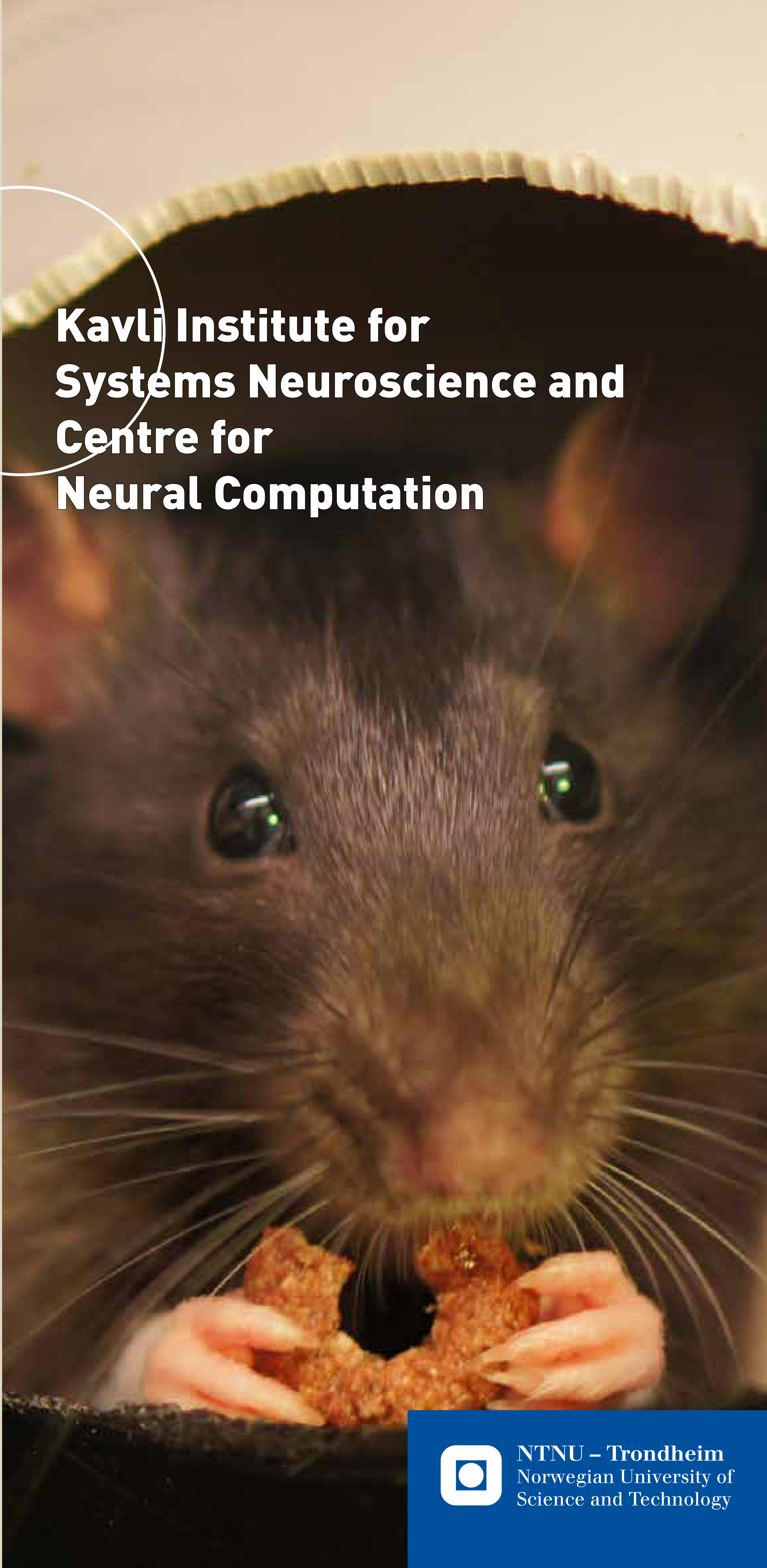
Kavli Institute for Systems Neuroscience and Centre for Neural Computation

Annual Report 2013



Norwegian Centre of Excellence

NTNU – Trondheim
Norwegian University of Science and Technology

The people at KI/CNC March 2014. (Photo: Thor Nielsen)

Facts about KI /CNC

May-Britt and Edvard Moser established the Laboratory for Memory Studies at the Norwegian University of Science and Technology (NTNU) in Trondheim in 1996.

In 2002, a ten-year-long grant from the Research Council of Norway enabled the laboratory to expand to become a Centre of Excellence (CoE). The new institution was named the Centre for the Biology of Memory (CBM), with Edvard Moser as director and May-Britt Moser as co-director.

In 2007, the Norwegian-American physicist, businessman, billionaire and philanthropist Fred Kavli selected the CBM as one of 15 prestigious Kavli Institutes worldwide. The centre accordingly changed its name to the Kavli Institute for Systems Neuroscience and the Centre for the Biology of Memory (KI/CBM).

The first CoE period expired in 2012, but the Research Council of Norway decided at the same time that the Trondheim research group should be awarded new funding. At the end of 2012-2013 the centre changed its name to the Kavli Institute for Systems Neuroscience and the Centre for Neural Computation (KI/CNC). The Kavli Institute is led by Edvard Moser, while the CNC is led by May-Britt Moser. KI/CNC is part of the Norwegian Brain Centre at NTNU, and contains perhaps the largest infrastructure for systems neurophysiology in the world.

The centre's basic research approach has always been to understand the sense of location as a model for developing a deeper understanding of memory and the workings of the brain. The sense of location is closely linked to the hippocampus, where place cells were discovered in 1971. In 2005, the centre discovered grid cells in the adjacent entorhinal cortex. Since 2005, KI/CNC researchers have uncovered the elements of an entire entorhinal brain circuit devoted to the encoding of space.

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From research group to institute

