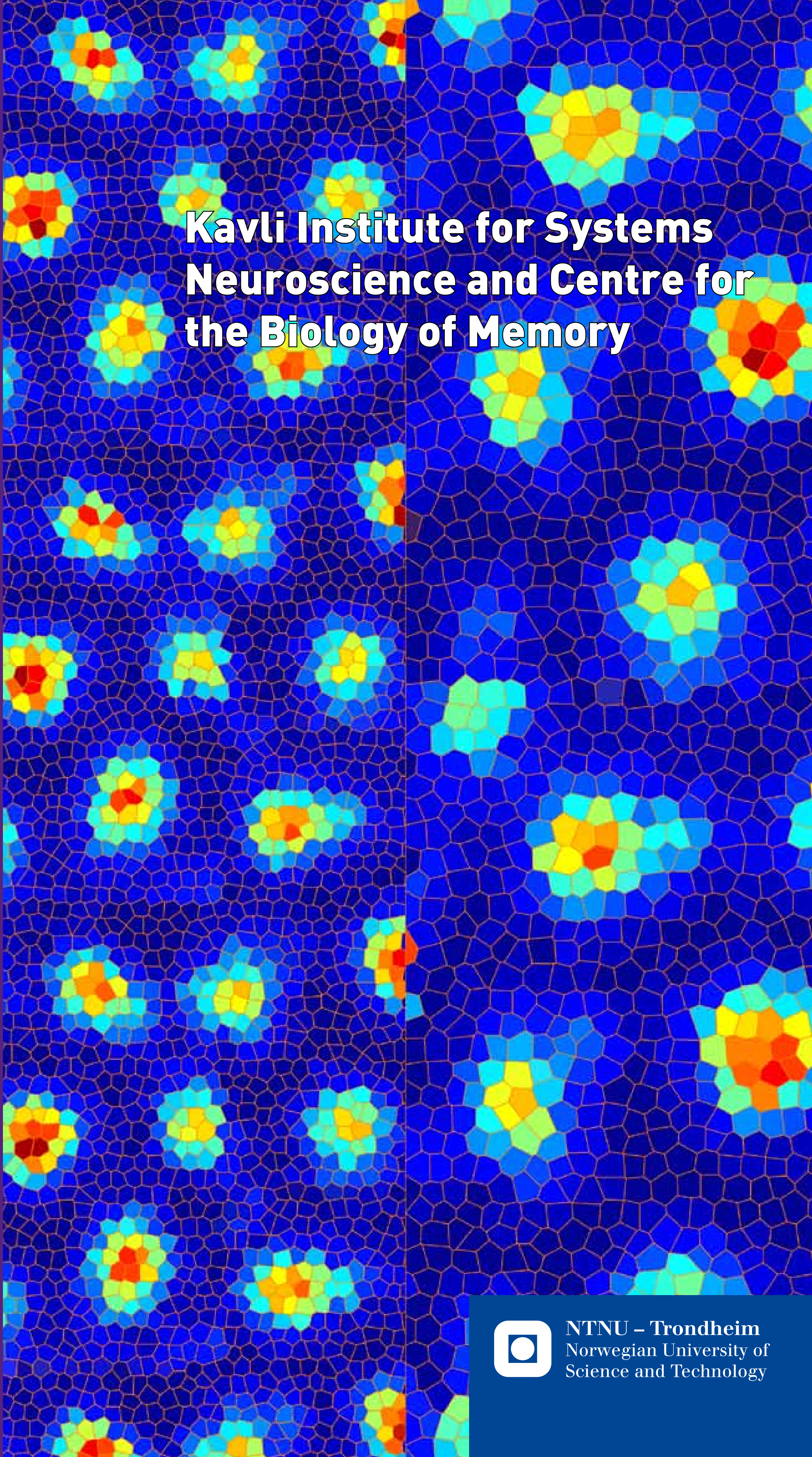
Annual report 2011

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



NTNU – Trondheim
Norwegian University of
Science and Technology

The KI/CBM staff, March 2012. *(Photo: Matias Okawa)*

Front page: The cover image shows the firing rate plot of a single entorhinal grid cell, with blue indicating a low firing rate and red indicating a high firing rate. The different spatial scales of grid cells along the dorsal-ventral axis of the medial entorhinal cortex suggest the presence of multiple spatial maps, as represented by the mosaic appearance of the grid cell. Illustration: Lisa Giocomo

NTNU
Kavli Institute for Systems Neuroscience and Centre for the Biology of Memory

Norwegian Centre of Excellence

Centre of Excellence
Medical-Technical Research Centre
NO-7489 Trondheim, Norway

Telephone: + 47 73 59 82 42
Telefax: + 47 73 59 82 94
E-mail: contact@cbm.ntnu.no
Internet: ntnu.no/cbm

Annual Report published by the Kavli Institute for Systems Neuroscience and Centre for the Biology of Memory.

Editor:
Director Edvard Moser

Text:
Bjarne Røsjø, BR Media
Hege Tunstad, KI/CBM

Translation:
Nancy Bazilchuk, Bazilchuk Ink

Layout & print:
Fagtrykk, NO-7005 Trondheim

Number printed:
400

Download:
ntnu.no/cbm/publications

CONTENTS

KI/CBM – a brief history

The Centre for the Biology of Memory (CBM) was established at the Norwegian University of Science and Technology (NTNU) in 2002 as a Centre of Excellence (CoE) with funding for ten years from the Research Council of Norway.

In 2007, the Norwegian-American physicist, businessman, billionaire and philanthropist Fred Kavli selected CBM as one of 15 prestigious Kavli Institutes. The CBM is the only Norwegian institute to be thus honoured to date. The appointment means the department gets about NOK 7 million in annual support from the Kavli Foundation for the foreseeable future, in addition to tremendous international recognition.

As a result of its history, the centre now has two names: the Kavli Institute for Systems Neuroscience and the Centre for the Biology of Memory (KI / CBM). After 2012, when the CoE period expires, the centre will "only" be the Kavli Institute for Systems Neuroscience. The Norwegian Ministry of Education and Research has indicated a willingness to continue with funding after the CoE period ends.

The protein that controls the brain's "zoom function"

The brains of rats and mice make mental maps of their surroundings at multiple levels, from coarse overviews to fine-grained, detailed maps. Researchers at the KI/CBM have shown that a specific protein controls the brain's "zoom function": If the protein does not work, the brain loses its ability to create detailed maps.

Lisa Giocomo came to the KI/CBM in Trondheim as a postdoctoral fellow in 2008 and now leads a research group at the Institute. (Photo: Lisa Giocomo)

In 2005, KI/CBM researchers discovered that the brains of rats contain grid cells, which are specialized neurons that work together to create a grid for the mental map that a rat makes of its surroundings. The grid in the rat brain bears an amazing resemblance to the coordinate lines on a normal map, except that the grids in a rat's map are triangular instead of square. Grid cells are found in the part of the brain called the entorhinal cortex.

Four years after this finding, KI/CBM researchers discovered that the grid cells in the rat brain create a number of different maps of varying resolution, from coarse overview maps that cover larger areas, to maps where the grid's "mesh" is much finer and contains many details. It was later shown that grid cells are also found in mice and bats, and there are indications that they are found in most species of mammals.

Detailed maps disappear

All cells – including grid cells – are surrounded by a biological membrane that separates the cell's interior from its external environment. Among other things, the cell membrane includes a number of channels or pores that regulate the transport of ions (electrically charged atoms or molecules) in and out of the cell. These ion channels often consist of a single protein, and researchers at KI /CBM are now studying which functions can be controlled by the channels.

Everybody knows how to zoom in and out on an online map to get the level of resolution you need to get you where you want to go. In the 16 November 2011 edition of the scientific journal *Cell*, researcher Lisa Giocomo and colleagues at the KI/CBM described how they knocked out a specific kind of ion channel in the grid cells in the brains of mice. When the HCN1 channels were disabled, the resolution of the maps created by the brain became coarser. "This is comparable to losing every other longitude and latitude line on a regular map, which would mean you wouldn't get a good representation of the environment at a detailed level," Giocomo explains.

The neuron's power supply

The ion channels in cell membranes can be described as the neuron's power supply. "If the cell is compared to a light bulb, then turning on an ion channel can be thought of as supplying a little bit more electricity to the light bulb. And if enough ion channels are active, or the right combination is active, you 'll get enough electricity to turn on the light bulb. But a neuron is much more complicated than a light bulb, of course," Giocomo adds.

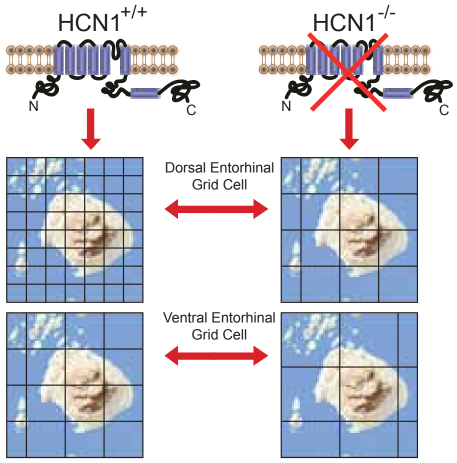
A grid cell or any other type of neuron that is "turned on" by the electrical currents through ion channels is then in a position to react by firing an electrical signal – an action potential - to another neuron. Action potentials are the technique that cells use to communicate with each other.

