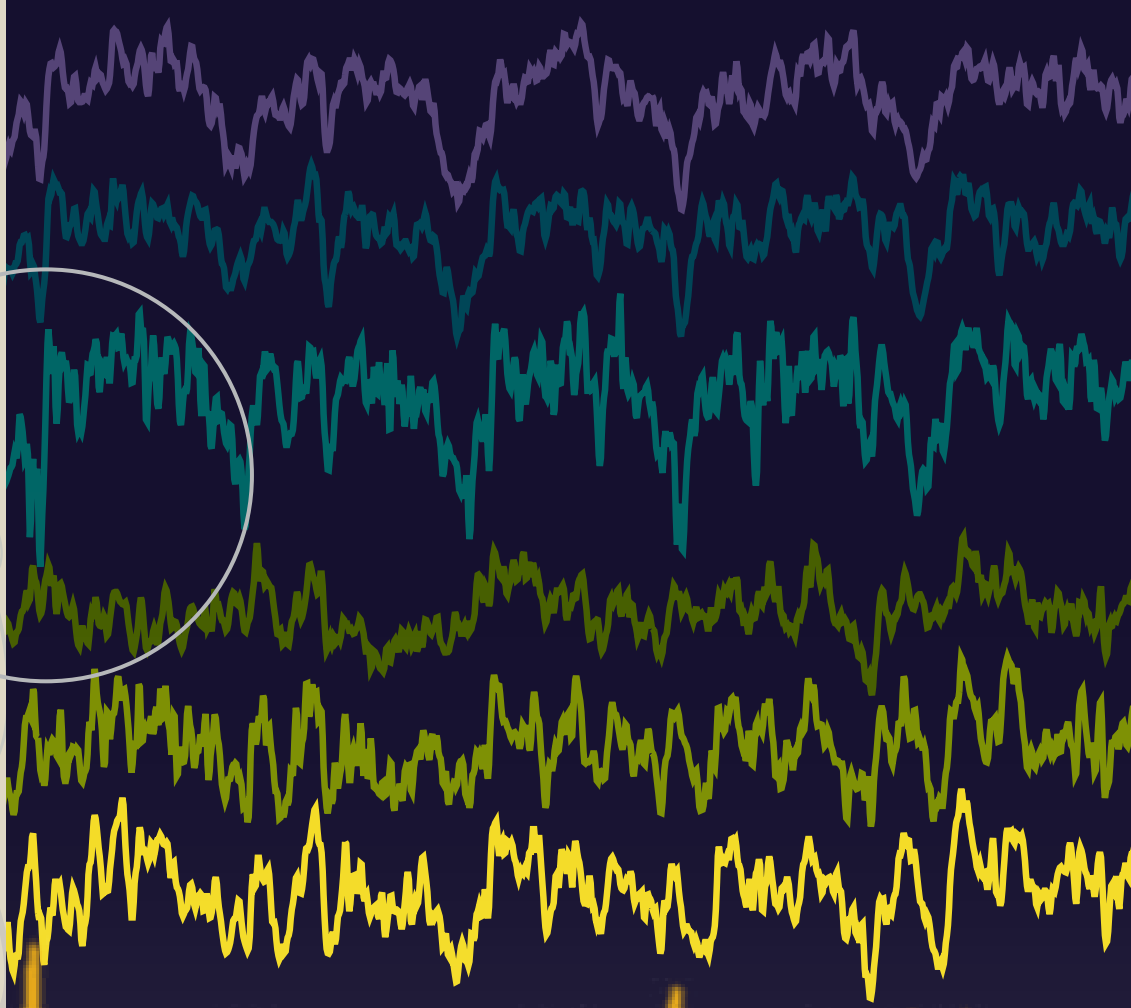

Kavli Institute for Systems Neuroscience and Centre for the Biology of Memory

Annual Report 2009

Norwegian Centre of Excellence

NTNU
Norwegian University of Science and Technology

The people at KI/CBM March 2010. (Photo: Gorm Kallestad)

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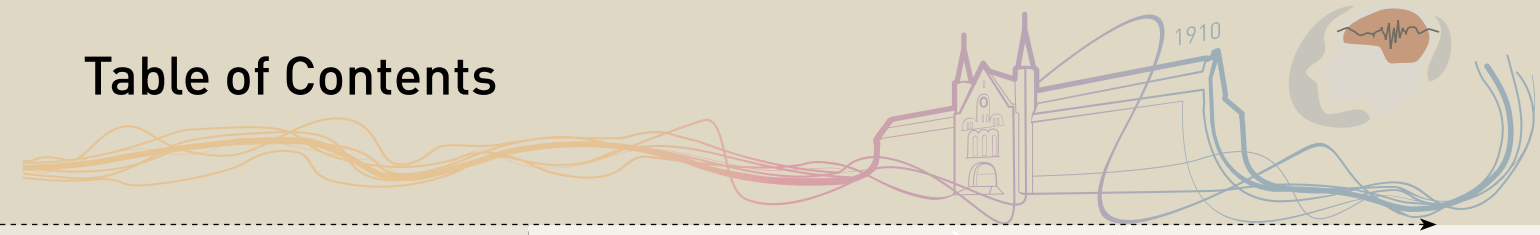

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KI / CBM – a brief history

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 an amount that gradually increases to about NOK 7 million in annual support from the Kavli Foundation, the Ministry of Education and Research and NTNU 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.

Discovering the key to human memory

"We don't know which discovery is going to be the key to a fundamentally deeper understanding of human memory. But the hope is that some time in the future, we will have both a cure for Alzheimer's disease and methods for improving the memory in normally aging brains," says Professor Carol Barnes.

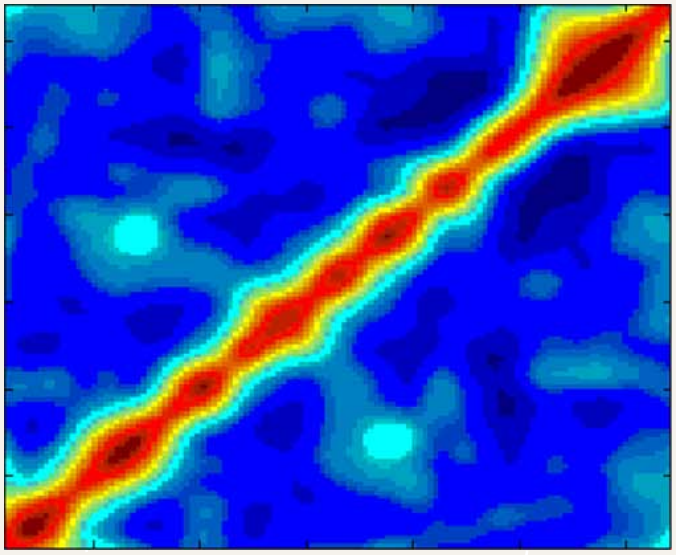
The main purpose of Professor Barnes' research is to understand how human memory changes as people grow older. This is of obvious interest from a curiosity-driven scientific point of view, but the research also holds potential for applications such as developing a cure for the dreaded Alzheimer's disease.

"Alzheimer's is one of the worst diseases from my perspective, because the patients effectively lose themselves. Who are you as a person, if not a collection of your memories? This is one of the reasons for studying memory: I don't believe you can understand diseases such as Alzheimer's until you understand the normally aging brain," Barnes says.

Good news about memory

Carol Barnes has good news about older people and their memories. "You would be surprised to know how much it is possible for older people to remember. When I started studying the brain in the late 1970s, everybody believed that as people aged, they lost many cells in their brain every day, and that this was the cause of the weakening of their memories. There was apparently nothing you could do about the decay. But this is simply wrong – older people do not lose substantial numbers of brain cells!"

"What really happens is that the ability to maintain strong connections between the cells that we think are important to memory changes. This means that older people can still learn and remember, but their ability to maintain their memories tends to fade more quickly," Barnes says.



Hippocampal cells that fire together during a specific behavioral experience (as shown in this spatial population correlation heat map) also tend to fire together during quiet waking or slow wave sleep after this behavior (as shown first by Bruce McNaughton, a visiting professor at the Centre). This may reflect a memory consolidation process. Old rats show disrupted "network replay", in that sequences of the experience can be played back out of order, which could contribute to the instability of memory observed in older animals.

Writing the future's textbooks

Professor Barnes has been a visiting member of the Centre for the Biology of Memory in Trondheim since the centre started in 2002, but she has known the Mosers since 1995, when Barnes was called to Oslo as an external examiner for May-Britt Moser's PhD thesis.

