are neither degraded nor seen by cellular sensors. For this work, Trude Flo was awarded funding by the Olav Thon Foundation (7) to further explore how this compartment can be targeted as an adjunct HDT strategy to treat mycobacterial infections.

The use of **advanced imaging approaches** to study host-pathogen interactions has thus led to seminal discoveries from CEMIR not possible to obtain otherwise, and there is increasing appreciation in the scientific community of the importance of spatiotemporal studies of sub-cellular events to understand infections and to discover drug targets (5). Flo's group recently developed a platform for live-cell fluorescent imaging combined with high-resolution 3D electron microscopy (CLEM) and used this to reveal how *M. tuberculosis* disrupts host cell membranes, resulting in activation of **inflammasomes and cell necrosis**. In the lungs of tuberculosis patients, this causes tissue pathology. The study is under review and was downloaded from the preprint server bioRxiv more than 150 times within a week, and actively shared on twitter e.g. by Keystone Symposia (https://doi.org/10.1101/747014). The platform and special moulds made at NTNU Nanolab by the Flo group to be used for 3D CLEM are shared with scientists from several countries. The platform will be further developed and adapted for microscopy-based screening purposes, which is highly relevant for drug screening by pharmaceutical companies.

Researchers at CEMIR contributed substantially to reveal how both *M. tuberculosis* and Yersiniae activate inflammasomes resulting in host cell killing and release of IL-1b. Images of *Y. pestis* cytotoxicity from Lien's group (CEMIR & UMass) made the front cover in PNAS (8) along with media attention, and the most recent findings were corroborated by another group (9) right after they were published in Science. Inflammatory cell death and IL-1b release is an area of great medical interest. CEMIR adjunct professor Latz and others founded a company, IFM therapeutics, to target inflammasome activation. Novartis recently (2019) acquired IFM in order to further develop compounds for clinical trials (10). Tuberculosis is the leading cause of death

from infectious agents and drug-resistance is increasing (https://www.who.int/tb/en/). Tissue damage is a main driver of tuberculosis pathology, thus targeting host cell death is an attractive HDT strategy to shorten the duration of conventional chemotherapy and reduce lung injury (2, 11).

5. Sources to corroborate the impact

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3.7.2 Scientific impact: Inflammatory responses induced by cholesterol, defining new therapeutic targets to treat atherosclerosis

Institution: Norwegian University of Science and Technology		
Name of SFF: CEMIR		
Title of case study: Inflammatory responses induced by cholesterol, defining new therapeutic targets to treat atherosclerosis		
Period when the underpinning research was undertaken: 2010-2019		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF: 2013-19**
Terje Espevik	**Prof., PI and CEMIR director**	
Eicke Latz	**Adjunct professor CEMIR**	
Jan Kristian Damås	**Prof. CEMIR**	
Tom Eirik Mollnes	**Adjunct professor CEMIR**	
Period when the impact occurred: 2014-2019		

1. Summary of the impact

Inflammation plays a key role in cardiovascular disease, a major cause of illness and death worldwide. Formation of cholesterol crystals (CC) is central to the pathogenesis of atherosclerosis. Scientists at CEMIR have played an essential role in analyzing the mechanisms of inflammatory responses that CC mediate. They have made significant discoveries on the NLRP3 inflammasome that is activated by CC and the complement system leading to production of the potent proinflammatory cytokine IL-1b. This has led to a search for NLRP3 inhibitors and clinical trials inhibiting IL-1b as well as IL-1b-induced cytokines like IL-6.

2. Underpinning research

Professors Latz and Espevik and their teams published that cholesterol itself can cause inflammation in its crystalline form by activating the NLRP3 inflammasome leading to IL-1b release. In this work they showed that NLRP3 is required for atherogenesis and that CC are formed early on in arteries during atherosclerotic disease. This study indicated new potential molecular targets for the therapy of this disease such as components involved in NLRP3 activation, IL-1b and IL-1b induced cytokines (Ref 1). These findings contributed to the big CANTOS trial to test the efficacy of IL-1b inhibition to treat cardiovascular disease in 10.000 patients. Although Latz and Espevik found that CC activate NLRP3, the endogenous initiator for this activation was not well understood. Thus, in the period 2010-2013 Espevik, Mollnes, Damås and Latz carried out studies that demonstrated that CC induced activation of NLRP3 by a complement dependent mechanism (Ref 2). The results from this work showed that the complement system is a key trigger in CC-induced inflammation and activation of NLRP3, suggesting that complement inhibition is an interesting target for treatment of cardiovascular disease. These findings were extended and proved that CC also induced coagulation through a complement dependent manner, which further supports complement inhibition as a clinical strategy for treatment of thrombosis associated with atherosclerotic plaque rupture (Ref 3).

Because of the potent pro-inflammatory effects of CC, therapeutic strategies aimed at prevention of cholesterol phase transition, or removal of CC, could reduce tissue inflammation and atherogenesis. This hypothesis was tested in the paper by Latz, Espevik, and their collaborators. It was found that 2-Hydroxypropyl-beta-cyclodextrin (CD), an FDA-approved drug

for entrapment of lipophilic pharmaceuticals, markedly induced regression of atherosclerotic lesions by dissolving CC, inducing reverse cholesterol transport and reduced pro-inflammatory gene expression. This study provided preclinical evidence that CD could be developed into an effective therapy for atherosclerosis in humans (Ref 4). Since IL-1b is a cytokine that drives the IL-6 signaling pathway, it was considered important to test if inhibition of IL-6 reduced atherosclerotic disease in humans. This work was a collaboration between researchers at St. Olavs Hospital (Kleveland and Wiseth), Oslo University Hospital (Aukrust, Gullestad) and CEMIR (Damås, Espevik). The underpinning research produced by CEMIR was to contribute to the study design, finding patients for the trial, and analysis and interpretation of the results. It was found that the IL-6 receptor antagonist tocilizumab attenuated inflammation and reduced troponin release (Ref 5). The trial provides encouraging data concerning short term inhibition of IL-6 in patients with atherosclerosis.

A key risk factor for atherosclerosis is a Western diet (WD), typically described as high in calories and rich in sugars, trans and saturated fats, salt and food additives, but low in complex carbohydrates, fibre, vitamins and minerals. A WD leads to formation of CC which drive inflammation in atherosclerotic lesions. Latz, Espevik and collaborators made a significant discovery demonstrating that a WD induced systemic inflammation, myeloid precursor re-programming and innate immunity memory through the NLRP3 inflammasome (Ref 6). This opens therapeutic opportunities to interfere with WD-associated pathologies.

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4. Details of the impact

Impacts include:

1. New detailed knowledge on the mechanisms causing cardiovascular disease and pathologies associated with unhealthy lifestyle

2. Identification of targets for treating cardiovascular disease

3. New awareness for life-style associated pathologies

Main beneficiaries include:

The scientific community, biotech industry, patients, politicians, the public

Inflammation plays a key role in cardiovascular disease, a major cause of illness and death worldwide. Accumulation of lipids, like cholesterol, in the artery wall has been thought to play an important role in the inflammatory process, although the exact mechanisms behind this effect has been unclear. When the cholesterol concentration exceeds a certain level, it will precipitate out as cholesterol crystals (CC). Formation of CC is a hallmark of atherosclerotic plaques. Researchers at CEMIR have made significant discoveries that the NLRP3 inflammasome and the complement system are activated by CC. A consequence of NLRP3 activation is production of the potent proinflammatory cytokine IL-1b which is among the strongest drivers of inflammation. Normally, IL-1b is transiently produced and is used by the immune system to fight infection and to heal wounds. During cardiovascular disease the immune system is not able to remove the CC and production of IL-1b leads to chronic inflammation. **The research at CEMIR opened up the understanding of the inflammatory mechanisms involved in cardiovascular disease.** The underpinning research demonstrating that CC activate NLRP3 was a significant finding that pointed to the **NLRP3-IL-1b axis as a possible target for treating cardiovascular disease.** This was corroborated in the large CANTOS trial with 10.000 patients performed by Novartis and published in 2017**. Here they used a neutralizing IL-1b antibody (canakinumab) and showed a significant decrease in the risk of major adverse cardiovascular events (1, 2).** As NLRP3 is upstream of IL-1b, **many biotech companies have been on the search for inhibitors of NLRP3 activation for treatment of chronic inflammatory diseases such as cardiovascular- and Alzheimer's disease.** IFM therapeutics has

successfully developed such an inhibitor. Novartis recently (2019) acquired IFM in order to further develop this compound for clinical trials (3). The interest in NLRP3 has greatly increased during the last 5 years. This is due to the fact that this receptor controls host responses to infections as well as sterile inflammatory responses involved in many chronic diseases. CEMIR researchers (Lien) have also produced a lot of research that has revealed how inflammasomes control infections. **Chronic inflammation is associated with obesity and consumption of a Western diet.** Results published by CEMIR researchers in 2018 have provided new understanding on how consumption of a Western diet along with sedentary behavior cause chronic metabolic inflammation and epigenetic cellular reprogramming. This leads to lifestyle-associated pathologies that now start to reach epidemic proportions. **CEMIR researchers found that life-style associated pathologies are also mediated through NLRP3 activation.** The impact of this research should **alert politicians to put more attention on health education**, particularly for children, that focuses on the risk associated with Western lifestyle (4).

A potential effective treatment strategy for cardiovascular disease is to reduce the amount of CC in plaques by solubilization and catabolism of cholesterol. This should reduce inflammation in the atherosclerotic lesions. A compound with such property is 2-Hydroxypropyl-beta-cyclodextrin (CD), an FDA-approved drug for entrapment of lipophilic pharmaceuticals. **CEMIR researchers found in 2016 that CD markedly induced regression of atherosclerotic lesions.** This finding generated a lot of attention with news coverage in several media like Wall Street Journal and Science Daily (5). CD is already in clinical use in humans for the delivery of lipophilic drugs and has not shown relevant toxicity. Hence, repurposing CD for the treatment or prevention of atherosclerosis would be feasible. The studies reported by CEMIR provide **a proof of principle that therapy with CD increase the solubility and removal of macrophage cholesterol could be an effective strategy for the treatment of atherosclerosis.**

Research at CEMIR also demonstrated that the complement system plays an essential role in the initiation of inflammation by CC. Importantly, it was found in 2014 that **the complement system was needed for activation of the NLRP3 inflammasome by CC.** This finding was corroborated in the study by Fung who found similar involvement of the complement in uric acid crystal-mediated inflammasome activation which occurs in gouty arthritis (6). The impact of the complement-CC research performed by CEMIR **points to the use of complement inhibitors for treating cardiovascular disease.** Our results also demonstrate that the actual coagulation and thrombosis that occur during plaque rupture are due to CC-induced complement activation (front page of these data in *J. Immunology* 203, 15 Aug 2019). A lot of **biotech companies are now pursuing development of complement inhibitors for large areas of diseases (7).** One would anticipate that cardiovascular disease will be an important indication for complement inhibition in future trials.

Dissemination of the results presented here is essential in order to discuss impact. Thus, **CEMIR organized two international conferences on Molecular Inflammation Research in Trondheim** in 2016 and 2019 where these finding and other novel discoveries in the inflammation field were presented. These conferences were very successful with around 200 delegates from around the world attending each time.

5. Sources to corroborate the impact

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3.8 CERAD - Centre of Excellence for Environmental Radioactivity

3.8.1 Scientific impact: Reducing the overall uncertainties in impact and risk assessments associated with ionizing radiation, also combined with other stressors

Institution: Norwegian University of Life Sciences (NMBU)		
Name of SFF: CERAD Centre of Excellence for Environmental Radioactivity		
Title of case study: Reducing the overall uncertainties in impact and risk assessments associated with ionizing radiation, also combined with other stressors		
Period when the underpinning research was undertaken: 2012 -		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Brit Salbu **Per Strand** **Ole Christian Lind** **Deborah H- Oughton** **Lindis Skipperud** **Hans Christian Teien** **Dag A. Brede**	**CERAD Director/Professor NMBU** **CERAD Deputy Director/Dir DSA** **CERAD Dir. Science/Ass. Prof NMBU** **CERAD Dir. Science/ Prof NMBU** **CERAD Dir. Education/ Prof NMBU** **Researcher, NMBU Researcher, NMBU**	**All from 2013 -**
Period when the impact occurred: 2015 -		

1. Summary of the impact

A series of nuclear sources has contributed, is still contributing, or has the potential to contribute to radioactive contamination of the environment in the future. To protect the environment from radioactive contamination, impact and risk assessment models have been developed, although uncertainty estimates are most often ignored. The overall objective of CERAD is to improve the ability to accurately assess the radiological risks from environmental radioactivity, combined with other stressors. To improve assessments, the CERAD research focusing on key factors contributing the most to the overall uncertainties has influenced the EC research priorities within radiation protection program from 2015.

2. Underpinning research

Many nuclear sources have affected and may affect the same territory in the future. Based on a series of NMBU field work at contaminated sites, radionuclides released from a source and deposted in an ecosystem will co-occur with other stressors. A series of natural processes will influence the ecosystem transfer of radionuclide species and the actual exposure of living organisms. A multitude of stressors may interact and influence the uptake of radionuclide species and responses in exposed organisms. Thus, integrated models linking source term and deposition, via ecosystem transfer, uptake and effects to impact and risks, are complex, and the prognostic model output is confounded by large uncertainties that stem from a series of sources. This understanding formed the basis for CERAD CoE (2013-2022), with research contributions from all mentioned above. At the Int. Conf. Radioecology and Environmental Radioactivity meeting 2016, Salbu, the director of CERAD, was invited to give the opening plenary lecture. She presented "Environmental risk assessments and factors contributing to the overall uncertainties", a topic that should be of international interest (Salbu, 2016). During the ICRER meeting she was awarded the

4th International Union of Radioecology V.I. Vernadsky award "in recognition of her outstanding contribution to the development and dissemination of Radioecology".

The radiation protection research within EC has been performed within EURATOM, and in 2015, EC outsourced the program to the EC funded project CONCERT: Concert - European Joint Programme For the Integration of Radiation Protection Research (2015 – 2020). Within CONCERT, CERAD partners have actively contributed to the development of the Strategic Research Agenda, and to priorities for new research. We were therefore very pleased to see that the CERAD research and focus on the uncertainty issue were given a major priority. The EC CONCERT first call 2016, topic 2**: Reducing uncertainties in human and ecosystem radiological risk assessment and management in nuclear emergencies and existing exposure situations, including NORM.** As a bases for the call: "In emergency management and long term rehabilitation uncertainty information on the current situation, or predicted evolution of the situation, is an intrinsic problem of decision making. To protect the population, often conservative assumptions are taken which may result in more harm than good due to secondary causalities as observed following the Chernobyl and Fukushima accidents. Therefore, the reduction of uncertainty, and how to deal with uncertainty information, is crucial to improve decision making for the protection of the affected population." These statements are fully in accordance with the CERAD CoE application in 2013. Following the call, 2 CONCERT funded projects: CONFIDENCE focusing on situations short term after an accident, and TERRITORIES focusing on long term after a release were funded. CERAD is partner in both ongoing projects, dealing with model developments, focusing on key factors, underlying processes and phenomena that are contributing most to the overall uncertainties, using hypothetical scenarios such as a nuclear accident in Europe and deposition at the Western coast in Norway. Major progress achieved is/has also been reported as part of the EC project deliverables.

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A series of Deliverables to the CONCERT funded projects Confidence and Territories (2016 – 2020) has focused on uncertainties, and will be available to public when projects are

- D 9.1 - Guidelines ranking uncertainties for atmospheric dispersion
- D9.60 Guidance to reduce sampling uncertainty,
- D9.61 Guidance to select the desirable fit-for-purpose level of complexity for models as

applied in risk assessment

- D9.62 Guidance on uncertainty analysis for radioecological models
- D9.63 Guidance about exposure scenario
- D9.65 TERRITORIES 150-page synthesis report about decision making processes has enabled a preliminary understanding of how uncertainty management comes into play in decision making processes for existing exposure situations that have arisen from major nuclear accidents and from NORM activities and provides a framework for the future development of discussions and exercises in interactive experts/stakeholders panels and reflection groups

4. Details of the impact

How the research underpinned the impact:

The aim of the CERAD research is to reduce the overall uncertainties in impact and risk assessments and thereby increase the protection of man and the environment from harmful effect from ionizing radiation, also in combination with other stressors. The research is organized around four Research Areas (RA) outlined in the CERAD Strategic Research Agenda (SRA). By interfacing generic and specialized models (fig.1) by linking source term and release scenario (Research Area 1) via ecosystem transfer (RA2) to biological effects (RA3) and impact for humans, the environment, for society and economy (RA4), the overall uncertainty should be assessed. The work is focusing on key factors contributing the most to uncertainties, in order to improve the predicting power of the assessment models. Improvements made, or relevance to the international community;:

Source term RA1 (O.C. Lind): Following severe nuclear events, a major fraction of refractory radionuclides will be released as radioactive particles. A key issue is to characterize particles utilizing advance tecnologies

Beneficiaries: Radiation Protection Authorities using emergency preparedness models associated with large uncertainties, IAEA working groups

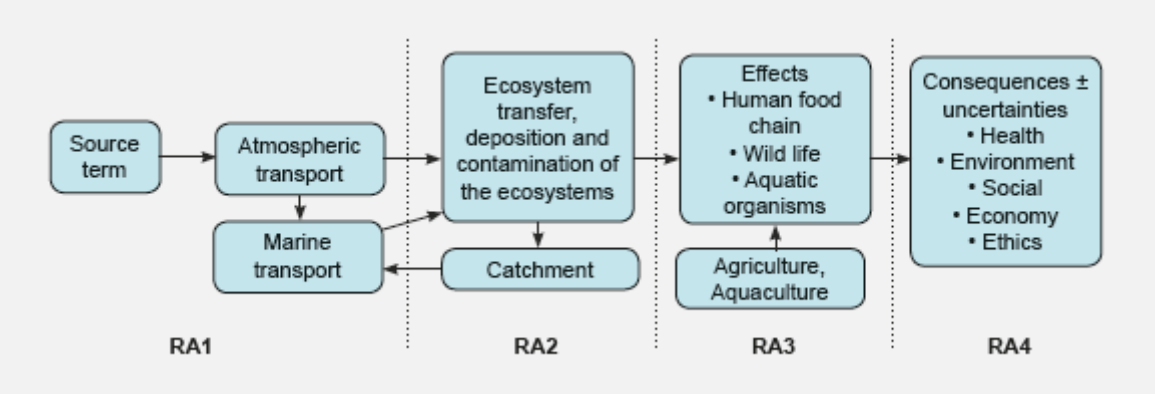
Changes to improve the source term characteristics: Within RA1, major improvements have been obtained as a comprehensive particle archive has been established, and particle codes based on particle characteristics are implemented in air transport and marine transport models. CERAD scientists has contributed significantly to an international recognition that it is crucial to include information on radioactive particles in environmental and risk assessments related to nuclear events. The research has demonstrated that releases of radioactive particles should be expected in most nuclear events and that such particles can carry a substantial amount of radioactivity posing risks to man and the environment. This aspect is also essential in an IAEA context

Beneficiaries: Radiation Protection Authorities using emergency preparedness models associated with large uncertainties, IAEA working groups including CRP on particles, relevant to nuclear forensic

Changes to improve transport modelling: Within RA1, the uncertainties in air transport has been estimated using the Ensemble method, both in the case of the Fukushima accident and in case of hypothetic accidents in Europe (Confidence Deliverable). The marine transport modeling has been significantly improved by implementing elemental speciation in the input river runoff, transformation processes occurring in the estuary mixing zones and the transport

of different radionuclide species in the coastal zones. This part is implemented in the ALLIANCE Roadmap for marine ecosystems.

