

EVALUATION OF RESEARCH IN BIOLOGY, MEDICINE AND HEALTH IN NORWAY 2010–2011

Self-assessment

# Centre for the Biology of Memory (CBM)

The Kavli Institute for Systems Neuroscience

- PANEL 2:
  - Centre for the Biology of Memory (CBM) / The Kavli Institute for Systems Neuroscience



## Introduction

The Research Council of Norway is responsible for conducting evaluations of Norwegian research. In 2010 the Council launched a comprehensive evaluation of biology, medicine and the health sciences, including psychology. Included in the evaluation were Norwegian universities, university hospitals, relevant research institutes and relevant university colleges. The results will be available in the autumn of 2011.

The objectives of the evaluation are to:

- perform a critical review of research in biology, medicine and the health sciences in an international perspective;
- obtain feedback on how Norwegian research can meet future challenges, especially in relation to new interdisciplinary research fields and social challenges;
- provide recommendations for measures to increase the quality and effectiveness of research;
- serve as a tool for institutions' strategic planning and scientific development activities;
- strengthen the basis for the Research Council's research policy input to government authorities.

### *Internal evaluations by the institutions/units under review*

Each institution included in the evaluation was asked to carry out an internal evaluation to provide the panels with information about the institution's organisation, strategic goals, research activity, infrastructure and other relevant factors.

The research groups of the Faculty of Medicine at NTNU and the St.Olavs Hospital-Trondheim University Hospital was evaluated together, since their research and innovation activities are highly integrated. The research groups were divided into 28 evaluation units. Self-assessments including information about the organization and resources, as well as future plans, was provided by each of the evaluation units.

This document presents the self-assessments that were produced by Centre for the Biology of Memory (CBM), the Faculty of Medicine.

Trondheim January 2011

## **Self-assessment –**

### **Centre for the Biology of Memory and the Kavli Institute for Systems Neuroscience**

#### **Table of Contents**

1.1.1. Organization of the Institute	2
1.1.2. Research Leadership	5
1.1.3. Strategy	6
1.1.4. Scientific quality – strong and weak research areas	9
1.1.5. Resources	15
1.1.6. Training, mobility and career paths	16
1.1.7. Research collaboration and interdisciplinarity	17
1.1.8. Other	18
2.2. Publication list for CBM / Kavli Institute	19
2.3 Facts sheet	24

## Summary

**Centre for the Biology of Memory (CBM) has developed into one of the world's leading convergence arenas for experimental and theoretical studies of memory in brain networks. The Centre became a Kavli Institute in 2007. During the eight years since its inauguration, CBM has been able to provide some of the most groundbreaking insights so far into how spatial location and spatial memory are computed in the brain and, more generally, how the brain generates its own neural patterns. The most remarkable contribution was perhaps the discovery of grid cells in the entorhinal cortex, in 2005, which immediately pointed to the entorhinal cortex as a hub for the brain network that makes us find our way through the environment. The discovery led to a complete revision of established views of how the brain calculates position and how the results of these computations are used by memory networks in the hippocampus. The results will ultimately benefit the development of tools for diagnosis and treatment of Alzheimer's disease, which commonly begins in just the brain area that contains the grid cells.**

The following outline is a self-assessment of the Kavli Institute for Systems Neuroscience. Because of the small size of the institute, Levels 1 and 2 have been merged.

### 1.1.1. Organization of the Institute

The Kavli Institute is a relatively new organizational unit of NTNU and the Institute is still developing. Because of the rapid change in organizational structure, the institute will be presented historically, as instructed.

The origins of the Kavli Institute can be traced back to 1996, when May-Britt and Edvard Moser were appointed associate professors at NTNU, a few months after they defended their Ph.Ds with Per Andersen at the University of Oslo. They started with empty space in the basement of the Department of Psychology at NTNU, without existing facilities for animal experiments. The new laboratories were operative from 1997 and by 1999 the first technician and a graduate student had joined the group. In 1999, the Mosers received their first major research grant, under the European Framework 5 (FW5) programme, with Edvard Moser as the coordinator for a consortium of 7 leading groups aiming to jointly perform the first integrated neural-network analyses of hippocampal memory in Europe. The group also received strategic funding from NTNU, allowing the group to grow from 2 to 6-7 persons. As part of the development of neuroscience at NTNU, the research group was invited to move to new laboratory premises in the Medical Technology Centre at the Faculty of Medicine in 2001.

In 2002, the Moser group was appointed a Research Council-founded Centre of Excellence. The **Centre for the Biology of Memory (CBM)** was established with Edvard Moser and May-Britt Moser as Director and Co-Director, together with 5 prominent visiting research colleagues from Europe (Witter, Treves, Morris, Menzel, Paulsen) and 2 from the U.S. (McNaughton, Barnes). The ambition of the Centre was to understand how information is encoded, stored and used in cortical systems and microcircuits.

The first scientific breakthrough came just before the inauguration of the Centre, in 2002, when the Moser group reported in *Science*, together with FW5 partner Menno Witter, that the intrinsic circuit of hippocampus was not necessary for basic hippocampal place signals. This led the Mosers and Witter to direct their search instead to the entorhinal cortex, which has dense direct inputs to CA1. In 2004, in a Research Article in *Science*, they provided the first evidence for strong position-related activity in this area, as predicted by the 2002 study, and in 2005 the work culminated in the discovery of grid cells as the principal functional cell type in the entorhinal spatial map. These findings were published as an Article in *Nature*. During the subsequent years, new insights were obtained at a high rate, with 1-3 papers published in *Nature* or *Science* every year since 2004. The new insights led to at least four major changes in the organization of the institute, as outlined below.

First, the host faculty was changed in 2005, when the **Faculty of Medicine** took over the Moser group from the Faculty of Social Sciences. This change led to a stronger integration with the strategies of the Faculty of Medicine. CBM was initially organized as a subunit of the Institute of Neuromedicine but due to the special character of the Centre, CBM was put directly under the Faculty from 2007-2008. Since then, the Director speaks directly to the Dean of the Faculty and all services are linked directly to the central administration of the Faculty. CBM is a strategic priority of the Faculty of Medicine.

The second major change was a burst of **recruitment to the Moser group**, starting around 2005. The discovery of grid cells led to an explosion of interest among young and talented postdoctoral researchers from all corners of the world. During the past 5 years, the Moser group has attracted candidates from MIT, Boston University, UC Irvine, Beijing University, University of Heidelberg, Salk Institute, Tokyo University, Weizmann Institute, Rockefeller University, and a number of other leading PhD-producing institutions. Although only a small fraction of the applicants are considered, the Moser group has now grown to a size of 9 post-docs and 11 graduate students, which is near the limit of what the two group leaders can handle. The researchers are funded by several major grants to the Moser group, including two Advanced Investigator Grants from the European Research Council to Edvard Moser and May-Britt Moser (total of 2.5 million Euros to each) and a European Framework VII RTD collaborative grant from the European Commission, coordinated by Edvard Moser. Several postdoctoral candidates also bring their own funding.

The third major change was the **recruitment of Menno Witter to a full professorship** at CBM in January 2007. Witter was one of the 7 visiting members of CBM and the closest collaborator of the Moser group, participating in the discovery of the entorhinal spatial map. Until he left his professorship in the Netherlands, Witter was the Scientific Director of the Neuroscience Institute of the VU University Medical Center in Amsterdam. Witter is probably the world's leading expert on the neuroanatomy and microcircuitry of the parahippocampal cortex, including entorhinal cortex. He established the role of the entorhinal cortex as the major interface between hippocampus and entorhinal cortex. Using novel combinations of electrophysiological, optical and neuroanatomical imaging techniques, he has revealed some of the key organizational principles of microcircuitry in the hippocampus and parahippocampus. His new lab at CBM was operative by the end of 2007. Since then Witter has trained technical assistants and recruited several skilled postdoctoral researchers and graduate students. His group has now 10-15 members. The recruitment of Witter to a permanent faculty position was followed by the hiring of two younger faculty on temporary contracts – Ayumu Tashiro, who received an ERC Startup grant from 2009, and Yasser Roudi who began on October 1<sup>st</sup>, 2010.

The fourth significant change was the appointment of CBM as a Kavli Institute in 2007. The **Kavli Institute for Systems Neuroscience** at NTNU is the 15th in the world and the 4th in neuroscience. The majority of Kavli Institutes are at leading universities in the U.S. (e.g., Harvard, MIT, Stanford, Yale, Caltech, Columbia, UCSD). Three are in Europe (Delft, Cambridge and NTNU). The Kavli Foundation provides an endowment of 7.5 million US dollars to each institute. In Trondheim, this is matched by an equivalent of 7.5 million dollars by NTNU and 7.5 million dollars by the Norwegian government. The annual disbursement provides the fundament for extending the scope of CBM's research programme. The objective of the research programme of the Kavli Institute is to establish how information is represented, encoded, stored and retrieved in neural microcircuits and networks of the hippocampus and associated cortex. Because spatial representation and navigation are among the first 'cognitive' functions to be understood in reasonable mechanistic detail, partly as a result of recent work at CBM, the Kavli Institute will use the network dynamics of navigation as a starting point for exploring principles and functions of cortical microcircuits more generally. The time perspective is much longer, however, and the aims and visions reach much wider than for CBM.

During its life time, CBM and the Kavli Institute have attracted considerable funding from research programmes of the European Union. Edvard Moser coordinates a Framework VII RTD project with 7 partners in European countries ('SPACEBRAIN'). Edvard Moser and May-Britt Moser have received Advanced Investigator Grants from the European Research Council (2009-13 and 2011-15, respectively) and Ayumu Tashiro has obtained an ERC Startup Grant (2009-2013).