"The Mosers and their research centre in Trondheim have made a number of astonishing new findings in the field of neuroscience. The excitement that the data emerging from this group has caused has clearly been worldwide among neuroscientists. I am sure that these results will be in future textbooks, and it is of great value for me and my students to know about their work. I also hope that the Mosers and their students benefit from knowing my students and their findings. The whole field

Carol Barnes

Carol Barnes is a Regents' Professor of Psychology and Neurology at the University of Arizona, where she directs the Evelyn F. McKnight Brain Institute, and is associate director of the university's BIO5 Institute. She was president of the Society for Neurosciences (SFN) in 2004-2005. Barnes conducts animal behavioural studies at the Arizona Research Laboratories while charting brain cell activity, with a focus on differences between young and old animals.

During her postdoctoral work at the Institute of Neurophysiology in Oslo in 1979, where she collaborated with Professor Per Andersen, Barnes provided some of the first evidence that age-linked deterioration in the normal brain was quite different from diseased brains at the cellular and neural levels.

Professor Barnes is one of the most frequently cited scholars regarding the ability to create memories at synapses, a phenomenon called long-term potentiation (LTP), discovered in Per Andersen's lab in 1966 by Professor Terje Lømo, who was then a student. When functioning well, LTP can stabilize brain circuits and prevent lab rats – and old people – from getting disoriented or lost on the street.

of brain research moves faster when you are able to share information and inspire each other," Barnes says.

From normal to even better memory

The memory research in Trondheim and in Barnes' lab in Arizona relies on experiments with lab rats, because their memories work in much the same way as in humans. Professor Barnes believes that the neuroscientific research community is on the verge of a breakthrough in terms of finding out what is special about individuals who age successfully and have very good memories, compared to those who do not.

"Even among rats in the laboratory, there are some individuals with much better memories than regular rats. This is despite the fact that lab rats are heavily inbred and genetically almost identical. They have all been raised in the same cages, they have eaten the same food, have been given the same exercise, and they have had the same caretakers who have treated them in the same way. Therefore, we are beginning to think that the expression of the genes that influences memory can be altered by behaviour or maybe by random events. This makes it possible to think that genetic pathways can be manipulated in ways that could make it possible, even for a person with normal memory, to have an even better memory," she says.

One of the latest findings from Professor Barnes is that aging in rats impairs the consolidation of memories during sleep – and she suspects the same is probably true in humans. "The traces of your daily experiences are played back in the brain during sleep. The interesting thing we found in older animals is that the replay could be out of order in terms of the actual sequence of events, and it is possible that this defective replay makes it harder to stabilize memories on a long-term basis. The replay is generated in the hippocampus, which passes information on to the cortex, where the memory is stabilized for the long term."

A new age of molecular biology

Professor Barnes is impressed by the results from the electrophysiological, behavioral and computational research on memory in Trondheim, and she is glad that researchers plan to continue pursuing these lines of inquiry. "But there is also a whole set of new and important skills out there on the horizon. The age of molecular biology is upon us, and the molecular methods that are being developed to study the brain are more and more exciting. These methods make it possible to identify the actual genetic composition of individual cells well enough to determine if they are sick or healthy, and if they are involved in projections to a specific target of the brain. The KI/CBM is already expanding in this direction but without abandoning their original focus, and that seems to be a very good strategy for the future".

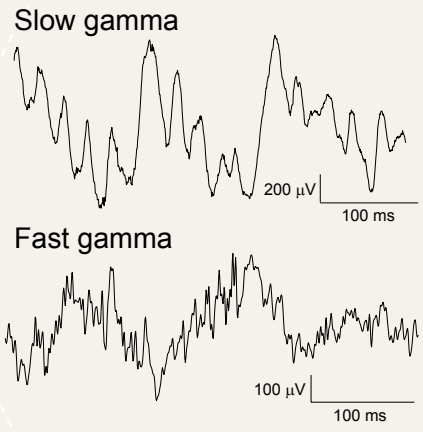
Carol Barnes, one of 7 visiting professors at KI/CBM.

The brain uses different wavelengths to separate experiences

How does the brain distinguish between different experiences, like old memories and new sensations, when several types of signals are hurtling through the brain simultaneously? The answer is that the brain works a bit like a radio: Different types of signals are separated via different frequencies and wavelengths.

All brain cells produce electrical signals that convey information to other brain cells. When a large number of brain cells work together in a network that sends electrical signals at the same time, brain waves are the result. Gamma waves, which are seen throughout the cortex, are a good example of these waves. Brain researchers have long wondered why the brain has several types of gamma waves with different wavelengths and frequencies, but in November 2009, a group of scientists from KI/CBM published their sensational findings in an article in the journal Nature.

"The brain uses lower frequency gamma waves when it calls up memories of past experiences. But if the brain wants to address what is happening here and now, such as sensory input about where you are and what you are experiencing, it uses gamma waves with higher frequencies. The different frequencies make it possible to distinguish between different types of information, for example, between memories and the news, even if the brain is working with them simultaneously," explains postdoctoral fellow Laura Colgin, who was first author of the Nature article.



There are two distinct types of gamma oscillations in CA1. One type is slow (~40 Hz), and the other type is fast (>65 Hz). Both ride on top of slower theta waves, but they tend to occur at different theta phases and on separate theta cycles.

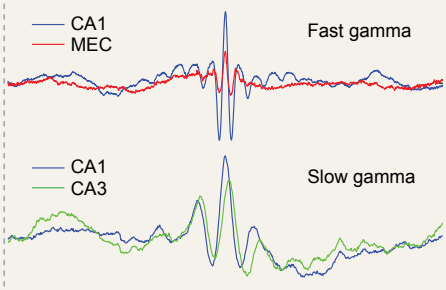
Postdoc Laura Colgin at KI/CBM. (Photo: Raymond Skjerpeng, KI/CBM)

On the same wavelength

Brain researchers knew from previous research that gamma waves - the fast waves in the brain, with frequencies between 25 and 150 Hz - resulted from advanced brain activities, such as the interpretation of sensory inputs. Researchers have also thought that these waves are linked to the formation of consciousness, but no one really knew why the frequency of the gamma waves differed so much from one region to another in the brain, and from one moment to the next. Information is carried on top of gamma waves, just like songs are carried by radio waves.

The new research results from Trondheim have given the old expression about "being on the same wavelength" a whole new meaning. "You know how when you feel like you really connect with someone, you say you are on the same wavelength? When brain cells want to connect, they literally tune into each other's wavelength. Our research shows that the differentiation between 'memory frequencies' and 'current experience frequencies' in the brain occurs at about 60 Hz," says Colgin.

"The cells can rapidly switch their activity to tune in to the slow waves or the fast waves," she adds, "but it seems as though they cannot listen to both at the exact same time.



CA1 fast gamma is synchronized with medial entorhinal cortex (MEC) fast gamma. CA3 slow gamma is synchronized with slow gamma in CA3.

This is like when you are listening to your radio and you tune in to a frequency that is midway between two stations: You will hear nothing but noise."

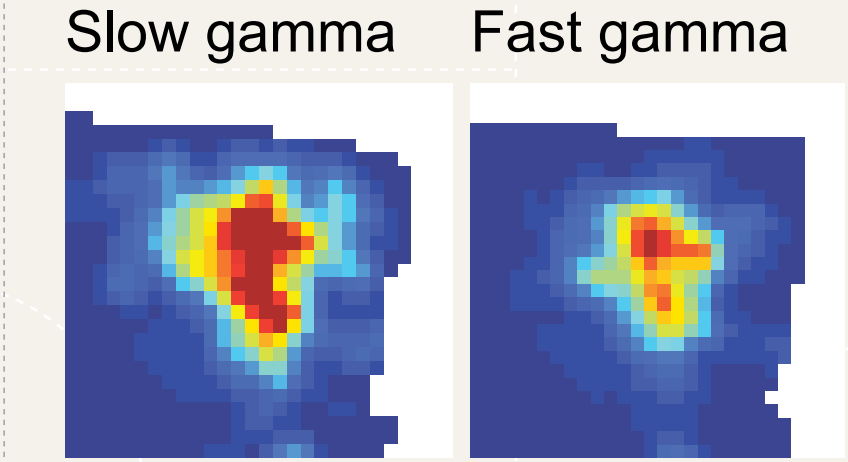
Who decides the frequency?

Colgin and her colleagues measured brain waves in rats in three different parts (CA1, CA3 and medial entorhinal cortex) of the

hippocampal region, which is a key memory centre in the brain. "What we actually measure is the variation in electrical voltages in the space between neurons, and these voltages are the result of the transport of ions through nerve cell membranes. The voltages are the result of large groups of brain cells that contact each other and send electrical signals at the same time," she explains.
Researchers in Trondheim have so far examined gamma waves and their frequencies in a small part of the brain, but Colgin thinks it is possible to find similar mechanisms in other parts of the brain. Gamma waves can actually be detected in many areas of the brain, such as in the visual cortex and olfactory cortex and in the amygdala.

The senders and recipients in the brain distinguish signals from each other by using different frequencies. But – what is responsible for deciding the frequencies?