There are thousands of individual ion channels in a single neuron. No one knows for certain how many of them are HCN1 ion channels, but there might be several hundred to as many as a few thousand in a grid cell. Entorhinal grid cells have a much higher proportion of HCN channels compared to many (but not all) other types of neurons in the brain.

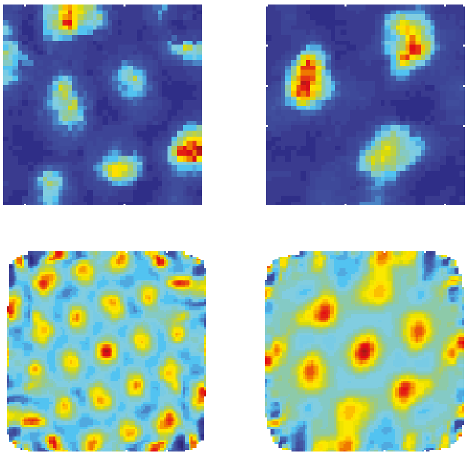
Researchers at the KI/CBM have thus found that a small part of the grid cells' power supply, specifically the ion channels known as HCN1, regulates the neuron's ability to create detailed maps of the animal's surroundings. But what do all of the other ion channels do? Giocomo doesn't know the answer yet, but she would like to find out more. "There are a lot of obvious follow-up questions to this research. Maybe there are other types of ion channels that are contributing to the larger scale maps in the brain, or maybe there are entirely other types of mechanisms that are generating the larger scale representations of the environment," she suggests.

Head of a new Kavli group

Lisa Giocomo completed her PhD at Boston University in 2008 with a project that focused on examining how the grid



Entorhinal grid cells are reminiscent of a longitude and latitude coordinate system. The scale of the brain's grid map is set by HCN1 channels, so when HCN1 is lost, the resolution of the grid map is decreased. (Photo: Lisa Giocomo)



Grid cells are found in the entorhinal cortex, which is found in close proximity to the hippocampus in the brain of rats, mice and other mammals. (Illustration: Lisa Giocomo)

cells in the entorhinal cortex communicate. It was during this work that she began to suspect that the HCN1 channels play an important role in the formation of grid cells. Later in 2008, she came to the KI/CBM as a postdoctoral research fellow with Edvard and May-Britt Moser to pursue the question further. When Giocomo's postdoc was completed, she became the head of her own research group, which in the future will continue to focus on the cellular mechanisms underlying spatial memory.

Lisa Giocomo's findings could prove useful for future research on Alzheimer's and related diseases, particularly because the area that is damaged in Alzheimer's is the same area that she is investigating. "One of the first things to go wrong with Alzheimer's is that you suddenly start to lose your sense of direction. We do not know yet if there is any connection between Alzheimer's and the mechanisms we are studying, but it might be worth looking into," she says.

Two cooperating Kavli Institutes

The article in *Cell* was published simultaneously with a companion article in the scientific journal *Neuron*, authored by researchers at the Kavli Institute for Brain Science at Columbia University in New York. The institute is headed by Professor Eric Kandel, who won the Nobel Prize in Physiology or Medicine in 2000.

The mice without an HCN1 ion channel were developed using genetic engineering by the Kavli Institute in New York, which also investigated the effect of missing ion channels in the place cells in the hippocampus. Place cells are thought to base their spatial response on the calculations of the grid cells. "We believe that this is a great example of collaborative research. We discussed and debated our findings and gave each other lots of feedback and input," says Edvard Moser, director of the KI/CBM at NTNU.

Another aspect of the story is that the same mice that lost the ability to create detailed maps of their surroundings have been shown to perform better at a different kind of task. Researchers at Eric Kandel's laboratory have demonstrated that if the mice are placed in a so-called Morris water maze, which is a water-filled basin with a platform that is hidden under the surface, the mice that lacked the HCN1 channel were actually better at remembering where the platform was located. The recent study by Giocomo and colleagues demonstrated that while their mental maps had become larger, they also became more stable. "We believe this increase in stability helps the mice navigate better in certain types of spatial tasks," says Giocomo.

Facts about the entorhinal cortex

The entorhinal cortex is located in close proximity to the hippocampus, a key centre for episodic memory. hippocampus. At the bottom of the entorhinal cortex, near the bottom of the mouse brain, are the grid cells that mark points that are at a distance from each other. The ever-finer and denser grids are created by the grid cells that are higher up in the entorhinal cortex.

"It is tempting to think that you need the densest networks to operate over short distances with high resolution, and that the largest mesh sizes are necessary for long distances. But I rather think that the different grid mesh sizes have to be combined to enable the animal to navigate well," says Edvard Moser.

Bats have grid cells, too

Menno Witter at the KI/CBM and two Israeli scientists have discovered that the brains of bats have cells that create a grid in the animals' mental maps of their surroundings. The discovery confirms the assumption that grid cells are found in most mammals, and sheds new light on theories of how this cell type is formed.

The Egyptian fruit bat is an impressive animal with a wing span that averages 60 cm. Grid cells in bats fire electrical signals that that combine to create a triangular grid of the animal's environment.
(Photo: Michael Yartsev and Nachum Ulanovsky)

Grid cells have been previously found in the brains of rats and mice, which adds importance to the discovery by the Norwegian-Israeli research group in 2011 that this cell type also is found in Egyptian fruit bats *(Rousettus aegypticus)*. The discovery was published in the scientific journal *Nature* on 3 November 2011, in an article written by Professor Menno Witter at the KI/CBM in colla-oration with Professors Michael M. Yartsev and Nachum Ulanovsky at the Weizmann Institute of Science in Israel.

"Bats are in a mammalian order which, seen from a phylogenetic and evolutionary perspective, is far from rodents. This finding thus confirms the assumption that grid cells are a widespread phenomenon among mammals. The assumption is also confirmed by the fact that the brains of all mammals are built the same way in the areas where we find grid cells," explains Professor Witter.

Two grid cell theories

Grid cells are specialized neurons in the mammalian brain and were discovered by researchers at the KI/CBM in 2005. Grid cells in rats, mice, and now bats have been found in the part of the brain called the entorhinal cortex, and what makes these cells special is that they fire electrical signals when an animal passes by well-defined points in the environment. The combined signals from the grid cells form a triangular and Chinese checkers-like network that is rolled out over the environment when an animal navigates. The signals from grid cells are sent to the hippocampus and the so-called place cells, which fire electrical signals each time the animal is in a specific area of the environment. In other words, grid cells draw a kind of coordinate system, while the place cells are specific to a particular environment and mark where the animal is at any time in relation to the coordinates.

It has hitherto been a mystery as to how the grid cells are formed, but researchers have launched two major competing theories. One of the theories suggests that the spatial periodicity of grid cells is in some way related to the theta rhythm, which is a prominent hippocampal-entorhinal network oscillation – a brain wave – in the 6–10 Hz frequency range. The studies of the Egyptian fruit bats contradict this theory, because the bats lack the clear theta rhythms seen in rodents.

"The theta frequency oscillations in rodents are almost continuous when the animal is moving around, and they disappear when the animal stops. The bats have only sporadic and intermittent theta frequency oscillations, typically with one-second-long bursts separated by an average interval of 37 seconds. We found that the variation in the theta frequency oscillations in bats did not correspond to any changes in the firing properties of the grid cells. The reasonable conclusion is that the grid cells in bats are not derived from the theta rhythm," explains Witter.

Will test flying bats

The Egyptian fruit bat is found in the Middle East and Africa outside of the Sahara, and is often considered a pest because a flock can strip a fruit tree bare in just minutes. These fascinating animals are equipped with a sonar system similar to the one used by insect-eating bats to locate bugs, but the fruit bats use sonar to determine whether a fruit is ripe.

The experiments with fruit bats were

conducted in Nachum Ulanovsky's laboratory in Rehovot outside Tel Aviv, on animals that were crawling around looking for food. Proponents of the theta frequency oscillation theory have argued that the animals were not moving at the right speed for the theta frequency oscillations to start, and that the frequency with which the cells fire would essentially mask the theta rhythm. Professor Witter disagrees.

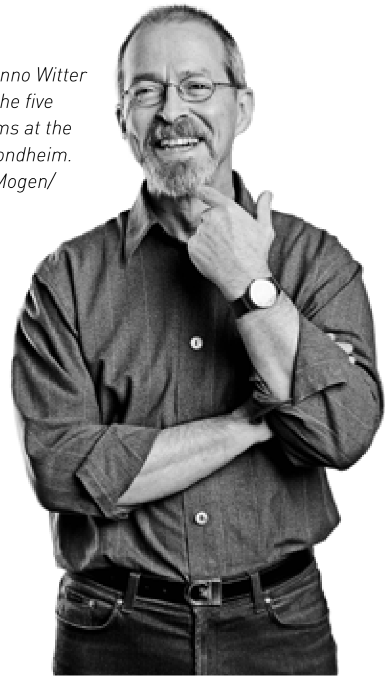
"We essentially did two things sequentially. We started by analysing the activity in the grid cells during the period when we did see theta oscillations, and compared this information to activity in the grid cells during the period with no such oscillations. There was no obvious difference in the results from both samples. Secondly, we did a statistical analysis of grid cell data in the rat, in which we resampled data such that the neurons would show a firing frequency in rats similar to what we observed in the bat. The result was that even in the case of such low firing frequencies, the neurons would still show the properties of grid cells. Therefore, we feel that the data observed in Israel are a really strong argument against the oscillatory model," explains Witter.