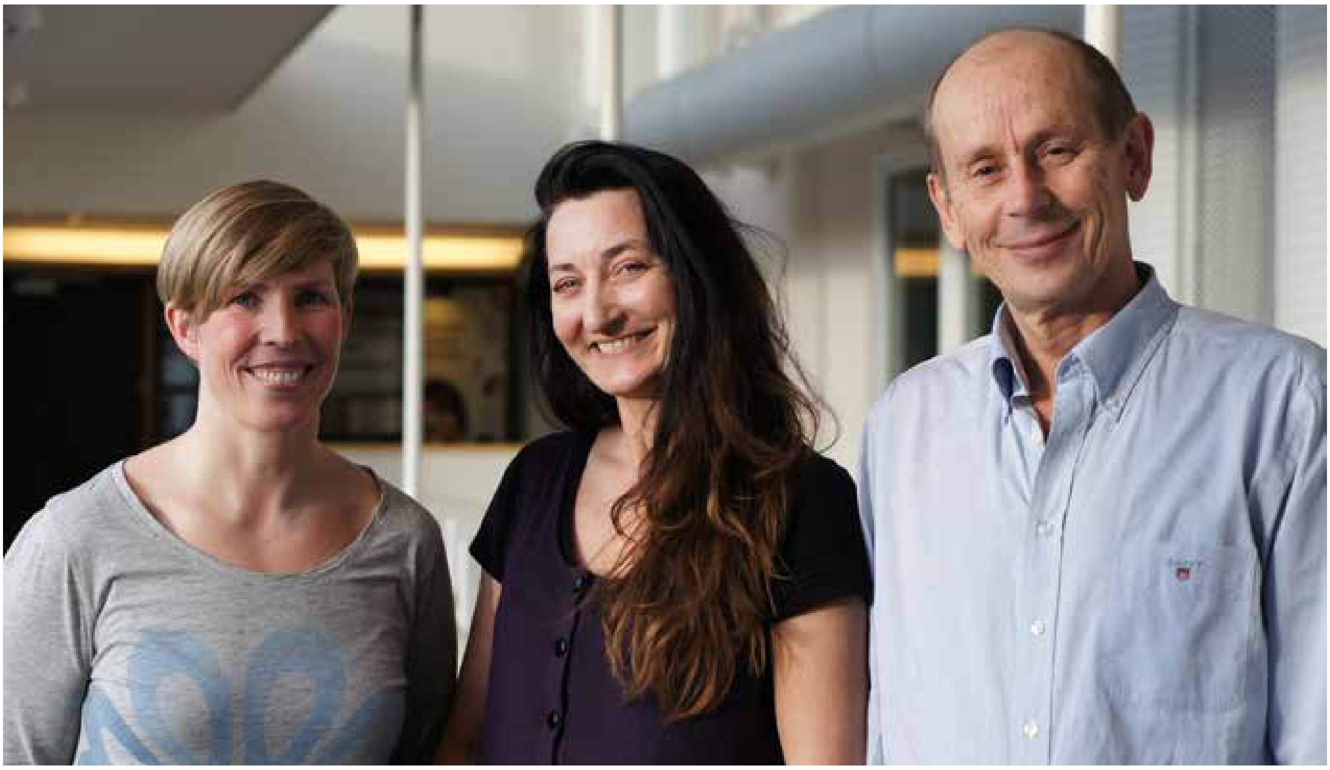
When the Centre for the Biology of Memory (CBM) was established in 2002, it consisted of Professors May-Britt and Edvard Moser and their research group of approximately 10 people, including PhD candidates and technical staff. During the next 12 years of growth, an increasing percentage of the staff has been postdoctoral fellows who come from all over the world to learn about grid cells and neural circuits in the hippocampus and entorhinal cortex.

With its recognition as a Kavli Institute, the Centre was able to recruit Professor Menno Witter from Amsterdam in 2007 and Professor Yasser Roudi from Stockholm in 2010. Most recently, Professor Cliff Kentros was headhunted from the University of Oregon in 2012.

The Centre is now no longer a single research group, but an institute composed of five groups. Nearly 100 people, including students, researchers and staff, work together towards the common goal of understanding neural computation in the cortex. The centre is currently recruiting another faculty member in systems and circuit neuroscience.

Passion, collaboration and ever-larger toolboxes

Professor May-Britt Moser has an ambitious vision and a plan. "We are eager to understand the basic mechanisms that give rise to the brain's mental functions. We are reaching for this goal with the help of passionate, eager researchers, aided by a rich variety of scientific tools and excellent technicians and administrative staff," she says.



Head of Office Nora Gullbekkhei, Professor May- Britt Moser and Senior Adviser Tor Grønbech ensure that a passionate staff can do their best. (Photo: Haagen Waade, KI/CNC)

The mammalian brain is an extremely complex organ with billions of neurons that continually exchange information with each other. Neuroscientists know quite a lot about how sight is processed in one part of the cortex, how auditory stimuli are processed in another part of the cortex, and so on. In contrast, the cellular mechanisms and computations underlying cognitive or mental functions were thought to be unreachable.

But not anymore. The scientists at the Kavli Institute for Systems Neuroscience and Centre for Neural Computation (KI/CNC) in Trondheim are well on their way towards unravelling how the brain generates cognitive functions from its network of connections between billions of neurons. They have managed this by focusing on how the brain handles navigation and memory, which are cognitive tasks that offer neuroscientists a big advantage in understanding the brain.

The internal computations of the brain

"Navigation and memory are computed mainly in the hippocampus and the entorhinal cortex, which are the two brain areas that are farthest from the pure sensory functions. This allows us to use them to study the internal computations of the brain," explains Professor Moser, director of the CNC.

May-Britt is married to Professor Edvard Moser, who leads the KI section of the institute. The couple and their colleagues in Trondheim confirmed the validity of their approach in 2005, when they discovered grid cells in the entorhinal cortex. When rats – and other mammals – navigate in an environment, the grid cells in the brain react and send electrical signals at spatial points that combine to form a triangular, Chinese-checkers-like grid.

"The grid pattern is not extracted from the outside world but is generated by the brain itself. Thus, grid cells have put us on the track of neural codes for cognitive functions," the Mosers say.

Attracting the best young researchers

When the KI/CNC was established in 2002 it was quite small, but it has now grown to include more than 100 employees, including some of the best young researchers in the world. What is the reason for this success?

"Our long-term funding from the Research Council of Norway and the Kavli Foundation have been very helpful. Among other things, the funding makes it possible for us to spend more time on difficult problems when we encounter them, instead of feeling pushed to publish a scientific paper as soon as we can," May-Britt Moser says.

"But money is not enough!" she adds. "We also need passionate scientists who have the ability to focus, who feel the joy of asking and addressing questions, who have a rich variety of tools in their toolboxes, and who are highly talented in working with others. Neuroscience is right in the midst of a technological revolution that provides us with new methods and approaches every day, and it has become impossible for one or a few scientists to master everything. That's why we now have five research groups with very different areas of expertise. That's also why we spend a lot of time and effort in stimulating and facilitating cooperation between the groups."

The institute in Trondheim has formalized several important collaboration forums, in addition to the casual meet-ups around the coffee machine. The research groups hold their own meetings every Monday, inviting researchers from other groups to participate. There are also weekly meetings between the group leaders and the managers of the institute, a 'journal club' where recently published articles are discussed, and a 'd club', where projects are briefly presented but long debated. The meetings are heavily fuelled by pizza, coffee and enthusiasm.

The Mosers and their colleagues also participate actively in different collaborative efforts with other international research groups. One result that demonstrates the value of cooperation is the publication of two papers simultaneously in Nature Neuroscience in January 2013 (see pages 4-5).

"The articles were the result of several groups sharing their specific science questions and data. The cooperation made it possible to solve a puzzle we have been pondering for eight years," May-Britt Moser says.

Starry eyes

Over the years, May-Britt Moser has been involved in hiring many young scientists. "I tend to look for people who have 'stars in their eyes'," she says.

"Or let me put it another way: I'm looking for people who are smart and who also have a passion for research. I believe that science is a lifestyle, and if you are not passionate about it, it is hard to go very far. But it is quite hard to walk around with stars in your eyes all the time, so we also have to take good care of our people," she says.

"We have hired a talented senior consultant with a background in both organizational psychology and therapy, who will spend a great deal of time helping to develop a good working environment and good working relationships. The centre should never become so large that it becomes difficult for employees to be seen and connect emotionally to each other."