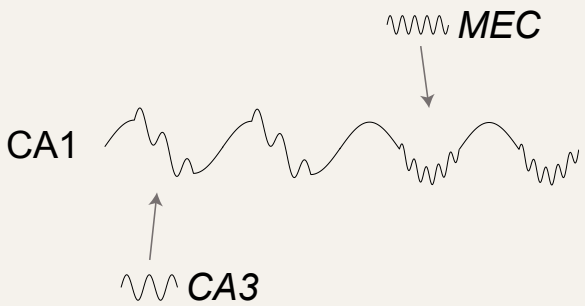
"We do not know yet. But if I were to guess, I would say it depends on the general conditions in the brain, for example how much attention is focused on the external world versus internal thoughts. These questions begin actually to approach issues related to consciousness, which have been very controversial among brain researchers," responds Colgin.



Color-coded firing rate maps constructed separately for spikes that occurred during slow (left) or fast (right) gamma for an example CA1 place cell. CA1 place fields were larger during periods of slow gamma, signifying that CA1 place cell firing was less tied to the precise location of the animal during slow gamma. This suggests that CA1 relies less on current environmental input during slow gamma and instead retrieves information from previously stored maps.

A general principle

The cells that tune into different wavelengths can be compared to a person zapping between radio stations that are already programmed into a radio. "They can switch back and forth between different channels several times per second. The switching allows the cells to pay attention to one piece at a time, sorting out what's on your mind from what's happening and where you are at any point in time. This is probably an underlying principle for how information is handled throughout the brain," says Edvard Moser, Kavli Institute for Systems Neuroscience director and co-author of the article in Nature. "The classical view has been that signaling inside the brain is hardwired, subject to changes caused by modification of connections between neurons. Our results suggest that the brain is a lot more flexible. Among the thousands of inputs to a given brain cell, the cell can choose to listen to some and ignore the rest, and the selection of inputs is changing all the time."



A schematic illustrating the main finding of the study. Slow gamma oscillations occur preferentially on the descending portion of the underlying theta waves. Fast gamma oscillations occur at a different time, near the trough of theta waves. Slow gamma serves to synchronize CA1 with memory inputs arriving from CA3, and fast gamma synchronizes CA1 with input about current location from the medial entorhinal cortex (MEC).

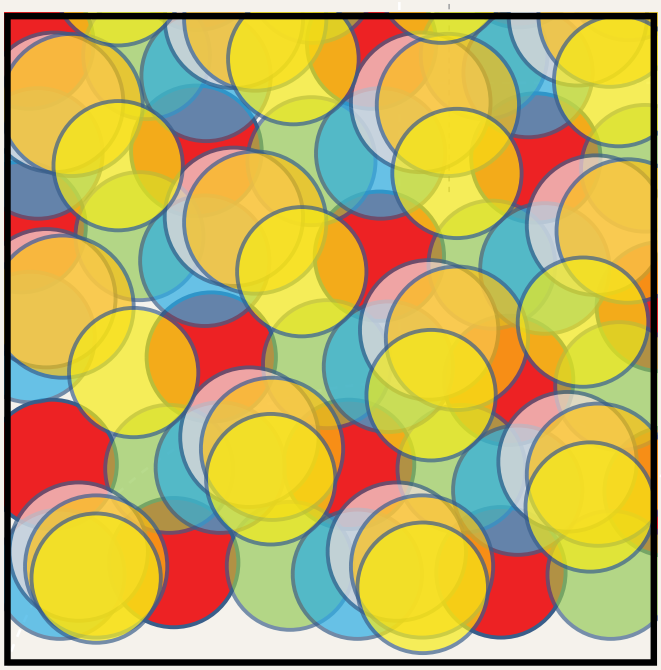
A cure for schizophrenia?

One of the goals of the research in Trondheim has been to find a cure for Alzheimer's disease. Laura Colgin may instead have come closer to unraveling the reasons behind schizophrenia. "We do know that gamma waves are abnormal in schizophrenic patients. Their perceptions of the world around them are mixed up, like a radio stuck between stations. It would be very interesting to investigate the role of gamma waves in other diseases of the brain," she says.

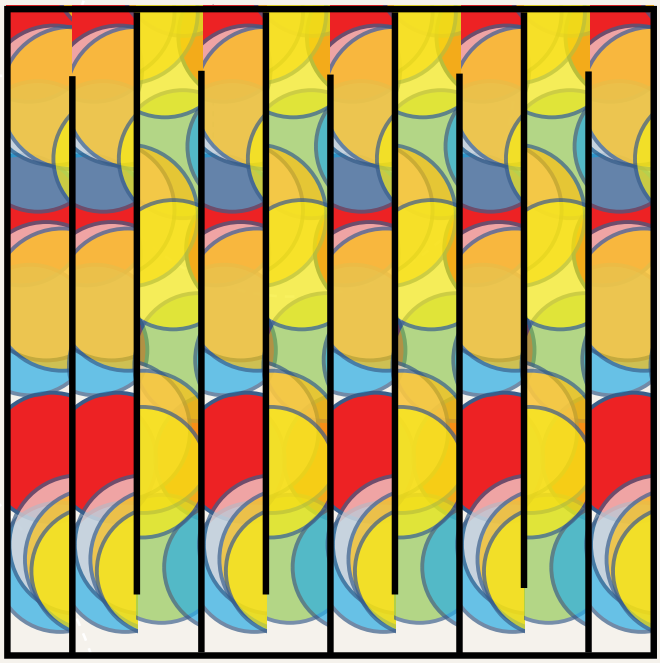
Colgin received her doctorate in the United States at the University of California at Irvine, for which she examined tissue samples to map out what roles the brain's different rhythms and frequencies play. "I met Edvard and May-Britt Moser at a conference in France, and was very interested in both their working methods and approach to animal experimentation. I'm very glad I got to come to Trondheim as a postdoc, because this is an excellent research institute with a great academic environment, along with very nice people," she says.

The brain creates its own library of maps

In 2005, scientists in Trondheim discovered that the brains of rats and other mammals make maps of the environment, and that these maps have grids that are strikingly reminiscent of actual manmade maps. Ongoing research shows that the brain does not create a single map with every detail, but instead creates an entire file of maps that includes both overview maps and more detailed maps for orientation.



A rat searching for food in a square box uses an overview map of the entire box. (Illustration: Dori Dedrikman, KI/CBM)



If the square box is equipped with a labyrinth with hairpin turns, the rats begin to create detailed maps for each corridor. (Illustration: Dori Dedrikman, KI/CBM)

The mapping function in the rat brain – and in the brains of humans and other mammals – is found in what are called grid cells in the entorhinal cortex, which is a small area near the memory centre found in the hippocampus. Each time a rat runs past a particular point in the environment, an electrical signal is fired from the same small group of grid cells in the entorhinal cortex. These cells tell the rat's brain: "Now you're right here!" When the rat passes a second point, a second electrical signal is fired from a second group of grid cells, and so on. In this way, the grid cells provide markers for all the locations in the rat's surroundings.

Rats are very good at orienting themselves. "If we put a rat in Box A, it naturally uses the map for Box A. If we then move the rat over to a new Box B, it makes a new 'Map B', even if the two boxes are identical. Rats can actually keep track of which of the boxes in the lab they are in," says Dori Derdikman, a postdoc at KI/CBM.

Every time the rat explores a new environment, the brain makes a new map using the grid cells. But if the rat returns to an environment where it has been before, the brain doesn't make a new map. Instead, the map that had been made previously is retrieved from storage in the brain, so the rat can use it again for navigation. Effectively, the same grid cells say to the rat brain, "Now you're back here again!" This discovery of the brain's map-making ability won international recognition for researcher Marianne Fyhn, including the Donald Lindsley Prize for the world's best doctoral thesis in behavioural neurobiology in 2005.