**Future and planned changes.** CBM and the Kavli Institute consist currently of three senior faculty – Witter, Moser and Moser – and two junior group leaders on temporary contracts – Roudi (2010-2014) and Tashiro (2009-2013). A major goal for the next 5 years of the Kavli Institute is to further increase the number of laboratories and to include more faculty members. The first steps have already been taken.

First, NTNU is preparing new premises for the Institute. The Medical Technology Centre is being converted into a **Brain Centre** housing the expanding Kavli Institute as well as the Medical Imaging laboratories and a few other groups. The Kavli Institute is the coordinator of a far-reaching proposal to the Research Council's Large Scale Infrastructure Programme, NORBRAIN, which, if funded, will provide highly needed state-of-the-art equipment to the growing number of scientists at the Kavli Institute. The facilities will be part of a national facility open to qualified users from all parts of Norway as well as other countries. Skilled personnel will provide users with training and technical support.

The Kavli Institute is also expanding its scientific scope and number of research programmes. During the next few years, the Institute will increase its faculty with at least two more permanent positions, one in systems-oriented molecular neuroscience and one in computational neuroscience or neurophysics. These are areas that contain the knowledge and tools needed for a mechanistic understanding of spatial cognition specifically and cortical network operations generally. The cost of these new positions will be covered entirely by NTNU, as negotiated with the Kavli Foundation before the inauguration of the Institute in 2007. In preparation for these developments, the Institute has recruited Dr. Yasser Roudi to a group leader position in neurophysics and computational neuroscience. Dr. Roudi started on October 1<sup>st</sup>, 2010. He will be evaluated for a permanent position by an external advisory board in 3-4 years. In addition, the Institute is encouraging young

researchers to apply for startup funding from the European Research Council for a period of 5 years. Ayumu Tashiro at CBM received the first **ERC Startup Grant** in Norway, beginning in 2009. His group of 5 post-docs and 2 graduate students works on the function of neurogenesis in the hippocampus. Other young researchers will apply in 2010 and 2011.

The most immediate challenge of CBM is its **finite funding period**. The contract period covers 10 years, starting in 2002, and the grant is not renewable. The Directors of CBM and the Kavli Institute are working together with NTNU and the Board of the Institute to secure continued funding after 2012. While the Centre grant provides only 25-30% of the funding of CBM and the Kavli Institute today, much of the infrastructure is supported by this grant. Alternative funding sources may not allow for similar funding of support staff, interim contracts and running expenses. The Kavli Institute will apply for a new Centre of Excellence appointment, with a different focus than in 2002, but NTNU has been asked to consider a backup to prevent sudden termination of the activity.

### 1.1.2. Research leadership

**Leadership structure.** CBM and the Kavli Institute are co-directed by May-Britt Moser and Edvard Moser. The two units (CBM and Kavli) are virtually identical, except for the funding sources, and the units consist of the same permanent faculty – currently Witter, Moser and Moser. The key difference is that CBM is temporary, lasting for another two years (2012), whereas the Kavli Institute is permanent.

The Director of CBM and the Kavli Institute speaks to the Dean of the Faculty of Medicine as well as the Boards of the Kavli Institute and CBM (see Organization chart in the supplement). The Boards meet jointly twice a year. They have no formal authority but the central management of NTNU is strongly represented and brings relevant issues to the attention of the Rector and the Board of NTNU. The Board of the Kavli Institute is chaired by the Vice Rector for Research at NTNU whereas the Board of CBM is chaired by the Dean of Social Sciences. The Deans of Medicine and Natural Sciences are members. CBM also has an Advisory Board of internationally renowned neuroscientists (Larry Squire, UCSD; Terrence Sejnowski, Salk Institute; Erin Schuman, Max Planck Institute for Brain Research; Earl Miller, MIT). The Advisory Board meets three times during the 10-year long funding period of CBM.

**Funding and allocation of resources.** CBM and the Kavli Institute get most of their funding from external sources. The joint annual budget for the two units amounts to approximately 50 million Norwegian Kroner (6 million Euro; 8 million US dollars). Twenty to thirty percent of the funding is obtained from the European Research Council (2 Advanced Investigator Grants and 1 Startup Grant) and the RTD and Marie Curie programmes of the European Commission, 30 per cent is obtained from the Research Council of Norway (20% Centre of Excellence contribution; 5% Functional Genomics Programme FUGE), and 5% comes from the Kavli Foundation. Almost 30% is provided by NTNU as the host institution's contribution to match the Centre of Excellence grant from the Research Council and the endowment from the Kavli Foundation. The annual funding is more or less evenly divided among the three research groups working at the institute during the evaluation period (Moser and Moser, jointly 33 MNOK; Witter 8 MNOK; Tashiro 9 MNOK). In addition, NTNU has allocated 42 MNOK to construction of lab facilities for the Kavli Institute in the new Brain Centre.

The major expenses are the personnel costs. More than 32 MNOK (65-70%) of the funding is used to pay salaries of visiting professors (5% positions), postdoctoral researchers, graduate students, and technical and

administrative support staff. The Institute has several support positions that serve all members of the Institute, such as two administrative positions, one information officer, one IT expert, a laboratory administrator, and three animal technicians, as well as support staff associated with individual groups (histology, electronics, programming, molecular biology). The remaining funds cover laboratory running expenses, scientific equipment, expenses for visitors, and travel.

The budget has **balanced** around zero since the inauguration of the Centre in 2002. For 2010, we expect an underspending of approximately 6 MNOK, which is a bit more than in previous years. The surplus is largely related to the withholding of funds to pay for extra costs incurred by the construction of new laboratory premises; major costs during 2010 are likely not to be invoiced until 2011.

**Division of time between research, teaching, consultancy and clinical work.** The focus of the Kavli Institute is on basic research. The Director is exempted from lecturing whereas the Co-Director has only a few lectures per year; both are advisors for a number of post-docs and graduate students, however. Menno Witter is responsible for the Master's programme in neuroscience and so spends considerable effort on teaching and organization of teaching in addition to his research. The Master's programme was inaugurated before his arrival at the Kavli Institute but he has developed it from a small-scale lecture series to an international Master with links to complementary master programmes in other European countries, including a formal agreement with the VU University in Amsterdam. The Institute is not involved in consultancy or clinical work.

### 1.1.3. Strategy

**Vision and mission.** Neuroscience is one of the fastest-developing areas of science, but it is fair to say that we are still far from understanding how the brain produces subjective experience. Simple questions about the origin of thought, imagination, social interaction, or feelings lack even rudimentary answers. During the past decades, we have learnt much about the workings of individual cells and synapses, but psychological phenomena cannot be understood only at this level. These phenomena all emerge from interactions between large numbers of diverse cells in intermingled neural circuits. A major obstacle in the development of the brain sciences has been the absence of concepts and tools for investigating neural computation at the circuit level. The mission of the Kavli Institute is to establish how information is represented, encoded, stored and retrieved in microcircuits and networks of the cortex. The research programme takes advantage of our emerging understanding of the computational functions of specific networks involved in spatial representation and memory; however, the perspective is wider, in that the **ultimate goal is to understand neural computation underlying subjective experience in general**.

The experimental study of brain-behaviour relationships has a long history, dating back to the studies of Fritsch and Hitzig in the 1870s and Karl Lashley, who started in the 1920s. Many new paradigms have been developed since then and a lot has been learned about the function of specific brain regions. However, inferences were until recently based almost exclusively on experimental lesions and pharmacological interventions. These traditional approaches lack the spatial and temporal specificity required to determine exactly how each brain area or each neurochemical population contributes to a particular brain function. Because of this lack of resolution, brain-behaviour studies have remained somewhat descriptive, not telling us much about how brain functions are generated. The mission of the Kavli Institute is **to develop concepts and methods for studying operations at the intersection**

**between neurons and behaviour, at the level of neural circuits**, where myriads of individual, highly differentiated cells operate together in anatomically defined neural networks. We wish to determine how individual circuits are wired, which of their cell types are firing under which conditions, how their signals are passed and stored between the different cell types, and how cells cooperate within systems of dynamically variable architecture during complex mental operations. Only by fully understanding the operation of neuronal circuits will we eventually be able to grasp, mechanistically, how subjective experience can arise out of component synaptic and cellular processes.

The Kavli Institute is pioneering the development and use of tools for analyzing interactions between the large and heterogeneous cell assemblies in a neural circuit in a number of ways:

- (1) First, the Kavli Institute is developing detailed wiring diagrams for key neural circuits involved in spatial representation. Detailed **quantitative analysis of microcircuitry** is necessary if we are to understand how network components interact to generate specific functions and such analysis is absolutely essential to the development of computational network models.
- (2) A second line of development exploits advances in molecular biology to develop tools for investigation of **how specific cell types in a neural circuit contribute to the function** of a brain region. There are generally two strategies that can be employed. One involves conditional mouse knockouts where gene deletions are controlled by promoters that are, or can be, activated only in desired brain regions and only during the animal's adult life. This technology is not generally available for other mammalian species than the mouse and mice are not, at the moment, optimal for multi-site high-density recording, as the implants are larger and heavier than can be accommodated by their skulls. The resources required for breeding are enormous and each conditional mouse strain takes years to develop. An alternative and potentially faster strategy involves gene delivery by viral vectors. Neural populations can be targeted selectively in mammalian species that are sufficiently large to allow recording of large numbers of cells in multiple interconnected regions, such as the rat. The tool chest of viral vectors is expanding rapidly and several complementary methods can be used to target transgene expression to specific cell types in the rat (Zhang et al., Nat. Rev. Neurosci., 2007; Luo et al., Neuron 2008). Researchers at the Kavli Institute are combining these new and specific transgenic tools with large-scale single-cell recording from multiple locations in the spatial representation system of the rat in order to determine how a basic cognitive function is generated by interacting neurons with different morphological and physiological identities. This unique endeavour will pioneer the functional analysis of neural circuits and may, perhaps for the first time, provide us with a mechanistic understanding of the neural fundament of a mammalian cognitive process.
- (3) The third development is the most recent one, starting formally only with the appointment of Yasser Roudi as a group leader at the Kavli Institute as of October 1<sup>st</sup>, 2010. This line of development shall advance our understanding of neural population coding using **theoretical approaches and tools**, particularly those from statistical physics and information theory.