The KI/CBM's Lisa Giocomo and Edvard Moser wrote a commentary and expressed strong support for Witter's point of view. "The demonstration of grid cells in the absence of detectable theta oscillations in Egyptian fruit bats is a fresh input which undoubtedly will guide theoretical and experimental studies in the coming years. It would be extremely surprising if a dual set of mechanisms resulted in grid cells with exactly the same properties and an identical functional organization," the two believe.

What is the mechanism?

The theory about theta waves as a driving force behind grid cells is thus weakened. But what then is the mechanism? "We feel that the so-called attractor network theory has become a more plausible candidate. The theory states that the grid patterns are generated from local network activity, but we can't be sure about this before we have conducted more experiments," Witter says.

Nachum Ulanovsky and Michael M. Yartsev are now at work on a new approach in which they will investigate the activity of grid cells in bats as they fly. This research presents major technical challenges, because it will not be possible to connect a cable from the animal's head to a computer. Researchers must instead use a small wireless transmitter on the fruit bat's head.



Professor Menno Witter leads one of the five research teams at the KI/CBM in Trondheim. (Photo: Geir Mogen/ NTNU)

"Previously, we investigated how rats, mice and crawling bats navigate, but in that case what we are talking about in principle is navigation in two dimensions on a surface. The experiments with bats can provide answers as to whether grid cells also create a grid in three dimensions. We will also get an answer as to whether theta waves occur in bats when they fly instead of crawl," explains Witter.

People also navigate

Several international research groups are currently investigating whether there are grid cells in other animal species, and there have been published studies that suggest that they exist in both humans and primates in general. But the verdict is not in yet on this research.

"There is certainly no doubt that we humans have a navigation system, and it is reasonable to assume that the system is linked to the hippocampus and entorhinal cortex too. Research on rodents and bats can therefore contribute to increased knowledge about how the human brain works," concludes Witter.

Hippocampus

The hippocampus is a small structure at the bottom of the mammalian brain, closely connected to the entorhinal cortex. The hippocampus plays a very important role in the brain and is also essential for the sense of place and memory. Researchers at the KI/CBM hope that studies of the hippocampus and the sense of place can also lead to a deeper understanding of memory – which can create a better understanding of the brain's functioning.

Brain Waves

Brain waves occur when the billions of neurons in the brain communicate with each other using small electrical impulses (action potentials) that fluctuate in time. Hippocampal theta waves in rats have a frequency range of 6-10 Hz and appear mainly when the animal is engaged in active motor behaviour such as walking or exploratory sniffing.

Two neurons in the same pub are not necessarily friends

It's no easy task recording the electrical signals from multiple firing neurons in the brains of rats and mice, but figuring out the configuration of the underlying neuronal networks is even more of a challenge. "The problem can be compared to figuring out who are real friends in a group of people at the pub," explains Yasser Roudi.

The physicist Yasser Roudi came to the KI/CBM in 2010, with the purpose of establishing a new research group dedicated to analysing and processing massive amounts of incoming information from an environment chock full of data, like the brain. Roudi's group is studying the issue from a theoretical point of view, using methods from the worlds of mathematics and statistical physics.

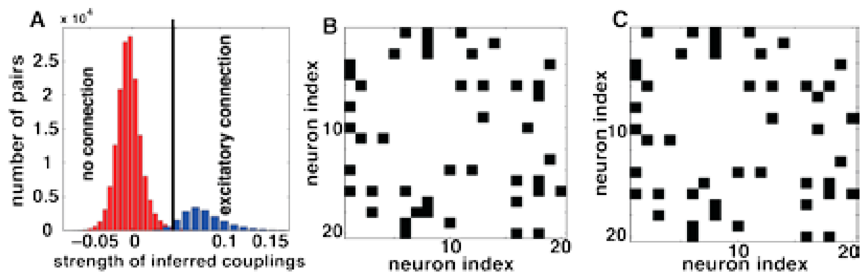
When Edvard and May-Britt Moser established the predecessor of the KI/CBM in Trondheim in 1996, the focus was to study the biological roots of memory by detecting and analysing electrical signals in the brain. The human brain is an extremely complex structure with approximately 100 billion neurons, each connected to approximately 10 000 other neurons. The neurons use weak electrical signals – action potentials – when they communicate with each other. The researchers at the KI/CBM use the rat brain as a "stand-in" to make scientific models of the human brain.

One important technique used at the KI/CBM is to insert tiny electrodes into the rat brain to record the action potentials from neurons. It is difficult enough to place one electrode with great precision in a brain and listen to the signals from a few cells, but the technique has now been advanced to the point that it is common practice to use multiple electrodes for listening to several hundred or even thousands of networking neurons at the same time.

Correlation is not a proof of connection

One challenge is to figure out which signal comes from which specific neuron in a big group, but that problem has been solved to some degree by other researchers. Yasser Roudi's research group is focused on a much more difficult question: They are using the recorded signals to infer the connections – the networks – between neurons. "Making that inference represents a big leap forward: It allows us to find out how network properties influence the firing of neurons, monitor how these properties are modified through behaviour, and thus eventually, how computation is performed in the nervous system. It is also a difficult question because correlation is not a proof of connection. Simply by finding that two neurons fire together, one cannot infer that they are necessarily connected," Roudi says.

The problem of mapping the connections between neurons in the brain is similar to mapping the relationships among ten people who go to different pubs and bars, adds Roudi. "You might assume that they are all friends, or you might think that one of them is a 'hub' that has invited nine friends who were not previously acquainted with each other. In fact, you can have all sorts of different patterns of friendship among these people. We are trying to establish the connections between individual neurons in a group by looking at their electrical signals, much like you could figure out the friendships between people by looking at their activity in a bar," he explains.



Histograms of couplings inferred by applying a non-equilibrium Ising model to synthetic data from a simulated cortical network (see Roudi & Hertz 11). Only the connections between excitatory neurons are shown. Putting a vertical line between the peaks as a decision boundary, we can reconstruct the network: an inferred coupling that falls on the right (left) of the line would be taken to indicate an excitatory (the absence of a) connection. B shows an example of such reconstruction for a subset of 20 neurons from a network of 1000 neurons. The true connectivity is shown in C. (Il.: Yasser Roudi)

A hot topic

The relationship between activity and connectivity is a hot topic and has implications for the studies of systems biology, genetic networks, protein networks, neuronal networks, social networks, and so on. "Our understanding of biological networks has been very limited because until recently, experimental tools only allowed us to study the properties of one or a few elements at a time. Luckily, technological breakthroughs and advances have changed this situation. Biologists can now use state-of-the-art technology to look at many elements of a biological network at the same time. But there is still a major problem: What do we do with the data that we get using these modern tools? This is where statistical physics becomes important. Statistical physics is the discipline that has been developed over the last century to deal with large systems of interacting elements," Roudi says.

Roudi's basic idea is to start with data from multiple electrode recordings of action potentials in a rat brain, delivered by researchers from Edvard and May-Britt Moser's group. They then try to reverse engineer the network that could have generated the signals.

"We are in fact building digital models of networks of neurons, and then we tweak the models until they send signals that are similar to those that were recorded," he says.

A dynamic approach

Most researchers in Roudi's field have until now mainly been focused on the study of equilibrium systems, but these are very far from biological systems. Yasser Roudi and John Hertz from NORDITA and the Niels Bohr Institute in Denmark introduced a new approach in 2011, with an article in the academic journal *Physical Review Letters*. "What we did was to build a platform that allowed the analytical investigation of simulated cortical networks. We showed that when we look at data generated from simulated cortical networks, the dynamic models work a lot better than equilibrium models," explains Roudi. The research community greeted the article as a breakthrough and its publication has already spurred other groups to take up the approach.

Models of Grid Cells and Path Integration

Yasser Roudi's group is also active in another line of research that aims at building computational models of the entorhinal cortex and the hippocampus, to better understand the generation of grid cell firing and path integration. In this effort, and in collaboration with Edvard and May-Britt Moser and Menno Witter, Roudi uses knowledge about the anatomy of these networks to make realistic models of them and to relate the output of the models to what could be measured in vivo. It is not surprising that this line of research is related to and benefits from efforts to solve the network inference problem.

"Our present knowledge about the way neurons interact with each other, to a large extent, comes from in vitro recordings, where researchers have found connections from studying slices of brain tissue under a microscope," Roudi says. "But connectivity in the living brain is constantly modulated by behaviour and cognitive processes, so in vitro connectivity may be very different from in vivo connectivity. This is a particularly important issue in parts of the brain such as the hippocampus, where memory formation through modification of synaptic connectivity is the main function. Therefore, we are now trying to use the technological breakthroughs in multi-unit spike recordings in a completely new way. To put it simply, we are trying to go from studying in vitro connectivity to studying spike trains recorded in live animals. We will use the recordings to infer functional connectivity, and then we will build computational models based on those connections. The models can then be used for analysis and designing new experiments. We hope that this will give us a better understanding of the general principles of network operation in complex systems, and will also allow us to learn more about the formation and function of grid cells," Roudi adds.