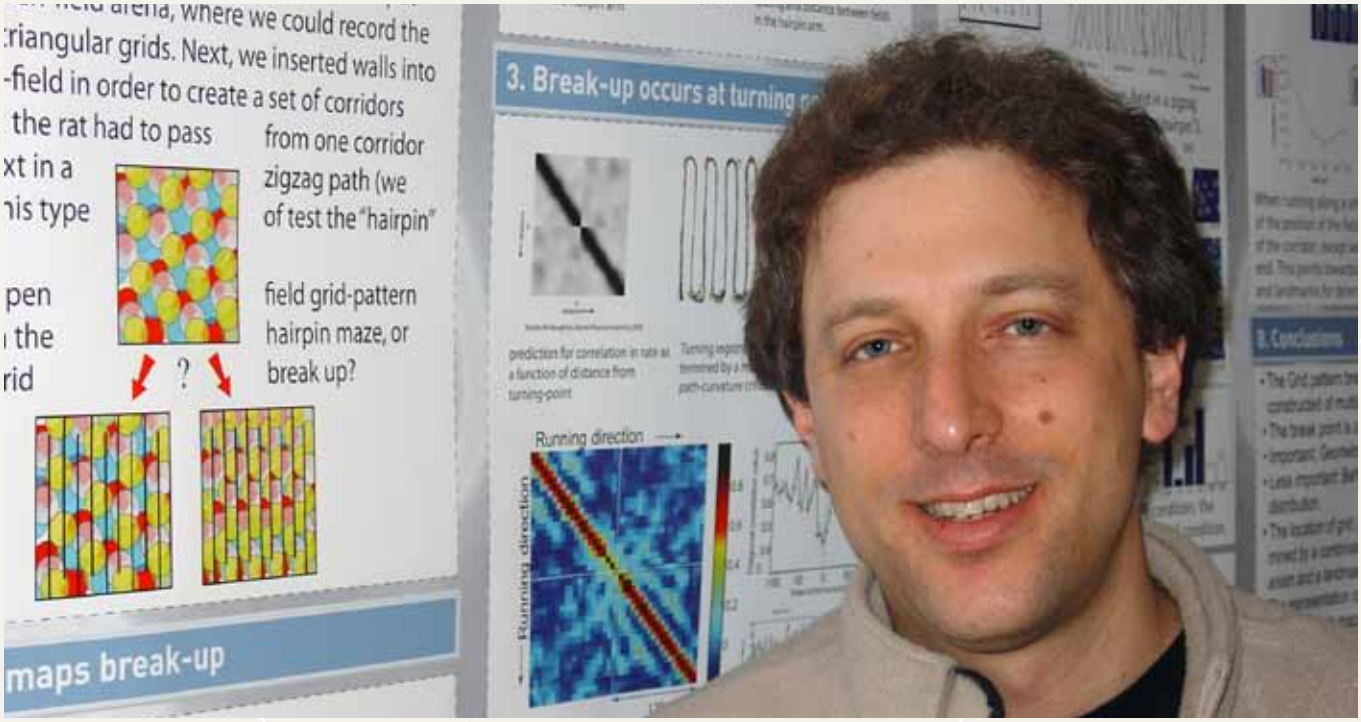
A multitude of different maps

A researcher who discovers something new soon begins to ponder the next new thing. That's exactly what happened with Dori Derdikman. "We didn't know whether all the map information in the brain is stored in a big map, or whether the brain creates multiple maps for different purposes. So we hatched a plan to answer the question," Derdikman says.

His answer to the question was published in Nature Neuroscience in October 2009: The brain saves a multitude of different maps. Some are overview maps, while others are detail maps. It's almost like Google Earth: You can zoom your way to Trondheim with an overview map, but you have to upload a detailed map to locate something on the campus of the Norwegian University of Science and Technology.

The maze becomes a labyrinth

Derdikman describes in the Nature Neuroscience article how researchers measured the brain activity of laboratory rats allowed to roam freely in a small compartment. Once the researchers had a



Postdoc Dori Derdikman at KI/CBM. (Photo: Haagen Waade, KI/CBM)

clear understanding of what the rats' mental maps looked like, they changed the layout of the compartment. Instead of an open area, the rats were now confronted with a labyrinth of long, narrow corridors in a hairpin maze - created by the insertion of walls in the compartment.

"When the walls were inserted, something happened with the rats' maps. First we recorded the same map. But when the rats came around a hairpin turn in the maze, the map changed totally. This happened several times, always when the rats went around a wall and came into a new corridor. If the rat had been using the same map that it had created for the open compartment, the map would have remained unchanged," Derdikman says.

But the "old" map of the entire box was not deleted either. Instead, the rat brain retains the general map, but also makes a "submap" of each single corridor.

The physical environment is the trigger

Derdikman also checked to see if it was confusing for the rats to change direction all the time because of the maze walls. Rats were trained to run the same route formed by the hairpin maze, but in a compartment without partitions. In this case, the rat used the same map as when it ran freely in the open compartment. That means that it was the physical environment that triggered the creation of a new map, not the rat's learned behaviour.

How is it that so many different maps are linked to the surroundings? A recently discovered cell type, border cells, which are active along certain walls in a given environment, may shed light on this question. Border cells describe the limits of where one environment ends and another begins.

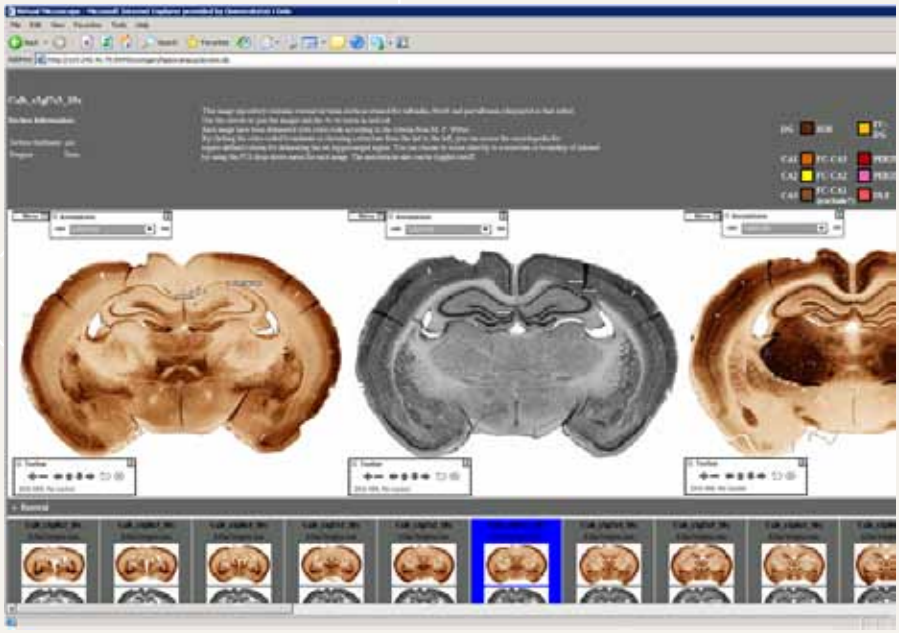
"Maybe these border cells are what signal the brain to switch maps when you move over a border in your environment," says Derdikman's colleague at the Kavli Institute, Trygve Solstad, who was lead author of a 2008 article in Science magazine that reported the presence of the cells. But the definitive answer to that question will have to wait until a research project examines how border cells behave in a fragmented environment.

Planning new research

Scientists now know that the brain's map system consists of three types of entorhinal nerve cells, all of which were discovered in Trondheim: Grid cells, border cells and head direction cells. "These nerve cells tell the brain where the rat is located, but we do not yet know exactly how cells supply the information to the brain. We think that we can find out more about this by examining the regions that take care of the 'input' and 'output' from the entorhinal cortex," suggests Derdikman.

Derdikman is originally from Israel and was awarded his PhD in neurobiology from the Weizmann Institute of Science in Rehovot, outside of Tel Aviv. His interest in May-Britt and Edvard Moser's research in Trondheim was awakened when he heard a lecture by the Kavli Institute's visiting professor Alessandro Treves. Derdikman has never regretted coming to Trondheim to work at one of the world's best laboratories in brain and memory research.

The rat brain gets its first digital atlas



The rat brain atlas. An interactive digital atlas of the parahippocampal-hippocampal system. Adjacent sections stained for different chemicals in the brain that assist in establishing borders. Snapshot taken with permission from The Rodent Work Bench; www.rbwb.org

Modern neuroscience and brain researchers have made so many advances that it is impossible for scientists to keep track of everything that is known. In order to organize all the available data, researchers are working to create a digital brain atlas.

The rationale for creating a digital brain atlas is similar to the rationale for creating a world atlas: It is useful to have an overview of how the world and the brain are divided, what is going on in different countries, and brain sections, and what kinds of communication exists between the different areas. Professor Menno Witter is leading the effort to create a map of the "countries" that are called the hippocampus and parahippocampus in the rat brain.
"There are already a number of printed brain atlases available, and researchers use them like you would use any other atlas: they help us to find out where we are and what we know about this particular place, where we want to go from here, and how to navigate to the next location. The goal behind the digital atlas is first of all to make information about the brain more easily accessible, so that we don't have to carry heavy books around. The second aim is to make the information much more detailed and specific," explains Professor Witter.

The brain in three dimensions

A digital atlas published on the Internet offers many more possibilities than a printed atlas. It can be continuously updated, as new research results are made available.
A world atlas often contains geopolitical, social, religious and demographic statistics, as well as geographical features and political boundaries. The brain atlas will be constructed in a similar way: At any given time, it will contain what researchers know about the brain's physical divisions, along with the features that have been found in the individual parts, the kinds of information exchanged between different parts of the brain, and so on. The atlas will also feature lists and links to published scientific articles that describe main features of each part of the brain.
"We will also be able to use the atlas to visualize where in the brain our experiments are being conducted. That means the atlas has to be three-dimensional and quantitative, in the sense that it should give us the ability both to find the part of the brain that we studied in each project, and where the electrodes we used were located, as an example," added Witter.