**Previous Research Council evaluations.** CBM has been evaluated by the Research Council on two previous occasions. In 2003, CBM was evaluated 'excellent' by the Panel for Psychology and Psychiatry. In 2006, the midterm evaluation of CBM rated the centre as 'exceptionally good'. There were no specific requests for organizational change.

**Strengths and weaknesses.** The Kavli Institute has become a magnet for scientists interested in understanding neural computation in the performing brain, yet the Institute also faces some significant challenges. The following is a list of perceived strengths and threats:

**Strengths:**

- We have made some of the most intriguing scientific discoveries of systems neuroscience during the past 10-20 years.
- We have pioneered new technologies for systems and network analysis in neuroscience, including most recently the use of virus-based gene intervention to study neural network interactions in the spatial representation circuit of behaving animals.
- CBM and the Kavli Institute host the world's leading expertise on micro- and macroanatomy of the entorhinal cortex.
- CBM and the Kavli Institute have strong collaborations with leading computational neuroscientists allowing researchers to merge experimental and theoretical approaches in the study of neural circuits.
- The Institute has a continuous flow of highly talented postdoctoral researchers as well as adequate funding and a highly skilled technical support team.
- The Institute has active collaborations with the best scientists in their field – some as visiting members of CBM, others with a more project-specific connection.
- CBK and the Kavli Institute are currently very well-funded. The funding allows for flexibility in hiring of new personnel as well as initiation of high-risk high-gain research projects.

**Threats:**

- CBM has a finite funding period. The contract expires in 2012 and the grant is not renewable. The Centre grant provides only 25-30% of the funding of CBM and the Kavli Institute today; however, the loss of this funding source would be serious, considering that much of the Institute's infrastructure (technical support, interim contracts, running expenses) is covered by the Centre of Excellence grant and most other grants cannot be used extensively for such purposes. The Kavli Institute will apply for a new centre but success is of course not guaranteed.
- The fast development of technology in systems neuroscience requires a high degree of sensitivity to the development of the field as well as willingness and funds to change the methodological approach to follow this development.
- Funding for new equipment is uncertain. If NORBRAIN is not funded, the institute will not be able to realize its plans for a national reservoir of next-generation equipment for systems neuroscience. This would in turn seriously hamper efforts to integrate activities at the Kavli Institute with those of the rest of the Norwegian neuroscience community. It would also restrict the opportunities for accepting candidates for short-term training visits.
- To be able to follow the fast conceptual and technological advances of the field, the Kavli Institute may need additional faculty with expertise in the new areas.
- The Kavli Institute is vulnerable in its strong dependence on two research groups – the Moser group and the Witter group. All three principal investigators have received, and are receiving, generous job offers at leading institutions in other countries. If any of the groups leave, the remaining institute will be quite amputated. The best way to dam up against this vulnerability is undeniably to increase the staff of the Institute – to recruit strong scientists

to fill new positions, bringing the total staff up to a size where the Institute can move on in the presence of staff change. NTNU and the Kavli Foundation are aware of this threat; the addition of two new staff positions at the Kavli Institute is part of the university's strategy to consolidate the new institute.

#### 1.1.4. Scientific quality – strong and weak research areas

The Kavli Institute has a coherent research agenda. The overall research programme was outlined in Section 1.1.3. It was shown that the focus of the Institute is on understanding principles of neural computation in circuits and systems of the cortex, with a particular focus on the mechanisms of spatial representation and memory. All four research groups of the centre are involved in this endeavour, each addressing a unique aspect of this general mission. The following is a brief outline and evaluation of the more specific research visions and plans of the individual groups.

**Moser group.** The Moser lab is interested in neural network computations in the cortex, with particular emphasis on memory and dynamic spatial representation in the hippocampal-entorhinal system. This research is at the core of the activity of the Kavli Institute and formed the basis for the institute when it was inaugurated. Twelve of the Moser group's original research articles since 2004 have been published in *Nature* and *Science*. May-Britt and Edvard Moser share the responsibility for the group. The group has approximately 20 post-docs and PhD students.

The Moser group has discovered some of the key elements of the brain's mechanism for computation, representation and storage of self-position. Their first breakthrough came in 2002, when they found, together with Menno Witter, that hippocampal place signals do not require the intrinsic circuit of hippocampus (Brun et al., *Science*, 2002). This led them to search for positional signals in the entorhinal cortex, outside the hippocampus, which culminated in the discovery of grid cells soon after (Fyhn et al., *Science*, 2004; Hafting et al., *Nature* 2005). Grid cells are place-modulated entorhinal neurons whose spatial firing fields in a freely moving rat define a periodic triangular array covering the entirety of the animal's environment, like the cross-points of graphic paper rolled out over the surface of the test arena, but with equilateral triangles as the repeating unit rather than squares (Figure 1). The array of firing is maintained in spite of continuous changes in the animal's speed and direction, and grid cells are thought to form an essential part of the brain's coordinate system for metric navigation

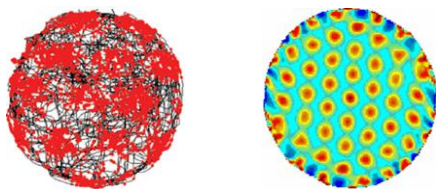


Figure 1. Grid cell in entorhinal cortex. Left panel: Trajectory of the rat in a 2 m diameter wide cylinder (black) with spike locations of one grid cell superimposed (red). Each red dot corresponds to one spike. Right: colour-coded spatial autocorrelogram for the same experiment showing periodicity of firing across the entire environment (radius 2 m).

(Hafting et al., 2005; McNaughton et al., *Nat Rev Neurosci*, 2006). To understand the function of grid cells, the Moser group went on to characterize the wider network in which these cells are embedded. In 2006, the group found that entorhinal cortex also contains cells that signal the animal's head direction and cells that signal direction and position conjunctively (Sargolini et al., *Science* 2006), and in 2008 they found a third cell type – border cells – which fires exclusively along boundaries of the local environment (Solstad et al., *Science* 2008). The group also reported that grid cells determine how

memory is stored in the hippocampus (Fyhn et al., Nature 2007), one synapse downstream in the network, and they showed that gamma oscillations are instrumental in routing information between grid networks in the entorhinal cortex and place and memory networks in the hippocampus (Colgin et al., 2009). Collectively, these studies have outlined the basic properties of the entorhinal spatial representation system. The search for the functions of the hippocampal-entorhinal networks has made spatial orientation and spatial memory become one of the best understood non-sensory cognitive functions to date. Grid cells have attracted attention because the crystal-like structure underlying their firing fields is not, like in sensory systems, imported from the outside world, but it is created within the nervous system itself. Grid cells thus provide scientists with direct access to some of the most basic operational principles of cortical circuits.

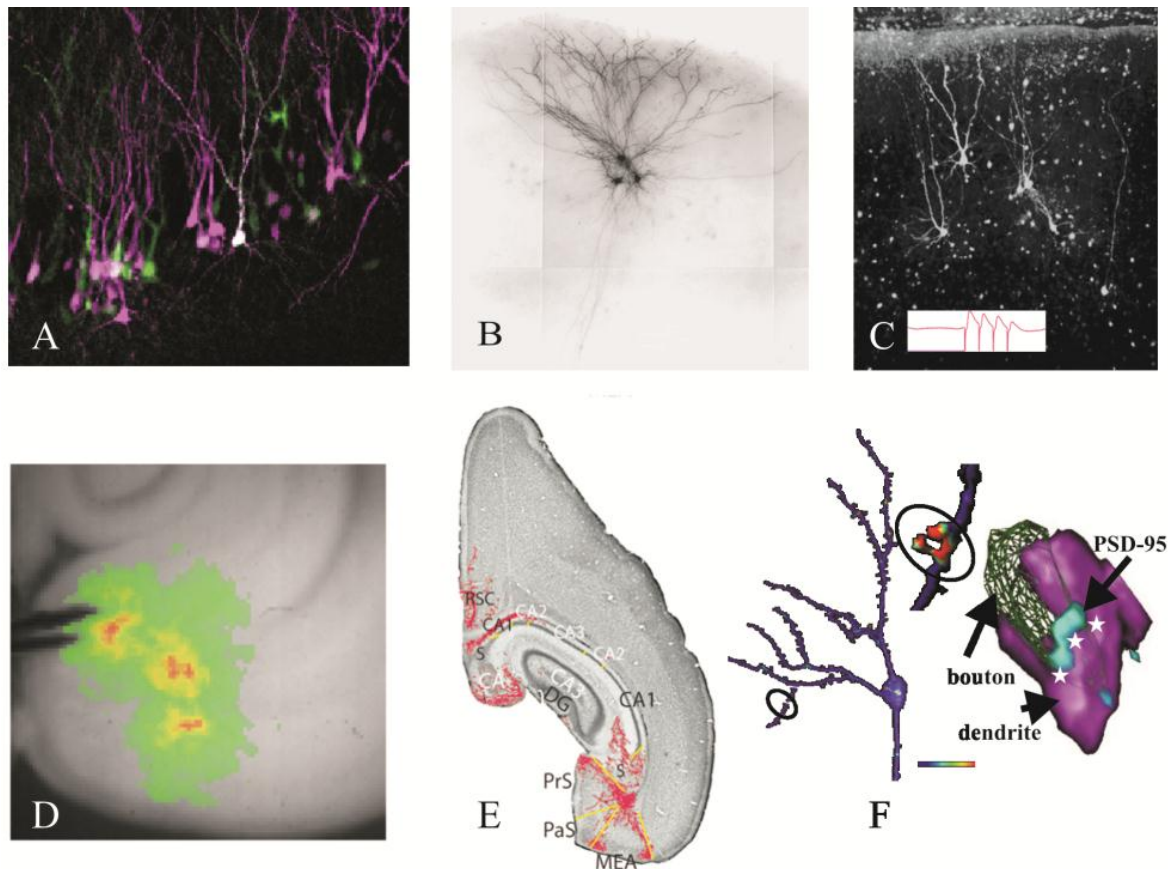
The Moser group is now digging into the mechanisms behind the formation of spatial representations. They wish to gain insight into the functional wiring of the circuit and manipulate its key components, one at a time, to determine the contribution of each part and to understand how the parts influence each other. The Mosers are using viral vectors (AAV) to target genes to defined neural populations, and photoinducible proteins such as channelrhodopsins and halorhodopsins (Boyden et al., Nat Neurosci. 2005; Zhang et al., Nature 2007; Gradinaru et al., Cell 2010) are expressed selectively in the target population in order to turn on or off its activity selectively. Using these novel tools, the researchers in the Moser group can, in principle, determine how the activity of each cell type contributes to the global computations of the entorhinal-hippocampal circuit. The first results of this endeavour will be reported at the Society for Neuroscience meeting in November 2010 (Zhang et al., 2010).