Beneficiaries: Meteorologist and Radiation Protection Authorities using emergency preparedness models associated with large uncertainties, IAEA working groups on transport



Changes in ecosystem transfer concept RA2 (H.C.Teien): Most ecosystem transfer models are based on thermodynamic constants, assuming the equilibrium conditions in the environments. Improvements have been made to models describing human food chain as well as to river transport models describing run-off of radionuclides from contaminated catchments. Research within RA2 has fully demonstrated that the transfer is dynamic, that dynamic modeling has to be implemented, and that the transfer constants should be replaced by time functions (Confidence Deliverables).

Beneficiaries: Radiation Protection Authorities utilizing radiological models to estimate impact and risks.

Changes in endpoints relevant for ionizing radiation RA3 (D.A. Brede): Research focus has been put on effects on a series of organisms exposed to low ionizing radiation doses, utilizing the unique gamma radiation facility at NMBU. In addition, mixed exposure are applied. A similar facility has now been established in France, UK and Belgium. A comprehensive Biological effect toolbox has been developed, and knowledge gaps related to sensitive life stages, reproduction, transgenerational and epigenetic effects utilizing advanced instrumentations are highlighted.

Beneficiaries: radiobiology and Radiation Protection Authorities setting intervention levels to protect man and the environment

Changes in conceptual understanding

Impact and risk assessment concepts (RA4): By linking generic and specialized models in a chain; from source and release scenarios to impact and risk, key factors contributing to the overall uncertainties are: Source term characterization, dynamic ecosystem transport, life history stages, and mixed exposure as well as conceptual uncertainties which is assigned to model bias or discrepancy from real life due to lack of knowledge or to deliberate exclusion of relevant mechanisms, processes or phenomena. Thus, field experiments has proved crucial to cover the extrapolation gap from lab to the filed. This concept has been implemented in new application to EC.

Beneficiaries: Radiation Protection Authorities estimating potential impact and evaluating the need of countermeasures

The importance of the impact: By focusing on key factors contributing the most to uncertainties, the predicting power of environmental impact and risk models associated with radioactivity should be improved. As pointed out by CERAD, the model predictions are only valid within the boundaries of the uncertainties, and the model predictions are only relevant when uncertainties are estimated, communicated and understood. This aspects has gradually been accepted internationally, and is the dominant issue within the EC CONCERT funded projects CONFIDENCE and TERRITORIES. A series of deliverables has been submitted since 2016, and the uncertainty issue will be highlighted during the final meetings 2019/2020.

Influence outside SFF: In addition to influencing 2 ongoing EC projects, CERAD research focusing on impact assessments and associated uncertainties has also influenced roadmaps within the ALLIANCE, has impacted the IAEA Co-ordinated Research Program (2013 – 2018) focusing on the characteristics and environmental behavior of radioactive particles in the environment, where the CERAD director acted as chair, as well as influencing new proposals submitted to the EC CONCERT 2.call September 2019.

Evidence or indicators of the extent of the impact described:
Asked to Chair the IAEA CRP on radioactive particles (2013 – 2018)
Asked to join the EC CONCERT project
Asked to join the EC CONFIDENCE and TERRITORIES projects with focus on uncertainties
Asked to join 3 new EC proposals

According to the RCN International Midterm evaluation of CERAD 2016:

- "CERAD is a global Centre of Excellence and a flagship for Norwegian science with an agenda that is also highly relevant for society."
- "CERAD is highly regarded and well known among the professional stakeholders globally. This provides Norway with a high profile and a trusted status in radioecology. Supporting evidence is provided by the UNSCEAR Fukushima report presented to the UN General Assembly and the contribution to ICRP." – ref Societal case.
- "There are excellent international connections, as well as policy and professional links".
- "Network building both nationally and internationally, also with practitioners and politicians, has been outstanding."

Timespan when these impacts occurred – from 2015

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Awards/prizes:

- Brit Salbu, the director of CERAD, was awarded the 4th International Union of Radioecology V.I. Vernadsky award "in recognition of her outstanding contribution to the development and dissemination of Radioecology".
- The Chernobyl 30 year memorial medal was awarded CERAD Director Brit Salbu, 26 April 2016.
- *Norwegian Academy of Science and Letters: Research Director D.H. Oughton appointed member 2015*

Key researchers who have witnessed the impact and could be contacted:
Professor Sisko Salomaa, STUK, Finland

3.8.2 Scientific impact: The impact of radioactive particles

Institution: Norwegian University of Life Sciences		
Name of SFF: Centre for Radioactivity in the Environment (CERAD)		
Title of case study: The impact of radioactive particles		
Period when the underpinning research was undertaken: 2013-2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): **Brit Salbu, Professor, Centre Director**	**Name(s):** **Ole Christian Lind, Associate Professor, Research Director**	**Name(s):**
Period when the impact occurred:		

1. Summary of the impact

Research performed by NMBU/CERAD scientists have contributed significantly to an international recognition that it is crucial to include information on physico-chemical forms of radionuclides (speciation) such as radioactive particles in environmental impact assessments following nuclear events. Releases of radioactive particles should be expected in most nuclear events and such particles can carry a substantial amount of radioactivity posing risks to man and the environment. IAEA also acknowledged the importance of the problem and asked the CERAD director to chair two IAEA Coordinated Research Projects (2001-2008 and 2013-2018) focusing on the characteristics and environmental behavior of radioactive particles.

2. Underpinning research

Over the last 30 years CERAD scientists Salbu and Lind have headed research initiatives which have demonstrated that refractory radionuclides such as U and Pu released during nuclear events such as the Chernobyl and Fukushima nuclear reactor accidents are predominately present as radioactive particles with characteristics of relevance for impact and risk assessments. Together with the University of Antwerp, CERAD has developed advanced analytical techniques for characterization of nanometer - micrometer sized radioactive particles and utilized them to document that particle composition depends on the source, while the release scenario conditions are essential for the particle size distribution, structure and oxidation states i.e., key variables of importance for weathering and remobilization of associated radionuclides and metals. As releases of radioactive particles can be expected in future nuclear events and since such particles can carry a substantial amount of radioactivity posing a risk to man and the environment, the particle issue represents a challenge. Although this is internationally recognized, particle characterization is most often ignored as the technology needed to characterize particles is rather demanding. The relevance of the problem was also acknowledge by IAEA, setting up two Coordinated Research Programs focusing on characteristics and environmental behavior of radioactive particles, chaired by Salbu. The IAEA CRP's have resulted in an IAEA TecDoc report, a special issue in Journal of Environmental Radioactivity as well as a series of other publications on the subject, e.g., [1-3].

CERAD laboratory experiments have demonstrated that particle retention in non-human organisms (e.g. blue mussels, earthworm, nematodes) may be more frequent than previously assumed. Furthermore, retained mm sized highly radioactive particles induced effects such as skin burn, reproduction failure and DNA damage in blue mussels [4]. The work demonstrates, as one of the first papers, that radioactive particles retained in non-human organisms induce effects at the molecular level, reflecting non-targeted effects.

Recent advances in technology and method development within CERAD have enabled us to accurately quantify and visualize retention of micrometer [2] and nanometer [5] sized particles in environmental matrices including within biota and thereby characterize the exposure they represent to specific organs and cells. Utilizing these the state-of-the art methods, retention could also be observed in field samples, e.g., U/Pu particles in snails from Palomares [2]. In another study, our synchrotron radiation based nanoanalytical 3D images showing the distribution of cobalt nanoparticles within intact C. elegans, including nanoparticle retention associated with the nematode uterus [5], was selected as ESRF Beauty of Science, 2015.
Based on the experience from 30 years of radionuclide speciation research, CERAD has also improved atmospheric and marine dispersion models for predicting transport of radioactive releases by implementing codes for particles (SNAP atmospheric model [6]) and dynamic speciation (ROMS ocean model [7]).

3. References to the research

1. Geckeis, H., et al., *Environmental Chemistry of Plutonium*, in *Plutonium Handbook*, D.L. Clark, D.A. Geeson, and R.J. Hanrahan, Editors. 2019, American Nuclear Society. p. 1979-2118.
2. Salbu, B., et al., *Challenges associated with the behaviour of radioactive particles in the environment.* Journal of Environmental Radioactivity, 2018. **186**: p. 101-115.
3. Lind, O.C., et al., *Micro-analytical characterisation of radioactive heterogeneities in samples from Central Asian TENORM sites.* Journal of Environmental Radioactivity, 2013. **123**: p. 63-70.
4. Jaeschke, B.C., et al., *Retention of radioactive particles and associated effects in the filter-feeding marine mollusc Mytilus edulis.* Sci Total Environ, 2015. **502**(0): p. 1-7.
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6. Bartnicki, J., et al., *Atmospheric transport of radioactive debris to Norway in case of a hypothetical accident related to the recovery of the Russian submarine K-27.* Journal of Environmental Radioactivity, 2016. **151, Part 2**: p. 404-416.
7. Simonsen, M., et al., *Coastal transport of river-discharged radionuclides: Impact of speciation and transformation processes in numerical model simulations.* Science of the Total Environment, 2019. **669**: p. 856-871.

4. Details of the impact

Impacts include: Taking into account the presence of radioactive particles in releases from nuclear events and implementing particle codes in air transport, marine transport or radioecological models is contributing to reduction of the overall uncertainties in environmental impact and risk assessments.
Beneficiaries include: The International union of radioecology, IUR; International Atomic Energy Agency (IAEA); Norwegian Radiation and Nuclear Safety Authority; Norwegian Meteorological Institute.

<u>The research has influenced research outside the SFF</u>
The research has made large impact on the IAEA Co-ordinated Research Program on radioactive particles, The IAEA CRP includes scientists from all nuclear weapon countries and the technologies developed and the assessment methods use are most useful internationally.

CERAD has been partner I several EC funded project related to radioactive particles, latest COMET – RATE. Due to the particle competence, CERAD was also invited to contribute to the Plutonium handbook, 2nd edition, with a chapter describing events leading to Pu releases to the environment.
Furthermore, CERAD is utilized as expert, giving advises to authorities associated with the Fukushima accident. The CERAD Director was also invited to japan to give a few hrs lecture on radioacticve particles.
Particles codes have been implemented in air transport and marine transport models to improve assessment of environmental impact and risks
Beneficiaries include: Meteorological Institutes and radiation Protection Authorities

Indicators of the impact.
The two IAEA CRPs reflect the international recognition of the importance of taking radioactive particles into account within radioecological studies (IAEA, 2011; Salbu et al., 2019). Several review and impact assessment papers have taken into account recommendations by CERAD scientists regarding the importance of assessing the impact of radioactive particles e.g., (Batuk et al., 2015; Chen et al., 2019; Raskob et al., 2018; Sancho and Garcia-Tenorio, 2019; Steinhauser, 2018).

Timespan when these impacts occurred – from 2013

5. Sources to corroborate the impact

1. Chen, F., Hu, J., Takahashi, Y., Yamada, M., Rahman, M.S., Yang, G., 2019. Application of synchrotron radiation and other techniques in analysis of radioactive microparticles emitted from the Fukushima Daiichi Nuclear Power Plant accident-A review. Journal of Environmental Radioactivity 196, 29-39.
2. Batuk, O.N., Conradson, S.D., Aleksandrova, O.N., Boukhalfa, H., Burakov, B.E., Clark, D.L., Czerwinski, K.R., Felmy, A.R., Lezama-Pacheco, J.S., Kalmykov, S.N., Moore, D.A., Myasoedov, B.F., Reed, D.T., Reilly, D.D., Roback, R.C., Vlasova, I.E., Webb, S.M., Wilkerson, M.P., 2015. Multiscale Speciation of U and Pu at Chernobyl, Hanford, Los Alamos, McGuire AFB, Mayak, and Rocky Flats. Environ Sci Technol 49, 6474-6484.
3. IAEA, 2011. Radioactive Particles in the Environment: Sources, particle characteristics and analytical techniques, IAEA-TECDOC. IAEA, Vienna, p. 90.
4. Raskob, W., Almahayni, T., Beresford, N.A., 2018. Radioecology in CONFIDENCE: Dealing with uncertainties relevant for decision making. Journal of Environmental Radioactivity 192, 399-404.
5. Salbu, B., Fesenko, S., Ulanowski, A., 2019. Radioactive particle characteristics, environmental behaviour and potential biological impact. Journal of Environmental Radioactivity 201, 56-57. Editorial Preface, Special Issue IAEA CRP.
6. Sancho, C. and R. García-Tenorio, *Radiological evaluation of the transuranic remaining contamination in Palomares (Spain): A historical review.* Journal of Environmental Radioactivity, 2019. **203**: p. 55-70.
7. Steinhauser, G., 2018. Anthropogenic radioactive particles in the environment. Journal of Radioanalytical and Nuclear Chemistry 318, 1629-1639.

Awards /prizes:

At the Int. Conf. Radioecology and Environmental Radioactivity (ICRER) meeting 2016, Salbu, the director of CERAD, was awarded the 4th International Union of Radioecology V.I. Vernadsky award "in recognition of her outstanding contribution to the development and dissemination of Radioecology". Assumedly, the extensive radioactive particle research of Salbu contributed to the Award panel decision.

3.8.3 Societal impact: Impact assessments for ionizing radiation on the environment with focus on the Fukushima-Daiichi accident

Institution: Norwegian Radiation and Nuclear Safety Authority (DSA)

Name of SFF: CERAD

Title of case study: Impact assessments for ionizing radiation on the environment with focus on the Fukushima-Daiichi accident

Period when the underpinning research was undertaken: 2011-present

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting SFF:
Per Strand	Director, DSA CERAD Deputy Director Adjunct Professor at NMBU	2013-present
Justin Brown	Senior Adviser	2013-present
Mark Dowdall	Senior Adviser	2013-present
Ali Hosseini	Senior Adviser	2013-present

Period when the impact occurred:

1. Summary of the impact

Research at CERAD has led to a reliable methodology for determining risks to wildlife from ionizing radiation following releases of radioactivity to the environment. DSA/CERAD was invited to support a United Nations led assessment on levels and effects of radiation exposure due to the Fukushima-Daiichi nuclear accident and the subsequent review processes. DSA/CERAD lead the work on environmental impact. Various UN reports and publications from the DSA/CERAD group augmented scientific understanding of environmental impacts from radioactivity following a major nuclear accident. This has influenced developments in international recommendations and guidance on environmental protection and approaches for regulating releases of radioactivity.

2. Underpinning research

The development of methodologies to assess the risks to wildlife from ionising radiation have been a key research theme for DSA since the late 1990s. In recent years (2011 – present), a team led by Professor Per Strand/CERAD/DSA and involving the support of Dr. Justin Brown, Dr. Mark Dowdall and Mr. Ali Hosseini (MSc.), have provided specialist advice to the United Nations Scientific Committee on the Effects of Atomic Radiation, UNSCEAR, in relation to the environmental impacts from the Fukushima-Daiichi nuclear accident in Japan. These, along with other inputs on human dosimetry and health from other scientific groups, have culminated in the production of several white papers on the levels and effects of radiation exposure due to the accident [e.g. 1-3]

The accident at the Fukushima-Daiichi Nuclear Power Station on March 11, 2011, led to significant contamination of the surrounding terrestrial and marine environments. In the period 2012 to 2016, Strand and co-workers applied a suite of approaches to calculate exposure and thereafter infer effects on wildlife through comparison with compiled dose−response relationships [4]. From the assessment performed, it was inferred that, although effects on sensitive biological endpoints (e.g. effects on morbidity) in individual plants and animals might

have occurred in the weeks directly following the accident in the most contaminated areas, impacts on population integrity would have been unlikely because of the short duration of the most highly elevated exposures.

Recent years have seen a significant body of work conducted on the assessment of the accident's impacts on both the terrestrial and marine environment. Such assessments have been undertaken at various levels of biological organisation, for different species, using different methodologies and providing often divergent conclusions on the effects of the accident on the environment. In the period 2013 to 2017, Strand and co-workers provided an overview of the work conducted in relation to the environmental impacts of the Fukushima-Daiichi accident, critically comparing and contrasting methodologies and results and analysing discrepancies [5]. The review work continues under the auspices of UNSCEAR.

A new version of the ERICA Tool, was developed by Brown and co-workers during the UNSCEAR assessments, and constituted the first major update of the Tool since its initial release in 2007 [6]. Key features of the Tool have been updated. Of particular note are: new databases of environmental transfer data; and modified extrapolation approaches to select transfer data where information is not available; and the application of Bayesian approaches to draw on relevant information that would otherwise have been excluded in the derivation of transfer data. These developments led to the need to update the screening criteria incorporated in the tool.

3. References to the research

[1] UNSCEAR, 2014. UNSCEAR 2013 Report. UNITED NATIONS, Sources, Effects and Risks of Ionizing Radiation (Report to the General Assembly), vol. I. Scientific Annex A: Levels and Effects of Radiation Exposure Due to the Nuclear Accident after the 2011 Great East-Japan Earthquake and Tsunami, Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), UN, New York (2014).

[2] UNSCEAR, 2015. Developments since the 2013 UNSCEAR Report on the Levels and Effects of Radiation Exposure Due to the Nuclear Accident Following the Great East-Japan Earthquake and Tsunami. A 2015 White Paper to Guide the Scientific Committee's Future Programme of Work. United Nations Scientific Committee on the Effects of Atomic Radiation, United Nations, New York, 2015.

[3] UNSCEAR, 2016. Developments since the 2013 UNSCEAR Report on the Levels and Effects of Radiation Exposure Due to the Nuclear Accident Following the Great East-Japan Earthquake and Tsunami. A 2016 White Paper to Guide the Scientific Committee's Future Programme of Work. United Nations Scientific Committee on the Effects of Atomic Radiation, United Nations, New York, 2016.

[4] Strand, P., Aono, T., Brown, J.E., Hosseini, A., Garnier-Laplace, Sazykina, T., Steenhuisen, F., Vives I Batlle, J., 2014. Assessment of Fukushima-derived radiation doses and effects on wildlife in Japan. *Environ. Sci. Technol. Viewp.* **2014 (1)**, 198-203.

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[6] Brown, J.E., Alfonso, B., Avila, R., Beresford, N.A., Copplestone, D., Hosseini, A. (2016). A new version of the ERICA tool to facilitate impact assessments of radioactivity on wild plants and animals. *J. Environ. Radioact.* **153**, 141–148.