"The borders in the brain are not as clear as they are between countries?"

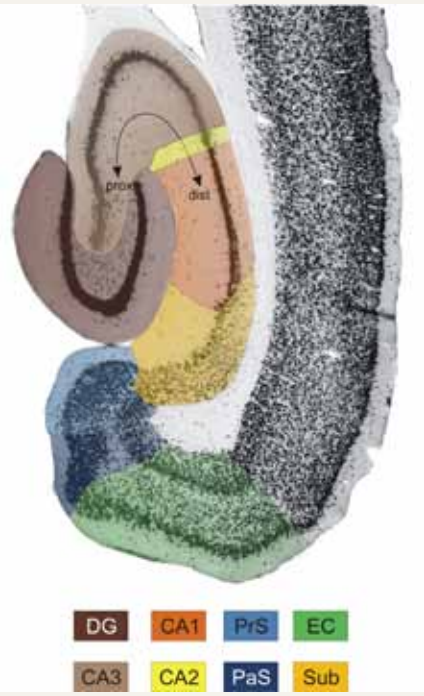
Menno Witter. (Photo: Haagen Waade, KI/CBM)

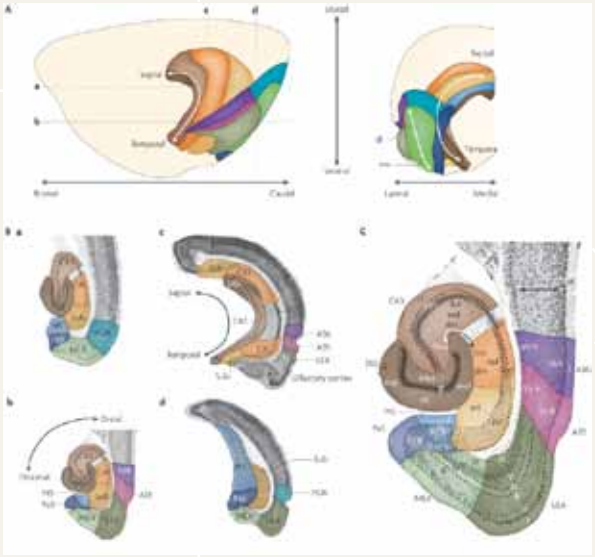
"Yes, and no," Witter answers. "It all depends on your definitions. Most neuroscientists agree on a lot of things, such as the location of the hippocampus and how it is defined. But there are also a number of areas and functions where the borders are vague in the brain. If you talk about memory in a general way, for example, it is hard to find any clear borders. But if you refer to episodic memory – the experiences you can talk about, the things that happened to you at a particular time in a particular place – most of us agree that you cannot build and store such memories if you don't have a hippocampus. We also agree that the memory for skills, like when you learn to ride a bicycle, is not stored in the hippocampus but in another part of the brain that is called the striatum," Witter answers.

An international project

The development of the digital brain atlas is in keeping with the goals of the International Neuroinformatics Coordinating Facility (www.incf.org), an organization that has 14 member countries. INCF is supporting the development of the brain atlas for a variety of animals such as primates (apes and humans) and rats. The American National Institutes of Health (NIH) recently launched a project that focuses on connections in the human brain, the human connectome[1] , as one of the three blueprint projects in neuroscience for the coming five years. All these initiatives together will contribute to our further understanding of the functions of the brain. The work on the rat brain atlas is being led by Professor Jan G. Bjaalie, who heads the Institute of Basic Medical Sciences at the University of Oslo and who was founding director of the INCF. Professor Witter and researchers at KI / CBM are helping with information about the parts of the rat brain that have been the research focus at KI/CBM, primarily the hippocampus and parahippocampus, including the entorhinal cortex. The project in Oslo has received a special grant from the Research Council of Norway, while the efforts in Trondheim have been supported by the Research Council through general research project grants.

Atlassing the rat brain. Color-coded subdivisions of the entorhinal-hippocampal system as seen in a horizontal section.





Atlassing the rat brain. Color-coded subdivisions of the entorhinal-hippocampal system as seen in 3-D representations (A) or in differently oriented sections (B). Reproduced with permission from Nat rev Neurosci. 10:272-282. www.temporal-lobe.com

INCF is also supporting the development of a digital registry of all the different types of cells found in the brain, with information about their morphology, physiology, the kinds of chemicals they contain, and how they respond to stimuli. Both the brain atlas and the cell index are based on information from published research data from around the world. Menno Witter is a member of the task force that runs the neuron registry. "These databases will make scientific data more accessible, but they will also make it possible to mine the data, so that people can use information from other researchers in novel ways. This makes it possible to speed up research and make it more efficient," Witter says.

"It is also important to reduce the likelihood that scientists will spend time on something that has already been mapped. It's sad to work for years to map an area that you think is a blank spot, if Stanley or Livingstone has already been there and mapped it," he adds.

A hundred years of brain research

The development of the digital brain atlas is not starting from scratch. Menno Witter and his colleagues have already developed a new database that describes the connections of the hippocampus in the rat's brain, which was described in an article in a 2009 issue of Nature Review Neuroscience. The database has also been published on www.temporal-lobe.com, with a list of all papers, references and figures ever reported on any particular connection.

"It is the nature of this project that the digital brain atlas perhaps will never be completely finished. We're talking about work that could continue for 100 years," suggests Witter.

1 The connectome is the complete description of the structural connectivity (the physical wiring) of an organism's nervous system.

Five good stories for 5000 brain researchers

Professor May-Britt Moser's lecture on brain research was very well received by more than 5,000 researchers at the annual meeting of the Society for Neuroscience in Chicago. The society has more than 38 000 members and is the world's largest organization of scientists who study the brain and nervous system.

Professor Moser initiated her special lecture "The Brain's Mechanisms for Mapping External Space" in October 2009 by displaying an image of "my dear husband and colleague Edvard Moser, lost in Australia" – and thus captured her audience's attention for the rest of her hour-long talk. The overarching theme was how the rats - and humans – understand where they are in their environment. Moser told the group five good stories that shed light on the question.

Place cells, which are brain cells that fire electrical signals each time an animal or a human is at a particular location, were discovered by John O'Keefe at University College of London in 1971. The discovery triggered a whole new understanding of how the brain orients itself in the environment, and has been the basis for a number of new discoveries made by KI / CBM. Moser's first story was about grid cells in the entorhinal cortex, which were discovered by five researchers in Trondheim in 2006. Grid cells contain a complete map system with a grid where coordinate points are recorded corresponding to locations in the environment.

From black boxes to labyrinths

The research that has been conducted on place cells, grid cells and other types of nerve cells in the brain has so far largely been conducted by studying rats that run around in simple situations, such as square black boxes with sides that are a little over a metre. So Moser's second story was about how KI / CBM researchers decided to study rats in environments that more closely approximate reality, such as a labyrinth with a number of hairpin turns. Postdoc Dori Derdikman has recently shown that "the map" in the rat brain is reset each time the rat begins on a new corridor in the labyrinth (see separate article on page 6).

By the time Moser came to story number three, her audience was intrigued. This third story was about researcher Rosamund Langston, whose work is an attempt to answer a classic evolutionary question: Are spatial representations in the brain innate or learned? Langston's findings will be published during 2010.

Story number four added another captivating question to the list: How does the brain avoid mixing different types of information? By changing the lighting in the laboratory, postdoc Karel Jezek is able to make rats believe that they have been moved from one place to another in milliseconds – much like the science fiction-inspired method known as teleportation. His experiments are all about determining how the brain handles information that can initially be confusing.

Gamma waves and the Hall of the Mountain King

The fifth story was about postdoc Laura Colgin, who has shown how the brain manages to sort large amounts of information by using different frequencies for communication between different cells (see separate article on page 4). When Moser concluded her lecture by showing a video of gamma waves, with the Pirum student choir in the background singing "In the Hall of the Mountain King," her podium was surrounded by scientists eager to learn more about the research being done in Trondheim.

May-Britt Moser plenary lecturer at SfN 2009. Copyright © 2009, Society for Neuroscience. All right reserved. Photo by Joe Shymanski.

Informal meetings for young brain researchers

"Everybody makes a lot more noise and asks more questions when the bosses aren't around," Rosamund Langston says. Langston organizes the Junior SpaceBrain Meeting, where PhD students and postdocs from European and Israeli brain research institutions meet once a year to solve practical problems and learn from each other.

The second Junior SpaceBrain meeting was held in Rhodes, Greece in 2009. (Photo: Emilio Kropff).

Seven universities and research organizations from Europe and Israel initiated the SpaceBrain project in 2008 with the goal of developing a comprehensive understanding of the brain. The project is being coordinated by Professor Edvard Moser at KI/CBM and is funded by the European Union's Seventh Framework Programme for research. Its goal is to search for the principles behind microcircuit computation in the spatial representation system of rodents, using a powerful combination of novel computational, electrophysiological, optical and molecular research tools. Much of the laboratory work is being done by young PhD students and postdocs, says KI/CBM postdoctoral fellow Rosamund Langston.