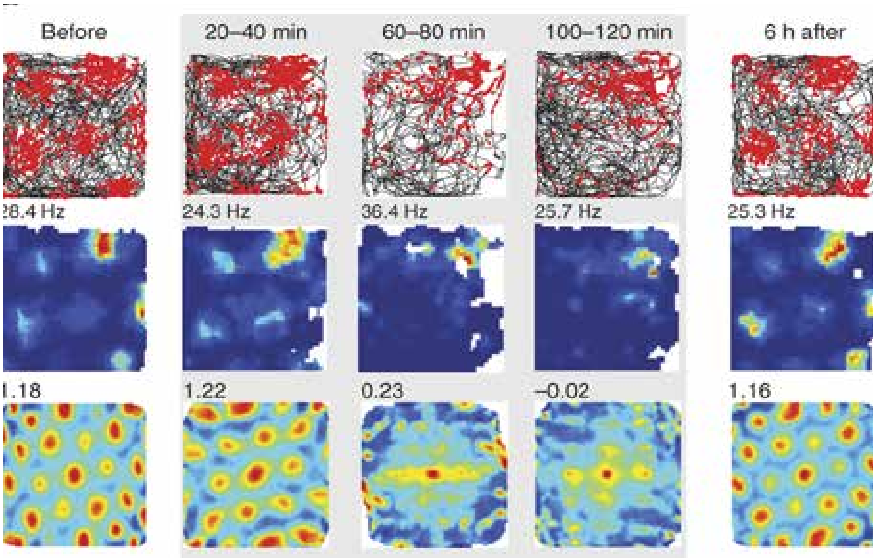
I have a dream

The centre has also hired a new head of office in 2013, who does an outstanding job of keeping track of everything, Moser says. The technicians are also excellent in every way, she adds, noting that if a research centre is going to work well, it must have the best people for every single job.

"I have a dream that our centre will become a national and international showcase, at the forefront of technological developments and delivering groundbreaking research. We'll do this while also ensuring we have the best possible environment for both animals and humans. I actually feel that we are well on our way towards these goals," says May-Britt Moser, who is obviously both proud and happy about the centre and her staff – because she always has stars in her eyes when she talks about them.

Combined approaches reveal the secrets of grid cell networks

It is generally a good idea to keep quiet if you want to keep a secret, but that won't work when neuroscientists are around. Instead, silencing the hippocampus in a rat's brain was exactly what it took to reveal what makes neurons in the entorhinal cortex act like grid cells.



When the input from the hippocampus was silenced, the entorhinal cortex stopped producing grid cell patterns. Illustration: KI/CNC

In January 2013, 16 scientists from three different research groups at the KI/CNC published two articles simultaneously in Nature Neuroscience. The articles described two findings: that a specific property of the network between stellate cells in the medial entorhinal cortex is able to generate grid-cell firing patterns, and that grid cells won't work unless they receive excitatory signals from neurons in the hippocampus.

The entorhinal cortex is the main interface between the hippocampus and the neocortex, and consists of a thin sheet of brain cells that covers a large area of the surface of the forebrain. In 2005, Professors May-Britt and Edvard Moser and three of their students made one of the most important discoveries in neuroscience over the last decade, namely that the entorhinal cortex in rats contains specialized cells that create a grid which allows the brain to make a generalized map of the surroundings. These grid cells were later found in mice, bats, monkeys, and humans, and are likely to exist in other animals.

The discovery meant in practice that researchers had gained an insight into how the brain's cognitive processes work, such as making decisions on the basis of sensory input. Any new information about the inner workings of the hippocampus and the entorhinal cortex is also important because a number of devastating brain diseases have their roots or links to this area of the brain – both in rats and in humans.

Stellate cells

Stellate cells are neurons with several dendrites radiating from the cell body, giving them a star shape.

The hippocampus plays important roles in the consolidation of information from short-term memory to long-term memory and spatial navigation. The entorhinal cortex and the hippocampus together play an important role in declarative memories, including spatial memories.

Alzheimer's often starts here

Prior to the publications in Nature Neuroscience, the researchers had studied grid cells in layer 2 of the entorhinal cortex.

"Layer 2 is only a couple of cells thick and is interesting because the dreaded Alzheimer's disease starts here in many human patients. We also know that temporal lobe epilepsy starts in the neighbouring layer 3, and the whole of the entorhinal cortex develops pathology in people with Parkinson's disease. I sincerely hope that our research might one day contribute to developing a cure for Alzheimer's and other brain diseases," says Professor Menno Witter. Witter is the leader of the Kavli Institute research group that is studying the wiring of neural networks and their function, and was an author of one of the articles in Nature Neuroscience.

Grid cells become head direction cells

When the Trondheim researchers discovered grid cells in 2005, they quickly began to wonder what kind of information the cells used to generate their special grid. An important contribution to answering this question came in 2013, after researcher Tora Bonnevie and her colleagues in the Kavli Institute's Moser group had conducted an experiment where they knocked out activity in the hippocampus.

"That is how we discovered that the grid cells in the entorhinal cortex stopped functioning, and became head direction cells instead. We had the first part of this data as early as 2006, but the results were unexpected and we couldn't explain what had happened. So we decided to wait to publish until we understood the data better," said Bonnevie.

Three thoughts fall into place

While Bonnevie was pondering the significance of her own finding and working on other projects, a postdoc in Witter's research group, Jonathan Jay Couey, was conducting in vitro experiments to figure out the connections between stellate cells in the entorhinal cortex. Some of these stellate cells are grid cells, and Couey realized that none of these cells were talking directly to each other.

"This was a great surprise! The only neuron a stellate cell in the entorhinal cortex wants to talk to is the neuron between each of them, and that interneuron is inhibitory. Think of it like this: Imagine that there was a third person between you and me when we were talking to each other. Every time I said something that might make you excited, this third person would say that what I said was not interesting. This is how the network between stellate cells in the entorhinal cortex works, and the result struck us as very strange," explains Witter.

The breakthrough came when Bonnevie, Edvard and May-Britt Moser, Couey and Witter discussed their respective results with group leader Yasser Roudi, who uses statistics and mathematical modelling to study the connections in the brain. Roudi immediately became enthusiastic about Bonnevie's findings, because based on Couey's data he had developed a model showing that an inhibitory network would be able to generate a grid network.

The only thing such a network would need was an excitatory drive to get it going, and Bonnevie had shown in vivo that exactly this kind of drive was coming from the hippocampus. Roudi's model even predicted that the grid cells would become directional when the input from the hippocampus was silenced.

Tora Bonnevie, lead author of the paper that showed the importance of hippocampal excitatory drive for grid-cell firing in the entorhinal cortex

"We were very happy when all of these pieces fell into place, and so we sat right down and began to write the articles for Nature Neuroscience. This story is a good example of the benefits of cooperation between researchers with very different 'toolboxes'. This story also demonstrates that there are real benefits from taking the time you need to better understand a complicated finding," says Witter.

Answers generate more questions

The researchers in Trondheim are still not completely satisfied.

"In science, every answer generates more questions. Tora Bonnevie managed to silence the input from hippocampus to the entorhinal cortex and produced impressive results. But there are also other inputs to the entorhinal cortex, so now we are planning to silence them and see what happens," Witter says.

Bonnevie has now completed her doctorate and is beginning a postdoc at St. Olavs Hospital in Trondheim. She will make use of data collected at the hospital during surgery to treat brain diseases such as Parkinson's disease with deep brain stimulation.