Yasser Roudi received his PhD from the International School for Advanced Studies (SISSA) in Trieste in 2005. He is now a corresponding fellow at the Nordic Institute for Theoretical Physics (NORDITA) in Stockholm and a research group leader at the KI/CBM. (Photo: Yasser Roudi)

The brain as a machine

Yasser Roudi's work is truly interdisciplinary, because he uses statistical and physical methods that could equally be used to study the mixing of gases or chemicals in a solution. "You might say that I am studying the brain as a machine, which is possible because the general laws of physics apply across all of nature. This is also the reason why different sciences can benefit from exchanging tools with each other. My aim as a scientist is to use the laws of physics to further our understanding of information processing and of computations in the brain as far as possible," Roudi says.

Eric Kandel receives honorary doctorate from NTNU

Professor Eric Kandel at Columbia University in New York was awarded an honorary doctorate by the Norwegian University of Science and Technology (NTNU) in 2011. Kandel is a Nobel Prize winner and a close associate of the KI/CBM.

Professor Eric Kandel was named an honorary doctor at NTNU in 2011. (Photo: Thor Nielsen/ NTNU Info)

Eric Kandel is a senior investigator at the Howard Hughes Medical Institute, a professor of neuroscience, biochemistry and biophysics at Columbia University, and a Fred Kavli professor and director of the Kavli Institute for Brain Science at Columbia.

Dr. Kandel collaborates with members of the KI/CBM on cellular mechanisms of spatial map formation in the brain, and has visited the Trondheim research community on several occasions. He has given three public lectures at NTNU. The first lecture – about the cellular mechanisms of memory – caused so much excitement that the regional newspaper announced in a two-page spread that the "rock star of brain science" had visited Trondheim.

Professor Kandel started studying sea slugs in 1962 and was able to show how learning is caused by changes in the synaptic connections between specific neurons, and what cellular mechanisms are responsible for simple forms of short-term and long-term memory formation. His more recent work has shown that these mechanisms are universal across species.

Eric Kandel's work, stretching over a period of more than 50 years, has had an enormous influence on our understanding of how memory is generated in the brain, and our understanding of brain function more generally. He has been recognized with a long list of honorary degrees and awards, including the National Medal of Science in the United States and the Nobel Prize for Physiology or Medicine in 2000.

ERC Grant to May-Britt Moser

Professor May-Britt Moser was awarded an Advanced Investigator Grant from the European Research Council (ERC) in November 2010. The grant goes to the funding of a research programme that started in 2011 and runs to 2015.

The ERC Advanced Grant is considered international recognition at the highest level, and will provide €2.5 million towards May-Britt Moser's research projects over five years. Professor Moser will also receive additional financial support from NTNU, which together will give the KI/CBM NOK 5 million (€0.62M) extra per year until 2015.

The grants will fund a broad research programme, ranging from the basic phenomenology of the transition between hippocampal representations to the role of gamma oscillations, thalamic activity and anatomy and development. The aim is to determine how environments and experiences are represented in a short-term time domain and how groups of cells (ensembles) involved in one representation fade into those associated with another.

The ERC's Advanced Investigator Grant is linked to the EU's 7th Framework Programme for research. Professor Edvard Moser received an ERC Advanced Investigator Grant in 2008.

Professor May-Britt Moser's research at the KI/ CBM is financed by an Advanced Investigator Grant from the European Research Council until 2015. (Photo: Geir Mogen/NTNU)

NORBRAIN receives MNOK 80 grant

The Norwegian Brain Initiative received MNOK 80 in a grant from the Research Council of Norway in October 2011. The contribution will be used to set up state-of-the-art neuroscience equipment to enable a broad spectrum of molecular and systems neuroscience research in Trondheim and Oslo.

Post doctoral researcher Jonathan Couey uses multiple simultaneous patch clamp recording in brain slices to quantify synaptic connectivity in the MEC. Understanding the local microcircuit from which grid patterns emerge will be essential to understanding how this neuronal computation is performed by the brain. (Photo: Geir Mogen/ NTNU)

The idea behind the Norwegian Brain Initiative – NORBRAIN – is that neuroscience is one of the fastest-developing areas of science, on the brink of discovering the mechanisms for complex mental functions. We will soon be able to understand how neurons enable us to think, decide, remember, and feel, and how these processes may fail during disease. For this potential to be realized, however, scientists need to change the way they do their research. It is necessary to establish research platforms for scientists with complementary skills and insights, and it is necessary to combine forces. These scientists must also have access to high-cost state-of-the-art equipment needed to address the most fundamental questions in the field.

A coordinated national initiative

This was the background for the Norwegian University of Science and Technology (NTNU) and the University of Oslo's decision in 2010 to work cooperatively to establish NORBRAIN as a national infrastructure for neuroscience research. Professor Edvard Moser and NTNU coordinated a joint application to the Research Council of Norway, which had announced the availability of NOK 400 million for competitive grants for new large-scale research infrastructure investments. In November 2011, the two universities got the good news that the Research Council had granted NOK 80 million (€10.2 million) to NORBRAIN.

NORBRAIN is an NTNU-coordinated national infrastructure for neuroscience. The project is structured around two Centres of Excellence – the KI/CBM at NTNU and the Centre for Molecular Biology and Neuroscience at the University of Oslo – as well as one Centre for Research-based Innovation – the Medical Imaging Laboratory (MI-Lab) at NTNU.

One of the best infrastructures

The grant provides an unprecedented opportunity for coordinated investment in the kinds of high-cost state-of-the-art equipment needed to sample large amounts of data at high resolution and at a high rate over large numbers of synapses, cells and brain systems. The approach will give researchers the tools and data they need to understand the fundamental mechanisms of brain function and dysfunction.

"The aim is to build one of the best neuroscience infrastructures in the world, with the equipment made available to neuroscientists from the whole of Norway. The project has an international aspect as well, in that it makes it easier for us to welcome guest researchers and researchers in training," Professor Edvard Moser says.

The timing of the RCN grant was very favourable because new space will be available at the beginning of 2012 for NORBRAIN at all three host centres. NTNU has converted its Medical Technology Centre into a Brain Centre, which is home to the expanding KI/CBM as well as the MI Lab and other groups. The University of Oslo is building an annex to Domus Medica, which will house the CMBN and activities developing around the centre.

"Teleportation" shows that memories have a quantal nature

Memories are divided into discrete individual packets, analogous to the way that light is divided into individual bits called quanta. The brain can swap between different memories as often as eight times in one second, and different memories are not mixed.

The brain does not create gradual transitions between similar memories, says Karel Jezek.Photo: Karel Jezek

Researchers at the KI/CBM showed in 2011 that memories are "quantal," meaning that they are organized into small packages, and that memories do not come in a continuous stream. Instead, the brain can switch between different memories in just 125 milliseconds, and two different memories are kept separate, even though they might seem quite similar to each other. The new findings were published in *Nature* in September 2011, in a scientific article with a former postdoc at KI/CBM, Doctor Karel Ježek at the Institute of Physiology of the Academy of Sciences of the Czech Republic, as the first author.

The study of how memories are organized at the millisecond level has received support from the European Research Council Advanced Investigator Grant, which was awarded to Professor May-Britt Moser in 2011. "There are no gradual transitions between memories. The brain will not let itself get confused. It never mixes different places and memories together, even though you might perceive it that way," says Professor Moser.

Memories of past Christmases

The new article in *Nature* built on results from 2004, when researchers in Trondheim explained how the hippocampus and the brain can distinguish between memories that seem similar to each other. "The ability to distinguish memories of one Christmas Eve from another is due to the encoding of the different memories in different networks of neurons in the brain. But the memories of various Christmas evenings also share many similarities and are stored in the same area of the brain, so that you can quickly 'switch' between memories. This is similar to a rat remembering that it has been looking for food in two different rooms," says May-Britt Moser.

But how does the brain call up the correct memory out of the chaos of competing memories? Researchers at the KI /CBM decided to investigate this further and came up with a new and intricate challenge for their research rats in Trondheim. The eager animals first hunted for chocolate bits in a dark box that had a lighted pattern on the floor, and then again in another dark box that had a lighted pattern on one wall. While the rats hunted for treats, the memories of the two places were stored in two different but similar networks of nerve cells in the hippocampus.

"Teleporting" rats

The two spaces were then converted to a single room in which the landmarks and patterns could be controlled by an electric switch. After the rats had learned their way in the two variants of the same space, the researchers could simply "teleport" the rats from one space to another by flipping a switch. This resulted in a conflict where the rat's visual system told it that it was in a new place, but the number of footsteps it had taken, the smell of the box, and other variables said that it was still in the old one.

The researchers measured the electrical activity of as many as 100 neurons in the CA3 section of the hippocampus during and right after the rats were "teleported", and saw that the rat brain first flickered several times between the two different memories. The flickering could last up to several seconds, but eventually the rat brain decided which room it was in, and the flickering stopped. It turned out that the memories were not mixed while the flickering was going on. There was no gradual transition between memories of the two places, which led to the conclusion that memories come in packets or quanta.