4. Details of the impact

Impacts include : Improving the basis and methodologies for environmental protection and for communicating the impact of a major nuclear event to stakeholders

Beneficiaries include: The International union of radioecology, IUR; The International Commission on Radiological Protection, ICRP; the scientific community working with impacts of radioactivity on the environment and UNSCEAR, International Atomic Energy Agency (IAEA) and national regulators.

Providing input to international deliberations on the theme of environmental protection from ionizing radiation.

The results performed by DSA/CERAD in the UNSCEAR assessments of environmental impact stimulated refinements of international assumptions and findings relevant to environmental radiological protection systems. The work provided support for the extension of the system of radiological protection of the environment to encompass ecosystem function and interactions between components within the ecosystem. The findings of the work have fed into scientific debate in the form of consensus conferences [1] and have resonance in other initiatives promulgated by the IUR [2]. The IUR may therefore be considered a beneficiary of the ongoing analysis.

Until recently, the ICRP system of radiological protection was focused on the protection of humans. Previous related work demonstrated the need to extend this system to address protection of the environment and this work further influenced the extension of the ICRP environmental protection framework to encompass all exposure situations, including those associated with nuclear accidents. It has been recognized that, after the occurrence of such an event, information regarding indicative population impacts may be useful in communicating the implications of the situation to stakeholders. This is particularly important when environmental conditions are such that humans have been removed from the area, and food chains leading to human exposure have been severed [3]. The work of the DSA/CERAD in relation to the environmental impacts following the Fukushima-Daiichi accident is an important input to such aspirations. The ICRP may therefore be considered a beneficiary of this ongoing analysis.

Furthermore, DSA was also involved in an assessment of environmental impacts of the Fukushima-Daiichi accident, as part of the IAEA assessment of the causes and consequences of the accident. This built on the UNSCEAR assessment and ensured that the results were considered by a broader community, including national regulators.

Instigating scientific debate regarding the environmental impacts of the Fukushima accident

The review conducted by DSA/CERAD under the auspices of UNSCEAR on the environmental impacts of the Fukushima-Daiichi accident led to the questioning of some published results. Dialogue among colleagues within CERAD were critical in crystalizing these views. The criticism was mainly centered on the significance of reported impacts at the population level, which did not correspond to current radiobiological understanding. Nonetheless, the large uncertainties involved in assessments of this type and the limitations to our existing understanding of radiation effects on environmental systems were recognized. The authors of the research that received criticism have since responded. One group [4] provided greater insights into their methodologies and the rationale for presenting certain forms of measurement that had been subject to criticism. This has had the general result of providing greater transparency and the scientific community's understanding of the aforementioned research. Another group, shared some of their underlying datasets allowing external research organizations to provide their expertise in performing dose reconstructions for birds in areas affected by the Fukushima accident [5]. This has also led to greater transparency and insights into work that has caused controversy.

Societal outreach

UNSCEAR have arranged several workshops and meetings with locals for areas affected by the Fukushima-Daiichi nuclear accident [6]. The analysis performed therefore contributed to informing public understanding of impacts (including those associated with the environment) following a major nuclear event.

Developing environmental impact assessment tools for the international scientific community

Following its release, the ERICA Tool has been widely employed in various applications worldwide. The tool has been used in quantifying environmental impacts from operating and planned nuclear power stations (e.g. [7]); to derive radiological quality guidelines for Australian U mining sites (e.g. [8]); assessments of the impact of near-surface radioactive waste repositories in Europe and Australia (e.g. [9]). In this way, the tool has contributed to the provision of a more rigorous and globally harmonised, evaluation of the environmental impacts associated with man's exploitation and use of nuclear technologies. The developmental work on the ERICA Tool has been performed under the auspices of CERAD and the beneficiary may be consider to be the scientific community (mainly environmental managers and assessors) working with impacts of radioactivity on the environment.

Another offshoot of the developmental work conducted on the ERICA Tool is the development and application of in situ methodologies for measuring exposures of wildlife in the field that have led to constructive recommendation for the improvements in impact assessment techniques [10].

The ERICA Tool has also been used by regulators as an input to the assessment and regulation of radioactive releases to the environment, thereby ensuring that potential environmental impacts are addressed in both management and in review processes.

5. Sources to corroborate the impact

[1] Bréchignac, F., Oughton, D., Mays, C., Barnthouse, L., Beasley, J.C., Bonisoli- Alquati, A., Bradshaw, C., Brown, J., Dray, S., Geras'kin, S., Glenn, T., Higley, K., Ishida, K., Kapustka, L., Kautsky, U., Kuhne, W., Lynch, M., Mappes, T., Mihok, S., Møller, A.P., Mothersill, C., Mousseau, T.A., Otaki, J.M., Pryakhin, E., Rhodes Jr., O.E., Salbu, B., Strand, P., Tsukada, H., 2016. Addressing ecological effects of radiation on populations and ecosystems to improve protection of the environment against radiation: agreed statements from a consensus symposium. J. Environ. Radioact. 158-159, 21-29.

[2] Bradshaw, C.L., Kapustka, L., Barnthouse, L., Brown, J., Ciffroy, P., Forbes, V., Geras'kin, S., Kautsky, U., Bréchignac, F., 2014. Using an ecosystem approach to complement protection schemes based on organism-level endpoints. J. Environ. Radioact. 136, 98-104.

[3] ICRP, 2014. Protection of the environment under different exposure situations. ICRP Publication 124, Ann. ICRP 43(1)

[4] Otaki J. M. and Taira W. (2017). Current Status of the Blue Butterfly in Fukushima Research Journal of Heredity, 2018, 178–187. doi:10.1093/jhered/esx037.

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[6] UNSCEAR (2016) http://www.unscear.org/docs/Web_story.pdf

[7] Vandenhove, H., Sweeck, L., Vives i Batlle, J., Wannijn, J., Van Hees, M., Camps, J., Olyslaegers, G., Miliche, C., Lance, B., 2013. Predicting the environmental risks of radioactive discharges from Belgian nuclear power plants. J. Environ. Radioact. 126, 61-76. http://dx.doi.org/10.1016/j.jenvrad.2013.07.004.

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[9] ANSTO, 2014. Safety Assessment of the Little Forest Legacy Site (LFLS). Australian Nuclear Science and Technology Organisation. ANSTO/T/TN/2013-10 rev 1. http://www.arpansa.gov.au/pubs/comment/lfls/ANSTO-T-TN-2013-10_LFLS_SafetyAssessment.pdf.

[10] Hinton, T.G., Byrne ,M.E., Webster, S.C., Love, C.N., Broggio, D.,Trompier, F., Shamovich, D., Horloogi, S., , Lance , S.L., Brown , J., Dowdall, M., Beasley , J.C. (2019). GPS coupled contaminant monitors on free-ranging Chernobyl wolves challenge a fundamental assumption in exposure assessments. Environment International. Volume 133, Part A, December 2019, 105152.

3.8.4 Societal impact: SHAMISEN Recommendations for preparedness and health surveillance of populations affected by a radiation accident

Institution: Norwegian University of Life Sciences		
Name of SFF: Centre for Radioactivity in the Environment (CERAD)		
Title of case study: SHAMISEN Recommendations for preparedness and health surveillance of populations affected by a radiation accident		
Period when the underpinning research was undertaken: 2015 - 2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): **Deborah Oughton** **Yevgeniya Tomkiv** **Alicja Jaworska** **Lavrans Skuterud**	**Role(s) (e.g. job title):** **Prof/Research Director, NMBU** **PhD Student (graduated June 2019), NMBU** **Researcher, DSA** **Researcher, DSA**	**Period(s) employed by submitting SFF:** **All 2014-present**
Period when the impact occurred: 2017 – 2019		

1. Summary of the impact

The SHAMISEN recommendations have had wide-reaching impact on the procedure and protocols for emergency preparedness in the event of a nuclear accident. These include changes in which health impacts on affected populations are monitored (to go beyond direct radiation effects and include well-being and mental health); the way that screening and epidemiological studies are carried (notably NOT to engage on population level thyroid screening), dosimetry and data registration (i.e., including personal dosimeters, social media and meeting GDPR), and support to affected populations (the importance of community resilience and sustainable infrastructure).

2. **Underpinning research**

The EU-OPERRA SHAMISEN project started in December 2015, with the goal of producing a set of recommendations that would contribute to health surveillance and related communication with affected populations after nuclear accidents. Experience, including previous work by CERAD participants, suggested that this was an area that had not been sufficiently addressed in current accident response planning in many European countries. It was also recognised that an update of emergency preparedness in this area was needed for a number of reasons. These included the fact that existing recommendations had a technical focus, with less attention paid to social, ethical, psychological issues and that the information tended to be directed towards the decisions made by experts rather than for support of affected populations . Finally, there had been a number of changes in legal and ethical requirements for health surveillance and epidemiological studies (e.g., related to data protection) that need consideration. SHAMISEN was co-ordinated by Elisabeth Cardis, ISGlobal, Spain, an internationally recognized epidemiologist.

Within the SHAMISEN project, Deborah Oughton (NMBU/CERAD) was WP leader and responsible for the final SHAMISEN Recommendation document [1]. Prior to SHAMISEN, CERAD participants from both NMBU and DSA had been involved in many EC and other international projects that highlighted the need for emergency preparedness and post-

accident management to address more than the direct radiological health impacts of an accident, and to include societal, ethical and economic aspects [2]. This approach is strongly reflected in the Shamisen recommendations, as well as other international activities at the time, including the IAEA Fukushima Comprehensive report, for which Oughton/CERAD co-ordinated the work on societal consequences [3], as well as ICRP work on Ethical Foundations of the System of Radiological Protection [4].

The SHAMISEN recommendations are based on reviews of guidelines in existence at the time of the Chernobyl and Fukushima accidents and of the actions which were taken, highlighting successes and limitations. The review includes case studies and lessons learnt from previous nuclear accidents. The 28 recommendations aim at improving health and living conditions of potentially affected populations. They cover health surveillance, epidemiological studies, dose reconstruction, evacuation and training of health personnel and other actors involved in liaising with affected populations. They also include a set of overarching and ethical recommendations, which have been elaborated further in subsequent articles [5, 6].

3. References to the research

1. Oughton, D., Albani, V., Barquinero, F., Chumak, V., Clero, E., Crouail, P., Fattibene, P., Kesminiene, A., Laurier, D., Liutsko, L., Ohba, T., Ostroumova, E., Pirard, P., Rogel, A., Sarukhan, A., Schneider, T., Tanigawa, K., Tomkiv, Y., Vale, L., Cardis E. 2017. *Recommendations and procedures for preparedness and health surveillance of populations affected by a radiation accident.* Shamisen report, pdf available at: https://issuu.com/isglobal/docs/recommendations_booklet
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3. IAEA, 2017. The Fukushima Daiichi Accident; Technical Volume 4/5. Radiological Consequences. IAEA: Vienna. Available from: https://www.iaea.org/publications/10962/the-fukushima-daiichi-accident
4. ICRP, 2018. Ethical Foundations of the System of Radiological Protection. (Authors: K-W. Cho, M-C. Cantone, C. Kurihara-Saio, B. Le Guen, N. Martinez, D. Oughton, T. Schneider, R. Toohey, F. ZöLzer), ICRP Publication 138, Sage Journals https://doi.org/10.1177%2F0146645317746010
5. Carr, Z., Maeda, M., Oughton, D., Weiss, W. 2018. Non-radiological impact of a nuclear emergency: Preparedness and response with the focus on health. *Radiation Protection Dosimetry*, 182: 112-119. https://doi.org/10.1093/rpd/ncy163
6. Kalman, C. and Oughton, D. (2019). Ethical considerations related to radiosensitivity and radiosusceptability. *International Journal of Radiation Biology*, in press (open access).

4. Details of the impact

Building on research carried out by CERAD (NMBU and DSA), a number of national and international organizations have, or are working on, strategies for nuclear emergency preparedness and health surveillance. The SHAMISEN Recommendations have had a impact at the international level, both by being recognized and endorsed by leading international

organizations, including a direct impact on the management of radiation risks in Fukushima. The SHAMISEN recommendations were presented and discussed at an International Stakeholder Workshop in Paris on 24th March 2017 [1]. The final recommendations were widely disseminated in a variety of different formats (including infographics) and translated into Japanese, Russian, Spanish and French [2].

Changes in which health impacts on affected populations are monitored.

Recognition that monitoring needs to go beyond assessment of the direct radiation effects and include well-being and mental health, has been endorsed by the OECD Nuclear Energy Agency (NEA/OECD) work on Integration of Non-Radiological Aspects of Emergency Planning [3] and WHO through its Radiation Emergency Medical Preparedness and Assistance Network (REMPAN) programme [4]. Although the psychological impacts of nuclear accidents have been noted since the Three Mile Island and Chernobyl accidents, this is the first time that international organisations have proposed practicable recommendations to tackle the issue. Previously these were sidelined as the consequences of public irrationality without a deeper understanding of the factors that lead (and can potentially alleviate) public anxiety. Improved understanding of public risk perceptions is also a central part of the CERAD Strategic Research Agenda (RA 4 Risk Assessment).

Changes in dosimetry and data registration

CERAD/NMBU was also responsible for assessment of the ethical aspects of health surveillance within SHAMISEN, which in turn built on Oughton's over 20 years experience working in the field. SHAMISEN called for an increased focus on the ethical challenges with the registration of personal data, as well as support for populations to make their own dosimetry measurements. This has been followed up by dedicated projects on the use of Health and Dosimetry Apps by affected populations [5], as well as examples of ethical challenges with personal dosimetry in Fukushima being addressed in other international projects on big data and machine learning [6].

Changes in the way that screening and epidemiological studies are carried

SHAMISEN has been critical of the prefecture level thyroid screening procedures carried out after Fukushima, including the communication protocol linked to the screening, which created more unease than reassurance and were open to misinterpretation in the media. SHAMISEN concluded that systematic population level screening should not be embarked on after an accident, but that screening should be offered, with appropriate counscelling, to resuested it. Debates on thyroid screening has been followed with publications and meetings with Japanese authorities and researchers [7].

Changes in the type of support offered to affected populations

Again, building on CERAD research, SHAMISEN stressed the importance of remediation that not only addressed dose reduction but also supports community resilience and ensure sustainable infrastructure (jobs, hospitals schools). After an accident populations are not only concerned about health effects, but also about whether they will be able to lead a normal life, and with

particular concern for children and future generations. These recommendations are supported by international developments including IAEA, NEA and ICRP [8],

Finally SHAMISEN, and more recently SHAMISEN-SINGS has had a high profile at the leading international radiological protection conferences, including invited lectures and special sessions over the past few years [9, 10].

5. Sources to corroborate the impact

1. SHAMISEN Stakeholder Workshop Paris, 2017. https://www.isglobal.org/en/new/-/asset_publisher/JZ9fGljXnWpI/content/el-proyecto-europeo-shamisen-concluye-con-una-reunion-de-actores-relevantes-en-paris
2. SHAMISEN Infographics and media pages. https://www.isglobal.org/en/-/recomendaciones-para-mejorar-la-salud-de-poblaciones-en-caso-de-accidente-nuclear
3. OECD/NEA Workshop "*Towards a better integration of Non-Radiological Public Health Aspects of protection strategies during Radiation Emergency Planning and Response*", March 2020. Specifically references SHAMISEN work. https://www.oecd-nea.org/hans/
4. WHO REMPAN The 15th meeting of the WHO Radiation Emergency Medical Preparedness and Assistance Network (REMPAN), Geneva 3-5th July, 2017. See July Newsletter and Dropbox for lectures and presentations: https://www.who.int/ionizing_radiation/a_e/rempan/en/
5. SHAMISEN-Stakeholder INvolvement in Generating Science (SINGS) Project. See https://www.isglobal.org/en/-/shamisen-sings and for CERAD/NMBU arranged Consensus Workshop on Ethical Aspects of Health and Dosimetry Apps and Citizen Science: http://radiation.isglobal.org/index.php/ca/shamisen-sings-news/consortium-meeting-and-consensus-workshop-on-ethics-1
6. UNESCO Committee for Ethics of Scientific Knowledge and Technology, COMEST. Concept notes on Artificial Intelligence (AI) and Internett of Things (IoT). http://www.unesco.org/new/en/social-and-human-sciences/themes/comest/
7. Fukushima Medical University, Nippon Foundation and IAEA meetings http://fmu-global.jp/workshop/symposium/4th-intl-expert-symposium-in-fukushima-convened/
8. ICRP Update of Publication 109 and 111 http://www.icrp.org/icrp_group.asp?id=85
9. 4th RICOMET conference on Social Sciences and Humanities in Ionising Radiation Research, Barcelona, 2019. Included a special Shamisen and Shamisen- Sings Session and an invited CERAD paper (Tomkiv et al.) on the Management of socio-psychological impact of radiation emergencies https://ricomet2019.sckcen.be/media/Files/Ricomet2019/BoA_RICOMET2019.pdf
10. 16th International Congress of Radiation Research, Manchester, 25–th August 2019. Keynote lecture by Oughton on Shamisen and Shamisen-sings http://icrr2019manchester.com/

3.9 CISMAC - Centre for Intervention Science in Maternal and Child health

3.9.1 Societal impact: Community initiated Kangaroo Mother Care improves the survival of low birth weight babies

Institution: University of Bergen		
Name of SFF: CISMAC, Centre for Intervention Science in Maternal and Child health		
Title of case study: Community initiated Kangaroo Mother Care improves the survival of low birth weight babies		
Period when the underpinning research was undertaken: August 2015-October 2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Sarmila Mazumder, Society for Applied Studies, India	**Principal Investigator**	
Sunita Taneja, Society for Applied Studies, India	**Principal Investigator**	
Halvor Sommerfelt University of Bergen and Norwegian Institute of Public Health, Norway	**Co-Principal Investigator**	**Complete SFF period 2013-2022**
Period when the impact occurred: From now onwards		

1. Summary of the impact

The ~20 million babies who are born with low birth weight (LBW) constitute ~15% of all births globally. These babies are at a much higher risk of severe illness, growth failure and death than full term babies.

CISMAC developed and tested an intervention, namely community initiated Kangaroo Mother Care (ciKMC), which has demonstrated the ability of mothers and families to successfully care for LBW babies who are not ill outside healthcare facilities in India. Our study shows a substantial survival benefit and improvement in early infant nutrition. On a population level, only ~80 LBW babies would need to receive ciKMC to prevent one death.

The findings will influence health policies on care of LBW babies at local, national and global levels.

2. Underpinning research

Babies born weighing less than 2500g are categorized as having low birth weight (LBW). They are at a substantially increased risk of death and impaired long-term development from childhood to adult life. LBW babies constitute around 15% of all births globally, in India, almost every third child is born with LBW.