"I will look at the signals that we have to record during these operations anyway, and will use them to learn more about the human brain," says Bonnevie.

She points out an important motivation for studying the brain in rats: Rats are intelligent animals, and much of what scientists learn by studying rat brains will also be valid for human brains.

Clever virus technique illuminates place cell network

The hippocampus in the rat brain contains a special type of neuron that plays the same role as the red mark on a tourist map – these neurons say, "You are here." Researchers at the KI/CNC showed in 2013 that these place cells listen to information from two other types of cells as they determine location.

Group leader Sheng-Jia Zhang and researcher Jing Ye showed that the place cells use information from two different types of neurons in the entorhinal cortex. (Photo: Haagen Waade, KI/CNC)

The British neuroscientist John O'Keefe discovered place cells in the hippocampus of rats more than four decades ago, in 1971. A small area in the hippocampus of the mammalian brain contains neurons that send an electrical signal each time the animal passes specific points in the environment, but until now the mechanism that enables place cells to do this has remained an unanswered question. The answer came in April 2013 in an article in Science, written by a group of researchers at the Kavli Institute in Trondheim. Group leader Sheng-Jia Zhang was the first author of the article.

"We have shown that place cells use information from at least two different types of neurons in the entorhinal cortex area outside the hippocampus when making this calculation," says Edvard Moser, who directs the Kavli Institute.

Signals at the foundation of cognitive processes

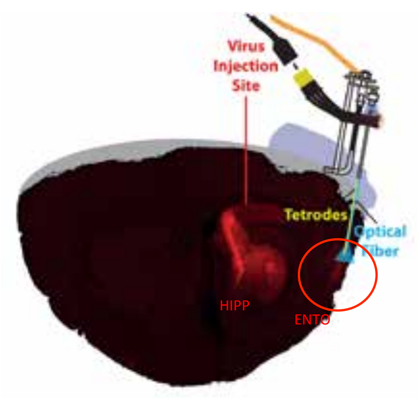
Place cells and other neurons in the brain generally consist of a central cell body and a large number of thin branches or axons, which the neurons use to send electrical signals to each other. The grape-sized rat brain contains about 50 million neurons, and each neuron sends axons to a few thousand other neurons. If you can prove that a specific neuron sends an axon to another specific neuron, you also know that the first neuron can send electrical signals and thus information to the second neuron.

These signals between neurons underlie both the simplest and the most complex processes in the brain, which is why scientists are very interested in studying the network formed by the 'information channels' between neurons in the brain. Researchers at the Kavli Institute study the connections between neurons around the hippocampus because this part of the brain contains one of the cognitive processes that is easiest to understand: the ability to navigate and find your way.

Neurons that navigate

The Trondheim researchers discovered in 2005 that the entorhinal cortex, close to the hippocampus, contains cells that draw a grid over the environment and create a generalized map in the brain. Later, they also identified entorhinal cells that send signals whenever the rat approaches a wall or another kind of boundary, and other entorhinal cells that send signals every time the rat's head points in a certain direction. The rat brain uses these three cell types actively when the animal navigates in the environment.

When the Mosers and their colleagues, including first authors Sheng-Jia Zhang and Jing Ye, initiated the experiment that led to the article in Science, they knew that neurons in the entorhinal cortex send axons to the hippocampus where place cells are located. But they did not know whether it was grid cells, head direction cells or border cells, or some combination of the three that sent these axons.



Section of rat brain. The image shows cells in the entorhinal cortex that are infected by a virus that has been inserted into the hippocampus. The virus carries the gene for a green fluorescent dye that makes it possible to see the infected cells. (Photo: Kavli Institute)

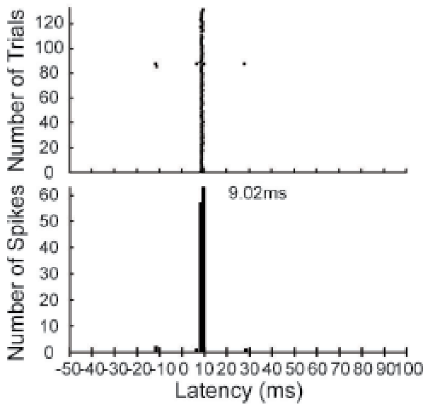
"It was unclear whether place cells in the hippocampus used information from all three cell types. We have wondered about this for years, and I'm glad that we finally managed to solve the puzzle," says Professor Moser.

A deep dive in the scientific toolbox

On pages 2 and 3, May-Britt Moser talks about the need for a very large 'toolbox' to conduct modern neuroscience research. Zhang and colleagues used a virus that is considered to be 'friendly', because it cannot make copies of itself or do damage. The only function that the virus has is that it can carry a foreign gene into a neuron and make sure the neuron sees the gene as its own. The gene enables the neuron to begin producing a protein for which the gene provides the 'recipe'. This in turn enables researchers to change the neuron's properties.

In this case, the Trondheim researchers used the friendly virus to transport a gene that originally comes from the algae world. Algae are photosynthetic and consequently have separate receptors that respond to light. When you put the gene for this kind of photoreceptor into a virus, which is then used to infect a neuron, the neuron develops a light-sensitive receptor. Researchers also surgically inserted optical fibres into the rat brain to transmit light to the cells in the hippocampus and entorhinal cortex. They also implanted thin microelectrodes to record the electrical signals from neurons in the area.

The virus technique gave the researchers the ability to examine which neurons in the entorhinal cortex send axons to place cells in the hippocampus. There are so many axons in this area that it is impossible to follow every single one visually, as you might be able to do in a serving of cooked spaghetti. Instead, scientists wanted to infect axons associated with the place cells in the hippocampus, and then let the axons carry the virus slowly back to their associated cell bodies in the entorhinal cortex.



Hippocampus-projecting entorhinal cells infected with ChR2 (rAAV-ChR2-FLAG) were identified as those that fired directly, at minimum latency in response to photostimulation.

After the virus had had a chance to work for a couple of weeks, the researchers began to turn lights on and off in the rat brains. They did this more than ten thousand times while microelectrodes recorded new light-sensitive neurons. That enabled the researchers to see that the grid cells and border cells in the entorhinal cortex had developed photosensitive receptors, and thus they knew that these very cells sent axons to place cells in the hippocampus.

A gold mine for neuroscientists

Edvard Moser considers the hippocampus and entorhinal cortex a gold mine for neuroscientists, because the sites contain signals that are easy to recognize. If scientists were instead to try to record electrical signals between neurons in many other areas of the cortex, they would just see random signals.

"But in the hippocampus and entorhinal cortex, we see signals that are almost as easy to understand as the ones we can find in the visual cortex, for example. There is nothing in the sensory apparatus that is similar to the grid pattern that is created in the entorhinal cortex, so we can be reasonably sure that this is something the brain has designed all by itself. That makes it a good starting point for understanding how computations are made in the rat brain - and in the brains of other mammals," says Edvard Moser.

A shortcut through the circuitry of memory

The brain consists of billions of neurons that communicate by sending electrical signals to each other through an extremely complicated network of tiny wires in electrical circuits. Researchers knew that the hippocampus holds a simple and important circuit for memory, but now they have discovered a shortcut through the circuit.