**Witter group.** Menno Witter was offered a professorship at the Kavli Institute in 2007. Before he moved in 2007, he had worked as a visiting member at CBM for 5 years. He was the closest collaborator of the Centre and the moved was motivated to a large extent by the wish to extend this collaboration. Since 2007, Witter has built up an active state-of-the-art neuroanatomy group. The group has approximately 10 post-docs and PhD students.

The objective of research in the Witter group is to reveal relationships between neural-network architecture and function. Witter and his colleagues have developed a pragmatic strategy to combine data on connectivity of groups of similar neurons with sparse sampling of individual neurons. In combination, these approaches allow for an analysis of the full wiring diagram of a network. The lead hypothesis for the next years is that striking differences in functional properties of the lateral and medial entorhinal cortex, as demonstrated through the collaboration with May-Britt and Edvard Moser, emerge from subtle differences in intrinsic wiring combined with differences in input relationships. The research will allow the group to determine not only the correlation of known functional differences with differences in local architecture but will also open to study the effects of subtle changes in cortical architecture on functional performance. The latter has significant translational capacity in that understanding the effects of specific changes can be used as models for neurodegenerative diseases, in particular Alzheimer's disease (see Translational research and societal relevance, page 14, for further details).

Before Witter moved to Trondheim, he outlined the basic concepts of the entorhinal network in a number of influential papers. The initial phase of his lab in Trondheim, now coming to its end, was used to pilot and implement the methodologies essential to carry out the proposed research. These include retrogradely and transsynaptically transported rabies virus that express different fluorophores,

and multiple whole cell recordings ( $>3$  cells) as a superior method to quantify local microcircuitry in the cortex *in vitro*. These are complemented with a new approach to express the photo-inducible molecule channelrhodopsin-2, which allows researchers to stimulate axons that cannot be easily maintained in an *in vitro* slice preparation. This application builds on the group's recently developed approach of *in vivo* tracing of input-output connectivity followed by *in vitro* recording, combined with the approaches implemented in the Moser group. With the use of voltage sensitive dye imaging, the group can assess efficiently whether the connectivity of interest is maintained in the slice, and Witter and his colleagues have developed efficient methods to combine all these approaches. The new methods will be complemented with traditional, yet powerful, anterograde and retrograde tracing of input and output pathways and newly developed confocal analyses in thick slices using sequential immunohistochemical staining procedures on intracellularly filled neurons. Changes in neuronal networks naturally occur during development and the group has implemented all the above approaches to study developmental changes in neuron networks (Figure 2). Some of the methods and transgenic animals are made possible through collaborations with Toshio Iijima (Tohoku Univ, Sendai, Japan), Yuchio Yanagawa (Gunma University, Japan), and Cliff Kentros (Univ. of Oregon, USA).



**Figure 2. The functional anatomy toolbox.** **A.** Single (purple and green) and double labeled (white) retrogradely transsynaptically infected pyramidal cells in CA3 following bilateral infection in entorhinal cortex (Ohara et al., *Front. Neuroanat.*, 2009). **B.** Four layer II stellate cells intracellularly filled with biocytin on P18 (Couey & Witter). **C.** *In vitro* patch of retrogradely labeled identified entorhinal-hippocampal projection neurons in layers II and III, receiving anterogradely labeled input from presubiculum. Four impaled and filled neurons are shown within a population of retrogradely labeled neurons; inset: response of deep layer II cell (Canto & Witter). **D.** Voltage sensitive dye imaging of presubicular activation of entorhinal cortex in adult rat (Koganezawa & Witter). **E.** Anterogradely labeled hippocampal-entorhinal projections on P16 (Krugé, O'Reilly & Witter). **F.** Sequential confocal analysis of synaptic connectivity of retrosplenial axons onto identified layer III neurons in presubiculum (Color code represents distance between elements of a potential synapse). Inset: bouton is characterized with the vesicular marker synaptophysin, postsynaptic element with PSD95 (Kononenko & Witter).

Through additional competitively obtained funding, the Witter group has expanded to its current size of 6 postdocs, 4 PhD students and 3 technicians. The group represents a unique combination of technical expertises and has already generated a new conceptualization on the interlaminar and intralaminar architecture of the entorhinal cortex. Currently, 1 paper is under revision, 2 papers are ready to submit, and 3-4 are expected to follow in the coming months. In order to make the network data available to the scientific community, Witter has initiated a collaborative digital brain atlas on the parahippocampal-hippocampal region (Univ. Oslo; <http://rbwb.org>), and published a connectional database in Nature Reviews Neuroscience (<http://www.temporal-lobe.com>). The latter activities are embedded in the Program on Ontologies of Neural Structures (PONS), initiated by the International Neuroinformatics Coordinating Facility (INCF). These activities, viewed as a whole, are considered to be at the absolute forefront of modern neuroanatomy.

**Tashiro group.** The Tashiro group was formed in March 2009, thanks to a starting investigator grant from European Research Council. Ayumu Tashiro initially joined CBM in 2006. As a postdoc in the Moser group, he contributed to setting up the first molecular biology lab at CBM, he has implemented virus-based genetic tools, and he has contributed to the development of optic fiber-coupled microelectrodes now used by Tashiro and the other groups.

The main focus of the group's research is to understand function of newly-generated neurons in the adult brain, which Tashiro has been working on and made important contributions to, as signified by high-impact publications in Nature and Journal of Neuroscience before Tashiro joined CBM. Generation of new neurons in the hippocampus is thought to be important in normal brain functions, such as memory formation and mood regulations, and brain diseases, such as depression epilepsy and schizophrenia. However, the mechanisms with which newly-generated neurons contribute to these functions and dysfunctions are not clear. The Tashiro group aims to advance our understanding of the roles of newly-generated neurons in adult brain by combining virus-based genetic manipulation, electrophysiological and anatomical techniques and behavioral analysis. In addition, with funding from the Research Council of Norway, the group aspires to understand cellular mechanisms of place cell activity.

The Tashiro group has 5 postdocs, 2 PhD students, 3 technicians and 4 master students and is expecting the arrival of 1 postdoc and 2 PhD students by early 2011.

**Roudi group.** Yasser Roudi has been recently hired and started a new group working on theoretical aspects of learning and memory and modelling of neuronal networks from Oct 2010. Roudi's research has two main aims: 1. to advance the understanding of general principles of computation and learning algorithms and the implementation of these algorithms in the nervous system. 2. developing advanced tools for high-throughput data analysis in systems biology. These aims are achieved using a theoretical approach, employing tools from statistical physics and information theory. This is a rapidly expanding research field which requires interaction between experimentalists and theoreticians and has proven to be very fruitful for understanding mechanisms of memory operations in the brain.

Roudi's recent work, outlined in several publications in the past two years, has made important advances in using multi-electrode arrays recording for reconstructing network connectivity. After carefully quantifying previous methods for analysing multi-electrode data and establishing that they

cannot offer the performance one would like to achieve, recently Roudi and Hertz have laid the ground for a different approach based on advanced tools in theoretical physics to use multi-electrode recording for understanding network connectivity (Hertz et al, BMC Neurosci. 2009; Roudi and Hertz, submitted available on <http://arxiv.org/abs/1009.5946>). This line of research will be pursued in the next few years by the establishment of this new theoretical group.

The group is now composed of Yasser Roudi and a postdoctoral fellow Aree Witoelar. Another postdoctoral fellow is expected to be hired during 2012. The group aims to expand also through collaboration with the Physics Department at NTNU, where Masters and PhD students with a quantitative background can be integrated into the research on biological questions.

**Distribution between research units.** Nearly all published results are from the Moser and Witter groups. This is natural given that the Tashiro and Roudi groups are starters in the field. For obvious reasons, their publication lists are dominated by papers from previous institutions at which they have worked. The average latency between startup of a project and publication at the Kavli Institute is ~3 years. The success of the Tashiro group in attracting funding provides recognition of the ideas pursued by this group. While Witter and the Mosers are internationally leading in their fields, Roudi and Tashiro have potential to achieve a similar position in the future.

**Strategy for publication.** It is the strategy of the Kavli Institute to communicate scientific results in the most respected and influential publication channels of the field, including, for experimentalists, such journals as *Nature*, *Science*, *Nature Neuroscience*, *Neuron* and *Cell*, and for theoreticians journals such as the *Physical Reviews* and *PLoS Comp. Biol.* We deliberately seek to maximize the impact of the publications by withholding data until a relatively complete and coherent understanding is obtained and all interpretations are well supported by the data. This necessarily lowers the number of publications but instead each advance will be sufficiently significant to be read by a wide neuroscience readership, including those working in unrelated fields, whom we wish to reach to maximally disseminate new knowledge about general principles. The strategy is reflected by the fact that all faculty members publish in the highest-ranking journals. Approximately 15 papers from CBM and the Kavli Institute have been published in *Nature* or *Science* during the last 5-6 years.