Before this study, we already knew that initiating kangaroo mother care (KMC), which consists of skin-to-skin contact and exclusive breastfeeding, in hospitals can reduce their risk of dying by

40%. However, in India and in many other countries in Asia and Africa, many babies are born outside of hospital or leave the hospital too early, before KMC is started. CISMAC researchers undertook a very large randomized controlled trial in India to examine the safety and benefit of community-initiated KMC (ciKMC) for such LBW babies who are otherwise healthy. The intervention was developed during one year of formative research, which was essential for designing the intervention to be initiated in the homes in a way that would be culturally acceptable for the families. The intervention reached almost all of the LBW babies identified in the population. Mothers, with support from their families, applied it with a high intensity (averaging almost 11 h of skin-to-skin contract per 24 h and exclusive breastfeeding).
The intervention reduced the risk of dying during the first six months of life among these fragile LBW babies by 30%. On a population basis, this intervention, which can be implemented in the Indian primary health care system with moderate investments, would require only ~80 children to receive ciKMC to prevent one death. The children receiving ciKMC also experienced lower risk of malnutrition and fewer disease episodes which may translate into additional benefits on child development.

The findings of the study fills an important research gap, supporting the extension of the promotion of KMC to all LBW babies who are not ill, even those born outside of health facilities or discharged from facilities without KMC.

In addition to the above-mentioned scientific and medical contributions, the findings of the ciKMC study will have important societal impact in terms of demonstrating the ability of mothers and families to successfully care for LBW babies outside health facilities. This is important in terms of maternal self-confidence, demonstrating how much the family functioning as a unit can improve care for vulnerable newborns, and also the importance of support from the health services in extending care to households in the community.

3. **References to the research**

Upadhyay RP, Martines JC, Taneja S, Mazumder S, Bahl R, Bhandari N, Dalpath S, Bhan MK. Risk of postneonatal mortality, hospitalization and suboptimal breast-feeding practices in low birthweight infants from rural Haryana, India: findings from a secondary data analysis. BMJ Open. 2018 Jun 22;8(6):e020384.

Mazumder S, Upadhyay RP, Hill Z, Taneja S, Dube B, Kaur J, Shekhar M, Ghosh R, Bisht S, Martines JC, Bahl R, Sommerfelt H, Bhandari N. Kangaroo mother care: using formative research to design an acceptable community intervention. BMC Public Health. 2018 Mar 2;18(1):307.

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Sarmila Mazumder, Sunita Taneja, Brinda Dube, Kiran Bhatia, Runa Ghosh, Medha Shekhar, Bireshwar Sinha, Rajiv Bahl, José Martines,. Maharaj Kishan Bhan, Halvor Sommerfelt, Nita Bhandari. Effect of community-initiated kangaroo mother care on survival of low birth weight infants: a randomised controlled trial. The Lancet. *In press*.

4. Details of the impact

The cKMC trial fills an important knowledge gap in available evidence which so far has been restricted to hospital-initiated KMC (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002771.pub4/epdf/full) . The new information CISMAC provides through this study will contribute to scale-up of cKMC for many more low birthweight babies. We expect this will influence child health promotion policies as presented in WHO newborn care guidelines over the next decade.

As part of the research activities, several postgraduate students have benefited from research by learning as being part of the research team as well as leading specific sub-studies within the main trial. Thus, it at least two postgraduate medical doctors will base their PhD studies on such studies.

5. Sources to corroborate the impact

The manuscript presenting the findings of the study will be published in The Lancet during September of 2019 accompanied by an editorial/comment commissioned by the journal that will highlight its importance. But even before this important publication, CISMAC's research is starting to influence local, Indian and international policymakers' thinking about newborn care. This is due to the briefings on the findings provided informally to state and national government representatives in India and WHO's Department of Maternal, Adolescent and Child Health at the global level.

3.10 CNC - Centre for Neural Computation

3.10.1 Scientific impact: Discovery of brain's mechanisms for space and navigation

Institution: Kavli Institute for Systems Neuroscience, NTNU		
Name of SFF: Centre for the Biology of Memory (2002-12) and Centre for Neural Computation (2012-22)		
Title of case study: Discovery of brain's mechanisms for space and navigation		
Period when the underpinning research was undertaken: 2002-19		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): May-Britt Moser and Edvard Moser and their team	**Role(s) (e.g. job title): Professor, Centre Directors**	**Period(s) employed by submitting SFF: 2002-**
Period when the impact occurred:		

1. Summary of the impact

Centre of Excellence funding enabled Edvard Moser (CoE Director 2002-12) and May-Britt Moser (CoE Director 2013-22), with their colleagues, to start a comprehensive long-term research program on mechanisms of memory and spatial mapping in the mammalian brain. They discovered grid cells, cells whose discharges map the spatial environment in a periodic coordinate system-like manner. They showed subsequently how a variety of functional cell types in the entorhinal microcircuit contribute to the formation of a map of self-location, and how the outputs of this map are used by memory networks in the hippocampus. Their work, which has fundamentally transformed our understanding of brain mechanisms for spatial location, was recognized with the Nobel Prize in Physiology or Medicine in 2014.

2. Underpinning research

During 1.5 decades of CoE funding, May-Britt and Edvard Moser and their colleagues have jointly shown how spatial location and spatial memory are computed in the mammalian cortex. Their most remarkable contribution, recognized by the 2014 Nobel Prize in Physiology or Medicine, is the discovery of grid cells in the mammalian entorhinal cortex. Grid cells are place-modulated neurons whose firing locations define a periodic hexagonal array over the entire local environment. These cells form an essential part of the brain's internal metric for navigation. Since the discovery, the Mosers have shown how space is mapped onto discrete neural populations and how these populations interact with other cell types to form a coherent internal map of location.

The simplicity and crystal-like structure of the grid cells offers unprecedented opportunities for understanding mammalian behaviour at the level of neuronal network computation, well beyond the domain of spatial mapping and navigation. Few if any other areas of systems neuroscience have reached this level of sophistication. The breakthrough has taken place within a period of 15-20 years, with the discovery of grid cells in 2005 – 3 years after the inauguration of the first CoE – as the most important eye-opener.

The first clues to the discoveries came when the Mosers showed, in 2002 and 2004, that spatial signals in place cells of a brain area called the hippocampus must originate from a neighbouring area, the entorhinal cortex, which has dense direct inputs to the hippocampus. In 2005, the Mosers showed that the activity of spatially-modulated entorhinal cells forms a grid pattern. After 2005, the Mosers have shown how entorhinal grid cells interact with other cell types to generate a

continuously updated representation of self-location that can be used in any environment, irrespective of shape and landmarks. These 'other' cell types, also discovered by the Mosers, include and speed cells (cells with firing rates that increase linearly with running speed, discovered 2015), border cells (cells that fire specifically along geometric borders, discovered 2008), and object-vector cells (cells that fire at specific distances and directions from prominent landmarks in the environment, forming a positional vector code, discovered 2019). The Mosers have also shown how the outputs of the entorhinal circuit are used to form distinct memories in the hippocampus (2004-2013) and they have shown that grid cells have strong innate components (2010). Finally, the Mosers have described how grid cells are organized into discrete modules, in a way that is different from map-like columnar arrangements in sensory cortices (2012).

3. References to the research

Hafting, T., Fyhn, M., Molden, S., Moser, M.-B., and Moser, E.I. (2005). Microstructure of a spatial map in the entorhinal cortex. **Nature**, 436, 801-806.

Fyhn, M., Hafting, T., Treves, A., Moser, M.-B. and Moser, E.I. (2007). Hippocampal remapping and grid realignment in entorhinal cortex. **Nature**, 446, 190-194.

Solstad, T., Boccara, C.N., Kropff, E., Moser, M.-B. and Moser, E.I. (2008). Representation of geometric borders in the entorhinal cortex. **Science**, 322, 1865-1868.

Stensola, H., Stensola, T., Solstad, T., Frøland, K., Moser, M.-B. and Moser, E.I. (2012). The entorhinal grid map is discretized. **Nature**, 518, 207-212.

Kropff E, Carmichael JE, Moser M-B, Moser EI (2015). Speed cells in medial entorhinal cortex. **Nature**, 523, 419-424.

Høydal, Ø.A., Skytøen, E.R., Andersson, S.O., Moser, M.-B., Moser, E.I. (2019), Object-vector coding in the medial entorhinal cortex. **Nature**, 568,400-404.

4. Details of the impact

Scientific impact: The discovery of grid cells and their control of population dynamics in the hippocampus has led to a complete revision of established views of how the brain calculates self-position. Spatial mapping is becoming one of the first non-sensory cognitive functions to be characterized at a mechanistic level in mammalian neuronal networks. With the discovery of a number of functionally specialized spatial cells in the entorhinal cortex, it has become possible to study neural computation at the high end of the cortical hierarchy, quite independently of sensory inputs and motor outputs. The presence of an abstract and easily monitored neural representation at the peak of mammalian cortex has provided direct access to some of the most fundamental operational principles of cell assemblies and microcircuits in the mammalian brain.

The research underpinning this breakthrough has been performed in its entirety at the Centre for the Biology of Memory and the subsequent Centre for Neural Computation at NTNU (2002-12 and 2012 – today, respectively). CoE funding has been necessary to conduct the high-risk high-gain research that led to the discoveries. The investigators had the time to investigate brain areas that were terra incognita at the time, they had the funds to afford failures and to take new directions, and they could compete for the best talents in recruitments for young-researcher positions.

The best indicator of the impact of the research is the 2014 Nobel Prize in Physiology or Medicine to May-Britt and Edvard Moser. The Nobel Prize is the world's most thorough research evaluation.

Societal impact: Understanding the neural codes of the cortex is fundamental to the development of treatments across the entire spectrum of neurological and psychiatric diseases. We still lack a mechanistic insight into diseases that affect the cortex, such as Alzheimer´s disease, schizophrenia, and depression. Revealing the neural codes of the cortex is a necessary if we are to understand causes of these diseases, which in turn is required to develop mechanistically-based treatments. Investigators of major diseases, such as Alzheimer's disease, including researchers at the Centre for Neural Computation, are taking note of these findings and directing their search for disease mechanisms to the very same cells found to encode location in the brain.

5. Sources to corroborate the impact

The research on the brain's system for space has been recognized by a series of scientific prizes and awards, not only the Nobel Prize. Here is selected list (all shared between M-B and E Moser):

2005: 28th annual W. Alden Spencer Award (College of Physicians and Surgeons of Columbia University)
2006: 10th Prix "Liliane Bettencourt pour les Sciences du Vivant" (Fondation Bettencourt, Paris)
2006: 14th Betty and David Koetser Award for Brain Research (University of Zürich)
2008 : 30th Eric K. Fernström's Great Nordic Prize (Fernström Foundation, University of Lund)
2011: 26th Louis-Jeantet Prize for Medicine (Louis-Jeantet Foundation)
2011: Anders Jahre's Great Nordic Prize for Medical Research (Univ. Oslo)
2013: 13th Perl/UNC Neuroscience Prize (Univ. of North Carolina)
2013: 102nd F. Nansen Award of Outstanding Research in Science and Medicine, Norwegian Acad. of Science
2013: 47th Louisa Gross Horwitz Prize for Biology or Biochemistry (Columbia University)
2014: 59th Karl Spencer Lashley Award (American Philosophical Society)
2014: 30th Koerber European Science Prize (Koerber Foundation)
2014: **Nobel Prize in Physiology or Medicine (Karolinska Institute, Stockholm)**
2018: Grand Cross of the Royal Norwegian Order of St. Olav (H.M. Harald of Norway)

May-Britt and Edvard Moser received the Nobel Prize "for their discoveries of cells that constitute a positioning system in the brain." The prize was shared with John O'Keefe. For prize motivation, see https://www.nobelprize.org/prizes/medicine/

3.10.2Scientific impact: Neural mechanisms of Alzheimer's disease

Institution: Kavli Institute for Systems Neuroscience, NTNU		
Name of SFF: Centre for Neural Computation (2012-22)		
Title of case study: Neural mechanisms of Alzheimer's disease		
Period when the underpinning research was undertaken: 2012-19		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Menno Witter, Cliff Kentros, May-Britt Moser and Edvard Moser and their teams	**Role(s) (e.g. job title): Professors**	**Period(s) employed by submitting SFF: 2012-**
Period when the impact occurred: 2012-2019		

1. Summary of the impact

Centre of Excellence funding enabled Menno Witter, Cliff Kentros, Edvard Moser and May-Britt Moser, with their colleagues, to start a long-term translational research program aimed at identifying mechanisms of neural degeneration in the brain's systems for space, time and memory. Following the discovery of grid cells and other cell types that map the spatial environment in a brain region called the entorhinal cortex, Witter and Kentros, and more recently the Mosers, have started attempts to localize the origin of Alzheimer's disease-like symptoms in mouse models. Witter and his colleagues have shown that cells in the entorhinal cortex – the home of the brain's mechanisms for spatial mapping – are the first to accumulating soluble amyloid-beta oligomers intracellularly. These observations point to the spatial mapping system as an origin of development of the disease.

2. Underpinning research

A major research ambition of Witter and his colleagues has been to describe the local networks underlying the existence of grid cells in layer II of the medial entorhinal cortex and the absence of such cells in its lateral counterpart. Using advanced combinations of cell-specific markers, tracers and recording of neuronal activity, Witter and colleagues discovered that principal cells in a key layer of this brain region come in two types, those expressing the protein calbindin and those expressing reelin. The reelin expressing neurons are the unique origin of projections to the hippocampal formation, and they are among the first to die in Alzheimer's Disease. This has led to the development of a successful translational research line in the Witter group, in which they address the underlying mechanisms of this specific vulnerability in Alzheimer's disease. Witter and colleagues found that reelin-expressing cells are the first to start accumulating soluble amyloid-beta oligomers intracellularly in both transgenic mouse models for Alzheimer's disease and in patient. They are currently investigating the molecular and metabolic pathways involved in this selectivity. In collaboration with the Kentros group, they have established a new enhancer-based genetic approach that allows them to selectively modify the disease starter-neurons. Such modifications may eventually lead them on the path to a cure for Alzheimer's disease.

3. References to the research

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Couey JJ, Witoelar A, Zhang S-J, Jing Y, Dunn B, Czajkowski R, Moser M-B, Moser EI, Roudi Y, Witter MP (2013) Recurrent inhibitory circuitry as a mechanism for grid cell formation. Nat Neurosci 16:318-324.

Kobro-Flatmoen A, Witter MP (2016) Reelin-immunoreactive neurons in entorhinal cortex layer II selectively express intracellular amyloid in early Alzheimer's disease. Neurobiol Dis. 93:172-183.

Nilssen ES, Jacobsen B, Fjeld G, Nair RR, Blankvoort S, Kentros C, Witter MP (2018) Inhibitory Connectivity Dominates the Fan Cell Network in Layer II of Lateral Entorhinal Cortex. J Neurosci. 38: 9712-9727.

Ohara S, Gianatti M, Itou K, Berndtsson CH, Doan TH, Kitanishi T, Mizuseki K, Iijima T, Tsutsui K-I, Witter MP (2019) Entorhinal layer II calbindin-expressing neurons originate widespread telencephalic and intrinsic projections Front. Syst. Neurosci, under revision

4. Details of the impact

Scientific impact: The brain's system for mapping of location is one of the first to be affected in Alzheimer's disease – one of the largest health burdens of modern society. There is currently no cure for this disease. A major reason for the lack of progress on the disease is that studies of Alzheimer's disease have looked for aberrant biochemical processes without taking into account the characteristics of the brain cells where the pathology starts and from which the disease progresses to the rest of the brain. Since the 1990s, accumulating evidence has pointed to neurons in entorhinal cortex as the site of the earliest degeneration in Alzheimer's disease. Unfortunately, this research has never reached out fully to the AD research community. A possible reason is that EC has long been a blank spot on the brain map. The discovery of a space circuit in the entorhinal cortex by the Mosers, in collaboration with Witter and their colleagues, has changed this situation. With the discovery of space-coding grid cells in entorhinal cortex, this brain area is becoming recognized as a hub of the brain´s network for spatial navigation, which often is the first cognitive function to be impaired in Alzheimer's disease. Investigators of Alzheimer's disease, including Witter and his colleagues at the Centre for Neural Computation, are now directing their search for disease mechanisms to the very same cells found to encode location in the brain. Witter's discovery that reelin-expressing cells in the entorhinal cortex are the first to start accumulating soluble amyloid-beta oligomers intracellularly has a huge potential in that it points researchers to possibly origins of Alzheimer's disease. While it is too early to tell whether the work will lead to a treatment eventually, the redefinition of Alzheimer's disease as a brain-region-related disease is thought to speed up research on the disease again.

5. Sources to corroborate the impact

It is too early to tell the extent to which Witter's observations will change our understanding of the mechanisms that initiate degeneration in Alzheimer's disease brains. However, the potential has been recognized by several grants to Witter and colleagues to work further on their findings, e.g. from the Thon Foundation. Witter and the Mosers are shortlisted for an Alzheimer Centre grant from the K.G. Jebsen Foundation, and Witter has been appointed visiting professor at Johns Hopkins University to pursue these questions.

3.11 MultiLing - Center for Multilingualism in Society Across the Lifespan

3.11.1 Societal impact: Collaborative Language Capacity Building

Institution: University of Oslo, Department of Linguistics and Scandinavian Studies		
Name of SFF: Center for Multilingualism in Society Across the Lifespan (MultiLing)		
Title of case study: Collaborative Language Capacity Building		
Period when the underpinning research was undertaken: 2013 - present		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Haley De Korne	Research/ now Postdoc	2016/ 2017 – present
Janne Bondi Johannessen	Professor	2013 – present
Pia Lane	Professor	2013 – present
Period when the impact occurred: 2013-2019		

1. Summary of the impact

There are hundreds of under-resourced languages (languages lacking teaching material, dictionaries, etc.) in many parts of the world. This poses a problem for education and hence democracy. Several research projects at MultiLing have resulted in language materials and contributed to language capacity building, including collaborative projects in Ethiopia, Norway, and Mexico. Collaboration with linguists, educators and policy makers in these countries has resulted in **teaching materials**, **professional development for teachers and scholars, and support from policy makers for the under-resourced languages**. It strengthens the social position of these languages and increases opportunities for their speakers.

2. Underpinning research

Ethiopia is a highly multilingual country. Through the NORHED project led in Norway by Janne Bondi Johannessen, Ethiopian staff and PhD students have done research on orthographies, grammars and lexical matters in a selected number of languages. This research has been published as chapters in the anthology of Mendisu and Johannessen (2016), and a summary has been published by Jekale, Mendisu and Johannessen (2019). Ethiopian sign language is one of the major under-resourced languages in Ethiopia, and Pawlos (2015) is a central work on sign language in Ethiopia. Around ten PhD candidates have been supported, and several have come to MultiLing's Summer and Winter Schools, which have enhanced the sociolinguistic understanding of the language situation, and added to the quality of their theses, of which four have been submitted and accepted so far. The Norwegian researchers have supervised, co-edited, and co-written papers, and produced speech corpora in collaboration with the Ethiopians (see Section 4, details of the impact).

Kven, a minoritised Finnic language primarily spoken in **Northern Norway**, is now in a process of revitalization after decades of decline in users. Lane has been PI of a number of projects documenting the Kven language, investigating language shift and revitalization, and analyzing the

standardisation of Kven, both as an academic and a participant in the standardisation process. The project *Minority Language Standardisation* shifted the main focus from linguistically oriented approaches and top-down perspectives to social actors and local practices, showing that the role of social actors is essential in order to understand the success or failure of minority language standardisation (Lane 2017). The project resulted in an acclaimed edited volume analyzing how individual social actors engage with, support, negotiate or reject aspects of language standardization processes and what the role of individual social actors is in standardisation processes on four continents (Lane, Costa & De Korne 2017).