Researchers at the KI/CBM tricked rats into believing that they had been teleported, and discovered that memories have a quantal nature. (Credit: Håkon Fyhn / Kavli Institute for Systems Neuroscience / NTNU)

It turned out that the packets lasted for 125 milliseconds. This corresponds to a time interval known as the theta cycle, which was discovered approximately 50 years ago. Theta cycles are formed when many cells in the hippocampus send electrical signals (action potentials) at the same time, and then are silent at the same time. This coordinated activity gives rise to measurable brain waves. However, it has not previously been shown that the brain is able to call up an entire memory in as short a period as the duration of a theta wave.

Stepping out onto the wrong floor

The teleportation effect in rats is similar to the momentary disorientation you would feel when the elevator doors open and you step out onto the wrong floor. The disorientation occurs because the place you expect to see and the place you actually do see are mutually exclusive.

Normally, the brain orients itself gradually as you move around. The hippocampus contains place cells, which record both your environment and your movement within it, in order to form memories that ensure you always know where you are. To update the brain on your position, place cells fire in a rhythm called a theta oscillation or cycle, which repeats every 125 milliseconds and is especially prominent when you're moving.

May-Britt Moser does not exclude the possibility that there may be more gradual transitions between memories within each theta cycle. The research published in 2011 showed that memories could mix to a certain degree during the first part of the cycle, but in the second part of the cycle, the hippocampus was completely engaged with one or the other memory.

A clock frequency in the hippocampus

Edvard and May-Britt Moser now suggest that the theta wave acts as a kind of clock that coordinates memories in the hippocampus. Neurons in the hippocampus are not very receptive to signals from other cells when they are in their quiet phase. "Without this kind of clock, everything would soon be chaotic, with cells that could not talk to each other because they were out of step," Professor Edvard Moser said in an article on the Norwegian research website Forskning.no.

The Trondheim scientists suggest that this system of theta waves and flickering between different memories is specific to the memory and the hippocampus, and it is unlikely that similar systems will be found in many other places in the brain. In the hippocampus, for example, the brain can take the time it needs to find the right memory, because it is to the animal's benefit. However, reaction time in the visual cortex can be critical to survival, particularly if the animal is unable to identify a danger in an unambiguous way in just a few milliseconds.

The researchers hope to look at other brain oscillation patterns in the future, such as the gamma wave, which repeats itself several times faster than the theta wave.

Norway has a new brain centre

"Here in Trondheim you have created a research environment that excels internationally," said Minister of Research and Higher Education Tora Aasland, as she laid the cornerstone for the Norwegian Brain Centre in Trondheim on 10 January 2011.

When it was first founded, the KI/CBM was located in NTNU's Medical Technical Research Centre. With the migration of a number of other research groups to the new University Hospital of Trondheim in 2010, NTNU was able to invest NOK 42 million to establish the Norwegian Brain Centre (NorBC), which will encompass the KI/CBM. The goal of the new centre is to become the world's largest laboratory for the measurement of electrical activity in neural networks. The investment represents a continuation of NTNU's long-term commitment to brain research, with the KI/CBM at the forefront.

The cornerstone laid by Tora Aasland is a crystal with a reconstruction of a real brain cell from a rat. "I am proud of what you have achieved and can promise that the government will also support this effort in the future. I hope the new centre will continue to evolve and find new answers that can benefit society," Minister Aasland said.

More space, upgraded standards

The expansion plans call for NorBC's area to expand by nearly tenfold to well over four thousand square meters, while at the same time the overall standard for the labs will be upgraded. The centre will explore a wide range of methodological approaches to understanding how the brain's networks function. The researchers started moving into the new facilities in January 2012. In addition to NTNU's contribution, the research activities at NorBC will be financed with contributions from the Research Council of Norway, the European Research Council (ERC), the Kavli Foundation and the EU's Framework Programme.

The Prime Minister was impressed

The Norwegian Prime Minister Jens Stoltenberg was very enthusiastic when he inaugurated the new research centre on 28 February 2012. "This has been a fascinating visit, and I shall remember that this is a world leading institution in the field of brain research," Stoltenberg said. Professor May-Britt Moser thanked the Prime Minister and gave him an extra brain cell, or more precisely a model of a brain cell from a rat.

The Norwegian Prime Minister Jens Stoltenberg was very enthusiastic when he opened the new research centre. (Photo: Matias Okawa)

Nordic and European awards go to KI/CBM leaders

Professors May-Britt and Edvard Moser were awarded two prestigious awards in 2011, the Swiss-based Louis-Jeantet Prize for Medicine and the Norwegian-based Anders Jahre's Award for Medical Research. The dual awards rank the researchers among the best in their field in both Scandinavia and Europe.

Edvard and May-Britt Moser were awarded the 2011 Louis-Jeantet Prize for Medicine for their pioneering work related to the discovery of grid cells and the mechanisms underlying the sense of place in the brain. The prize was shared with the German biologist Stefan Jentsch, director of the Max Planck Institute of Biochemistry in Martinsried. The Louis-Jeantet Prize for Medicine is awarded annually to the best European scientists in biology and biomedicine, and provided the researchers in Trondheim with more than NOK 4.2 million (SF 700,000).

Support for more research

The prize is awarded by a foundation that was established in the Swiss city of Geneva in 1982, after the French businessman Louis Jeantet bequeathed his entire fortune to the effort before he died of cancer in 1981. The purpose of the prize is to focus on the basic biological research that may some day be of importance in medicine and medical research.

Edvard and May-Britt Moser say that the prize will be used to continue their search for the sense of place in the brain, with a special emphasis on examining how grid cells work together with other cells in the entorhinal cortex and hippocampus. The two are very grateful for the recognition associated with the award of the Louis-Jeantet Prize.

"There is a large group of researchers who have worked to identify the basis for the sense of place, and all deserve a bit of credit. We are also very pleased by the economic aspect of the prize. It gives us the ability to launch ambitious research for which it can be difficult to find regular funding," the researchers said in an interview with the regional Norwegian newspaper Adresseavisen.

Torbjørn Digernes, rector of the Norwegian University of Science and Technology (NTNU) in Trondheim, congratulated the professors, saying that the prize makes him proud. "May-Britt and Edvard Moser are talented and dedicated scientists who repeatedly put Trondheim and NTNU research on the world map," Digernes said.

A Nordic honour

Edvard and May-Britt Moser were also recognized with the 2011 Anders Jahre's Award for Medical Research, which is valued at NOK 1 million and is awarded to outstanding Nordic researchers in basic and clinical medicine.

"Their findings have received broad international recognition since they provide a new understanding of how the brain works. With support from the Kavli Foundation and the Research Council of Norway (Centre of Excellence) the two scientists have established a very strong research environment in Trondheim and succeeded in attracting many researchers from abroad," the citation for the award said.

The Louis-Jeantet Prize for Medicine was presented to May-Britt and Edvard Moser at a ceremony in Geneva on 14 April 2011. (Photo: FONDATION LOUIS-JEANTET)

University of Oslo Rector Ole Petter Ottersen and University Director Gunn-Elin Aa. Bjørneboe presented the Anders Jahre Senior Medical Award to May-Britt and Edvard Moser on 14 October 2011. (Photo: Francesco Saggio, University of Oslo)

Excellent results give SPACEBRAIN an afterlife

The aim of the EU-funded SPACEBRAIN project was to study how complex mental functions originate from electrical and chemical processes. The project was so successful that the participants decided to continue to work cooperatively even after the end of the funding period.

Members of the EU-funded SPACEBRAIN consortium held their fourth annual meeting in Stechelberg in the Swiss Alps from 15 to 17 June 2011. (Photo: Karel Jezek)

The project Space coding in hippocampo-entorhinal neuronal assemblies (SPACEBRAIN) started in 2008 with funding from the European Union's Seventh Framework Programme (FP7) for research, and formally ended with a fourth annual meeting in the Swiss Alps in June 2011. The group decided to continue with a fifth meeting in 2012, in Heidelberg, despite the fact that the funding period is over.

"Despite impressive advances in almost every field of neuroscience, our understanding of brain function has largely been confined to the brain's building blocks at the microscopic level, and to phenomenological descriptions at the macroscopic level. We know much less about the link between these levels – how complex mental functions originate from electrical and chemical processes," explains Professor Edvard Moser, director of the KI/CBM. He was the project's coordinator from start to finish, and is very happy with the results.

Breaking new ground

The SPACEBRAIN project broke a lot of new ground in the understanding of the link between macroscopic and microscopic levels in the brain. Forty-two months of collaboration have produced significant advances in our understanding of how space is represented in neural networks of the entorhinal cortex and hippocampus, brain regions known to form internal maps of the local environment. Two papers with SPACEBRAIN funding have been published or accepted for publication in *Nature*, three in *Science*, one in *Cell*, and several are appearing in other high-impact journals such as *Nature Neuroscience* and *Nature Methods*. Key scientific advances include, first of all, new insights into the intrinsic wiring of the entorhinal cortex, according to the final report.