**Dissemination to the general public.** The Kavli Institute is strongly committed to better public understanding of science and the faculty members have been engaged in a number of activities relevant to this. Both Witter and the Mosers are members of the European Dana Alliance for the Brain (EDAB). The mission of EDAB, and its American counterpart the DANA ALLIANCE, is to inform the general public and decision-makers about the importance of brain research, to advance knowledge about the personal and public benefits of neuroscience, and to disseminate information on the brain in health and disease in an accessible and relevant way. In March each year, EDAB organizes Brain Awareness Week, when hundreds of public events and activities worldwide bring scientific progress in the neurosciences out to the general public. The Kavli Institute has participated actively in this endeavour, with an exhibition at the Science Museum by Witter and the Mosers, as well as a public lecture about fragile-X syndrome by Mark Bear, MIT.

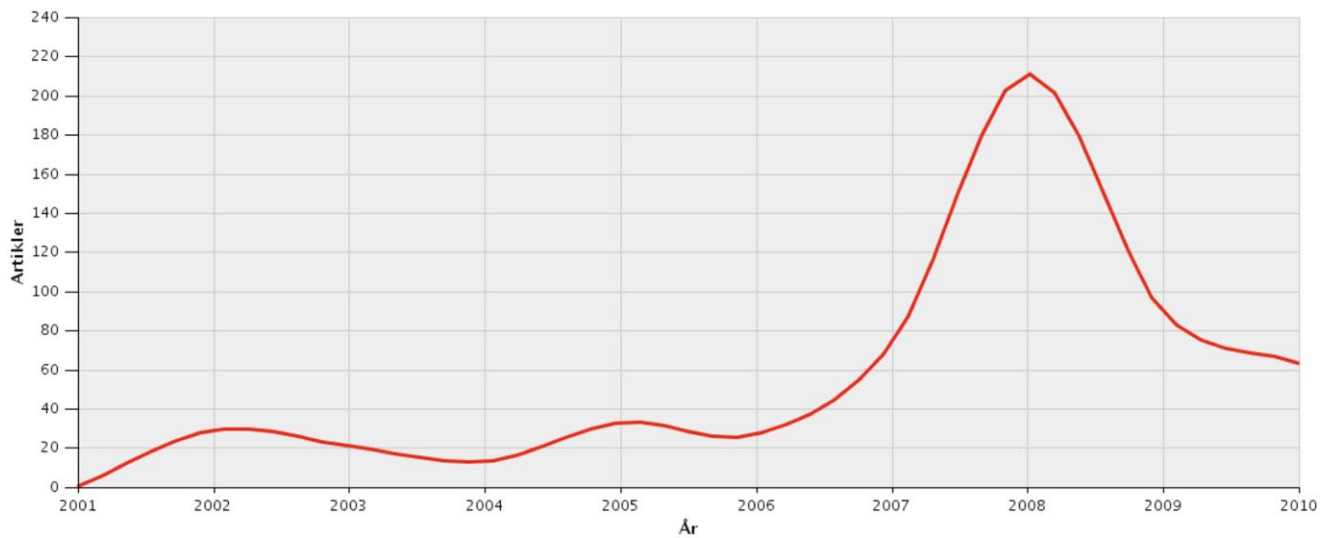


Figure 4. Number of articles referring to CBM or the Kavli Institute per year since 2001. In 2008 the Kavli Institute hired an information officer to promote dissemination to the lay public. Although the media coverage increased severalfold, we decided in 2009 to focus on a lower number of newspaper and radio/TV articles with higher impact. The count is not complete as several radio and TV programmes are not included. Many international media are included.

Witter and the Mosers are also active in the media on a regular basis, with almost 400 articles in media since 2008 as well as approximately 20 contributions on radio or on TV during the same years (Figure 4). May-Britt and Edvard were guests on ‘Grosvold’, the most watched television programme in Norway in 2009. They have been in the news on TV several times as well as in *Schroedinger’s Cat*, a primetime popular science magazine. A team from *Schroedinger’s Cat* accompanied Witter and the Mosers to Longyearbyen at 79 degrees North, where they organized a scientific conference in 2008, and in the same year *Schroedinger’s Cat* sent a series of programmes about memory based on a collaboration with the Kavli Institute.

**Translational research and societal relevance.** While the primary goal of the Kavli Institute is to understand cognition in the normal brain, the activity has considerable potential for translation to clinical applications. Such translation will primarily have to be carried out by interaction with relevant clinical researchers; however, Witter has initiated collaborative projects on the neural basis of Alzheimer’s disease. The group is investigating changes in neural networks in animal models for Alzheimer’s disease. Through a collaboration with Claudio Cuello at McGill University, Witter has set up a breeding colony of transgenic rats that carry the human A $\beta$ PP751 cDNA containing the entire coding region and approximately 900 bp of 3' non-translated sequence including the Swedish double mutation (K670N, M671L) in conjunction with the Indiana mutation (V717F) under control of the Thy-1 promoter (McGill-R-Thy1-APP). These rats express increased levels of soluble A $\beta$  in neurons of the entorhinal cortex as early as one week postnatally (Leon et al., *J Alzheimers Dis.*, 2010). The model faithfully mimics the time-dependent increase in amyloid plaque load as well as the typical time-dependent changes in spatial distribution of the amyloid. A quantitative stereological study is currently carried out, in which cell numbers and amyloid load is analyzed at different developmental stages from 3 – 15 months of age. This model will allow Witter and his colleagues to systematically study the development of the disease over time. Witter will study

functional and connectional changes in the entorhinal-hippocampal circuit resulting from changes levels of A $\beta$  load, based on the hypothesis that the entorhinal circuit is prone to be specifically susceptible to increases in amyloid load. The group has established collaborations with Scott Small at Columbia Univ, Brad Hyman at Harvard Med. School and Mike Hasselmo at Boston Univ., who are working on similar concepts using other transgenic models for this disease.

In addition to these explicit translational efforts, it is worth noting that because the entorhinal cortex is the first brain region to be affected in many patients with Alzheimer's disease, basic functional insight into the network basis of spatial representation in the entorhinal cortex, as obtained from ongoing work at the Kavli Institute, may by itself provide clinical neurologists and health workers with tools for early diagnostics, prevention and treatment of Alzheimer's disease. Insight into general mechanisms of network function may also benefit progress in understanding of other neurological or psychiatric diseases where similar computational mechanisms are affected.

### 1.1.5. Resources

The research group at CBM consists of 3 faculty, 2 young group leaders, approximately 20 postdocs and 20 PhD students, 10-15 master students and 21 technical assistants. The Centre has currently about 800 m<sup>2</sup> of lab space but with the new premises to be completed in 2011, the lab space will increase to more than 2500 m<sup>2</sup>. The present laboratories include about 10 fully equipped state-of-the-art high-density single-unit recording laboratories with different types of behavioural apparatus; this number will increase to more than 20 in the new premises. Most of the present recording rooms are for rats, but two are dedicated for mice. The center has five setups for surgery, extensive facilities for histology and neuronal tracing, several confocal and fluorescence microscopes, a patch-clamp and voltage sensitive dye imaging setup and two molecular biology laboratories with all facilities for generating viral-vector tools. There are separate housing facilities for rats and mice, hundreds of each species. Rats are generally bred in-house. There are three technicians working in the animal facilities. The Institute has an IT engineer, a laboratory manager, and 2-3 administrative staff; in addition, all experimental groups have histology and molecular biology technicians and the Moser group has technicians helping with programming, electronics and electrode preparation. The Centre has become a regular user of the national supercomputer facilities.

The scientific equipment is state-of-the-art but needs to be renewed. Major investments are needed during the next few years to accommodate new technologies such as STED-PALM microscopes, in vivo patch clamp recording, and nanoscale recording methods. CBM and the Kavli Institute coordinate an application for a 100-MNOK national upgrade of neuroscience equipment beginning in 2011. If the proposal is successful, the pressure on the equipment will be less than today and the facilities will be shared on a self-cost basis with researchers from other groups and institutions, in Norway and abroad. The upgrade and extension of the facilities would enable the centre to host an increasing number of scientists on training visits. Except for the uncertainty related to renewal of equipment, the resources are excellent. The scientific output of CBM/Kavli generally matches the resources available.

NTNU has supported the development of CBM and the Kavli Institute right from the beginning when May-Britt and Edvard Moser worked at the Psychology Department in the late 1990s and applied for a European Framework V project. The subsequent Centre of Excellence funding from the Research Council was matched by an equally large share from NTNU, which included stipends for post-docs and

graduate students, technical and administrative support, and support for consumables and travel. No overhead was charged on the contribution from the Research Council. The contribution from the Kavli Foundation in 2007 was also matched by an equal contribution from NTNU and from the Ministry. The Faculty of Medicine has established one new position – the professorship in neuroanatomy, now held by Menno Witter. The university put significant resources into offering Witter a competitive startup package and a state-of-the-art neuroanatomy lab. The Kavli Institute gets a significant share of strategic NTNU money allocated, for example, to advanced equipment and postdoctoral fellows. Finally, NTNU has allocated funding for new laboratory premises in 2011 (42 MNOK) and the university is working for a continuation of CBM after the contract period with the Research Council has expired. NTNU is also supporting NORBRAIN, a proposal for large-scale rearmament of Norwegian neuroscience infrastructure coordinated from the Kavli Institute.