There are 364 recognized Indigenous languages in **Mexico**, many of which lack pedagogical and civic resources. Although Mexico passed a law in 2003 that recognizes the rights of Indigenous language speakers to use their languages in education and other public domains such as the health and judicial sectors, these rights have yet to be implemented in many communities. Since 2013, De Korne has researched the programs and pedagogies used to teach Isthmus Zapotec, an Oto-manguean language spoken by around 100,000 people in the state of Oaxaca. Ethnographic observation of Isthmus Zapotec education programs and interviews with representative stakeholders resulted in insights into the shortcomings of the current education programs, and recommendations for strategic improvements at two university campuses (De Korne, López Gopar & Ríos Ríos 2018) and a community-based program. In collaboration with administrators and teachers in several programs, De Korne developed and helped to facilitate professional development courses and curriculum guides for teachers in this context. In autumn 2018, several researchers from Oaxaca participated in a seminar and exchange with language and education researchers at the University of Oslo.

3. References to the research

• Derib Ado Jekale, Binyam Sisay Mendisu and Janne B. **Johannessen**. 2019 "Linguistic Capacity Building in Ethiopia: Results and Challenges". In: T. Halvorsen, K. S. Orgeret & R. Krøvel (eds.). *Sharing Knowledge, Transforming Societies: The Norhed Programme 2013–2018.* Cape Town: African Minds.

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• **Lane**, P. (2015). Minority language standardisation and the role of users. *Language Policy*,14, 3, 263–283 https://link.springer.com/article/10.1007/s10993-014-9342-y

• Wright, S., U. **Røyneland** & P. **Lane** (eds.) *Language standardisation: Theory and practice* Special issue of *Sociolinguistica* 30. Mouton de Gruyter.

• **De Korne**, H., López Gopar, M. E., & Rios Rios, K. (2018). Changing ideological and implementational spaces for minoritised languages in higher education: Zapotequización of language education in Mexico. *Journal of Multilingual and Multicultural Development*, 0(0), 1–14. https://doi.org/10.1080/01434632.2018.1531876

4. Details of the impact

1) **Ethiopia:**

There are a large number of languages used as mother tongues in Ethiopia, but many of them are not developed for writing. This is a problem for instruction in the educational system (and goes against UNESCO's advocacy for multilingual education since 1953), as well as for democracy, as large groups of people do not get necessary information concerning civil rights. It also goes against the Ethiopian constitution, which states that people have the right to learn in their own language. The project *Linguistic Capacity Building: Tools for the inclusive development of Ethiopia (LCB)* (Cooperation between University of Oslo and the Universities of Addis Ababa and Hawassa.) enables more languages to be used in schools and in local administration. The result is increased resources and opportunities for children and adult speakers of disadvantaged spoken and signed languages to use their mother tongue in Ethiopia.

Some output of the LCB:

The following outputs contribute to augmenting literacy among the respective language group populations and to developing educational tools. The capacity-building of Ethiopian scholars through MA and PhD degrees contributes to carrying on the legacy of the project.

• Two primers on Kambaata. A total of 4000 copies have been published and handed over to the zone's administration.

• Sidaama Dictionary (Kjell Magne Yri & Steve Pepper). Available freely online: https://dictionaria.clld.org/contributions/sidaama

• Speech corpora for Hamar, Muher, Gumer, Haddiyyaa, Gamo Oromo and Amharic, at the University of Oslo website and accessible for free. (Valuable tools for dictionary and grammar writing, available freely online: http://tekstlab.uio.no/ethiopia/)

Under preparation:

- An Aari bilingual dictionary, a primer and a dictionary in Gumer, a bilingual dictionary in South Omo Zone.
- Two new MA programmes (Sign language, AAU, and Multiculturalism, HU)

Also:

- 10 Phd candidates (4 finished)
- 40 MA candidates (30 finished)

2) **Norway:**

During the period 2007-2010 Pia Lane was a member of the Kven Language Council whose task was to develop a written standard for Kven. Their work and the Ruija corpus of Kven dialects (developed by Lane) laid the foundations for the Kven standard launched in 2014 (Söderholm 2014). The standard was initially criticized for relying primarily on one of the Kven dialects, and

Lane's publications on the standardisation of Kven and users' reactions to the standard were used to inform further development of the Kven standard.

The Norwegian Ministry responsible for indigenous and minority affairs was an official partner of the project *Minority Language Standardisation* (directed by Lane), and this provided input to the *Goal oriented plan for the Kven language* (https://www.regjeringen.no/contentassets/b1bf2ee2a7824c06ac22443e011f0fd6/plan_kvensk_spraaak.pdf). Insights from the project were also used as a basis for the documentary film *The Secret Language* (Lightsource Productions) addressing language shift, revitalization and the standardisation of the Kven language. The documentary was screened by the NRK – Norwegian Broadcasting Corporation – and is available on NRK's website. The documentary is used as a teaching resource on several courses in higher education, thereby contributing to raising awareness of the Kven minority in Norway and also of multilingualism in general. Because of her expertise on Kven language and culture, Lane was appointed by the Norwegian Parliament to serve on the Norwegian Truth and Reconciliation Commission, a commission of inquiry to document injustices against Sámi and Kven peoples, for examining current consequences of oppressive policies, and to propose measures for further reconciliation.

3) **Mexico**

De Korne has used applied linguistic research and ethnographic monitoring to collect data on the practices inside Indigenous language classrooms, and to discuss the strengths and shortcomings of these practices with key stakeholders. Through consultation sessions and recommendations based on prior ethnographic research, De Korne worked with administrators and teachers at two university campuses in order to develop strategies for program improvement, including curriculum plans and professional development activities for trainee teachers (2013-2018). In 2014, she collaborated with administrators from one university campus to host a 2-day conference on Indigenous language teachers in Oaxaca, with the aim of fostering professional and supportive networks among teachers in the region. She was also part of an interdisciplinary team of linguists, botanists, and Isthmus Zapotec speakers lead by Gabriela Pérez Báez (Smithsonian Institute/ University of Oregon), and contributed to the production of learning and literacy materials (Pérez Báez 2015), as well as coordinating outreach workshops for children (Pérez Báez 2018).

5. Sources to corroborate the impact

- See publications in (3) for Ethiopia.

3.11.2Societal impact: Multilingualism on the social and political agenda

Institution: University of Oslo, Department of Linguistics and Scandinavian Studies

Name of SFF: Center for Multilingualism in Society across the Lifespan (MultiLing)

Title of case study: Multilingualism on the social and political agenda

Period when the underpinning research was undertaken: 2013 - present

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Valantis Fyndanis	Postdoctoral fellow / now Researcher	2014 – 2018/ 2019–present
Mira Goral	Professor/Core group	2015 – 2020
Pernille Hansen	PhD/Postdoctoral fellow	2014/ 2017 – present
Kristin Vold Lexander	Researcher/now postdoc	2013 – present
Marianne Lind	Researcher/Core group	2015 – 2018
Monica Norvik	Researcher/Core group	2013 – present
Else Ryen	Associate Professor/Core group	2015 – 2016 (retired)
Unn Røyneland	Professor/Core group	2013 – present
Hanne Gram Simonsen	Professor/ Core group	2013 – 2017 (retired)
Bente Ailin Svendsen	Professor/Core group	2013 – present
Ingebjørg Tonne	Professor/Core group	2018 – present

Period when the impact occurred: 2013 – 2019

1. Summary of the impact

Multilingualism has long been seen in the public eye as a problem to be overcome. MultiLing as a Centre of Excellence has greatly contributed to highlighting **multilingualism as a resource** for both the individual and society. The impact case presented here highlights the social impact of MultiLing's research and indicates (1) how new language assessment tools have been developed for multilinguals in Norway; (2) how citizen engagement has been brought to research on multilingualism in schools; and (3) how multilingualism has been brought more into the educational curricula and the political agenda.

2. Underpinning research

Since the establishment of MultiLing in 2013, **multilingualism as a resource** has been brought to the attention of the public and multilingualism has been increasingly on the public agenda.

1) To obtain full knowledge about the linguistic and communicative competence of a multilingual, all languages must be assessed. Whether it concerns a developing child or a person with aphasia often only the majority language is taken into consideration. This is due to the misconception that "language" means the majority language and to the lack of adequate **assessment and treatment tools** in other languages. MultiLing researchers (Fyndanis, Goral, Hansen, Lind, Norvik, Simonsen) have developed and adapted assessment tools for Norwegian and other languages, in order to assess multilinguals across their languages. MultiLing has provided new ideas and methods in the intersection between psycholinguistics and sociolinguistics, through two recent COST Actions on language assessment, resulting in several new tools developed collaboratively for more than 20 languages. These include the Cross-linguistic Lexical Tasks (CLT) and the Parents of Bilingual Children Questionnaire (PABIQ) for preschoolers as well as the Comprehensive Aphasia Test (CAT) for adults.

2) Norway does not have national census data on the extent of multilingualism in schools. To counter this, MultiLing researchers (Lexander, Ryen, Svendsen) launched **projects using *citizen science***: a) the engagement of pupils in a citizen science (CS) project where all pupils in Norwegian schools were invited to be language researchers; b) the development of a publicly available database where pupils registered their data; c) a national survey on multilingualism, in collaboration with the Norwegian Language Council, including teachers ('Room for languages?') (2015). In the CS project, which was part of the RCN's annual Research Campaign in 2014, Svendsen employed CS as used in natural sciences and further developed Citizen Sociolinguistics theoretically and methodologically. MultiLing developed a database for the pupils' registration of their data, publicly available for further research or citizen engagement. Based on these results, MultiLing developed, in collaboration with the Norwegian Language Council, a national survey on multilingualism in schools including teachers. Results demonstrate there is a vast linguistic diversity in Norwegian schools that is neglected for learning and teaching purposes.

3) MultiLing has brought multilingualism more into **educational curricula** and the **political agenda**. Based on her research on second language acquisition, Tonne was appointed by the Norwegian Directorate for Education and Training to the national group for the renewal of the curriculum for Norwegian as a school subject. The work is part of the curriculum renewal LK20 of all the subjects in the Norwegian school, grades 1 to 13, with implementation planned for the fall of 2020. In the final draft of the curriculum for Norwegian, multilingualism has been extensively incorporated, more than in previous curricula. Based on her research on linguistic diversity in Norway, Røyneland was appointed by the Norwegian Language Council to lead an Expert Committee to identify the most important challenges for Norwegian language policy for the future. Their report 'Language in Norway – Culture and Infrastructure' was presented in November 2018 to Norway's Minister of Culture and Equality, and has been highly influential (cf. the new Language Law). In this report, both old and new multilingualism in Norway is highlighted as an important resource to be addressed in society and contains a number of suggestions of specific policy measures.

3. References to the research

Goral, M., M. **Norvik** & B. Jensen. (2019). Variation in language mixing in multilingual aphasia. *Clinical linguistics & phonetics*, 1-15.

Hansen, P., Łuniewska, M., **Simonsen**, H. G., Haman, E., Mieszkowska, K., Kołak, J., & Wodniecka, Z. (2019). Picture-based vocabulary assessment versus parental questionnaires: A cross-linguistic study of bilingual assessment methods. *International Journal of Bilingualism*, *23*(2): 437-456.

Fyndanis, V. M. **Lind**, S. Varlokosta, M. Kambanaros, E. Soroli, K. Ceder, K. K. Grohmann, A. Rofes, H. G. **Simonsen**, J. Bjekić, A. Gavarró, J. Kuvač Kraljević, S. Martínez-Ferreiro, A. Munarriz, M. Pourquie, J. Vuksanović, L. Zakariás & D. Howard. (2017). Cross-linguistic adaptations of the Comprehensive Aphasia test: Challenges and solutions. *Clinical linguistics & phonetics*, 31(7-9): 697-710.

Røyneland, U. (2016). Språkleg mangfald i Noreg – problem eller ressurs? Fleirspråklegheit som forskingsfelt ('Linguistic diversity in Norway – Problem or resource? Multilingualism as a research field'). *Samtiden* 3-4. https://samtiden.no/2016/11/30/samtiden-3-4-2016/

Røyneland, U. (et al.) (2018). *Språk i Norge – kultur og infrastruktur* ('Language in Norway – Culture and Infrastructure'). https://sprakinorge.no

Svendsen, B. A. (2018). The dynamics of citizen sociolinguistics. *Journal of Sociolinguistics*, 22(2): 137–160. https://onlinelibrary.wiley.com/doi/abs/10.1111/josl.12276.

Svendsen, B. A., E. **Ryen** and K. V. **Lexander.** (2015). *Ta tempen på språket!* ('Taking the temperature of language!') Research Council of Norway. https://www.miljolare.no/innsendt/oppslag/1336/5502d9f97a260/rapport_fd2014.pdf.

The database: https://www.miljolare.no/aktiviteter/ord/

Tønne, I. (2019). Å ta telling. Språklig mangfold i fagfornyelsen LK20 ('To count. Linguistic diversity in the renewal of school subjects LK20'). *Prosa.* http://prosa.no/debatt/a-ta-telling-spraklig-mangfold-i-fagfornyelsen-lk20/

4. Details of the impact

Norway is a multilingual country yet there has been little awareness about what multilingualism actually is and it has long been seen in the public eye as a problem to be overcome and not as a resource. This is a great loss for both the individual and society and may result in discrimination, prejudice, lack of or inadequate education, exclusion from working life and from society at large, a potentially more dangerous working environment, poor diagnosis and assessment of health issues, and poverty. There is a need for language assessment for educational purposes and for treatment of pathologies; moreover, there is a need for a heightened awareness of multilingualism in education and in society as a whole. MultiLing as a Centre of Excellence has greatly contributed to highlighting **multilingualism as a resource**, and to meeting these challenges through the development of assessment tools, nationwide surveys of language use and a comprehensive language exhibition in Oslo, involvement in the formation of national curricula, and spearheading a specially commissioned report on the future of Norwegian language policy – a report the Government has anticipated for making a new national language law and a new White paper on language in Norway, due Spring 2020.

(1) In assessing the language skills of multilingual individuals, it is crucial to consider all their languages. For multilingual children, assessing only one language may lead to both over-diagnosis and under-diagnosis of developmental language disorder (DLD). However, tools adequate for assessment across languages are scarce. For adult multilinguals with aphasia, assessment in all their languages is necessary for a precise diagnosis and to give and evaluate appropriate treatment, in particular to measure possible generalization effects across languages. Current practices rarely allow for proper assessment, as few of the existing tools are designed for, or even suitable for, cross-linguistic assessment. Furthermore, there is a lack of awareness of the nature of multilingualism, and multilingual individuals meet monolingual language attitudes only focusing on Norwegian. We have developed useful assessment tools and methods that are used in research, and that provide new tools to practitioners within early childhood education and care, speech and language therapy, medical, educational and psychological counselling service. These tools and our targeted dissemination activities have communicated insights from both psycholinguistics and sociolinguistics, and are a result of MultiLing. Our dissemination efforts have generated interest across educators, therapists, administrators and politicians, and these along with the assessment tools have resulted in greater awareness of multilingualism as a resource and in more valid assessment of the language abilities of multilinguals.

(2) Although Norway is a multilingual country, we do not have national census data on the language competence and composition in schools or families. Multilingualism in the school is encouraged in Norwegian, Sámi, English and the traditional foreign languages, but other languages are left invisible. Researchers at MultiLing generated knowledge through a national research campaign where they invited all pupils to become language researchers, and they

developed a publicly available database. To reveal the linguistic diversity of Norway, the researchers developed a language exhibition, which included the pupils' work from the national campaign as well as results from other research projects at MultiLing (Oslo City Museum 2016–2018). Parts of the exhibit were presented at the Research Market (2014, 2018), and a "language lounge" was created at the Oslo City Museum (consisting of debates, lectures, quiz, city walks, conversations with writers 2016–2017). The language exhibition drew more than 150 000 visitors, ca 12 000 unique visitors searched the database, and the exhibition received substantial media coverage. Both pupils and teachers expressed their content with participation in the campaign. The language exhibition was in collaboration with Oslo City Museum, the Norwegian Language Council, Helge Persen (AD, Tank design), I. I. Ims (project coordinator) and Tommy Sørbø (project consultant). Anwar Saab (1001 Films), along with Svendsen, produced a documentary film of the language exhibition and the language lounge (https://www.youtube.com/watch?v=uTjRmGANx5k).

3) Focus on multilingualism has been insufficient in educational curricula and on the political agenda in Norway. MultiLing's researchers have been directly involved in rectifying this situation. In 2019 a renewed curriculum for Norwegian as a school subject was presented by an expert committee appointed by the Ministry of Education. MultiLing's researcher Tonne was active in the committee. The work is part of the curriculum renewal LK20 of all the subjects in the Norwegian school, grades 1 to 13. In the final draft of the curriculum for Norwegian, multilingualism has been extensively incorporated, more than in previous curricula. Most noticeably, this has been done through the new core element "Linguistic diversity", in interplay with the core element "Language as system and opportunity" and expressed in the competence goals throughout the school years. In November 2018, the report *Language in Norway – Culture and Infrastructure* (Røyneland et al. 2018) was presented to Norway's Minister of Culture and Equality. The report, commissioned by the Norwegian Language Council, has been highly influential and has had substantial impact on Norwegian language policy. MultiLing's Deputy Director Røyneland was appointed to lead the expert committee. In the report, both old and new multilingualism in Norway is highlighted as an important resource to be addressed in society. The report contains analyses of how globalization and migration impact languages and language users in Norway, and offers a number of suggestions of specific policy measures. The proposal of a new, comprehensive language law, presented by the Government in August 2019, states that it will contribute to an active language policy in a multilingual state.