A project with unique features

"The success of the project reflects several unique features of SPACEBRAIN. One is the integration of experimental and theoretical work. From the beginning, experimentalists and modellers have been working on complementary subprojects, exchanging information as soon as data or models were available. Another is the explicit attempt to combine methods and concepts from multiple levels of analysis, ranging from mechanisms of synaptic transmission to interactions between large distributed circuits. Finally, the success also reflects the open and positive working atmosphere of the consortium. Trust and an open attitude have formed the basis for constructive discussion and true collaboration from the first day of the project," concludes Edvard Moser.

"Undoubtedly excellent research"

The scientific quality of the research conducted by the KI/CBM is "undoubtedly excellent", according to an international evaluation carried out on behalf the Research Council of Norway.

The Research Council of Norway (RCN) carried out a comprehensive evaluation of Norwegian research in biology, medicine and health in 2010 and 2011. The evaluation panel concluded that the scientific quality at the KI/CBM is "undoubtedly excellent", and that the centre has developed into "one of the world's leading arenas for experimental and theoretical studies of memory in brain networks".

According to the evaluation, the KI/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 evaluation panel was also impressed by the societal impact of the research in Trondheim. In addition to the general importance of truly excellent neuro-science research, the present pro-gramme also addresses particular aspects of importance for understanding and diagnosing Alzheimer's disease, the report says.

The recommendation is that the funding should be continued after the Centre of Excellence award from the RCN expires in 2012. The members of the evaluation panel are confident that the importance of continued funding is understood by the Norwegian University of Science and Technology, the RCN and the Norwegian Government and "will be addressed in good time".

The evaluation was led by Professor Ulf Lerner at Umeå University and the University of Gothenburg, Sweden. The other eight members came from research institutions in Sweden, Denmark, the United Kingdom, Canada, Poland and France.

The KI/CBM has developed into one of the world's leading arenas for experimental and theoretical studies of memory in brain networks, according to an international evaluation in 2011. (Cover page of RCN Report)

The media love brain science

Everyone is interested in the brain, if last year's media attention to research conducted at the KI/CBM is any indication. More than 90 articles were written in the Norwegian media in 2011 about the institute and its research. There were nearly the same number of articles published in the international online media.

The Nordic media monitoring agency Retriever listed a total of 23 articles on the KI / CBM in the print editions of various Norwegian national newspapers over the year. There were also 26 articles in the online editions of different national newspapers, 42 articles in the print editions of Norwegian regional and local newspapers, and approximately 90 articles in the online media in the Nordic region and internationally.

Many of the editors at home and abroad were intrigued by the report that the KI / CBM researcher Lisa Giocomo and colleagues had "found the zoom button in the brain." Professor May-Britt Moser's research attracted attention as far away as India, where the large online newspaper The Hindu wrote that "Memories come in packages - eight times a second." The same news on the Italian La Stampa website was given the title "Il nostro Cervello divide i Ricordi in pacchetti as 125 millisecondi", while the online South Africa Star newspaper asked the timely question, "Did I sleep in my bed this time?"

Prizes and investments

The Norwegian media were also very interested in the establishment of the Norwegian Brain Centre (NorBC) at NTNU, and the awarding of the Swiss-based Louis-Jeantet Prize for Medicine and the Norwegian-based Anders Jahre's Award for Medical Research to Edvard and May-Britt Moser.

The Mosers were also the subject of a great deal of media discussion because they were finalists in the competition for the honour of being named "Trøndelag residents of the year", which is awarded by the regional newspaper Adresseavisen and the Norwegian Broadcasting Corporation's (NRK) regional Trøndelag office.

Norwegian regions and counties have a strong tradition of friendly rivalry, and the regional newspaper Sunnmørs-posten appreciated that the couple were highly valued in the neighbouring county. Edvard and May-Britt Moser are originally from Hareid and Fosnavåg in Sunnmøre County.

Brain science on TV

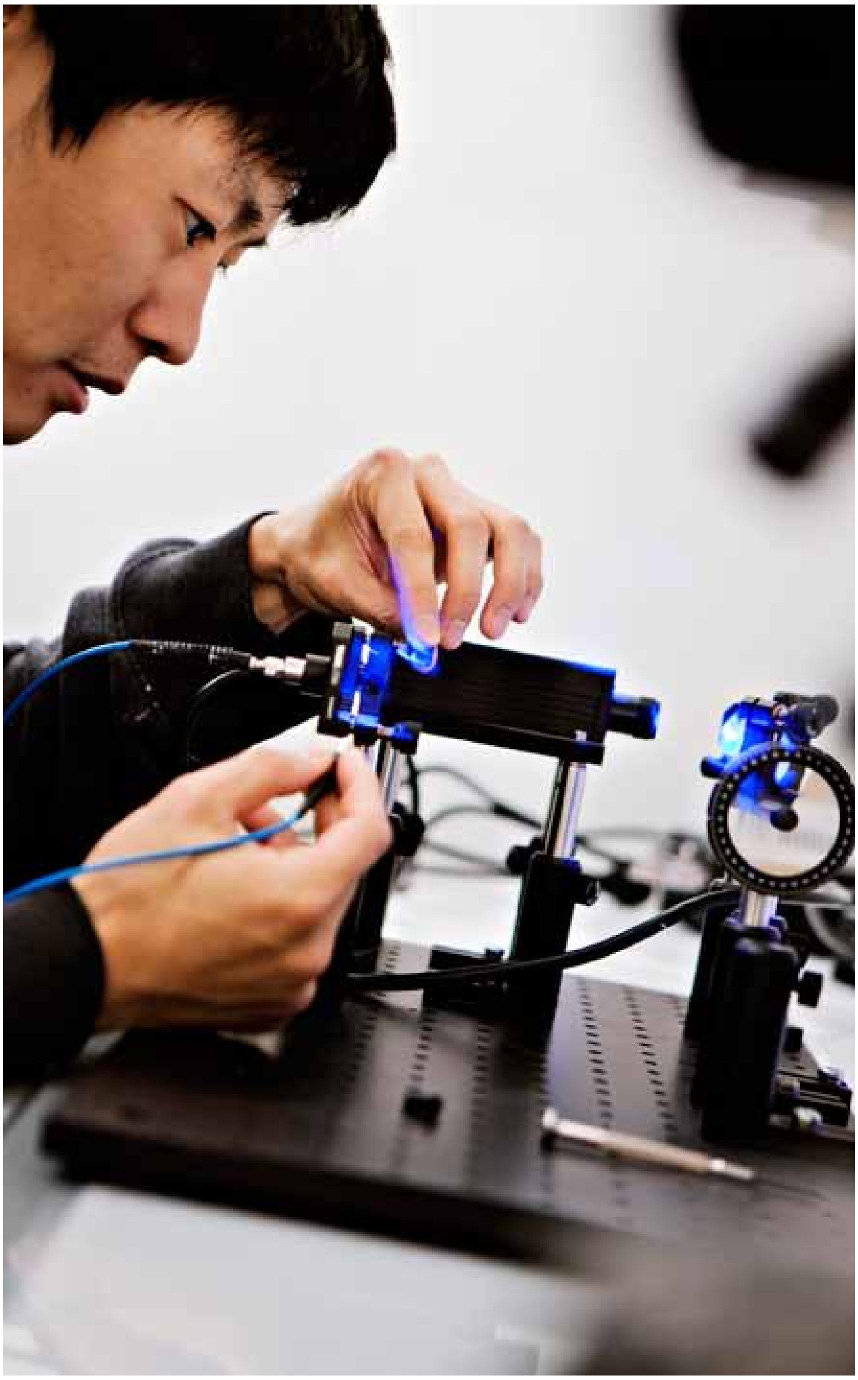
Edvard Moser was a participant in NRK's popular programme "Schrödinger's Cat", which took as its starting point the unique memory of Trondheim Symphony Orchestra conductor Krzysztof Urbanski, who can memorize an entire musical score in minutes. Moser drove a sports car with Urbanski to try to figure out why a man with such a good memory has a very poor sense of location.

Perhaps the biggest media event in 2011 came on Friday 7 October, when Edvard and May-Britt Moser participated in NRK broadcaster Fredrik Skavlan's eponymous talk show, "Skavlan". The talk show often has more than 1 million viewers in Norway and Sweden. The couple were guests in the studio along with the Swedish actress Noomi Rapace, the Swedish Foreign Minister Carl Bildt and the American singer Tony Bennett.

The Norwegian media were very interested in the awarding of the Swiss-based Louis-Jeantet Prize to Edvard and May-Britt Moser. (Photo: Elisabeth Lund/ Sunnmørsposten)

KI/CBM broadens into new research areas

In 2011, the KI/CBM decided to intensify its focus on molecular and systems neuroscience, two fields that can describe how the network of neurons in the brain can work together.



When May-Britt and Edvard Moser in 1996 established the research that has evolved into today's KI/CBM, the focus was on studying the biological roots of memory by recording and analysing electrical signals in the brain. The centre later expanded its activities to include molecular biology studies, and in 2009 the institute was further expanded with the establishment of a research group working on modelling and computational neuroscience. In 2010 the centre also began to develop virus-based techniques that can be used to turn on and off the activity of certain nerve cells, as well as developing a new technology for measuring the microscopic signals inside cells.

Beginning in 2012, the KI/CBM will intensify its focus on molecular and systems neuroscience as a tool in brain research. The institute has invited applications for a new faculty position in systems neuroscience. The institute is open to applicants with experience and interest in using state-of-the-art molecular and cellular technologies to understand neural networks and behaviour.