**Academic staff.** More than 80% of the academic staff (including post-docs and PhD students) are foreign citizens. They span a wide range of training backgrounds, from physics and computer science through biology and medicine to psychology. The gender balance among post-docs and PhD students is approximately 60% (males) – 40% (females). Nearly all members of the centre are younger than 40. The three permanent faculty are in their 50s (Witter) and 40s (Mosers).

### 1.1.6. Training, mobility and career path

The recruitment and training policy of the Kavli Institute has a strong focus on international exchange and mobility. The majority of PhD students and post-docs come from other countries, with an aim of using state-of-the-art systems approaches to understanding hippocampal-entorhinal circuits. These researchers are likely to go abroad after their work period at the Kavli Institute and they are encouraged to do so. The same holds for the minority of PhD students and post-docs with a Norwegian background; these are also encouraged to go abroad for further training and, when they return, to obtain faculty positions in other institutes or other universities than the Kavli Institute. Recruitment to new faculty positions is competitive on the international arena. All group leaders have so far been recruited internationally. The Kavli Institute aims to have an approximately equal number of male and female group leaders. Female post-docs are particularly encouraged to apply for ERC startup funding.

At the beginner's level, recruitment is encouraged through the International Master's programme in neuroscience, organized by a Programme Board chaired by Menno Witter. Students receive training across all levels of the field, from molecules to behaviour, but with a particular emphasis on systems neuroscience and network mechanisms. Visiting professors and post-docs at CBM participate in courses and direct training of Master and Ph.D. students, providing the students with knowledge of the diversity of thoughts and techniques in the field. There is a well articulated PhD program in which the Kavli Institute is strongly involved through the membership of Witter in the Programme Board. If the recently submitted large-scale infrastructure application (NORBRAIN) is funded, there is the ambition to further strengthen both master and PhD training through national and international collaborations.

During the 8 years since its inauguration, CBM has produced number of successful PhD students and post-docs. Among the graduate students, Marianne Fyhn, who worked here from 2000 to summer

2008, received the David Lindsley Prize for the best PhD thesis in neuroscience in 2005 and was a runner-up to the Science-Eppendorf Prize in 2007, also for her thesis. Together with postdoc Torkel Hafting in the Moser lab she received the Fridtjof Nansen Prize for Young Researchers in 2007. One of the centre's first post-doc was Stefan Leutgeb, who worked at CBM from 2002 to 2007. In 2007, he was appointed group leader at NTNU. In 2008, he received an ERC Startup Grant, which he eventually declined because he was offered a competitive assistant professor position at UCSD. He moved to UCSD in 2008. Jill Leutgeb received the Royal Norwegian Academy's Prize for Young Researchers in 2008. She has also an assistant professorship at UCSD. Francesca Sargolini has now a faculty position at the University of Provence in Marseille, Rosamund Langston is a lecturer at the University of Dundee and James Ainge at the University of St. Andrews, and Laura Colgin has just become an assistant professor at the UT Austin. Laura Colgin is the 2010 recipient of the International Gruber Prize, a prize received for the second time by researchers at the Kavli Institute (the first recipient was Ayumu Tashiro in 2008).

The Kavli Institute has attracted a number of talented researchers, who came after making fundamental discoveries in related fields. For example, Ayumu Tashiro came with a *Nature* paper from the Salk Institute; Jonathan Whitlock's paper on the role of LTP in hippocampal learning in *Science* in 2006 was chosen by *Science* as a 'highlight of the year'; and Lisa Giocomo and Rosamund Langston each have important *Science* papers on grid cell properties and hippocampal memory.

### 1.1.7. Research collaboration and interdisciplinarity

A unique feature of CBM and the Kavli Institute is the strong international anchor. To realize the integration of methods and concepts across disciplines, the Centre recruited 7 distinguished foreign members in 2002, each among the leaders in their fields, to work at the Centre periodically (1-2 visits each year, each of 1-2 weeks). These scientists, coming from the U.S., the U.K., Germany, Italy and the Netherlands, shared an interest in how memory forms in cell assemblies and brain circuits. Their goal has been to determine, using a combination of neurophysiological, behavioural, information theoretical and statistical methods, how information is computed and stored in neuronal networks of the hippocampus and the neocortex. Postdocs, graduate students and technicians from CBM have also visited most of the labs of the visiting professors to give seminars, learn new techniques, or conduct experiments and analyses for which equipment is not available at NTNU. The integration of wide expertise, crossing a number of scientific disciplines from physics and mathematics through biology and psychology, on a common set of research projects within a single lab has been enormously successful and been noticed world-wide. The collaborative and intellectually stimulating research environment at CBM and the Kavli Institute has attracted talented post-docs from several leading neuroscience labs (see above), and led directly to the recruitment of Menno Witter to a professorship at the Kavli Institute. The current team of visiting professors includes Alessandro Treves (SISSA, Trieste), Bruce McNaughton (Univ. Lethbridge), Carol Barnes (Univ. Arizona), Mayank Mehta (UCLA), Richard Morris (Univ. Edinburgh), Ole Paulsen (Cambridge Univ.) and Randolph Menzel (Free Univ. of Berlin).

More recent collaborations are based on funding from the European Commission and include the now almost completed SPACEBRAIN project coordinated by Edvard Moser. Collaborators on this project include John O'Keefe, Neil Burgess and Kate Jeffery (UCL, London), Fritjof Helmchen (Univ. Zurich), Hannah Monyer (Univ. Heidelberg), and Misha Tsodyks (Weizmann Inst., Israel).

The Mosers and Tashiro collaborate with Fred Gage (Salk Institute, La Jolla) through a James McDonnell grant, and the Mosers work on a joint project with Eric Kandel (Columbia Univ.). Witter has a number of international collaborations, including Nachum Ulanovsky at the Weizmann Institute, Toshio Iijima at Tohoku University, Cliff Kentros at Univ. of Oregon, Howard Eichenbaum and Michael Hasselmo at Boston University, Scott Small at Columbia University, and Brad Hyman at Harvard Medical School.

### **1.1.8. Other**

Please note that enclosed CVs and publications from postdocs primarily reflect their work at their previous host institutions. The lag between start of project and publication is normally around 3 years, such that their work at CBM/ the Kavli Institute is normally published only at the end of their postdoctoral contract.

## Publication list for CBM / Kavli Institute

The list includes papers published between 1 January 2005 and 30 June 2010. **Please note that only papers with CBM or Kavli Institute as author affiliation are included.** We have not listed papers by Centre members when these are published independently of the Centre. This applies to most papers by the Centre's visiting professors (Professor II), the post-docs and the earliest work of MP Witter (for post-docs and Witter, all work that they performed before their arrival at the Centre).

### 2005

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.

Leutgeb, S., Leutgeb, J.K., Barnes, C.A., Moser, E.I., McNaughton, B.L., and Moser, M.-B (2005). Independent codes for spatial and episodic memory in the hippocampus. **Science**, 309, 619-623.

Leutgeb, J.K., Leutgeb, S., Treves, A., Meyer, R., Barnes, C.A., McNaughton, B.L., Moser, M.-B., and Moser, E.I. (2005). Progressive transformation of hippocampal neuronal representations in 'morphed' environments. **Neuron**, 20, 345-358.

Steffenach, H.-A., Witter, M.P., Moser, M.-B., and Moser, E.I. (2005). Spatial memory in the rat requires the dorsolateral band of the entorhinal cortex. **Neuron**, 45, 301-313.

Leutgeb, S., Leutgeb, J.K., Moser, M.-B., and Moser, E.I. (2005). Place cells, spatial maps and the population code for memory. **Current Opinion in Neurobiology**, 15, 738-746.

Moser, E.I., Moser, M.-B., Lipa, P., Newton, M., Houston, F.P., Barnes, C.A. and McNaughton, B.L. (2005). A test of the reverberatory activity hypothesis for hippocampal place cells. **Neuroscience**, 130, 519-526.

De Hoz, L., Moser, E.I., and Morris, R.G.M. (2005). Spatial learning with unilateral and bilateral hippocampal networks. **European Journal of Neuroscience**, 22, 745-754.

### 2006

Sargolini, F., Fyhn, M., Hafting, T., McNaughton, B.L., Witter, M.P., Moser, M.-B., and Moser, E.I. (2006). Conjunctive representation of position, direction and velocity in entorhinal cortex. **Science**, 312, 754-758.

Colgin, L.L., and Moser, E.I. (2006). Rewinding the memory record. **Nature**, 440, 615-617.

McNaughton, B.L., Battaglia, F.P., Jensen, O., Moser, E.I., and Moser, M.-B. (2006). Path-integration and the neural basis of the 'cognitive map'. **Nature Reviews Neuroscience**, 7, 663-678.

Leutgeb, S., Leutgeb, J.K., Moser, E.I., and Moser, M.-B (2006). Fast rate coding in hippocampal CA3 cell assemblies. **Hippocampus**, 16, 765-774.

Solstad, T., Moser, E.I., and Einevoll, G.T. (2006). From grid cells to place cells: a mathematical model. **Hippocampus**, 16, 1026-1031.

Witter, M.P. and Moser, E.I. (2006). Spatial representation and the architecture of the entorhinal cortex. **Trends in Neurosciences**, 29, 671-678.

## 2007

Fyhn, M., Hafting, T., Treves, A., Moser, E.I., and Moser, M.-B. (2007). Hippocampal remapping and grid realignment in entorhinal cortex. **Nature**, 446, 190-194.

Leutgeb, J.K., Leutgeb, S., Moser, M.-B., and Moser, E.I. (2007). Pattern separation in dentate gyrus and CA3 of the hippocampus. **Science**, 315, 961-966.

Tse D, Langston RF, Kakeyama M, Bethus I, Spooner PA, Wood ER, Witter MP, Morris RGM (2007). Schemas and memory consolidation. **Science**, 316:76-82.

Moser, E.I. (2007). Atlas on our shoulders. **Nature**, 409, 406.