Clifford Kentros (Photo: Thor Nielsen)

When Professor Clifford Kentros came to the Kavli Institute to become a group leader in 2012, he brought a set of molecular and genetic tools that were specially designed to unravel the wiring and functioning of the brain. The Journal of Neuroscience chose to publish one important result from this research in September 2013, partly because Kentros and his colleagues at the Kavli Institute had discovered nothing less than a new pathway that constitutes a shortcut through the circuitry of memory.

The discovery was made in a close collaboration between Kentros and David C. Rowland, who was a student in Kentros's group and is now a postdoc in the Moser group at the Kavli Institute. Professor Menno Witter and his group at the Kavli Institute also contributed, along with four other researchers.

Anatomical discoveries of this magnitude in the brain are a rare thing nowadays, so the article made a big impact among neuroscientists. The article also proved the enormous potential of modern molecular neuroanatomical tools, because of their ability to determine the precise connectivity of the neuronal cell types that comprise the innate circuitry of the brain.

An amazingly simple circuit

"It is amazing to see how simple the circuitry of memory in the brain really is. The circuit is in fact a loop that starts with signals in the superficial layers of the entorhinal cortex," explains Professor Kentros.

"These signals are sent from the entorhinal cortex through projections or 'wires' to dentate granule neurons in the hippocampus, which transmit them further to neurons in the CA3 region of the hippocampus, which again transmit them further to neurons in the CA1 region. The next step is to send signals via the subiculum back to the deep layers of the entorhinal cortex, which completes the loop by sending signals to the superficial layers where the whole thing started," Kentros says.

Lose the circuit, lose your memory

It is easy to get lost among the names of all these small anatomical parts of the brain, but remember this: Each step in the circuitry of memory represents the processing of information, which is a very important process. If the circuit is broken, you will be unable to store new memories, explains Kentros.

The precise circuitry of the hippocampal region is interesting because studies of the rodent brain have shown that it contains a set of distinct cell types that represent position, environmental geometry, and direction. Four key cell types have been described in this broad neural circuit: place cells, grid cells, border cells, and head direction cells.

The entorhinal grid cells can be compared to a general map of the environment, whereas the place cells in the hippocampus can be compared to the red dot that says "This is where you are" on the map outside of your shopping centre, for example. The grid cells and the place cells need to talk to each other in order to keep your general map coordinated with your specific location. This is one of the important things that goes on in the circuitry of memory.

A rabid and useful virus

David Rowland and Clifford Kentros's discovery of a shortcut through the CA2 region suddenly made the circuitry of memory both more complicated and more interesting.

" Maybe you noticed that I mentioned CA1 and CA3 in the circuit, and that there was a number missing. Well, not anymore. We have known for a long time that the hippocampus also has a small region called CA2, but few neuroscientists have paid any attention to it. We discovered that the CA2 creates a shortcut that transmits signals directly from the hippocampus back to the superficial part of the entorhinal cortex, where the circuit starts," explains Kentros.

Rowland and Kentros used one of the many new smart tools in the neuroscientist's toolbox to discover the shortcut: A 'tamed' version of the otherwise very dangerous rabies virus.

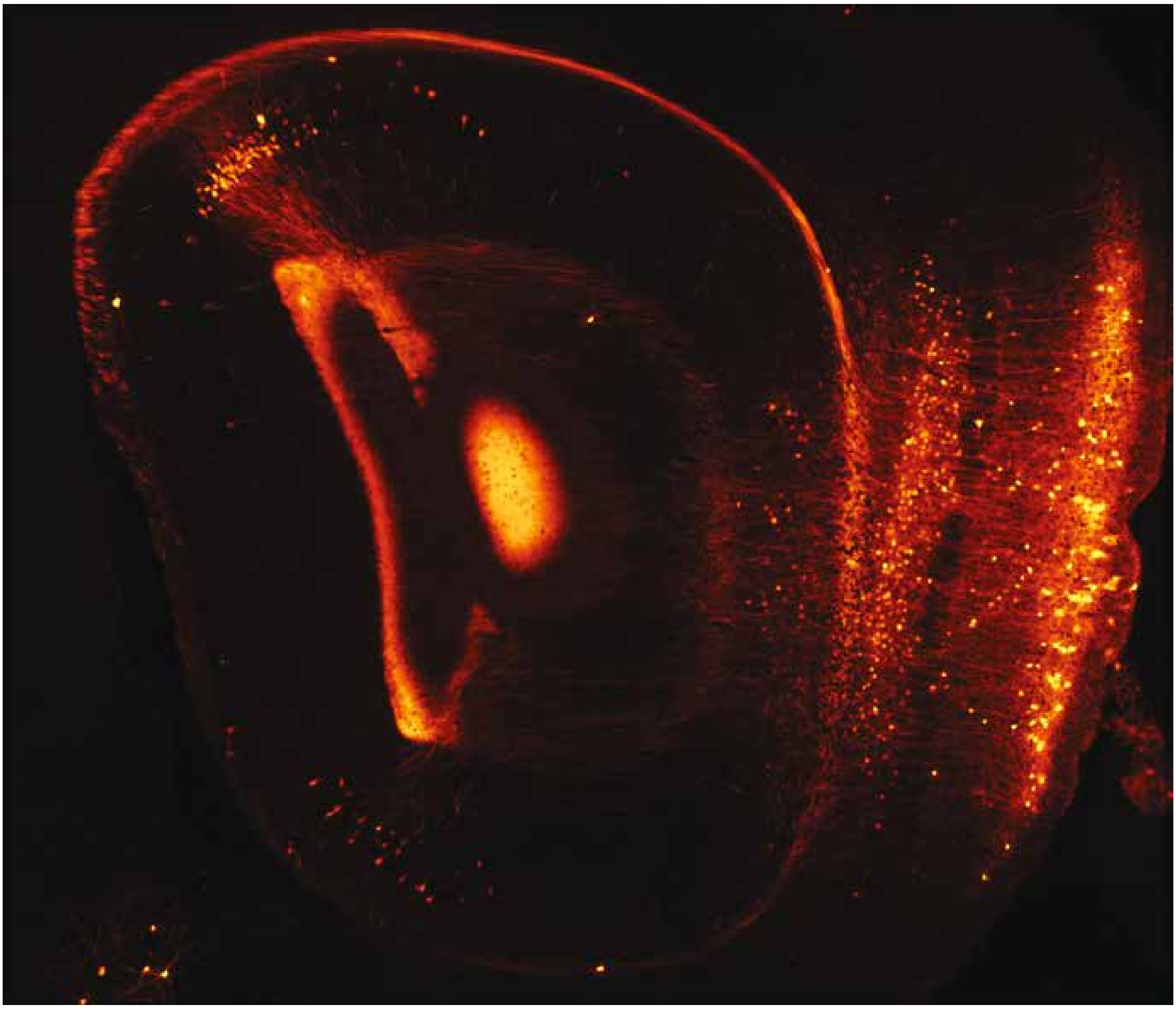
A normal rabies virus can infect the motor neurons in the part of the body where a person is bitten by a rabid animal. From there, the virus can jump into neighbouring neurons and infect them, and then make its way further up to the spinal cord and into the deep brain. Kentros and his colleagues instead used a genetically modified virus that can only jump once into a new neuron, so that it is 'friendly' to neuroscientists instead of dangerous to people in general. The virus carries with it a protein that causes infected neurons to glow when the researchers shine a special light on them.