"We hold the main meeting for the SpaceBrain project once a year, with all the project leaders and representatives from the funding agencies. This is very formal, with a great deal of discussion about strategies and deadlines. But the young researchers who are responsible for much of the work in the laboratories felt we needed more time together to talk about everyday problems in the laboratory and share ideas. After the first Junior SpaceBrain meeting in Marseilles in 2008, we agreed that it was very helpful to meet when we were away from the watchful eyes of the people we are trying to impress!" Langston says.

Asking about anything you want

The second Junior SpaceBrain meeting was held in Rhodes in 2009, and the third meeting will be held in Amsterdam in 2010, at the same time as the meeting of the Federation of European Neurosciences. The general idea is to create an informal environment for discussion.

"It has been amazing to see how much you can learn when young researchers from different disciplines, like biologists, physicists and psychologists, are together in the same room helping each other solve practical and theoretical problems. We can also ask the academic questions that we might otherwise be afraid to ask for fear of looking ignorant in front of our supervisors," she adds.

The SpaceBrain project has already made considerable progress, thanks to both its managers and younger noisy students. Langston and her colleagues at KI/CBM and University College London have a come a long way in answering an important question: Are the spatial representations and navigational skills in rats an innately defined property in the brain, or are they something that is learned from experience? "We have proven that there is a genetically predefined system for spatial representation in the rat brain, but the system is not as fully formed as it is in adults," she says. The details of Langston's findings will be available when the results from the project are published in a scientific journal.

Starting her own lab

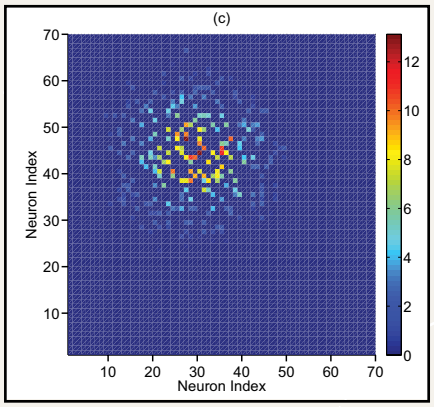
Rosamund Langston studied at the University of Edinburgh and came to Trondheim as a postdoctoral fellow in 2007 to study spatial representation in the brains of rats. In February 2010, she went back to the UK to start her own brain research lab at the University of Dundee. "Trondheim has been an amazing lab to work in, and I certainly want to continue collaborating with the Mosers," she says.

The SpaceBrain project participants are: KI/CBM in Trondheim (Norway), Axona Ltd (Great Britain), The International School for Advanced Studies (Italy), University College London (Great Britain), University of Zürich (Switzerland), Universitätsklinikum Heidelberg (Germany) and the Weizmann Institute (Israel).

The search engine, the cell and the brain

The individual who strolls a bustling city street, a blood cell that detects an invader, and a search engine on the Internet share many similar challenges: There is a vast amount of information and excessive environmental signals, but most of them are of little interest. How are these systems able to operate in the face of this constant flow of complex signals and information?

"This is a very general question. What are the efficient methods for analysing and processing massive amounts of incoming information from a noisy environment?" asks physicist Yasser Roudi. He is coming to the KI/CBM in 2010 to establish a research group to study the issue from a theoretical point of view, using methods from the worlds of mathematics and physics.
An Internet search engine, the brain and the immune cell detect the information that is useful for them and discover structure in the flood of information they receive. They do this using built-in mechanisms and, very importantly, their past experiences and memory. What they see depends upon what they're interested in and what has proven useful in the past. If you are out shopping, you'll probably look for shop windows and sales posters, but if you're driving a car you may be looking for a parking space.



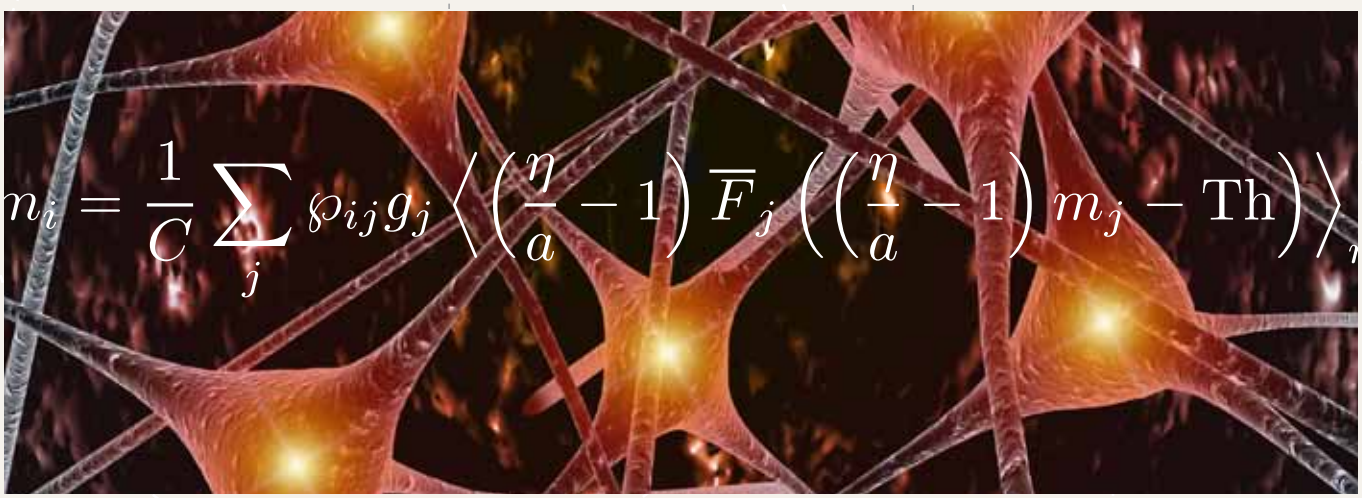
The figure shows the activity in a simulated network, where blue is less active and red is highly active. The position of the patch of activity on the network shows the position of an object in the visual scene, and the fine pattern of activity inside the patch shows which object is present. (Illustration: Y. Roudi)

Expanding research frontiers

When KI/CBM was established in 2002, the focus was the study of the biological roots of memory by detecting and analysing electrical signals in the brain. The center has since expanded its activities to include the study of molecular biology. Roudi's new research group represents the further expansion of the institute's efforts to include theoretical aspects of learning and memory. "We will focus on two issues in this new research. One problem is: What algorithms can be efficiently used to infer knowledge about the structures that exist in the environment? The other one is how they are implemented in biological systems." In most cases, the algorithms and their implementation involves the complex interactions of many elements, e.g. many neurons in the brain. This is where physics comes to the scene: it provides the tools necessary for studying such complex systems.

Among the best

Yasser Roudi is originally from Iran and received his PhD from the International School for Advanced Studies (SISSA) in Trieste in 2005. After 3 years as a Senior Research Fellow at UCL, London, he joined the Nordic Institute for Theoretical Physics (NORDITA) in Stockholm in 2008. He is now looking forward to establishing himself in Trondheim. "The Kavli Institute is among the best in the world in its field, and I will maintain contact with NORDITA. Thus, I have everything I need for my work with computational neuroscience. In this work, there is a great advantage to having access to the experimental data from the Kavli Institute. Even theoretical work is ultimately tied to experimental research in the sense that the results are only useful if they can be tested through experiments", Roudi says.



The brain contains billions of neurons, each connected to thousands of other neurons. (Illustration: Shutterstock)

Brain research in the media

The Norwegian mass media have discovered that researchers at KI / CBM are at the forefront in neuroscience and brain research, and that "most people" are interested in the topic. During 2009, the institute was featured in a number of popular features on the radio and television, and in newspapers and online media.

May-Britt and Edvard Moser as talkshow participants. (Facsimile from nrk.no)

On March 20, May-Britt and Edvard Moser were guests on Norway's most watched television programme, a talk show named after the programme's host, Anne Grosvold. The Mosers were guests along with two national icons, the Trøndelag rock king Åge Aleksandersen, who has sold more than 1.5 million albums in Norway, and wilderness explorer Lars Monsen, who has written 14 books and produced several television shows about his expeditions into the wilderness of Alaska, Canada and northern Scandinavia.
The talk show segment that included the Mosers was a part of the annual global event called Brain Awareness Week, which has as its goal to increase the general public's understanding of the progress that has been made in brain research. The programme had 915 000 viewers, which is a substantial number in a country with 4.8 million inhabitants.


HUKOMMELSE

May-Britt Moser was interviewed about 'digital Alzheimer's'. (Facsimile from VG)

Broad media coverage

Norway's largest newspaper, VG, featured an interview with May-Britt Moser on August 14, in a four-page story that highlighted the theme "Digital Alzheimer's," a condition that could be used to describe busy people who store phone numbers and appointments digitally instead of remembering this information themselves. "If you compare, people do know much more today than before the Internet," Moser said in an effort to comfort people.