5. Sources to corroborate the impact

1)
Nytt verktøy kan avdekke barns språkvansker på flere språk ('New tools can reveal children's language difficulties in several languages'). Interview, barnehage.no, Fall 2017.
http://barnehage.no/forskning/2017/11/nytt-verktoy-kan-avdekke-barns-sprakvansker-pa-flere-sprak/

Vil tilby verktøy for å teste flerspråklige barn i flere språk enn norsk ('Will provide tools for testing multilingual children in more languages than Norwegian'). Interview, *Uniforum*, Fall 2017.
https://www.uniforum.uio.no/nyheter/2017/10/vil-tilby-verktoy-for-a-teste-flerspraklige-barn-i.html

2)
Svendsen received the Knowledge Oslo award for the best Oslo research in 2017 with the impact case, as well as the Department's dissemination award 2017.
https://www.hf.uio.no/om/aktuelt/aktuelle-saker/2018/bente-ailin-svendsen-vant-pris-for-beste-osloforsk.html

A teacher involved in the Citizen Science project:
Henrik Krogvold Helset, teacher at Vassbonn School, Akershus, henhelse@365.oknett.no

3)
Curriculum LK20:
https://hoering.udir.no/Hoering/v2/347?notatId=741

https://www.regjeringen.no/no/aktuelt/fornyer-innholdet-i-skolen/id2606028/?expand=factbox2606062

Proposal for a new, comprehensive Language Law (2019):
https://www.regjeringen.no/no/dokumenter/spraklov/id2664141/

3.12 NORMENT - Norwegian Centre for Mental Disorders

3.12.1 Scientific impact: Connectome development and mental illness

Institution: University of Oslo and Oslo University Hospital		
Name of SFF: Norwegian Centre for Mental Disorders (NORMENT)		
Title of case study: illness		
Period when the underpinning research was undertaken: 2014 - 2017		
Details of staff conducting the underpinning research from the submitting unit:		
Names: Tobias Kaufmann Dag Alnæs Nhat Trung Doan Christine Lycke Brandt Ole A Andreassen Lars T Westlye	**Roles:** T.K. and L.T.W. conceived the study; T.K. analyzed the data with contributions from L.T.W.; D.A. N.T.D., C.L.B. and O.A.A. contributed with data preprocessing, quality assurance and interpretation of results; T.K. and L.T.W. wrote the first draft of the paper and all authors contributed to the final manuscript	**Periods employed by NORMENT:** 2014 – present (T.K., D.A.) 2014 – 2017 (N.T.D.) Full SFF period (C.L.B., L.T.W., O.A.A.)
Period when the impact occurred: 2017 to present		

1. Summary of the impact

Our research provided important new insight into the development of brain networks in youths, and its vulnerability to disorder. We have gained a better understanding of normal brain development and the diverging patterns this may take in some children who develop mental illness. This work is therefore an important step toward the identification of robust biomarkers that will enable us to detect signs of reduced mental health in the developing brain before the outbreak of severe symptoms.

2. Underpinning research

The brains of children and adolescents are highly plastic, which allows for an enormous potential for learning and development in this period, however, in some children this plasticity comes at a cost. In an alerting report, the World Health Organization attributed about one third of all years lived-with-disability worldwide to neuropsychiatric conditions and it is increasingly recognized that many severe mental disorders originate in neurodevelopment, likely long before the outbreak of severe symptoms and subsequent diagnosis. To date, little is known why the brain of those children and adolescents is vulnerable to mental illness. Biomarkers that allow for an early detection are urgently needed to reduce the duration of untreated illness and facilitate early support.

In this work, we studied the development of brain networks in a large US cohort of 797 individuals aged 8-22 using functional magnetic resonance imaging of the brain. We revealed that during neurodevelopment the connections of the human brain evolve into a unique pattern that – like a fingerprint – renders us distinct from one another. Maturation was particularly profound during adolescence, supporting that puberty is a sensitive period in which the brain undergoes tremendous changes, yielding stable and individualized brain networks in early adulthood. Importantly, individuals with pre-clinical signs of mental illness displayed a delayed maturation in their fingerprinting pattern. We found that brain connections in those individuals were less stable across different tasks and contexts and were less individualized. Consequently, less distinct network fingerprints were associated with higher level of symptom burden. This has triggered a number of follow up studies and sparked exciting new questions that we and other labs are currently pursuing.

The work was conducted by NORMENT researchers Kaufmann, Alnæs, Doan, Brandt, Andreassen and Westlye. It built on results from various prior studies on the brain functional connectome that NORMENT researchers have performed since the establishment of the centre

in 2013 (e.g. Brandt et al. (2015) Schizophrenia Bulletin, Kaufmann et al (2015) Schizophrenia Bulletin, Skåtun et al (2015) Schizophrenia Bulletin, Kaufmann et al (2016) NeuroImage). Following publication of the findings in the leading neuroscience outlet (Kaufmann et al (2017) Nature Neuroscience), several follow-up studies have been conducted at NORMENT (e.g. Kaufmann et al (2018) JAMA Psychiatry). Furthermore, the Research Council of Norway has funded a Young Research Talents project that follows up the findings with new dedicated studies on the identification of signs of mental illness in the developing human brain (project LifespanHealth).

3. References to the research

Main reference:

- Kaufmann, T., Alnæs, D., Doan, N.T., Brandt, C.L., Andreassen, O.A., Westlye, L.T. (2017). Delayed stabilization and individualization in connectome development are related to psychiatric disorders. **Nature Neuroscience**. https://www.nature.com/articles/nn.4511

Related work by NORMENT authors:

- Kaufmann, T., Alnæs, D., Brandt, C.L., Bettella, F., Djurovic, S., Andreassen, O.A., Westlye, L.T. (2018). Stability of the Brain Functional Connectome Fingerprint in Individuals With Schizophrenia. **JAMA Psychiatry.** https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2680567
- Kaufmann, T., Alnæs, D., Brandt, C.L., Doan, N.T., Kauppi, K., Bettella, F., Lagerberg, T.V., Berg, A.O., Djurovic, S., Agartz, I., Melle, I.S., Ueland, T., Andreassen, O.A., Westlye, L.T. (2017). Task modulations and clinical manifestations in the brain functional connectome in 1615 fMRI datasets. **NeuroImage**. https://www.ncbi.nlm.nih.gov/pubmed/27916665
- Skåtun, K.C., Kaufmann, T., Doan, N.T., Alnæs, D., Cordova-Palomera, A., Jönsson, E.G., Fatouros-Bergman, H., Flyckt, L., KASP, Melle, I., Andreassen, O.A., Agartz, I., Westlye, L.T. (2016). Consistent Functional Connectivity Alterations in Schizophrenia Spectrum Disorder: A Multisite Study. **Schizophrenia Bulletin**. https://academic.oup.com/schizophreniabulletin/article/43/4/914/2548978
- Brandt, C.L., Kaufmann, T., Agartz, I., Hugdahl, K., Jensen, J., Ueland, T., Haatveit, B., Skåtun, K.C., Doan, N.T., Melle, I., Andreassen, O.A., Westlye, L.T. (2015). Cognitive Effort and Schizophrenia Modulate Large-Scale Functional Brain Connectivity. **Schizophrenia Bulletin**. https://academic.oup.com/schizophreniabulletin/article/41/6/1360/2526022
- Kaufmann, T., Skåtun, K.C., Alnæs, D., Doan, N.T., Duff, E.P., Tønnesen, S., Roussos, E., Ueland, T., Aminoff, S.R., Lagerberg, T.V., Agartz, I., Melle, I., Smith, S.M., Andreassen, O.A., Westlye, L.T. (2015). Disintegration of Sensorimotor Brain Networks in Schizophrenia. **Schizophrenia Bulletin**. https://academic.oup.com/schizophreniabulletin/article/41/6/1326/2526034

4. Details of the impact

Improving our understanding of the pathophysiology of severe mental illness is key in their treatment and prevention. Over the past decades, it has become increasingly clear that these disorders originate in neurodevelopment yet we lack sensitive methods to detect abnormalities in brain development early. Because the disorders are typically diagnosed in early adulthood when severe symptoms manifest, it is likely that the period of untreated illness spans several (neurodevelopmental) years. Discovering biomarkers that allow us to trace patterns of abnormal brain development are therefore among the key challenges that the field is facing.

We at NORMENT have illustrated that the brain develops into a fingerprint-like pattern in youths and found that deviations from this neurodevelopmental trajectory are indicative of pre-clinical signs of mental illness. This is an important first step toward the development of biomarkers.

Consequently, the findings have received marked attention in the community as for example indicated by a highlighting commentary by UCLA Professor Adriana Galvan in the News and Views section of Nature Neuroscience, the high number of citations the paper has already received in the 2.5 years since publication, and the reception of the prestigious *Excellent Paper in Neuroscience Award 2018*.

The research has triggered new questions that we are following up at NORMENT, for example how the interplay between environmental and genetic risk factors influences the individualization of the brain during childhood and adolescence. We hope that future research building on this study will lead to the identification of robust biomarkers that will enable us to detect signs of reduced mental health in the developing brain before the outbreak of severe symptoms.

5. Sources to corroborate the impact

Kaufmann et al (2017) Nature Neuroscience

- was highlighted by Nature Neuroscience with a commentary in the *New and Views* section of their April 2017 issue: https://www.nature.com/articles/nn.4530
- was awarded the ERA-NET NEURON Excellent Paper in Neuroscience Award 2018 (3000€). https://www.neuron-eranet.eu/en/881.php
- was awarded the Best Publication Award 2017 by Oslo University Hospital (50k NOK). https://www.ous-research.no/home/ous/News/17883
- has been cited already 75 times since 2017 (status Sep. 2019). With an *Altmetric* score of 153, it is in the 98th percentile of all papers tracked by *Altmetric* of similar age in all journals (status Sep. 2019). https://www.nature.com/articles/nn.4511/metrics
- was outlined in the Research News of the University of Oslo https://www.med.uio.no/klinmed/english/research/news-and-events/news/2018/the-brain%E2%80%99s-fingerprint-reveals-early-signs-of-men.html
- led to funding of a Young Research Talent grant to the first author of the study that largely builds on the findings of this study and follows up the research toward the discovery of biomarkers for the early detection of signs of mental illness in the developing brain (Project 276082 LifespanHealth). https://prosjektbanken.forskningsradet.no/#/project/NFR/276082

3.12.2 Scientific impact: Novel methods for identifying polygenic architecture in complex diseases

Institution: Faculty of Medicine, University of Oslo		
Name of SFF: Norwegian Centre for Mental Disorders (NORMENT)		
Title of case study: Novel methods for identifying polygenic architecture in complex diseases		
Period when the underpinning research was undertaken: 2016-2019		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period employed by SFF:**
Olav B Smeland	Post.doc.	4 years
Yunpeng Wang	Post.doc	3 years
Oleksandr Frei	Post.doc.	2 years
Weng Li	Post.doc.	2 years
Verena Zuber	Post.doc.	2 years
Francesco Bettella	Researcher	5 years
Alexey Shadrin	Post.doc.	2 years
Anders Dale	Guest researcher	Collaborator
Ole Andreassen	Professor	Director of NORMENT
Period when the impact occurred: 2017/2019		

1. Summary of the impact

NORMENT has been involved in some of the first studies identifying novel genetic risk and protective loci for psychiatric disorders and other phenotypes through collaborative efforts in genome-wide association studies (GWAS). Building upon these discoveries, NORMENT has helped develop and apply novel biostatistical tools to improve risk variant discovery. This has allowed the discovery of more loci for complex disorders including psychiatric disorders without time-consuming and expensive additional data collection. The methods have been adapted in the toolbox of the Psychiatric Genetics Consortium and the new discoveries provide a fruitful framework for exploitation of polygenic information towards clinical utility.

2. Underpinning research

NORMENT is and has been involved in the identification of novel risk and protective loci for schizophrenia and bipolar disease in addition to genetic variants associated with the size of various brain structures, intelligence, Alzheimer's etc through large-scale genome- wide association studies (GWAS) conducted during the last decade. These discoveries from genome-wide association studies have transformed psychiatric genetics and provided novel insights into the genetic etiology of psychiatric disorders. Two major discoveries have emerged; the disorders are polygenic, with a large number of common variants each with a small effect and many genetic variants influence more than one phenotype, suggesting shared genetic etiology. Although growing sample sizes increase GWAS power, the small genetic effects are difficult to detect with traditional statistical methods and to this date most of the polygenic architectures underlying psychiatric disorders still remain undetected. This has motivated efforts to develop 'Big Data' analytical approaches that improve the yield of existing GWAS.

NORMENT has been central in developing and applying novel statistical approaches to improve the yield of existing genome-wide association studies for polygenic phenotypes. These methods were built on several assumptions: 1. Some genetic loci are more likely to harbor causal effects. 2. A large number of genetic variants are likely to influence more than one phenotype that is, they exhibit allelic pleiotrophy. Thus, NORMENT helped develop cross-trait analytical approaches such as the conditional False Discovery Rate (condFDR) approach which complements the standard measures of genetic correlation by allowing identification of individual overlapping variants that

did not previously reach genome-wide significance, and by allowing identification of variants regardless of their allelic effect directions. It leverages overlapping SNP associations (cross-trait enrichment) between two separate GWAS to improve statistical power for genetic discovery. The conjunctional FDR (conjFDR) is a natural extension of the condFDR, which allows discovery of overlapping loci by providing a conservative estimate of the FDR for a SNP association with both phenotypes simultaneously. Application of the condFDR and conjFDR approaches has increased genetic discovery and uncovered genetic overlap in a wide specter of complex human traits, including the psychiatric disorders schizophrenia, bipolar disorder and ADHD. Notably, the conjFDR approach has demonstrated genetic overlap between several phenotypes that are not genetically correlated, such as schizophrenia and brain structure volumes, schizophrenia and personality traits, and bipolar disorder and intelligence.

An example of the efficacy of the novel methods to identify variants based on 'fewer samples' come from the discovery of ADHD gene risk variants. The first published GWAS on ADHD (896 cases, 2455 controls) did not find any significant hits (Neale et al 2010). In 2017, Shadrin et al (2017) performed a conditional/conjunctional false discovery rate (condFDR/conjFDR) analysis to genome-wide association study (GWAS) data on ADHD (2,064 trios, 896 cases, and 2,455 controls) and educational attainment (n=328,917). This analysis identified five loci for ADHD. Four of these loci were later identified in a larger ADHD GWAS (Demontis et al 2019), effectively proving the validity of the approach.

3. References to the research

Identification of novel genes in schizophrenia and bipolar through GWAS:

1. Schizophrenia Working group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. Nature 511, 421-427 (2014).
2. Stahl, E.A., et al. Genome-wide association study identifies 30 loci associated with bipolar disorder. Nat Genet 51, 793-803 (2019).

Development of novel biostatistical methods for identifying novel loci in complex diseases:

3. Andreassen, O.A., et al. Improved detection of common variants associated with schizophrenia by leveraging pleiotropy with cardiovascular-disease risk factors. Am J Hum Genet 92, 197-209 (2013).
4. Andreassen, O.A., et al. Improved detection of common variants associated with schizophrenia and bipolar disorder using pleiotropy-informed conditional false discovery rate. PLoS Genet 9, e1003455 (2013).

Additional application of the novel methods:

5. Smeland, O.B., et al. Identification of Genetic Loci Jointly Influencing Schizophrenia Risk and the Cognitive Traits of Verbal-Numerical Reasoning, Reaction Time, and General Cognitive Function. JAMA psychiatry 74, 1065-1075 (2017).
6. Smeland, O.B., et al. Genome-wide analysis reveals extensive genetic overlap between schizophrenia, bipolar disorder, and intelligence. Mol Psychiatry (2019).

4. Details of the impact

The discovery of new loci involved in schizophrenia and bipolar revolutionized psychiatric genetics. The next step was to translate these genetic findings to obtain a greater understanding at the cellular and pathways level and also to determine the environmental influence on this genetic background. Since the 108 loci were published in 2014, a number of studies for the molecular underpinnings of schizophrenia has emerged. For instance, the results from the

first GWAS on schizophrenia led to the follow-up study and identification of the complement C4 in the associated MHC-region as a mediator of synapse elimination during postnatal development (Sekar et al 2016).

The novel biostatistical methods were developed in collaboration with Anders Dale and his team at the Center for Multimodal imaging genetics at University of California, San Diego. The NORMENT team has been particularly successful in applying the methods broadly to many complex traits and interpreting the results. For instance, the novel biostatistical methods have helped elucidate the complexity of the genetic relationship between many complex phenotypes, for example, that between schizophrenia and cognitive function. A gene-set enrichment analysis of the shared loci implicated biological processes related to neurodevelopment, synaptic integrity and neurotransmission, among others. Among the shared loci, schizophrenia risk was linked to lower intelligence at 61 (81%) of the loci. Thus, in addition to identifying more loci shared between schizophrenia and cognitive traits compared to the standard GWAS analysis, these conjFDR studies indicate that the shared genetic etiology between schizophrenia and cognitive function involves a mixture of agonistic and antagonistic effect directions, and is more complex than what is suggested by their moderate negative genetic correlation. This is clinically important and in compliance with some reports that not all patients with schizophrenia perform poorly on cognitive tests.

The use of the novel biostatistical methods is still in its infancy (first publication in 2013) and thus only NORMENT and the group of Anders Dale have published on them and adaptation in the broader scientific community is just starting. However, as a testament to the recognition of their validity and seeing the challenge of collecting enough samples to find all loci involved in the complex psychiatric diseases, the next analysis plan (2019) for the Psychiatric Genetics Consortium (PGC) involves the addition of conditional and conjunctional FDR.

The NORMENT team has also been efficient in interpreting the results for the broader benefit of society – for instance, the Norwegian newspaper VG chose to devote an article to narrate the findings of overlapping loci between bipolar and higher intelligence. This was later made publically available on the Norwegian bipolar association homepage (see below). Likewise, part of the work was recognized at Oslo University Hospital by awarding the first author of one of the papers - Olav Smeland - for an outstanding scientific paper (see below).

The number of citations of the original papers gives some indication to their importance for the field:

Paper 1 (Ripke): 1689 citations on Pubmed for paper 1, Altmetric score = 1070 (in the 99th percentile (ranked 47th) of the 192,253 tracked articles of a similar age in all journals).
Paper 2 (Stahl): 19 citations for paper 2, Altmetric score = 293 (in the 99th percentile (ranked 1,310th) of the 253,555 tracked articles of a similar age in all journals).
Paper 3 (schizophrenia + CVD): 118 citations
Paper 4 (schizophrenia + BIP, 2013): 93 citations.

5. Sources to corroborate the impact

A comment on "Over 108 genetic loci found for schizophrenia found" on the Norwegian popular science page:
https://sciencenorway.no/forskningno-mental-health-norway/over-100-genetic-loci-for-schizophrenia-found/1405323

Commentary on the identification of new risk loci for bipolar disorder - one in the science daily and one on the NORMENT homepage:
https://www.sciencedaily.com/releases/2019/05/190501131357.htm
https://www.med.uio.no/norment/english/research/news-and-events/news/2019/new-genes-linked-to-bipolar-disorder.html

Prize to Olav Smeland for outstanding scientific paper by Oslo University Hospital:
https://www.med.uio.no/norment/english/research/news-and-events/news/2018/prize-to-olav-smeland-for-outstanding-scientific-paper
Internal highlight at Oslo University Hospital on the award including statement about why the articles where chosen:
https://oslo-universitetssykehus.no/om-oss/nyheter/priser-til-halvarets-fremragende-forskningsartikler

Newspaper article on the bipolar disorder linked to higher IQ – a comment on the article of Olav Smeland on the genetic loci overlap between bipolar disorder and intelligence in an article from the Norwegian newspaper VG (available on the Norwegian bipolar association's homepage).
https://www.bipolarforeningen.no/content/download/11120/87091/file/VG%20pluss-artikkel%20IQ.pdf

Excellent Researcher Award to Centre Leader Ole A. Andreassen from Oslo University Hospital:
https://www.med.uio.no/norment/forskning/aktuelt/aktuelle-saker/2019/pris-for-fremragende-forskning-til-ole-andreassen.html

Bergesen-prize to Ole A. Andreassen: The Bergesen prize is an honorary prize given to a person or institution that has done an excellent piece of work within non-profit work/organizations.
https://www.med.uio.no/klinmed/om/aktuelt/aktuelle-saker/2018/bergesenprisen-til-professor-ole-andreassen.html

3.12.3Societal impact: Cardiovascular comorbidity in mental illness

Institution: University of Oslo and Oslo University Hospital

Name of SFF: Norwegian Centre for Mental Disorders (NORMENT)

Title of case study: Cardiovascular comorbidity in mental illness

The centre's cardiovascular research in severe mental disorders have yielded several articles in high impact journals and the centre leader has recently been successful in achieving a prestigious EU grant for a research project on cardiovascular disease (CVD). The most recent and clinical important study published is "Cardiovascular risk remains high in schizophrenia with modest improvements in bipolar disorder during past decade".