Leutgeb, J.K. and Moser, E.I. (2007). Enigmas of the dentate gyrus. **Neuron**, 55, 176-178.

Dickson B & Moser EI (2007). Editorial overview: Neurobiology of Behaviour. **Current Opinion in Neurobiology** 17, 672-674.

Moser, E.I. and Moser, M.-B (2007). Grid cells. **Scholarpedia**, 2:3394.

Moser, E.I. (2007). Plasticity: More than Memory. In Tulving E., Dudai Y., Roediger, H.L. and Fitzpatrick, S.: Science of Memory: Concepts.

Sargolini, F. & Moser, E.I. (2007). Entorhinal grid cells and the representation of space. In Bontempi, B., Silva, A.J. & Christen, Y.: Memories: Molecules and Circuits. Springer-Verlag Berlin, Heidelberg, Germany.

Leutgeb, S. and Leutgeb J.K. (2007). Pattern separation, pattern completion, and new neuronal codes within a continuous CA3 map. **Learn. Mem.**, 14: 745 - 757.

Witter MP (2007). Intrinsic and extrinsic wiring of CA3; Indications for connectional heterogeneity. **Learn. Mem.** 14:705-713.

Papp G, Witter MP, Treves A (2007). The CA3 network as a memory store for spatial representations. **Learn. Mem.** 14:732-744.

Wouterlood FG, Canto CB, Aliane V, Boekel AJ, Grosche J, Hartig W, Belien JAM, Witter MP (2007). Coexpression of vesicular glutamate transporters 1 and 2, glutamic acid decarboxylase and calretinin in rat entorhinal cortex. **Brain Struct Funct.** 212: 309-319.

Jones BF, Witter MP (2007). Cingulate cortex projections to the (para)hippocampal region in the rat. **Hippocampus** 17: 957-976.

Cappaert NLM, Wadman, WJ, Witter MP (2007). Spatiotemporal analyses of interactions between entorhinal and CA1 projections to the subiculum in rat brain slices. **Hippocampus** 17: 909-921.

Witter MP (2007) The Perforant path. Projections from the entorhinal cortex to the dentate gyrus. In: The Dentate Gyrus: A Comprehensive Guide to Structure, Function and Clinical Implications H. Scharfman (Ed). Progr. Br. Res, 163: 43-61, Elsevier Ltd Oxford.

**2008**

- Hafting, T., Fyhn, M., Bonnevie, T., Moser, M.-B. and Moser, E.I. (2008). Hippocampus-independent phase precession in entorhinal grid cells. **Nature** 453, 1248-1252.
- Kjelstrup, K.B., Solstad, T., Brun, V.H., Hafting, T., Leutgeb, S., Witter, M.P., Moser, E.I. and Moser, M.-B. (2008). Finite scales of spatial representation in the hippocampus. **Science** 321, 140-143.
- 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.
- Leutgeb S (2008). Detailed differences. **Science**, 319, 1623-1624.
- Moser, E.I., Kropff, E. and Moser, M.-B. (2008). Place cells, grid cells and the brain's spatial representation system. **Annual Reviews of Neuroscience**, 31, 69-89.
- Whitlock, J.R., Sutherland, R.J., Witter, M.P., Moser, M.-B. and Moser, E.I. (2008). Navigating from hippocampus to parietal cortex. **Proceedings of the National Academy of the Sciences USA**, 105, 14755-14762.
- Brun, V.H., Leutgeb, S., Wu, H.-Q., Schwarcz, R., Witter, M.P., Moser, E.I. and Moser, M.-B. (2008). Impaired spatial representation in CA1 after lesion of direct input from entorhinal cortex. **Neuron** 57, 290-302.
- Brun, V.H., Solstad, T., Kjelstrup, K.B., Fyhn, M., Witter, M.P., Moser, E.I. and Moser, M.-B. Progressive increase in grid scale from dorsal to ventral medial entorhinal cortex. **Hippocampus**, 18, 1200-1212.
- Fyhn M, Hafting T, Witter MP, Moser EI, Moser MB (2008). Grid cells in mice. **Hippocampus** 18:1230-1238.
- Treves A, Tashiro A, Witter MP, Moser EI (2008). What is the mammalian dentate gyrus good for? **Neuroscience** 154:1155-1172.
- Colgin, L.L., Moser, E.I. and Moser, M.-B. (2008). Understanding memory through hippocampal remapping. **Trends in Neurosciences**, 31, 469-477.
- Hasselmo, M.E., Moser, E.I. and Moser M.-B. (2008). Foreword: Special Issue on Grid Cells. **Hippocampus**, 18, 1141.
- Moser, E.I. and Moser, M.-B. (2008). A metric for space. **Hippocampus**, 18, 1142-1156. (lead article for special issue on grid cells).
- Wouterlood FG, Aliane V, Boekel AJ, Hur E, Zaborsky L, Barroso-Chinae P, Hartig W, Lanciego JL, Witter MP (2008) Origin of calretinin containing, vesicular glutamate transporter 2 co-expressing fiber terminals in the entorhinal cortex of the rat. **J Comp Neurol**. 506: 359-370.
- Kajiwara R, Wouterlood FG, Sah A, Boekel AJ, Baks-te Bulte LTG, Witter MP (2008). Convergence of entorhinal and CA3 inputs onto pyramidal neurons and interneurons in hippocampal area CA1. An anatomical study in the rat. **Hippocampus** 18: 266-280.
- Tse D, Langston RF, Bethus I, Wood ER, Witter MP, Morris RG (2008). Does assimilation into schemas involve systems or cellular consolidation? It's not just time. **Neurobiol Learn Mem** 89: 361-365.
- Canto CB, Wouterlood FG, Witter MP. (2008) What does the anatomical organization of the entorhinal cortex tell us? **Neural Plast**.2008:381243.

Kokanezawa N, Taguchi A, Tominaga T, Ohara S, Tsustui K-I, Witter MP, Iijima T (2008) Significance of the deep layers of the entorhinal cortex for transfer of both perirhinal and amygdale inputs to the hippocampus. **J Neurosci Res.** 61: 172-181.

Van Strien N, Scholte S, Witter MP (2008). Activation of the human medial temporal lobes by stereoscopic depth cues. **Neuroimage** 40:1815-1823.

Wouterlood FG, Boekel AJ, Aliane V, Beliën JA, Uylings HB, Witter MP. (2008). Contacts between medial and lateral perforant pathway fibers and parvalbumin expressing neurons in the subiculum of the rat. **Neuroscience.** 156: 653-661.

Tashiro A., Yuste R. (2008) Role of GTPases in morphogenesis and motility of dendritic spines. **Methods Enzymol.** 439:285-302.

## 2009

Colgin LL, Denninger T, Fyhn M, Hafting T, Bonnevie T, Jensen O, Moser M-B and Moser, EI (2009). Frequency of gamma oscillations routes flow of information in the hippocampus. **Nature**, 462, 353-357.

Colgin LL, Moser EI (2009). Hippocampal theta rhythms follow the beat of their own drum. **Nature Neurosci.**, 12, 1483-1484.

Derdikman D, Whitlock JR, Tsao A, Fyhn M, Hafting T, Moser M-B and Moser EI (2009). Fragmentation of grid cell maps in a multicompartiment environment. **Nature Neurosci**, 12, 1325-1332.

Marumoto T, Tashiro A, Friedmann-Morvinski D, Scadeng M, Soda Y, Gage FH, Verma IM. (2009). Development of a novel mouse glioma model using lentiviral vectors. **Nature Medicine** 15:110-6.

Van Strien NM, Cappeart N, Witter MP (2009) The anatomy of memory: An interactive overview of the parahippocampal/hippocampal network. **Nature Rev Neurosci** 10:272-282.

Lehn H, Steffenach H-A, Van Strien NM, Veltman D, Witter MP, Håberg A (2009). A specific role of the human hippocampus in recall of temporal sequences. **J. Neurosci.** 29:3475-3484.

Bast T, Wilson IA, Witter MP, Morris RGM (2009) From rapid place learning to behavioral performance: a key role for the intermediate hippocampus. **PLoS Biol.** 7: 0730: 0746; e1000089.

Dolleman-van der Weel MJ, Morris RG, Witter MP. (2009) Neurotoxic lesions of the thalamic reuniens or mediodorsal nucleus in rats affect non-mnemonic aspects of watermaze learning. **Brain Struct Funct.** 213:329-342.

Nielen MMA, Heslenfeld DJ, Heinen K, Van Strien JW, Witter MP, Jonker C, Veltman DJ (2009) Distinct brain systems underlie the processing of valence and arousal of affective pictures. **Brain Cogn.** 71:387-396.

Ohara S, Inoue K, Yamada M, Yamawaki T, Koganezawa N, Tsutsui K, Witter MP, Iijima T. (2009) Dual transneuronal tracing in the rat entorhinal-hippocampal circuit by intracerebral injection of recombinant rabies virus vectors. **Front Neuroanat.** 2009;3:1.

Moser, E.I. & Moser, M.-B. (2009). Hippocampus and Neural Representations. Encyclopedia of Neuroscience (L.R. Squire, Editor), Vol. 4, pp. 1129-1136. Oxford: Academic Press.

**2010 (before 30<sup>th</sup> of June)**

Langston RF, Ainge J, Cowey JJ, Canto CB, Bjerknes TL, Witter MP, Moser EI, Moser M-B (2010). Development of the spatial representation system in the rat. **Science**, 328, 1576-1580.

Derdikman D. and Moser M.-B. (2010). A dual role for hippocampal replay. **Neuron** 65, 582-584.

Colgin LL, Leutgeb S, Jezek K, Leutgeb JK, Moser EI, McNaughton BL and Moser M-B (2010). Attractor-map versus autoassociation based attractor dynamics in the hippocampal network. **J. Neurophysiol.**, 104, 35-50. Epub 2010 May 5.