The institute's most important scientific publications in 2009 are discussed in separate articles in this Annual Report, and many of them triggered popular news articles.
Postdoctoral fellow Laura Colgin's publication in Nature in November was discussed in a whole series of articles in Adresseavisen, the regional newspaper for mid-Norway. The newspaper began early in the week with an article that explained that Colgin was on the verge of publishing important news, which was then followed in the middle of the week by a two-page article that described Colgin's research. The series finished with a summary article on Friday.
Colgin's article in Nature was also featured on the Norwegian National Broadcasting Corporation's (NRK) national and regional TV news broadcasts, in NRK radio's popular science magazine, and on the online research news portal Forskning.no. The latter also presented postdoctoral fellow Dori Derdikman's research results in a separate article on November 19, 2009. Research at KI / CBM was also a main theme on Newton, NRK TV's youth-oriented magazine about science and technology, on December 13, 2009. In addition, research findings from the centre have been featured in several international media during the year, including the online publications Sciencemag.org, Science Daily.com, eBioNews, AlphaGalileo.org, Physorg.com, The Medical News (news-medical.net) and news service (CORDISNews) on the European Commission's research and development portal Cordis.


Adresseavisen

Blodsugende, men langdrygt

Vurderer massivt lakseslakt

Trondheims-forskere med sensasjonell oppdagelse:

Slik sorterer hjernen vår

Skyhøy festfaktor

Væpnet aksjon etter vold på Vikåsen

Tenåring fikk hjertestans på fotballbanen

Ukens Go'helg-produkt

Laura Colgin's Nature paper was the cover story of Adresseavisen. (Facsimile from Adresseavisen)

Who's who at KI/CBM

CBM Board

Jan Morten Dyrstad
Associate Professor
Dean, Faculty of Social Science and Technology Management, NTNU (chair)

Stig Slørdahl
Professor
Dean, Faculty of Medicine
NTNU

Bjørn Hafskjold
Dean
Faculty of Natural Sciences and Technology
NTNU

Tore O. Sandvik
County Council Chair
Sør-Trøndelag County

Kavli Board

Kari Melby
Prorector
NTNU (chair)

Stig Slørdahl
Professor
Dean, Faculty of Medicine
NTNU

May-Britt Moser
Professor and Co-Director
KI/CBM
NTNU

Menno Witter
Professor
KI/CBM
NTNU

The Advisory Board

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Professor
University of California, San Diego, USA (chair)

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

Erin Schuman
Professor
Max Planck Institute for Brain Research, Frankfurt, Germany

Earl Miller
Professor
Massachusetts Institute of Technology, Boston, USA

Faculty

Edvard I Moser
Professor and Director

May-Britt Moser
Professor and Co-Director

Menno P. Witter
Professor

Ayumu Tashiro
Group leader

Yasser Roudi
Group leader (2010)

Visiting professors

Carol Barnes
Professor
University of Arizona, USA

Bruce McNaughton
Professor
University of Lethbridge, Canada

Randolf Menzel
Professor
Free University of Berlin, Germany

Richard G. M. Morris
Professor
University of Edinburgh, UK

Ole Paulsen
Professor
University of Cambridge, UK

Alessandro Treves
Professor
International School for Advanced Studies, Italy

Mayank Mehta
Associate Professor
UCLA, USA

Administration

Iuliana Hussein
Head of office

Hege J. Tunstad
Communication Officer

Linda Katalin Veres
Executive Officer

Research scientists

Laura Colgin
Research Scientist
Moser group

Karel Jezek
Research Scientist
Moser group

Dori Derdikman
Research Scientist
Moser group

Jonathan Whitlock
Research Scientist
Moser group

Sheng-Jia Zhang
Research Scientist
Moser group

Natalia Kononenko
Post-doc (until 2009)
Witter group

Rosamund Langston
Post-doc
Moser group

Tiffany Cautier
Post-doc
Moser group

Jay Couey
Post-doc
Witter group

Emilio Kropff
Post-doc
Moser group

Noriko Kogenezawa
Post-doc
Witter group

Kally O'Reilly
Post-doc
Witter group

Jing Ye
Post-doc
Moser group

Hideki Kondo
Post-doc
Witter group

Lisa Marie Giocomo
Post-doc
Moser group

Hiroshi Ito
Post-doc
Moser group

Trygve Solstad
Post-doc
Moser group

Kei Igarashi
Post-doc
Moser group

Masato Uemura
Post-doc
Tashiro group

Rafal Czajkowski
Post-doc
Witter group

Takuma Kitanishi
Post-doc
Tashiro group

Who's who at KI/CBM

Graduate students

Cathrin Barbara Canto
PhD student
Witter group

Kirsten Brun Kjelstrup
PhD student
Moser group

Tora Bonnevie
Phd student
Moser group

Albert Tsao
Phd student
Moser group

Espen Joakim Henriksen
PhD student
Moser group

Charlotte Boccara
PhD student
Moser group

Grethe Olsen
PhD student
Witter group

Tor Kirksola
PhD student
Moser group

Hanne Stensland
PhD student
Moser group

Chenglin Miao
PhD student
Moser group

Li Lu
PhD student
Moser group

Charlotte Boermeester Alme
PhD student
Moser group

Mathias Lysholt Mathiasen
PhD student
Witter group

Ingrid Heggland
PhD student
Witter group

Project students

Jørgen Sugar
Witter group

Alessandro Luchetti
Tashiro group

Kristian Frøland
Moser group

Tale Litleré Bjerknes
Moser group

Master's students

Henriette Folkvard Hestvaag
Master (until 2009)
Moser group

Gry Fluge Vindedal
Master (until 2009)
Tashiro group

Nenitha Charlotte Dagslott
Master
Tashiro group

Ida Aasebø
Master
Tashiro group

Stefan Mattias Adriaan Blankvoort
Master
Tashiro group

Ingvild Ulsaker Kruge
Master
Witter group

Julia Dawitz
Master (until 2009)
Witter group

Asgeir Kobro-Flatmoen
Master
Witter group

Christian Gjeraker
Master
Witter group

Fan Zheng
Master
Moser group

William Espen Windsor
Master
Witter group

Øystein Rød Brekk
Master
Witter group

Sobia Islam
Master
Witter group

Technical team

Ingvild Hammer
Infrastructure
Support group

Haagen Waade
Computers, networks
Support group

Tommy Åsmul
Animal care
Support group

Kyrre Haugen
Histology
Moser group

Klaus Jenssen
Electronics
Moser group

Raymond Skjerpeng
Programming
Moser group

Ann Mari Amundsgård
Histology, hyperdrives
Moser group

Ellen Marie Husby
Anatomy
Witter group

Ragnhild Gisetstad
Anatomy
Witter group

Alice Burøy
Molecular biology
Moser group

Endre Kråkvik
Molecular biology, hyperdrives
Moser group

Bruno Monterotti
Anatomy
Witter group

Teruyo Tashiro
Neurogenesis
Tashiro group

Paulo Girão
Animal care
Moser group

Naomi Kitanishi
Technician
Tashiro group

Associated members

Gerit Pfuhl
PhD student

Hanna Mustaparta
Professor NTNU, (Biology),
Norway

Hanne Lehn
PhD student

Robert Biegler
Associate Professor
NTNU (Psychology),
Norway

On sabbatical leave

Marianne Fyhn
Research Scientist (now UCSF)
Moser group

Torkel Hafting Fyhn
Research Scientist (now UCSF)
Moser group

Annual accounts

Income

Transferred from 2008[1]	6 041 000
Research Council of Norway: Centre of Excellence	10 000 000
Research Council of Norway: other, including FUGE[2a]	11 691 000
International	
(EU 7th Framework Programme, Fondation Bettencourt-Schueller, James McDonnell Foundation)[2b]	7 693 911
Kavli Foundation and support from host institution and ministry	8 888 923
Return of overhead	12 076 132
Total income	50 349 966

Expenses

Net personnel costs	27 305 177
Overhead	14 327 527
Scientific equipment	996 646
Other expenses	655 483
Operational expenses	14 507 549
Total expenses	57 792 382
Transferred to 2010	-1 401 416

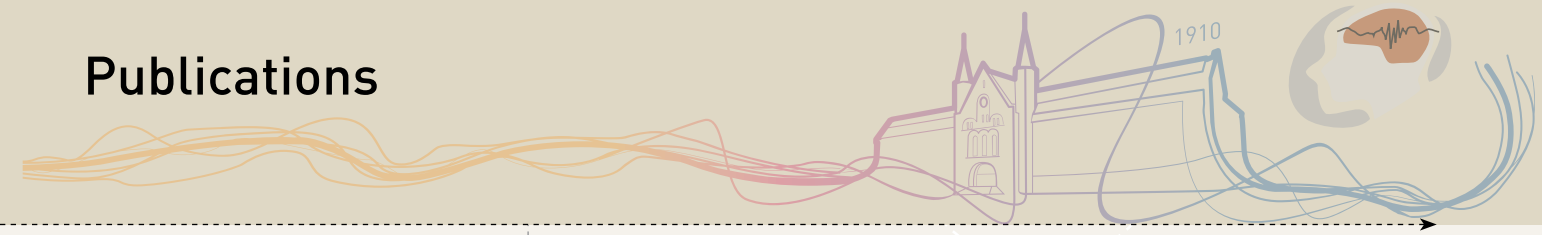
Amounts in NOK

1.
A correction has been made to the centre's financial statements for the 2007and 2008 fiscal years. The reasons for the corrections are:
In 2007, one project was missing for which NOK 4.8 million in expenses were charged for that year. There was a difference in the practices used to expense overhead and expenses charged to the incorrect account were not included.
In 2008 incorrect expenses were charged to a project and expenses that were charged to the centre without a cost code were not included. The balance as of 31.12.2008 has been corrected.