"This made it possible to see both the neurons that we had infected ourselves, and the neighbouring neurons that were infected when the virus jumped over one (but only one) synapse. If we saw light from a neuron that we had not infected, we knew that it had to be connected to one of the neurons that were infected in the first place. In other words: The virus made it possible for us to unravel the wiring between neurons," explains Kentros.

What is the circuit doing?

In science, every answer generates new questions. Professor Kentros now wants to find out what the shortcut through the CA2 is doing, and he has already started an investigation together with colleagues in Trondheim and at Columbia University in New York. This time, he is going to use a pharmacogenetic tool that makes it possible to turn the activity of neurons up or down, almost like when you adjust the volume on your amplifier with a knob. This tool will allow them to make recordings from neurons and see what happens in the CA1 – downstream from the CA2 – and in the entorhinal cortex itself, while they manipulate the activity of neurons in the CA2.

"I have a hunch about what we are going to find. Maybe the shortcut through the CA2 is a way of controlling that the processing in the longer circuit doesn't go wrong. But you cannot be sure without doing the experiments," Kentros says.



The dense cluster of cells in the upper left is the CA2 region of the hippocampus. The entorhinal cortex is to the right. (Illustration: NTNU)

What makes a motor neuron behave as if it has eyes?

Mirror neurons in the brain have some amazing properties. Many believe they allow us to recognize not only what other individuals are doing, but also how they feel and what they intend to do. But what makes a motor neuron behave as if it has eyes and can read minds?

Mirror neurons were originally discovered almost by accident in macaque monkeys, by a group of researchers led by Professor Giacomo Rizzolatti at the University of Parma in Italy in the early 1990s. These neurons were subsequently discovered in humans and in birds, and it is likely that they are found in many other social creatures.

A mirror neuron is a neuron that fires both when an animal acts, and when the animal observes the same action performed by another.

"Any social creature with mirror neurons has a huge adaptive advantage. When another creature approaches you, it is beneficial to find out quickly if the intention is to have sex or punch you in the face. Or make a meal of you," says Jonathan Whitlock, who is a researcher and a group leader at the KI/CNC.

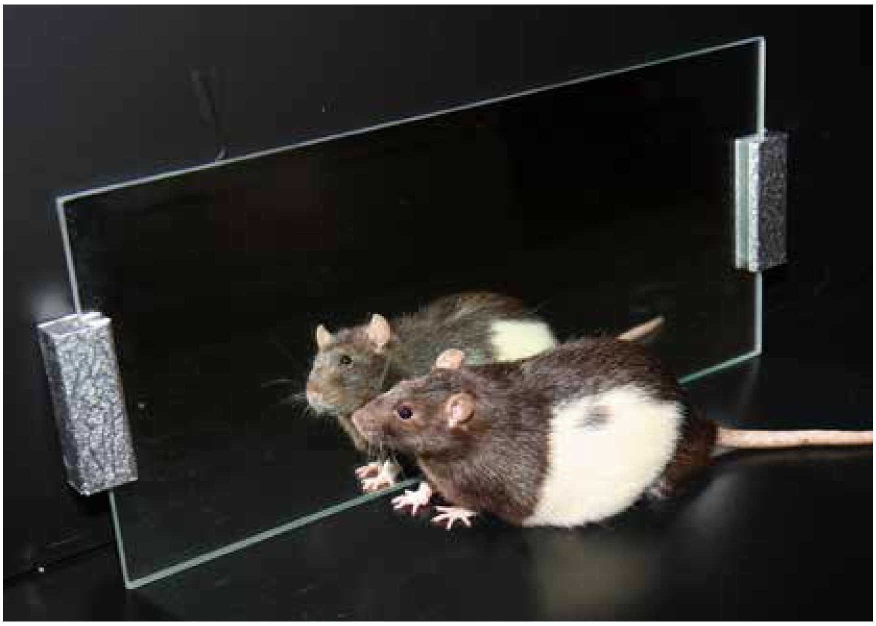
In 2013, Whitlock was awarded a prestigious €1.5 million start-up grant from the European Research Council. He is now using the grant to set up a research group on mirror cells in rodents. If Whitlock can find mirror cells in rodents, he will also be able to take the first steps towards understanding their circuit properties. This huge task could take the better part of five years.

Twinkle, twinkle, little neuron

Jonathan Whitlock needs a big box of tools in order to complete the project. The researchers at the Kavli Institute already have a lot of experience with using tetrodes, devices with four active microelectrodes, to record electrical signals from neurons in the rodent brain. Whitlock has a new trick up his sleeve: A miniature microscope that can be mounted on top of a mouse's head.

The brain cells of the mice that he will use are genetically modified, and have a protein that flashes a light when calcium ions stream through the membrane into the neuron. The stream of calcium occurs naturally when the neuron fires a burst of activity – and the flashes of light can be recorded through the microscope. This new technique should make it possible to study several hundred neurons at the same time. Whitlock hopes that at least some of the flashes will come from mirror neurons.

"Instead of looking at the stars in the sky, we can look at the twinkling neurons in the rodent brain and find out more about how this little 'universe' works," he says.



If mirror neurons are found in rodents, it will enable researchers to study them with all the fabulous tools that have been used to study grid cells and other neurons. (Illustration: KI/CNC)

A project that could open doors

If the project is successful, the first breakthrough will be proof that there are indeed mirror neurons in the rodent cortex. That would pave the way to the next step, with another tool: A genetically engineered virus that makes neurons sensitive to laser light, to study where the inputs to mirror neurons come from.

"The ultimate goal is to find out what makes a motor neuron into a mirror neuron. Today, nothing is known about how a motor cell can act as if it has eyes. If mirror coding can be shown in rodents, it will enable us to use all the fabulous molecular tools that already exist to study mirror neurons, their circuits and their functions in these animals. My dream is that this could open the door on a whole new field of study. Maybe we even could find out if it is true that a deficient mirror system really is part of the cause of autism," says Whitlock.

NORBRAIN fully operational after significant investments

The Norwegian Brain Initiative was awarded a large grant from the Research Council of Norway in 2011. The University of Oslo (UiO) and the Norwegian University of Science and Technology (NTNU) are now in the process of realizing their vision to build the world's best infrastructure for neuroscience research.

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 behind complex mental functions. Realizing this potential requires universities to join forces to establish research platforms for scientists with complementary skills and insights. Scientists must also have access to state-of-the-art equipment needed to address the most fundamental questions in the field.

Three outstanding centres

This was the perspective in 2010 when NTNU and UiO decided to establish NORBRAIN as a national infrastructure for neuroscience research. In November 2011, the Research Council of Norway granted NOK 80 million (€10.2 million) to NORBRAIN. The project is structured around two Centres of Excellence – the KI/CNC at NTNU and the Centre for Molecular Biology and Neuroscience at UiO – as well as one Centre for Research-based Innovation – the Medical Imaging Laboratory (MI-Lab) – at NTNU.

"Much of the funding is now being used to buy equipment that is divided between Oslo and Trondheim. This means that we will soon enter a normal operation phase, where we can emphasize training and the use of equipment," says Professor Edvard Moser. He was the initiator and is now coordinator of the major equipment project.