Alme CB, Buzzetti RA, Marrone DF, Leutgeb JK, Chawla MK, Schaner MJ, Bohanick JD, Khoboko T, Leutgeb S, Moser EI, Moser M-B, McNaughton BL and Barnes CA (2010). Hippocampal granule cells opt for early retirement. **Hippocampus**, 20, 1109-1123. Epub 2010 June 28.

Witter MP (2010). Connectivity of the Hippocampus. In: Hippocampal microcircuits, (V.Cutsuridis et al eds), Springer series in Computational Neuroscience 5. Springer pp. 5-26.

Moser EI, Corbetta M, Desimone R, Frégnac Y, Fries P, Graybiel A, Haynes JD, Itti L, von der Malsburg C, Melloni L, Monyer H, Singer W, Wilson M (2010). Coordination in Brain Systems. In von der Malsburg, C, Phillips WA, and Singer W, eds.: Dynamic Coordination in the Brain: From Neurons to Mind. Strüngmann Forum Report, vol. 5. Cambridge, MA: MIT Press.

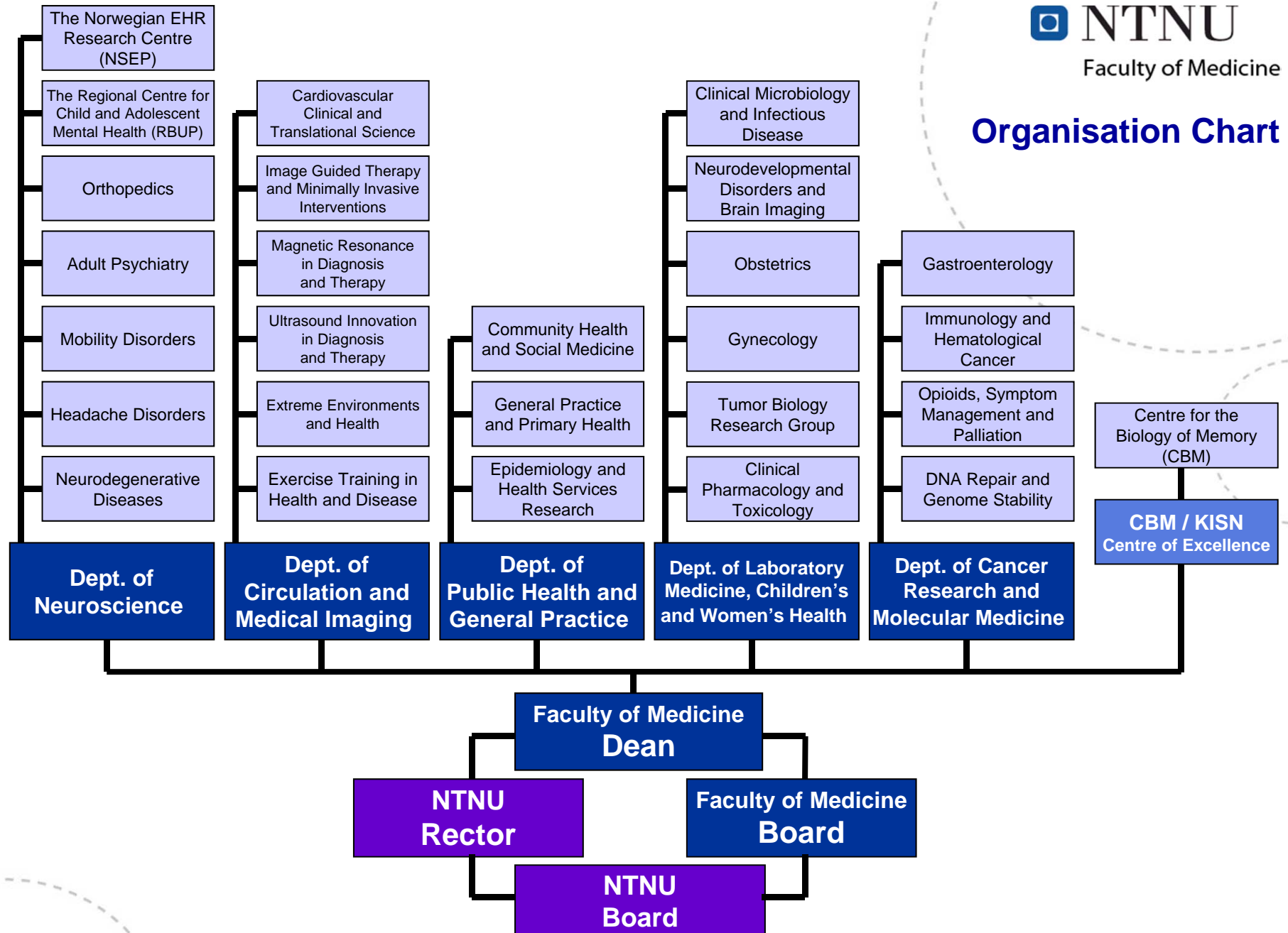
## Organisation Chart

Evaluation Units

Departments

Faculty

University



# FACT SHEET

**Name of institution: CBM**

**Organisation Chart (to be attached)**

**Table 1. R&D expenditures and sources of funding (1000 NOK)**

<i>Type of expenditures</i>	<i>2007</i>	<i>2008</i>	<i>2009</i>
Institution/university funding, salaries	3945	6771	10586
Institution/university funding, other current costs	3681	998	5163
Institution/university funding, instruments and equipment	113	457	4082
<b>Institution/university funding, total</b>	<b>7739</b>	<b>8226</b>	<b>19831</b>
Grants from The Research Council of Norway	16448	12186	24592
Other national funding/grants (public or private)		38	216
EU grants		1576	8048
Other international funding/grants	439	1046	1368
<b>Funding/grants, total</b>	<b>16887</b>	<b>14846</b>	<b>34224</b>
<b>Total expenditures (institution/university + support/grants)</b>	<b>24626</b>	<b>23072</b>	<b>54055</b>
Grants as % of total expenditures	69%	64%	63%

**Table 2. Number of graduates**

<i>PhD graduated</i>	<i>2007</i>	<i>2008</i>	<i>2009</i>
PhD/Dr.scient			1
PhD/Dr.med			1
PhD/Dr.odont			
PhD/Dr.psychol			
PhD/Dr.polit			
PhD/Dr.agric			
Dr.philos			
Others, specify			
<b>Total</b>			
<i>Master students graduated</i>	1	2	3

**Table 3. Number of personnel by December 31. 2009, by source of funding**

<i>Positions</i>	<i>Institution</i>		
	<i>Institution/University</i>	<i>External</i>	<i>Hospital</i>
Professor I	3		
Associate professor I			
Professor II	7		
Postdoctoral fellow	18		
PhD-student	14		
Senior Research Scientist*	2		
Researcher with doctoral degree**	5		
Clinician with PhD performing R&D and presently supervising PhD students			
Technical/administrative personell	18		
Others, <i>Project students</i>	4		

<b>Total</b>	71		
--------------	----	--	--

\* Senior research scientist equals researchers formally qualified for employment as professor

\*\* Encompasses several positions such as research scientist, chief scientist, principal scientist, researcher, senior researcher, researcher I, researcher II, researcher formally qualified for employment at associate professor level (see guidelines 2.3.5).

Table 4: Researchers submitting CV's (see guidelines 2.3.6)

Professor I, associate professor I, postdoctoral fellow, senior research scientist, researcher with PhD-degree and clinician with PhD performing R&D and presently supervising PhD students.

<i>Name</i>	<i>Position</i>	<i>Sex F/M</i>	<i>Year of birth</i>	<i>Research unit for evaluation</i>
Carol Barnes	Professor II	F	1949	
Laura Colgin *	Researcher	F	1972	
Jonathan Jay Couey	Post doctor	M	1972	
Rafal Czajkowski	Post doctor	M	1976	
Dori Derdikman *	Post doctor	M	1969	
Marianne Fyhn *	Researcher	F	1973	
Lisa Marie Giocomo	Post doctor	F	1981	
Torkel Hafting *	Researcher	M	1972	
Kei Igarashi	Post doctor	M	1978	
Hiroshi Ito	Post doctor	M	1977	
Karel Jezek *	Researcher	M	1973	
Takuma Kitanishi	Post doctor	M	1981	
Noriko Koganezawa	Post doctor	F	1978	
Hideki Kondo	Post doktor	M	1967	
Emilio Kropff	Post doctor	M	1977	
Rosamund Langston *	Post doctor	F	1980	
Bruce McNaughton	Professor II	M	1948	
Mayank Mehta	Professor II	M	1958	
Randolf Menzel	Professor II	M	1940	
Richard G. M. Morris	Professor II	M	1948	
Edvard Moser	Professor	M	1962	
May-Britt Moser	Professor	F	1963	
Rajeevkumar Raveendran Nair **	Post doctor	M	1974	
Kally O'Reilly	Post doctor	F	1977	
Ole Paulsen	Professor II	M	1961	
Yasser Roudi	Researcher	M	1981	
Trygve Solstad *	Post doctor	M	1979	
Ayumu Tashiro	Researcher	M	1977	
Alessandro Treves	Professor II	M	1960	
Masato Uemura	Post doctor	M	1977	
Tiffany Van Cauter	Post doctor	F	1981	
Jonathan Whitlock	Researcher	M	1977	
Aree Witoelar **	Post doctor	M	1978	
Menno Witter	Professor	M	1953	
Jing Ye	Post doctor	F	1979	
Calvin Young **	Post doctor	M	1980	
Sheng-Jia Zhang	Post doctor	M	1965	

\* Not employed at CBM any more

\*\* Employment started after 1. January 2010

**Date**

25.11.2010

**Signatures**

Neres Linda

Administrative responsible

Eduardo

Head of the institution