Molecular biology and systems neuroscience are essential tools to expand the understanding of neural networks and their behaviour neural networks and their behaviour. Here, Albert Tsao, a PhD candidate at the KI/CBM, works with a laser to be used in an optogenetic experiment. (Photo: Geir Mogen/NTNU)

Who's who at KI/CBM

CBM BOARD

Bjørn Hafskjold
Dean Faculty of Natural Sciences and Technology NTNU

Jan Morten Dyrstad
Dean of Faculty of Social Sciences and Technology Management NTNU (chairman)

Stig Slørdahl
Dean Faculty of Medicine NTNU

Tore O. Sandvik
County Council Chair, Sør-Trøndelag County

KAVLI BOARD

Kari Melby
Prorector NTNU (chairman)

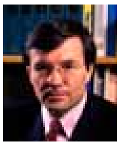
May-Britt Moser
Professor NTNU

Menno Witter
Professor NTNU

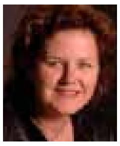
Stig Slørdahl
Dean Faculty of Medicine NTNU

ADVISORY BOARD

Larry Squire
Professor University of California San Diego, USA (chairman)



Terry Sejnowski
Professor Howard Hughes Medical Institute, Salk Institute, USA



Erin Schuman
Professor Max Planck Institute for Brain Research, Germany

Earl Miller
Professor Massachusetts Institute of Technology, USA

FACULTY

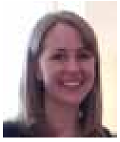
Edvard Moser
Professor and Director

May-Britt Moser
Professor and Director

Menno Witter
Professor

JUNIOR GROUP LEADERS

Ayumu Tashiro
Group leader



Lisa Giocomo
Group leader

Yasser Roudi
Group leader

Sheng Jia Zhang
Group leader

VISITING PROFESSORS

Alessandro Treves
Professor International School for Advanced Studies, Italy

Bruce McNaughton
Professor University of Lethbridge, Canada

Carol Barnes
Professor University of Arizona, USA

Mayank Mehta
Associate Professor UCLA, USA

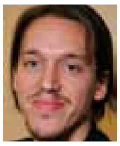
Ole Paulsen
Professor University of Cambridge, UK

Randolf Menzel
Professor Free University of Berlin, Germany

Richard Morris
Professor University of Edinburgh, UK

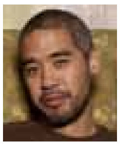
RESEARCH SCIENTISTS

Debora Ledergerber
Postdoc
Moser group



Emilio Kropff
Postdoc
Moser group

Hiroshi Ito
Postdoc
Moser group



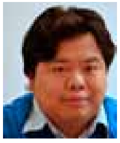
Homare Yamahachi
Postdoc
Moser group

Jing Ye
Postdoc
Moser group

Jonathan Whitlock
Researcher
Moser group

Kei Igarashi
Postdoc
Moser group

Tiffany Van Cauter
Postdoc
Moser group



Aree Widya Witoelar
Postdoc
Roudi group

Alexandre Daniel Surget
Postdoc
Tashiro group

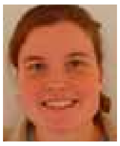
Calvin Young
Postdoc
Tashiro group

Masato Uemura
Postdoc
Tashiro group

Nils Borgesius
Postdoc
Tashiro group

Raveendran Rajeevkumar Nair
Postdoc
Tashiro group

Takuma Kitanishi
Postdoc
Tashiro group



Cathrin Canto
Researcher
Witter group

Hideki Kondo
Postdoc
Witter group

Jay Jonathan Couey
Postdoc
Witter group

Kally O'Reilly
Postdoc
Witter group

Kang Zheng
Postdoc
Witter group

Noriko Kogonezawa
Researcher
Witter group

Rafal Czajkowski
Postdoc
Witter group

ON SABBATICAL LEAVE

Charlotte Alme
PhD candidate
Moser group

Trygve Solstad
Researcher
Moser group

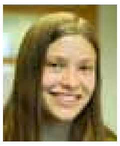
GRADUATE STUDENTS

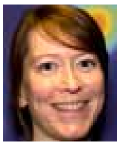
Albert Tsao
PhD candidate
Moser group

Charlotte Boccara
PhD candidate
Moser group

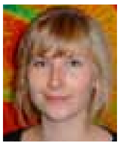

Chenglin Miao
PhD candidate
Moser group


Espen Joakim Henriksen
PhD candidate
Moser group


Hanne Stensola
PhD candidate
Moser group


Ingvild Kruge
PhD candidate
Moser group


Li Lu
PhD candidate
Moser group

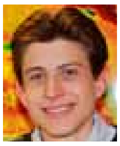

Nenitha Charlotte Dagslott
PhD candidate
Moser group


Tanja Wernle
PhD candidate
Moser group


Tor Stensola
PhD candidate
Moser group

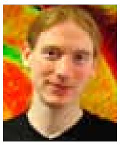

Tora Bonnevie
PhD candidate
Moser group

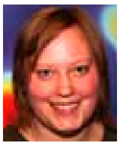

Benjamin Adric Dunn
PhD candidate
Roudi group


Alessandro Luchetti
PhD candidate
Tashiro group


Ingrid Amellem
PhD candidate
Tashiro group


Mehdi Fallahnezhad
PhD candidate
Tashiro group


Stefan Matthias Blankvoort
PhD candidate
Tashiro group


Grethe Mari Olsen
PhD candidate
Witter group


Ingrid Heggland
PhD candidate
Witter group

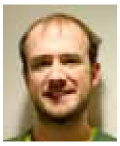

Mathias Mathiasen
PhD candidate
Witter group

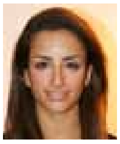
MASTER'S STUDENTS


Fan Zheng
Master's student
Moser group

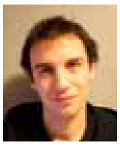

Torgeir Wåga
Master's student
Giocomo Group

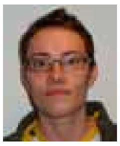

Vania Cuellar
Master's student
Giocomo group


James Carmichael
Master's student
Moser group


Atefe Rafiee Tari
Master's student
Tashiro group

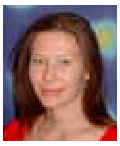

Katarzyna Anna Kapusta
Master's student
Tashiro group


Magnus Helgheim Blystad
Master's student
Tashiro group


William Espen Windsor
Master's student
Tashiro group


Øystein Rød Brekk
Master's student
Tashiro group


Abdala Mumuni Ussif
Master's student
Witter group


Annelene Gulden Dahl
Master's student
Witter group


Asgeir Kobro-Flatmoen
Master's student
Witter group


Christian Gjeraker
Master's student
Witter group


Christin H. Berndtsson
Master's student
Witter group


Hanna Haaland
Master's student
Witter group


Lilliane Hansen
Master's student
Witter group

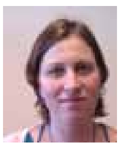

Sobia Islam
Master's student
Witter group

ADMINISTRATION


Hege Tunstad
Communication Officer
Support group


Iuliana Hussein
Head of office
Support group


Linda Veres
Executive Officer
Support group

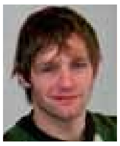

Marzena Grindal
Higher Executive Officer
Support group


Unni Iversen
Senior executive officer
Support group

TECHNICAL TEAM

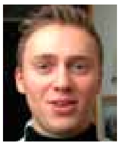

Alice Burøy
Molecular biology
Moser group

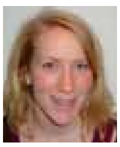

Ann Mari Amundsgård
Histology, hyperdrives
Moser group


Endre Kråkvik
Molecular biology, hyperdrives
Moser group


Klaus Jenssen
Electronics
Moser group


Kyrre Haugen
Histology
Moser group

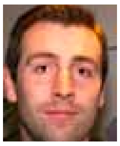

Raymond Skjerpeng
Programming
Moser group


Grethe Jakobsen
Animal care
Support group


Haagen Waade
Computers, networks
Support group


Ingvild Hammer
Infrastructure
Support group

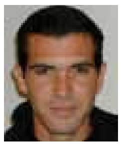

Merethe Andresen
Animal care
Support group


Tommy Åsmul
Animal care
Support group


Naomi Kitanishi
Research assistant
Tashiro group

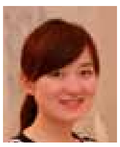

Teruyo Tashiro
Neurogenesis
Tashiro group


Bruno Monterotti
Anatomy
Witter group

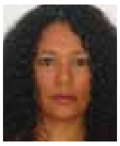

Paulo Girão Bettencourt
Anatomy
Witter group


Ragnhild Giestad
Anatomy
Witter group

RESEARCH ASSISTANTS


Chika Yoshii
Research assistant
Tashiro group

Vanja Cnops
Research assistant
Tashiro group



Yadira Ibarguen
Research assistant
Tashiro group

Ida Aasebø
Research assistant
Witter group

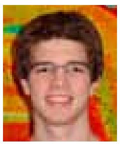
Juan Wu
Research assistant
Zhang group

PROJECT STUDENTS

Hannah Maria Eggink
Project student
Giocomo group

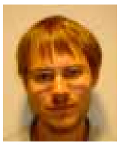
Paul Eduard Cornelis Mertens
Project student
Giocomo group