Professor Sten Grillner (left) was among the first Kavli Prize Laureates in neuroscience in 2008. He is shown here with Fred Kavli and Kavli Laureates Pasko Rakic and Thomas M. Jessell. (Photo: Scanpix)

NORBRAIN's new board

An important development in 2013 was that NORBRAIN established its own board, with Professor Sten Grillner as chair. Grillner is the director of Karolinska Institute's Nobel Institute for Neurophysiology in Stockholm and the leader of the International Brain Research Organization (IBRO), which aims to promote and support neuroscience training and collaborative research around the world. Grillner was also recently leader of the Federation of European Neuroscience Societies (FENS).

"Grillner is a distinguished neuroscientist with great vision and broad international experience. We are very pleased to have someone of his calibre as chairman," says Moser.

Professor Moser hopes NORBRAIN will provide Norwegian neuroscience research a boost in the years ahead, but he is already thinking about what needs to come next.

"We now have made great strides in establishing state-of-the art facilities in Oslo and Trondheim, but at the same time, the pace of technological advances in neuroscience research is blindingly fast. We will very likely need a more permanent source of financing in a few years if we are to keep up with the international competition," Moser says.

Fred Kavli (1927-2013)

The engineer, inventor, philanthropist, billionaire and businessman Fred Kavli died on 21 November 2013, after having fought a hard battle against cancer over the last year.

Fred Kavli (1927-2013), one of research's best friends. (Photo: Gorm Kallestad)

Fred Kavli, or Fridtjof as he was called before he moved to the United States, was born in 1927 in Eresfjord in Romsdal. He was awarded an engineering degree in theoretical physics from the Norwegian Institute of Technology (NTH), which later became the Norwegian University of Science and Technology (NTNU) in Trondheim. After graduating in 1956, he travelled to Canada and then to the United States. He founded the Kavlico Corporation in Los Angeles in 1958, a high-tech enterprise that became a world leader in the development and manufacture of sensors. The sensors used in the US space shuttles came from Kavlico. Kavli was the company's head until he sold it in 2000.

The sky over Eresfjord

We who were lucky enough to get to know Fred loved him dearly and were inspired by his great vision of research excellence, founded on passion and the thirst for knowledge. Fred used to talk about going skiing as a young man in Eresfjord and seeing the northern lights dance across the sky. Even then he began to think about big pictures issues, the laws of nature, and how everything fits together. He decided to learn as much as he could, and when he sold Kavlico in 2000 he used his wealth to realize his vision. The money was used to establish The Kavli Foundation, now one of the world's leading foundations for financial and strategic support for basic research. Fred believed that basic research helps humanity.

Obama listened to Kavli

It is hard not to be impressed by what The Kavli Foundation has achieved during its 13-year history. Politicians from around the world have listened to Fred's advice on scientific strategy. President Obama's planned billion-dollar investment in research on the brain and brain diseases has its direct origins in an initiative of The Kavli Foundation. It is largely due to Fred's efforts that the world's most powerful man sees brain research as the next moon landing.

In 2006, Fred was appointed Grand Officer, Commander with Star of the Royal Norwegian Order of Merit for his outstanding contributions to Norway and to humanity. He received an honorary doctorate from NTNU in 2008 and from the University of Oslo in 2011, and had been elected to numerous scientific academies.

The glory of life

Fred was passionate about building a deep and fundamental knowledge of nature, as he showed in the many inspiring speeches he gave, and which often brought tears to our eyes.

"For many of us, the greatest reward in life is to gain more knowledge about the human being and the universe in which we live, to open new horizons, new vistas for the human mind, and to discover and understand nature. It is a history of survival through increased skills and knowledge, and each day – as I look at nature – the meadows, the trees, the flowers, the birds, the dolphins, the animals, and the human being – I hear a victorious cry for the glory of life."

With Fred's death, research has lost one of its best friends, but it's comforting to know that he has built a scientific structure that remains.

The world takes note of KI/CNC research

Scientists at the KI/CNC in Trondheim saw once again in 2013 that their research has been noticed in professional circles and by the international media.

The rats Thelma and Louise are important KI/CNC employees, because they help remind the animal caretakers just what it takes to make a rat happy. In April 2013, Thelma was pictured on the front page of The New York Times Science Times section.

In December 2013, Professors Edvard Moser and May-Britt Moser together with John O'Keefe from University College London were awarded the 2013 Louisa Gross Horwitz Prize for discoveries that have illuminated how the brain calculates location and navigation.

Nobel Laureate Eric Kandel from Columbia University introduced the Mosers at the award ceremony on Columbia University in January 2014.

May-Britt Moser was awarded the Norwegian Madame Beyer award in 2013, at an annual regional business conference arranged by the Trondheim Chamber of Commerce in September.

The award recognizes brilliant female business leaders, and is meant to be an inspiration for female leaders and a recognition of superb leadership.

Featured in the science section of The New York Times

May-Britt and Edvard Moser have been popular interview subjects for the Norwegian and foreign media since the research centre was established. The centre changed its media strategy in 2008, in part because working with the media had become very time consuming.

Børge Brende, Norway's Minister of Foreign Affairs (left) visits the Kavli Institute labs.

The new strategy has been to prioritize the largest and most important research news and media, and the change has been very successful in subsequent years.

On 29 April 2013, The New York Times Science Times section published an account of May-Britt and Edvard Moser's story, from its beginning in Professor Per Andersen's office at the University of Oslo in 1988 when Andersen "yielded to the Mosers' combination of furious curiosity and unwavering determination and took them on as graduate students". Both Nobel laureate Eric Kandel and John O'Keefe were quoted as great admirers of the Mosers. The NYT also published a video interview with the Mosers.

Visit and grants

Mr. Børge Brende, Norway's Minister of Foreign Affairs, visited NTNU and gave an inspiring talk to staff and students about geopolitical changes. He was also presented with the Medical Faculty's ideas of how to work with global health, and was impressed by a tour of the Kavli Institute's lab.

Edvard Moser received his second Advanced Investigator grant from the European Research Council in 2013. The grant funds his investigation of the functional organization of cortical circuits. Jonathan Whitlock was awarded a highly competitive ERC start-up grant to set up a research group on mirror cells in rats (see page 10).

In October, a group of neuroscientists from the Nordic countries met in Trondheim to discuss the possibility of a Nordic neuroscience meeting. The scientists agreed to establish The Society for Nordic Neuroscience, and decided to organize the first Nordic Neuroscience meeting in Trondheim in June 2015.