Period when the underpinning research was undertaken: 2013 – 2019

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Linn Rødevand, Nils Eiel Steen, Torbjørn Elvsåshagen, Daniel Quintana, Elina Reponen Ragni Mørch, Synve Hoffart Lunding, Trude S. J. Vedal, Ingrid Dieset, Sherif Gohar, Trine V. Lagerberg, Ingrid Melle, Ole A. Andreassen	PhD students (LR, ER, SHL, TSJV), affiliated PhDs (RM, ID), Post docs (TE, SG), Researchers (DQ, TVL) Assoc. prof. (NES), Profs (IM, OAA)	2013- 2019: NES, TE, DQ, IM, TVL, OAA 2013 – 2017: ID 2014-2018: RM 2016- 2019: LR, ER, TSJV 2017- 2019: SHL, SG

Period when the impact occurred: 2014-2019

1. Summary of the impact

The life expectancy in patients with severe mental disorders (schizophrenia and bipolar disorder) are reduced by 10-20 years. A major cause of the excessive deaths is due to cardiovascular disease. The study by Rødevand et al (2019) documents levels and patterns of change of cardiovascular risk factors in schizophrenia and bipolar disorder during the recent years. The article builds on cardiovascular research in severe mental disorders by the NORMENT group during more than 15 years. This research has been a basis for targeted interventions in the clinics aiming to reduce the cardiovascular comorbidity and mortality in these patients.

2. Underpinning research

Patients with severe mental disorders have significantly higher mortality than the general population from unnatural causes (suicide, homicide or accidents); however, there is also a large excessive mortality due to natural causes (somatic conditions) such as CVD. Persons who have been hospitalized for a psychotic disorder have a two to three-fold increase risk of dying from CVD, and the gap in life expectancy between severe mental disorders and the rest of the population is increasing.

Cardiovascular risk and mechanisms in severe mental disorders have been focused by the research group of NORMENT for several years. We have demonstrated that certain antipsychotic agents (especially clozapine) stimulate cellular lipid biosynthesis and the existence of lipid dysregulations during antipsychotic treatment independent of body mass index. We have also identified lipid dysregulations related to antidepressant medication. The centre has contributed in identifying broad genetic overlap between severe mental disorders and cardiovascular risk factors, and corroborated the cardiovascular link by demonstrating

relationships between lipid profiles and clinical traits. The latest study, “Cardiovascular risk remains high in schizophrenia with modest improvements in bipolar disorder during past decade” investigate the potential preconditions for the cardiovascular mortality in this patient group, documenting broadly increased cardiovascular risk factors in schizophrenia and bipolar disorder compared to the general population. There was no decrease in cardiovascular risk factors in patients with schizophrenia during the past decade and only a small-moderate degree decrease in patients with bipolar disorder.
The study was designed by prof. Ole A. Andreassen, researcher Trine V. Lagerberg (supervisors) and Linn Rødevand (PhD student) and based on a collaboration between the Precision psychiatry research group and the Clinical research group of the centre. The study builds on previous studies related to cardiovascular risk and mechanisms by the centre such as Andreassen et al [2013], Ringen et al [2014], Quintana et al [2016], Fjukstad et al [2016], Gohar et al [2019]. These NORMENT studies are part of the basis for cardiovascular preventive interventional initiatives in mental health clinics.

4. **References to the research**

Main reference:

a. Rodevand L, Steen NE, Elvsashagen T, et al. Cardiovascular risk remains high in schizophrenia with modest improvements in bipolar disorder during past decade. Acta Psychiatr Scand Apr 2019;139(4):348-360.

Related work by NORMENT authors:

b. Fjukstad KK, Engum A, Lydersen S, Dieset I, Steen NE, Andreassen OA, Spigset O. Metabolic Abnormalities Related to Treatment With Selective Serotonin Reuptake Inhibitors in Patients With Schizophrenia or Bipolar Disorder. J Clin Psychopharmacol Dec 2016;36(6):615-620.
c. Quintana DS, Westlye LT, Kaufmann T, Rustan OG, Brandt CL, Haatveit B, Steen NE, Andreassen OA. Reduced heart rate variability in schizophrenia and bipolar disorder compared to healthy controls. Acta Psychiatr Scand Jan 2016;133(1):44-52.
d. Ringen PA, Engh JA, Birkenaes AB, Dieset I, Andreassen OA. Increased mortality in schizophrenia due to cardiovascular disease - a non-systematic review of epidemiology, possible causes, and interventions. Front Psychiatry 2014;5:137.
e. Andreassen OA, Djurovic S, Thompson WK, et al. Improved detection of common variants associated with schizophrenia by leveraging pleiotropy with cardiovascular-disease risk factors. Am J Hum Genet Feb 7 2013;92(2):197-209.
f. Gohar SM, Dieset I, Steen NE, Mørch RH, Vedal TSJ, Reponen EJ, Steen VM, Andreassen OA, Melle I. Association between leptin levels and severity of suicidal behaviour in schizophrenia spectrum disorders. Acta Psychiatr Scand. 2019 May;139(5):464-471.

4. Details of the impact

The research group has for several years been doing research of cardiovascular risk factors and comorbidity in severe mental disorders. The group has been a major national force in focusing the comorbidity in severe mental disorders as exemplified by a range of high impact publications in international journals encompassing national and international collaborations including the Psychiatric Genomics Consortium with 38 participating countries.
In addition to contributing to awareness among clinicians both nationally and internationally as exemplified by publishing review articles in core journals (Ringen et al [2014]), the research

have manifested in a program at the Division of mental health and addiction, Oslo university hospital (OUH) called “Hjertefrisk” (“Healthy heart”) initiated in spring 2017. The Hjertefrisk algorithm is a tool for health professionals to identify and monitor increased risk of diabetes and CVD in people with severe mental illness. The form defines appropriate monitoring measures during antipsychotic medication, and the complete Hjertefrisk algorithm is available in one page including characteristics of patients at risk and appropriate interventions. The program is implemented in the Division at OUH with a catchment area of about 500 000 individuals as well as in several other hospitals, forming a national multicentre project. This project is a major contribution towards adequate treatment of the cardiovascular risk at a national level in people with severe mental disorders, aiming to decrease the excessive mortality. The research has also initiated projects of high intensive aerobic training (HIT), benefitting these patient groups in Trondheim and Vestfold. Moreover, patients at OUS have had the possibility to attend a naturalistic interventional study applying motivational techniques to reduce cardiometabolic risk. Based on cardiovascular research initiatives, the NORMENT centre leader, prof. Ole Andreassen, has been successful in achieving a prestigious EU grant as the coordinator of the project “CoMorMent. Predicting comorbid cardiovascular disease in individuals with mental disorder by decoding disease mechanisms”. CoMorMent is a collaboration between eight countries.

5. Sources to corroborate the impact

g. Web links to the “Hjertefrisk” project:
   1) https://oslo-universitetssykehus.no/avdelinger/klinikk-psykisk-helse-og-avhengighet/hjertefrisk-hjelpemiddel-for-oppfolging-og-tiltak-hos-pasienter-med-psykiske-lidelser-eller-rusmiddelproblemer-i-kardiometabolsk-risikogruppe
   2) https://www.med.uio.no/norment/forskning/samarbeid/hjertefrisk/

h. Review articles from the centre:
   Ringen PA, Engh JA, Birkenaes AB, Dieset I, Andreassen OA. Increased mortality in schizophrenia due to cardiovascular disease - a non-systematic review of epidemiology, possible causes, and interventions. *Front Psychiatry* 2014;5:137.

i. Article on motivational techniques:
   Ringen PA, Falk RS, Antonsen B, et al. Using motivational techniques to reduce cardiometabolic risk factors in long term psychiatric inpatients: a naturalistic interventional study. BMC Psychiatry Aug 15 2018;18(1):255.

j. The centre leader received support from the Olav Thon foundation during 2016-2018 for research on CVD in severe mental disorders
   https://www.med.uio.no/norment/forskning/aktuelt/aktuelle-saker/2016/stotte-fra-olav-thon-stiftelsen.html

k. Dissemination activities:
   https://www.med.uio.no/norment/forskning/aktuelt/aktuelle-saker/2015/hjerte-karsykdom-og-psykisk-lidelse.html

3.12.4 Societal impact: Genetic research, dissemination and reduced stigma

Institution: University of Oslo and Oslo University Hospital

Name of SFF: Norwegian Centre for Mental Disorders (NORMENT)

Title of case study: Genetic research, dissemination and reduced stigma

Period when the underpinning research was undertaken: 2014-2019

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period employed by SFF:
Smeland OB	Post.doc.	4 years
Bahrami S	Post.doc	3 years
Shadrin A	Post.doc.	2 years
O'Connell K	Post.doc	2 years
Frei O	Post.doc	3 years
Bettella F	Researcher	5 years
Steen NE	Associate Professor	5 years
Ueland T	Associate Professor	5 years
Djurovic S	Professor	5 years
Dale A	Guest researcher	Collaborator
Andreassen OA	Professor	Director of NORMENT

Period when the impact occurred: 2019

1. Summary of the impact

The research about genetic overlap between intelligence and bipolar disorder was disseminated to users and user communities through all our different dissemination channels, reaching a large number of people. The research has thus been important in our aim to be a provider of knowledge about severe mental disorders that can help break down stigma in society.

2. Underpinning research

Postdoctoral fellow Olav B. Smeland and colleagues found that risk genes for bipolar disorder were associated with higher intelligence. Smeland and co-authors investigated DNA from more than 400.000 people, including 20.000 patients with bipolar disorder and 35.000 patients with schizophrenia. They found that 12 risk genes for bipolar disorder were also linked to intelligence. In 75 % of these genes, bipolar disorder risk was associated with higher intelligence. In schizophrenia, there was also a genetic overlap with intelligence, but a higher proportion of the genes was associated with cognitive impairment.

3. References to the research

- Smeland OB, Bahrami S, Frei O, Shadrin A, O'Connell K, Savage J, Watanabe K, Krull F, Bettella F, Steen NE, Ueland T, Posthuma D, Djurovic S, Dale AM, Andreassen OA (2019). Genome-wide analysis reveals extensive genetic overlap between schizophrenia, bipolar disorder, and intelligence. Molecular Psychiatry, Jan 4, doi: 10.1038/s41380-018-0332-x

4. Details of the impact

The research about genetic overlap between intelligence and bipolar disorder was disseminated to users and user communities through all our different dissemination channels, including the NORMENT website, websites of host institutions, through collaboration with user organizations through our User Council, in our social media and at our open lecture/event “Sinnssyk forskning: Arv og miljø”. The results where shared through our own website (www.norment.no) and it was featured by national newspaper VG. This article highlighted the research along with a personal story, and was written in a way that can help people associate bipolar disorder in a more positive and dignified light. This way, the research was featured national in a way that will help break down stigma.
The research was also shared on our Twitter account and featured in the websites of Oslo University Hospital (OUS). In addition to this, we have a close collaboration with the Norwegian Bipolar Association, and the news were also shared through their websites and social media, reaching a large combined audience of users, their families, healthcare personnel and researchers.

As a large centre, CoE NORMENT has employed a user representative and established a User Council that play an important part in our dissemination strategies. The user council consists of members who have personal experience with bipolar disorder, schizophrenia, major depressive disorder and as next of kin. In addition, the user council represent 3 different user organizations and provide links to society through their networks and experiences. The User Council played a pivotal role in taking initiative to, planning and organizing our open dissemination event this spring, called “Sinnssyk forskning: arv og miljø” (“Mad research: genes and environment”). The User Council unanimously came up with the name as a way to break down stigma. At the event, key research areas and findings were shared in a short lecture format, including the research in this case study on intelligence and bipolar disorder. After the lectures, a mingling session provided a chance for the audience to speak directly with the researchers asking questions and learning more.

The event also marked the official opening of our Facebook page, which has been started on initiative of the user council and is administered by the user representative. The aim of the Facebook account is to provide information about the research at NORMENT in a way that is easy to understand, with users, their families and the general population as the primary target group. Since the kick-off in May, the Facebook page now has over 400 followers, and information about the open event reached more than 16,000 people.

In sum, the dissemination of the results has reached a large number of people. By adding a new and more positive perspective on bipolar disorder, the results have become important in our work to share information and knowledge that will lead to less stigma around severe mental disorders.

5. Sources to corroborate the impact

- NORMENT website:
  - https://www.med.uio.no/norment/forskning/aktuelt/aktuelle-saker/2019/sinnssyk-forskning-arv-og-miljo.html

- https://www.med.uio.no/norment/english/research/news-and-events/news/2019/genetic-overlap-bipolar-disorder-intelligence.html
- OUS website:
  - https://www.ous-research.no/home/ous/news/19187
- Article in VG:
  - https://www.vg.no/forbruker/helse/i/gP26p1/tonje-har-bipolar-lidelse-sykdommen-knyttes-til-hoey-iq
- Twitter:
  - https://twitter.com/sffnorment
  - https://twitter.com/SFFNORMENT/status/1082641188312752128
- Facebook:
  - https://www.facebook.com/sffnorment/
  - https://www.facebook.com/events/638740883245927/

3.13 PluriCourts - Centre for the Study of the Legitimate Roles of the Judiciary in the Global Order

3.13.1 Societal impact: Responses to backlash against international investment treaty arbitration

Institution: University of Oslo, The Faculty of Law, Department of Public and International Law

Name of SFF: PluriCourts - Centre for the Study of the Legitimate Roles of the Judiciary in the Global Order

Title of case study: Responses to backlash against international investment treaty arbitration

Period when the underpinning research was undertaken: 2014-2019

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting SFF:**
Behn	Post doc/Associate Professor II	Behn, Fauchald 2014-2019
Fauchald	Professor, coordinator	St John 2016-2018
Langford	Professor, associated with PluriCourts	Squatrito 2014-2017
St John	Post doc	Berge 2015-2019
Squatrito	Post doc	Stiansen 2015-2019
Berge	PhD fellow	Letourneau-Tremblay 2014-2016/2017-2019
Stiansen	PhD fellow/Post doc	Lie 2017-2019
Letourneau-Tremblay	Researcher Assistant/PhD fellow	
Lie	Master student/researcher/PhD fellow	

Period when the impact occurred: 2017-2019

1. Summary of the impact

PluriCourts has, through the establishment of a database (PITAD) and a series of empirical studies, provided a basis for a fact-based discussion of proposals to reform mechanisms for the settlement of international investment disputes. Negotiations are carried out in the context of United Nations Commission on International Trade Law (UNCITRAL), largely on the basis of proposals from the European Union, and a key issue is whether and how one can establish a more permanent dispute settlement framework than the ad hoc regime that currently exists. PluriCourts was invited by the European Commission to present its findings to EU Member States in the early phases of the UNCITRAL negotiations, has been admitted observer status during the negotiations, and has been selected to head the Academic Forum that provides input to the negotiation process.

2. Underpinning research

The research has focused on the following main topics:

1) The strategies of states, arbitrators and private parties to investment disputes in terms of responding to the legitimacy crisis of international investment law: Our research has shown how states adjust their positions in negotiations of new investment treaties, reorient the arguments they present to investment arbitration tribunals, adopt new strategies when investors bring cases

against them (including, inter alia, the hiring of counsel and the use of domestic legal instruments against investors), and increasingly challenge decisions by investment arbitration tribunals through annulment proceedings or in domestic courts. It has also indicated that arbitrators are somewhat sensitive to criticism addressed to their decisions and that they are increasingly cautious when deciding cases in favor of investors. We have found that a broad variety of private parties bring investment treaty arbitration, but that their success in such cases vary significantly according to their size.

2) Claims that developing countries suffer disproportionately under the current regime of international investment law, in terms of restrictions on their political freedoms and losing cases at international tribunals: Our research has identified which countries are targeted in investment disputes and the economic sectors within which such disputes are most frequent. We have found that low and lower middle income countries according to World Bank income groups have had very few cases against them and that the dispute settlement element of the investment regime has had marginal importance to such countries. More research is needed to identify less visible effects of the regime, such as "regulatory chill".

3) Perceptions of the dispute settlement process as being dominated by western male arbitrators and lawyers, and that these actors frequently face conflict of interest situations (e.g. representing opposing parties or functioning as both arbitrators and counsel): Our research has confirmed that there is a relatively small group of particularly powerful persons associated with investment treaty arbitration, and that many of these perform several and sometimes conflicting roles. While this leads to challenges regarding lack of diversity and sociological legitimacy, it is also important for the stability, coherence and predictability of the regime.

3. References to the research

Malcolm Langford, Daniel Behn and Runar Lie, 'The Revolving Door in International Investment Arbitration' 20(2) *Journal of International Economic Law* 1 (2017);
Daniel Behn and Malcolm Langford, 'Trumping the Environment? An Empirical Perspective on the Legitimacy of Investment Treaty Arbitration' 18(1) *Journal of World Investment and Trade* 14 (2017);
Daniel Behn, Tarald Berge, and Malcolm Langford, 'Poor States or Poor Governance: Explaining Outcomes in Investment Treaty Arbitration' 38(3) *Northwestern Journal of International Law and Business* 333 (2018);
Malcolm Langford and Daniel Behn, 'Managing Backlash: The Evolving Investment Arbitrator?' 29(2) *European Journal of International Law* 551 (2018);
Malcolm Langford, Daniel Behn and Ole Kristian Fauchald, 'Backlash and State Strategies in International Investment Law' in Thomas Gammeltoft-Hansen and Tanja Aalberts (eds) *The Changing Practices of International Law* (CUP 2018) 70;
Daniel Behn, 'Performance of Investment Treaty Arbitration' in Theresa Squatrito, Oran Young, Andreas Follesdal and Geir Ulfstein (eds) *The Performance of International Courts and Tribunals* (CUP 2018) 77;
Ole Kristian Fauchald and Daniel Behn, 'World Peace and International Investment: The Role of Investment Treaties and Arbitration' in Cecilia Bailliet and Kjetil Larsen (eds), *Research Handbook on International Law and Peace* (Edward Elgar 2019) 182.

4. Details of the impact

The international regime for resolving investment disputes between foreign investors and host countries has been controversial for at least three decades. A serious backlash against the regime emerged in the early 2000s, much as a result of an increasing number of disputes and politically controversial cases. PluriCourts has since its start focused on building a database regarding such disputes in order to facilitate empirically informed research. When the UNCITRAL reform process started in 2017, this coincided with major output from PluriCourts researchers based on the data collected in PITAD.