2.a.
Research Council of Norway income is considered grant income for 2009.

2b.
A lag is expected in the income from the EU where a project year is considered to be 18 months. Income is expected in 2010.

Publications



Research Articles

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.

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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.

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Couey, J.J., Moser, E., Witter, M.P. (2009). Development of the entorhinal cortex layer ii stellate cell network. Society for Neuroscience Abstracts 35, 101.1.

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Canto, C.B., Mansvelder, H.D., Witter, M.P. (2009). Development of direct projections from presubiculum to identified neurons in medial entorhinal cortex. Society for Neuroscience Abstracts 35, 101.6.

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Olsen, G.M., Witter, M.P. (2009). Connections between the posterior parietal cortex and the hippocampal-parahippocampal system. Society for Neuroscience Abstracts 35, 101.12.

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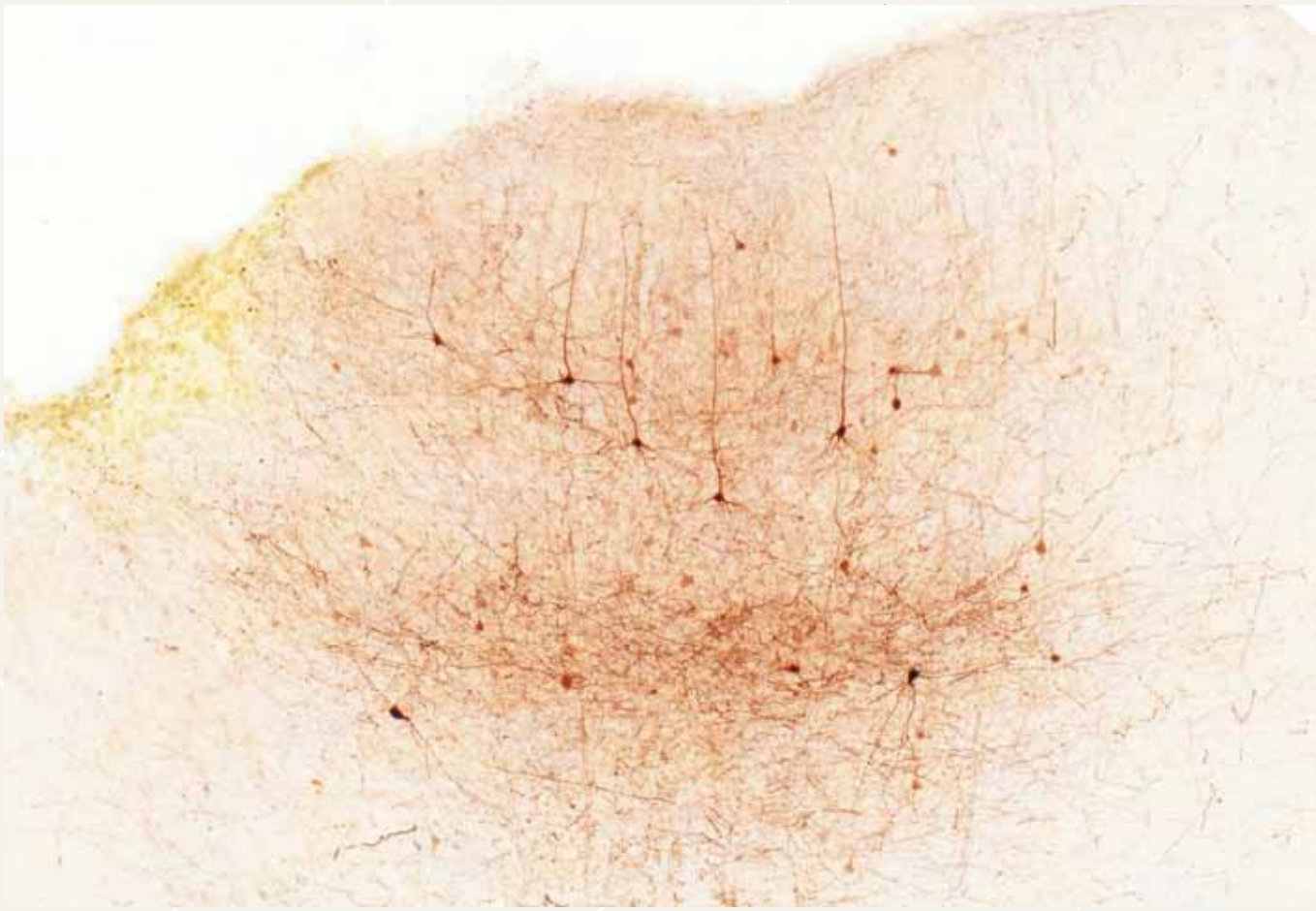
The Biology of Memory and Systems Neuroscience

The normal human brain is made up of about 100 billion nerve cells (neurons). Each nerve cell can have an average of approximately 10,000 to 20,000 points of contact with other nerve cells. These contact points are called synapses, which is where the storage of memories takes place.

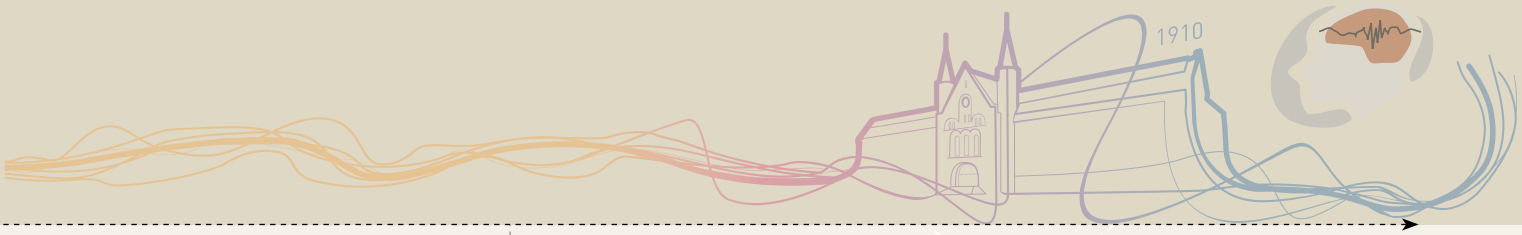
If one nerve cell in the brain wants to send information to another nerve cell, it generates an electrical signal that is sent through a nerve fibre to a synapse. The signal consists of one or more action potentials, which can have a value of "0" or "1". The action potential does not actually pass directly through the synapse, but instead results in the release of small signalling substances from the nerve terminals that activate or deactivate the next nerve cell. The next neuron can then either send a new electrical signal to a second nerve cell or not, according to the situation at hand.

Researchers at KI / CBM explore the brain's functioning by detecting and analysing the electrical signals in the brain, primarily in the regions of the brain called the hippocampus and entorhinal cortex. The hippocampus is an older part of the cerebral cortex and has a central role in the functioning of human and animal memory, while the entorhinal cortex contains grid cells, border cells and direction cells that together give the brain the ability to make highly advanced maps.

Since the centre's inception in 2002, KI / CBM researchers have used laboratory rats as study animals. The rats run around in boxes and corridors in search of food and have had very thin electrodes inserted into their brains, which enables researchers to detect brain activity. 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. In 2009, KI / CBM 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.



Labeled neurons in the posterior parietal cortex of the rat, filled with biotinylated dextran amine. Multiple neurons are labeled in the 3rd and 5th layer of the cortex, showing clear visualization of dendrites and axons. (courtesy of Grethe Mari Olsen and Menno Witter).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Illustration, frontpage: The image shows time-varying slow and fast gamma rhythms recorded simultaneously from gradually increasing depths in the hippocampus of a freely moving rat. Laura Colgin, KI/CBM

Annual Report for KI/CBM 2009

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