Who's who at KI/CNC

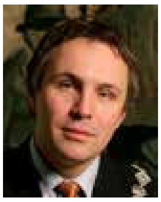
CNC BOARD

Stig Slørdahl
Dean
Faculty of Medicine
NTNU
Chairman of CNC Board

Anne Borg
Dean
Faculty of Natural Science and Technology
NTNU

Geir Egil Øien
Dean
Faculty of Information Technology, Mathematics and Electrical Engineering
NTNU

Nils Kvernmo
Managing Director
St. Olavs Hospital



Tore O. Sandvik
County Council Chair
Sør- Trøndelag County

May-Britt Moser
Professor
NTNU
Secretary of CNC Board

KAVLI BOARD

Kari Melby
Pro-Rector for Research
NTNU
Chairman of Kavli Board

Jan Morten Dyrstad
Associate professor
NTNU

May-Britt Moser
Professor
NTNU

Menno Witter
Professor,
NTNU

Stig Slørdahl
Dean
Faculty of Medicine,
NTNU

Edvard Moser
Professor
NTNU
Secretary of Kavli Board

ADVISORY BOARD

Carla Shatz
Professor
Stanford University
USA

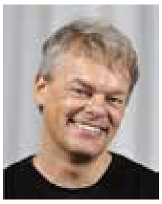
Erin Schuman
Professor
Max Planck Institute for Brain Research
Germany

Rainer Friedrich
Professor
Friedrich Miescher Institute for Biomedical Research
Switzerland

Thomas Jessell
Professor
Columbia University
USA

Tony Movshon
Professor
New York University
USA

LEADER GROUP



Edvard Moser
Professor and Director of Kavli Institute for Systems Neuroscience

May-Britt Moser
Professor Director of Centre for Neural Computation

Menno Witter
Professor

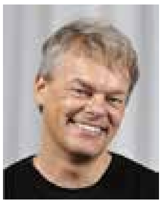
Clifford Kentros
Professor

Yasser Roudi
Professor

Nora Gullbekkhei
Head of administration

Tor Grønbech
Senior advisor

FACULTY



Edvard Moser
Professor and Director of Kavli Institute for Systems Neuroscience

May-Britt Moser
Professor Director of Centre for Neural Computation

Menno Witter
Professor

Clifford Kentros
Professor

Ayumu Tashiro
Group leader (until 2013)

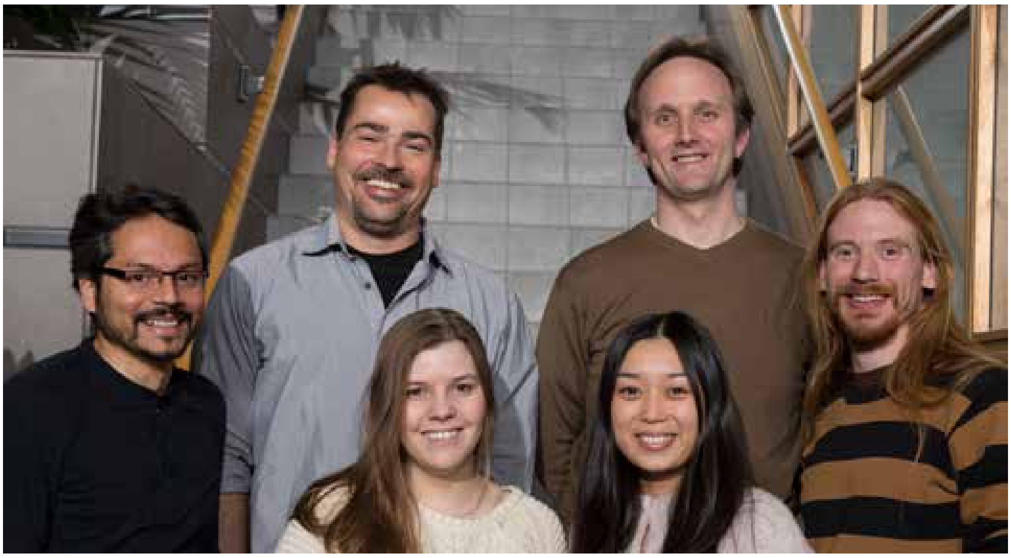
Yasser Roudi
Group leader

Sheng-Jia Zhang
Group leader

MOSER GROUP

From bottom left: Kei Igarashi, Nouk Tanke, Grethe Jakobsen, Nenitha Dagslott, Ingvild U. Kruge, Charlotte B. Alme, May-Britt Moser, Qichen Cao, Jing Ye, Torgeir Waaga, Øyvind Høydal, Tanja Wernle, David C. Rowland, Flavio Donato, Martin Hägglund, Merethe Andresen, Homare Yamahachi, Chenglin Miao, Hanne Stesola, Tor Stensola, Håvard Tangvik, Alice Burøy, Vadim Frolov, Espen J. Henriksen, Jens F. Andersen, Endre Kråkvik, Klaus Jenssen, Kyrre Haugen, Tor Grønbech, Ryo Iwai, Hiroshi Ito, Debora Ledergerber, Nora Gullbekkhei, Edvard I. Moser, Bjarte B. Løfaldli, Haagen Waade, Jørgen Sugar

KENTROS GROUP



From bottom left: Christin H. Berndtsson, Qiangwei Zhang, Rajeevkumar R. Nair, Clifford Kentros, Cornelis H. Z. Borgesius, Stefan M. A. Blankvoort

ROUDI GROUP

From left: Ariel Haimovici, Aree W. Witoelar, Claudia Battistin, Yasser Roudi, Maria Mørreaunet, Trygve Solstad, Nicola Bulso, Benjamin A. Dunn

WITTER GROUP

From bottom left: Kamilla G. Haugland, Ai Lan Phan, Bruno Monterotti, Paulo J. B. Girão, Teri Sakshaug, Inge Storkaas, Mathias L. Mathiasen, Heidi Kleven, Asgeir K. Flatmoen, Hanne T. Soligard, Ingrid Heggland, Menno Witter, Bente Jacobsen, Maria José L. Donate, Konstantinos Tsamis, Amy Robinson, Grethe M. Olsen, Eirik S. Nilssen, Michele Gianatti, Karoline Hovde, Peter Bennett, Øyvind W. Simonsen, Thanh P. Doan, Pål Kvello, Jørgen Sugar

WHITLOCK GROUP

From left: Jonathan Whitlock, Tuce Tombaz, Tadiwos F. Mergiya

TECHNICIANS AND ADMINISTRATION GROUP

From bottom left: Kyrre Haugen, Endre Kråkvik, Qiangwei Zhang, Klaus Jenssen, Bruno Monterotti, Nora Gullbekkhei, Espen J. Henriksen, Hanne T. Soligard, Vadim Frolov, Grethe M. Olsen, Jens F. Andersen, Grethe Jakobsen, Alice Burøy, Merethe Andresen, Håvard Tangvik, Paulo J. B. Girão, Bjarte B. Løfaldli, Haagen Waade

Annual accounts 2013

Income

Norwegian Research Council: Centre of Excellence	12 500 000
Norwegian Research Council: other	23 447 000
International (European Commission, EMBO, Louis Jeantet Foundation)	11 654 000
Other Public/Private (Kavli foundation, Norwegian Health authorities)	2 797 000
Norwegian University of Science and Technology	30 746 000
Total income	81 144 000

Expenses

Net personnel costs	41 345 000
Indirect costs including floorage	14 058 000
Equipment	7 758 000
Operational expenses	17 983 000
Total expenses	81 144 000

Amounts in NOK

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Photo, frontpage:
Rat eating a chocolatey hoops (Photo: Haagen Waade, KI/CNC)

Annual Report for KI/CNC 2013

NTNU – Trondheim
Norwegian University of
Science and Technology

NTNU – Norwegian University of Science and Technology

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, teacher education, the arts and humanities, medicine, architecture and fine art.

NTNU's cross-disciplinary research delivers creative innovations that have far-reaching social and economic impact.

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