Eline Kristindatter Storm
Project student
Moser group

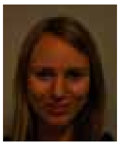


Kristian Frøland
Project student
Moser group

Tale Litlere Bjerknes
Project student
Moser group



Inge Storkaas Røysland
Project student
Witter group



Juliane Kristine Andreassen
Project student
Witter group

Jørgen Sugar
Project student
Witter group

Øyvind Wilsgård Simonsen
Project student
Witter group

Annual Accounts 2011

Income	
Transferred from 2010	**6 886 000**
Norwegian Research Council: Centre of Excellence	10 000 000
Norwegian Research Council: other	7 663 000
International (EU, ERC, Marie Curie, James McDonnell Foundation)	16 448 000
Other public/private (Kavli Foundation, Contact Committee)	1 035 000
Norwegian University of Science and Technology	
Funding (RSO/Kavli/RD)	16 722 750
Own contribution BOA	6 882 607
Incentive funds EU/ERC	1 055 009
Total income	**66 692 366**
Expenses	
Net personnel costs	35 304 000
Indirect costs including floorage	17 032 000
Scientific equipment	2 394 000
Operational expenses	12 211 000
Total expenses	**66 941 000**
Transferred to 2012	**- 248 634**

Amounts in NOK

Publications

MAY-BRITT OG EDVARD MOSER
Moser EI, Moser M-B (2011). Seeing into the future. **Nature**, 469, 303-304.

Moser EI (2011). The multi-laned hippocampus. **Nature Neurosci**. 14, 407-408.

Moser M-B, Moser EI (2011). Crystals of the brain. EMBO Mol. Med. 3, 1-4.

Giocomo LM, Moser M-B and Moser EI (2011). Computational models of grid cells. **Neuron**, 71, 589-603.

Moser EI (2011). A bat's perspective on navigation. **Proc. Natl. Acad. Sci.**, 108, 15665-15666.

Jezek K, Henriksen EJ, Treves A, Moser EI and Moser (2011). Theta-paced flickering between place-cell maps in the hippocampus. **Nature**, 478, 246-249.

Giocomo LM, Hussaini SA, Zheng F, Kandel ER, Moser M-B and Moser EI (2011). Grid cells use HCN1 channels for spatial scaling. **Cell,** 147, 1159-1170.

Giocomo LM, Moser EI (2011). Spatial representation: Maps in a temporal void. **Current Biology**, 21, R962-R964.

AYUMU TASHIRO
Aasebø IE, Blankvoort S and Tashiro A (2011). Critical maturational period of new neurons in adult dentate gyrus for their involvement in memory formation. **Eur J Neurosci**, 33, p1094-100

YASSIR ROUDI
Sakallariu J., Roudi Y., Hertz J., Mezard M. (2011). Effect of coupling asymmetry on mean-field solutions of direct and inverse Sherrington-Kirkpatrick model. preprint

Hertz J., Roudi Y., Tyrcha J. (2011). Ising Models for Inferring Network Structure From Spike Data. "Principles of Neural Coding", edited by Stefano Panzeri and Rodrigo Quian Quiroga, preprint

Roudi Y., Hertz J. (2011). Dynamical TAP equations for non-equilibrium Ising spin glasses, **J. Stat. Mech.**, P03031

Roudi Y., Hertz J. (2011). Mean Field Theory for Non-equilibrium Network Reconstruct Phys. **Rev. Lett.**, 106, 048702

MENNO WITTER
Kononenko N, Witter MP (2011) Presubiculum layer III conveys retrosplenial input to the medial entorhinal cortex. **Hippocampus**, DOI 10.1002/hipo.20949

Kjonigsten LJ, Leergaard TB, Witter MP, Bjaalie JG (2011) Digital atlas of anatomical subdivisions and boundaries of the rat hippocampal region. Front. Neuroinform. 5:2. doi: 10.33 9/fninf.2011.00002.

Sugar J, Witter MP, van Strien NM, Cappaerts NLM (2011) The retrosplenial cortex: intrinsic connectiviuty and connections with the (para)hippocampal region in the rat. An interactive connectome. **Front. Neuroinform**. 5:7. doi: 10.3389/fninf.2011.00007

Small, SA, Schobel SA, Buxton R, Witter MP, Barnes CA (2011) A pathophysiological framework of the hippocampal circuit in aging and disease. **Nature Rev Neurosci**, 12: 585-601.

Yartsev M, Witter MP, Ulanovsky N (2011) Grid cells without theta oscillations in the entorhinal cortex of bats. **Nature**, 479: 103-107.

Canto CB, Witter MP (2011) Cellular properties of principal neurons in the rat entorhinal cortex. I. The lateral entorhinal cortex. **Hippocampus**, DOI 10.1002/hipo.20997

Canto CB, Witter MP (2011) Cellular properties of principal neurons in the rat entorhinal cortex. II. The medial entorhinal cortex. **Hippocampus**, DOI 10.1002/hipo.20993

Witter MP (2011) The Hippocampus. In: The Mouse Nervous System. Eds G. Paxinos, L- Puilles & C. Watson. **Acad. Press**, ch. 5, pp 112-139.

Witter MP (2011) Entorhinal cortex. **Scholarpedia**, 6(10):4380.

LISA GIOCOMO
Giocomo LM, Hussaini SA, Zheng F, Kandel ER, Moser MB, Moser EI (2011). Increased spatial scale in grid cells of HCN1 knockout mice. **Cell**, 147:1159-1170.

Yoshida M, Giocomo LM, Boardman I, Hasselmo ME (2011). Frequency of subthreshold oscillations at different membrane potential voltages in neurons at different anatomical positions on the dorso-ventral axis in the rat medial entorhinal cortex. **Journal of Neuroscience**, 31:12683-94.

Navratilova Z, Giocomo LM, Fellous JM, Hasselmo ME, McNaughton BL (2011). Phase precession and variable spatial scaling in a periodic attractor map model of medial entorhinal grid cells with realistic after-spike dynamics. **Hippocampus,** 10.1002/hipo.20939

Giocomo LM, Moser EI (2011). Spatial Representation: Maps in a temporal void. **Current Biology**, 21:R962-R964.

Giocomo LM, Moser MB, Moser EI (2011). Computational models of grid cells. **Neuron**, 71:589-603.

The Biology of Memory and Systems Neuroscience

Researchers at KI / CBM explore the brain's functioning by detecting and analysing the electrical signals in the brain. In 2009, KI / CBM also began an active expansion into genetics and molecular biology in order to increase its tool box for studies of neural network actions in the performing brain.

Since the centre's inception, KI / CBM researchers have used laboratory rats as study animals. The rats run around in boxes and corridors in search of food and have very thin electrodes inserted into their brains, primarily in the regions of the brain called the hippocampus and entorhinal cortex. This enables researchers to detect brain activity.

The hippocampus is an older part of the cerebral cortex and has a central role in the functioning of human and animal memory. The entorhinal cortex contains grid cells, border cells and direction cells that together give the brain the ability to make highly advanced maps.

The electrodes don't need to be inserted directly into the nerve cells, but instead are placed gently in the space outside of the cells. Each electrode can then record the electrical activity in many brain cells at once, but the electrodes are so sensitive that it is possible to distinguish between the different signals from each individual neuron.

A series of important findings

The KI/CBM has produced a series of sensational scientific findings. In its first year, researchers found that direct inputs from the entorhinal cortex to the hippocampus are responsible for spatial orientation. In 2004, they showed that the entorhinal cortex contains an accurate spatial map of the animal's environment. 2005 was marked by the discovery of grid cells in the entorhinal cortex, which form a map with coordinates comparable to those on a map you can buy in a bookshop. The following year researchers found cells that function like a compass and a speedometer.

The discovery of a completely new type of brain cell that registers borders and barriers caused scientific excitement worldwide when it was published in the American journal Science in 2008. In the same year, it was also discovered that the hippocampus has an inbuilt map with a number of different scales.

In 2009, researchers at the KI/CBM discovered both that the brain uses different wavelengths to separate experiences, and that the brain is able to create its own library of maps for specific purposes.

In 2010, it was discovered that rats are born navigators. The brain in newborn rats comes hard-wired with working navigational neurons. The researchers also found grid cells in two new areas of the brain, outside the entorhinal cortex where grid cells and border cells had been found earlier.

NTNU – Trondheim
Norwegian University of
Science and Technology

Annual Report for KI/CBM 2011

NTNU

The Norwegian University of Science and Technology (NTNU) is Norway's primary institution for educating the nation's future engineers and scientists. The university also has strong programmes in the social sciences, the arts and humanities, teacher education, medicine, architecture and fine art. NTNU's cross-disciplinary research delivers creative innovations that have far-reaching social and economic impact.

Kavli Institute for Systems Neuroscience and Centre for the Biology of Memory
Centre of Excellence Medical-Technical Research Centre,
NO-7489 Trondheim, Norway
Telephone: +47 73 59 82 42
Telefax: +47 73 59 82 94
E-mail: contact@cbm.ntnu.no