Eventually, PluriCourts and its associated project 'Responses to the "legitimacy crisis" of international investment law (LEGINVEST)' have become providers of data and research output for the reform process. Researchers from PluriCourts (Behn and Langford) have been elected to key positions in the Academic Forum which was established among a network of researchers to provide research input to the reform process. Through these avenues, PluriCourts and LEGINVEST have provided funds and administrative support for activities of the Academic Forum during a very important consolidating phase after the initial enthusiasm associated with its start-up.

PluriCourts researchers (Behn and Langford) have participated very actively during the deliberations in the UNCITRAL Working Group, and other researchers (Berge and StJohn) have interviewed participants in the reform process for the purpose of separate research projects. The UNCITRAL process is scheduled to continue for several more years, and PluriCourts participation will continue for the foreseeable future based on funding made available as part of the LEGINVEST project.

5. Sources to corroborate the impact

PluriCourts acting as administrator for the Academic Forum on ISDS, see

- https://www.cids.ch/academic-forum
- https://www.jus.uio.no/pluricourts/english/projects/leginvest/academic-forum/

Organization of key workshop for the Academic Forum for the discussion and further development of input to the negotiation process

- https://www.jus.uio.no/pluricourts/english/projects/leginvest/events/reforming-international-investment-arbitration.html

PluriCourts researchers have been central in working groups of the Academic Forum, data from PluriCourts has been a key component of reports, and findings from PluriCourts have been frequently referenced in many Academic Forum reports, see in particular:

- PluriCourts database (PITAD) provided important data for WG 2 on duration of proceedings: https://www.cids.ch/images/Documents/Academic-Forum/2_Duration_-_WG2.pdf
- D Behn and M Langford participated in WG 4 on incorrectness of ISDS decisions: https://www.cids.ch/images/Documents/Academic-Forum/4_Incorrectness_of_ISDS_Decisions_-_WG4.pdf
- Literature from PluriCourts is extensively cited by WG 5 on diversity: https://www.cids.ch/images/Documents/Academic-Forum/5_Diversity_-_WG5.pdf

- The report of WG 7 on empirical perspectives is authored by researchers from PluriCourts: https://www.cids.ch/images/Documents/Academic-Forum/7_Empirical_perspectives_-_WG7.pdf

Papers from PluriCourts are extensively used as background materials for papers elaborated for negotiators by the Secretariat of UNCITRAL

- See http://undocs.org/en/A/CN.9/WG.III/WP.169, footnote 4 referring to publications by PluriCourts researchers Squatrito, Stiansen, St John, Langford and Behn
- See references to Langford, Behn and Lie in http://undocs.org/en/A/CN.9/WG.III/WP.151, https://undocs.org/en/A/CN.9/WG.III/WP.152 and https://undocs.org/en/A/CN.9/WG.III/WP.167

PluriCourts has been allowed two observers to sessions of the UNCITRAL Working Group and the work of the Academic Forum has been extensively referred to in reports from its sessions:

- Report from session 37: http://undocs.org/en/A/CN.9/970
- Report from session 36: http://undocs.org/en/A/CN.9/964

4 Appendices

4.1 Appendix A – Templates

4.1.1 Template 1 Societal impact

<table>
<tr><td colspan="3">Societal impact
Impact case template</td></tr>
<tr><td colspan="3">Institution:</td></tr>
<tr><td colspan="3">Name of SFF:</td></tr>
<tr><td colspan="3">Title of case study:</td></tr>
<tr><td colspan="3">Period when the underpinning research was undertaken:</td></tr>
<tr><td colspan="3">Details of staff conducting the underpinning research from the submitting unit:</td></tr>
<tr><td>Name(s):</td><td>Role(s) (e.g. job title):</td><td>Period(s) employed by submitting SFF:</td></tr>
<tr><td colspan="3">Period when the impact occurred:</td></tr>
<tr><td colspan="3">1. Summary of the impact (indicative maximum 100 words)
This section should briefly state what specific impact is being described in the case study</td></tr>
<tr><td colspan="3">3. Underpinning research (indicative maximum 500 words) This section should outline the key research insights or findings that underpinned the impact, and provide details of what research was undertaken, when, and by whom. This research may be a body of work produced over a number of years, but at least some of the results should have been reported as a result of the SFF. References to specific research outputs that embody the research described in this section, and evidence of its quality, should be provided in the next section (section 3).

Details of the following should be provided in this section:
• The nature of the research insights or findings which relate to the impact in the case study.
• An outline of what the underpinning research produced by the centre was.
• Any relevant key contextual information about this area of research.</td></tr>
<tr><td colspan="3">3. References to the research (indicative maximum of six references)
This section should provide references to key outputs from the research described in the previous section, and evidence about the quality of the research. Underpinning research outputs may include, but is not limited to journal articles, book chapters, edited volumes, monographs, patents, prototypes etc.

Include the following details for each cited output:
l. author(s)
m. title
n. year of publication
o. type of output and other relevant details required to identify the output (for example, DOI, journal title and issue)</td></tr>
</table>

4. Details of the impact (indicative maximum 750 words).

This section should provide a narrative, with supporting evidence, to explain:

p. how the research underpinned (made a distinct and material contribution to) the impact;
q. the nature and extent/importance of the impact.

The following should be provided:

r. An explanation of the process or means through which the research led to, underpinned or made a contribution to the impact (for example, how it was disseminated, how it came to influence users or beneficiaries, or how it came to be exploited, taken up or applied).
s. Where the centre's research was part of a wider body of research that contributed to the impact (for example, where there has been research collaboration with other institutions), the case study should specify the particular contribution of the centre's research and acknowledge other key research contributions.
t. Details of the beneficiaries – who or what community, constituency or organisation has benefitted, been affected or impacted on.
u. Details of the nature of the impact – how they have benefitted, been affected or impacted on.
v. Evidence or indicators of the extent of the impact described, as appropriate to the case being made.
w. Timespan when these impacts occurred.

5. Sources to corroborate the impact (indicative maximum of ten references)

This section should list:

x. References to sources that could corroborate key claims made about the impact of the centre's research (policy papers, reports, reviews, web links or other documented sources of information in the public domain, web links to companies that has taken up new technology, media items, individual users/beneficiaries who could be contacted to corroborate claims, etc.)
y. If relevant, external users or others who have witnessed the impact and could be contacted to corroborate the claims made in the reported cases.

4.1.2 Template 2 Scientific impact

<table>
<tr><td colspan="3">Scientific impact
Impact case template</td></tr>
<tr><td colspan="3">Institution:</td></tr>
<tr><td colspan="3">Name of SFF:</td></tr>
<tr><td colspan="3">Title of case study:</td></tr>
<tr><td colspan="3">Period when the underpinning research was undertaken:</td></tr>
<tr><td colspan="3">Details of staff conducting the underpinning research from the submitting unit:</td></tr>
<tr><td>Name(s):</td><td>Role(s) (e.g. job title):</td><td>Period(s) employed by submitting SFF:</td></tr>
<tr><td colspan="3">Period when the impact occurred:</td></tr>
<tr><td colspan="3">1. Summary of the impact (indicative maximum 100 words)
This section should briefly state what specific impact is being described in the case study</td></tr>
<tr><td colspan="3">2. Underpinning research (indicative maximum 500 words) This section should outline the key research insights or findings that underpinned the impact, and provide details of what research was undertaken, when, and by whom. This research may be a body of work produced over a number of years, but at least some of the results should have been reported as a result of the SFF. References to specific research outputs that embody the research described in this section, and evidence of its quality, should be provided in the next section (section 3).

Details of the following should be provided in this section:
z. The nature of the research insights or findings which relate to the impact in the case study.
aa. An outline of what the underpinning research produced by the centre was.
bb. Any relevant key contextual information about this area of research.</td></tr>
<tr><td colspan="3">3. References to the research (indicative maximum of six references)
This section should provide references to key outputs from the research described in the previous section, and evidence about the quality of the research. Underpinning research outputs may include, but is not limited to journal articles, book chapters, edited volumes, monographs, patents, prototypes etc.

Include the following details for each cited output:
cc. author(s)
dd. title
ee. year of publication
ff. type of output and other relevant details required to identify the output (for example, DOI, journal title and issue)</td></tr>
<tr><td colspan="3">4. Details of the impact (indicative maximum 750 words).
This section should provide a narrative, with supporting evidence, to explain:

gg. how the research underpinned (made a distinct and material contribution to) the impact;
hh. the nature and extent/importance of the impact.</td></tr>
</table>

The following should be provided:

ii. An explanation of how the research has influenced/benefited subsequent research outside the SFF.

jj. Where the centre's research was part of a wider body of research that contributed to the impact (for example, research collaboration with institutions outside the SFF), the case study should specify the particular contribution of the centre's research and acknowledge other key research contributions.

kk. Details of the nature and scope of the impact – what fields/research groups/scholarly communities are impacted and how.

ll. Evidence or indicators of the extent of the impact described, as appropriate to the case being made.

mm. Timespan when these impacts occurred.

5. Sources to corroborate the impact (indicative maximum of ten references)

This section should list:

nn. References to sources that could corroborate key claims made about the impact of the centre's research (research papers/reports/review articles (from outside the SFF) that in some way describe or illustrate the impact; awards/prizes: if possible links to award panel's statements explaining the background for the prize)

oo. If relevant, key researchers or others outside the SFF who have witnessed the impact and could be contacted to corroborate the claims made in the reported case.

4.2 Appendix B - Overview of the submitted impact cases

SFF I-III	*Name of SFF*	*Scientific/ societal impact*	*Name of impact case*
SFF I	CASTL - Center for the Advanced Study of Theoretical Linguistics	Scientific impact	Formal Framework for Lexical Verb Meaning
			Microvariation in the Input & Multilingualism
			The Nordic Center of Excellence in Microcomparative Syntax
		Societal impact	Mávsulasj Spoken Lule Saami Documentation
	CeSOS - Centre for Ships and Ocean Structures	Scientific impact	Analysis of sloshing in tanks by a multi-modal approach
		Scientific and societal impact	Integrated dynamic analysis of floating wind turbines
			Ship control in extreme conditions
			Vortex Induced Vibrations
	CMA - Centre of Mathematics for Applications	Scientific impact	
		Societal impact	Computing and programming is tightly integrated in all science programs at the University of Oslo*
			Education in computational mathematics
	CSCW - Centre for the Study of Civil War	Scientific impact	A platform for theoretical exchange on civil war
		Societal impact	Conflict is Development in Reverse
			Debunking Conflict Myths
			Defining Global Policy on Climate and Conflict
	PGP - Physics of Geological Processes	Societal impact	Computing and programming is tightly integrated in all science programs at the University of Oslo*
SFF II	CEES - Centre for Ecological and Evolutionary Synthesis	Scientific impact	Centre for Ecological and Evolutionary Synthesis
			The Atlantic cod genome - discovering a unique immune system
		Societal impact	Marine population dynamics under anthropogenic induced stress
			Saxitoxin – a story of innovation
	CBC - Center for Biomedical Computing	Scientific impact	CSF flow
		Societal impact	Computing and programming is tightly integrated in all science programs at the University of Oslo*
	CGB – Centre for geobiology	Scientific impact	Discovery and characterization of a new group of microbes - Lokiarchaeota
		Societal impact	Deep-sea mineral resources, unique ecosystems and bioprospecting potential within Norwegian territorial waters - hydrothermal vent fields at

SFF I-III	*Name of SFF*	*Scientific/ societal impact*	*Name of impact case*
			the Arctic Mid-Ocean Ridges (AMOR) in the Norwegian-Greenland Sea.
SFF II	CIR – Centre for Immune Regulation	Scientific impact	Cell surface IgA and IgM expression in plasma cells
			Long lived gut plasma cells
			Idiotypes and T cells in autoimmunity and B cell malignancies
		Societal impact	Extending in vivo half-life of IgG therapeutics and albumin fused biologics
	CSMN – Centre for the Study of Mind in Nature	Scientific impact	Philosophy without Intuitions
		Societal impact	Health Impact Fund
SFF III	AMOS – Centre for Autonomous Marine Operations and Systems	Scientific impact	An efficient numerical hydrodynamic method for fully-nonlinear analyses in marine technology
			Development of analysis methods for design against accidental ship and iceberg collisions
			Marine robotic platforms – Underwater Snake Robots
		Scientific and societal impact	Icing Protection for Unmanned Aerial Vehicles
	BCSS – Birkeland Centre for Space Science	Scientific impact	Understanding the Asymmetry of Geospace
			Building Space Instrumentation to Understanding Hard Radiation from Thunderstorms
		Societal impact	Space Weather, Climate and Lightning Protection
	CAGE - Centre for Arctic Gas Hydrate, Environment and Climate	Scientific impact	Ice sheet - methane hydrate interactions
		Societal impact	Ice sheet - methane hydrate interactions
			Innovation in Monitoring of Marine Methane Release
	CBD - Centre for Biodiversity Dynamics	Societal impact	Generic ecological impact assessments of alien species
	CCBIO - Centre for Cancer Biomarkers	Scientific impact	Repurposing identified new molecular target and mechanism of old drug
			Targeting AXL receptor tyrosine kinase to improve cancer therapy
		Societal impact	Co-Creation of Reflexive Cancer Research
	CEED - Center for Earth Evolution and Dynamics	Scientific impact	Linking Surface Processes to the Deep Earth
			Understanding ARCTIC's geodynamics and paleoenvironment

SFF I-III	*Name of SFF*	*Scientific/ societal impact*	*Name of impact case*
SFF III		Societal impact	Improving the Public's Understanding of today's Climate Crisis
			Planetary Sciences - A new research and education direction in Norway
	CEMIR - Centre of Molecular Inflammation Research	Scientific impact	Cell biological studies of host-pathogen interactions for identifying new therapeutic targets to treat infections
			Inflammatory responses induced by cholesterol, defining new therapeutic targets to treat atherosclerosis
	CERAD - Centre of Excellence for Environmental Radioactivity	Scientific impact	Reducing the overall uncertainties in impact and risk assessments associated with ionizing radiation, also combined with other stressors
			The impact of radioactive particles
		Societal impact	Impact assessments for ionizing radiation on the environment with focus on the Fukushima-Daiichi accident
			SHAMISEN Recommendations for preparedness and health surveillance of populations affected by a radiation accident
	CISMAC - Centre for Intervention Science in Maternal and Child health	Societal impact	Community initiated Kangaroo Mother Care improves the survival of low birth weight babies
	CNC – Centre for Neural Computation	Scientific impact	Discovery of brain's mechanisms for space and navigation
		Societal impact	Neural mechanisms of Alzheimer's disease
	MultiLing - Center for Multilingualism in Society Across the Lifespan	Societal impact	Collaborative Language Capacity Building
			Multilingualism on the social and political agenda
	NORMENT - Norwegian Centre for Mental Disorders	Scientific impact	Connectome development and mental illness
			Novel methods for identifying polygenic architecture in complex diseases
		Societal impact	Cardiovascular comorbidity in mental illness
			Genetic research, dissemination and reduced stigma
	PluriCourts - Centre for the Study of the Legitimate Roles of the Judiciary in the Global Order	Societal impact	Societal impact: Responses to backlash against international investment treaty arbitration

* The same case was sent in by three centres to the evaluation (CMA, CBC, PGP).

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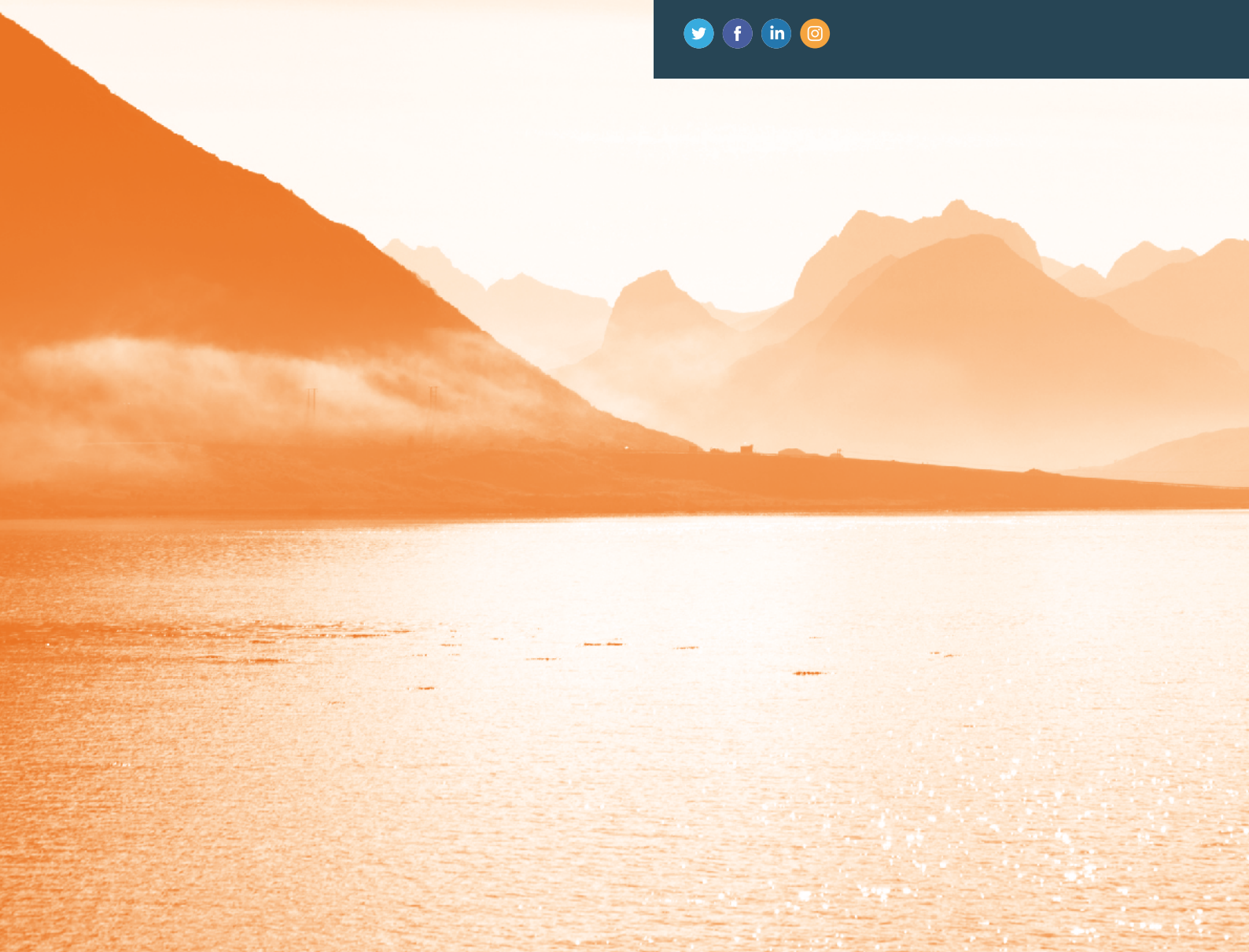
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