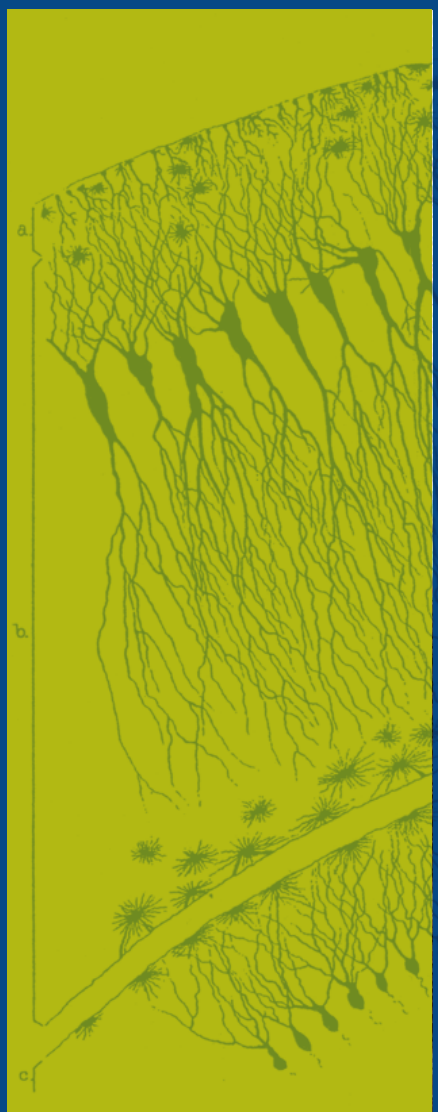
Annual Report 2003 Centre for the Biology of Memory

NTNU
Norwegian University of Science and Technology



Contents

Annual Report from The Centre for the Biology of Memory

Editors: Edvard and May-Britt Moser, CBM, N-7489 Trondheim
Text: Bjarne Røsjø, Faktotum Informasjon as, N-1253 Oslo
Translation: Patrick Chaffey, N- 0596 Oslo
Graphic Design: Birgitte Kolbeinsen, Melkeveien Designkontor as, N-0196 Oslo
Printed by: Tapir Uttrykk, N-7005 Trondheim
ISBN: 82-471-6006-4

Understanding the Biology of Memory

The scientific goal of the Centre for the Biology of Memory (CBM) is to understand the biological processes responsible for memory. This ambitious aim requires a multidisciplinary and multi-level approach which can only be accomplished by close collaboration between experts in several disciplines.

The three Centres of Excellence in Trondheim were inaugurated on 18 November 2002. From the left: Professor Peder Emstad of the Centre for Quantifiable Quality of Service in Communication Systems, Professor Edvard Moser of the CBM, Professor Torgeir Moan of the Centre for Ships and Ocean Structures, Christian Hambro, Director of the Norwegian Research Council, and Kristin Clemet, Minister of Education and Research (Photo: Rune Petter Næss, NTNU Info).

The CBM brings together internationally leading neuroscientists in a Centre associated with the Norwegian University of Science and Technology (NTNU) in Trondheim, Norway. These scientists share an interest in memory and contribute complementary expertise. The activities of the Centre include theoretical work, experiments, and training of students, all centred around the main scientific goal of the Centre. The goal is to determine, using a combination of behavioural and neurophysiological methods, how groups of neurons in the hippocampus and neocortex give rise to specific memory operations such as encoding, storage, consolidation and retrieval.

Memory has been studied using either a top-down or a bottom-up strategy. The top-down approach starts by studying cognitive or behavioural memory, and then works its way towards identifying the brain regions involved, the individual cells and molecules responsible. The bottom-up strategy begins by studying the basic molecular mechanisms of synaptic modification, and thence upwards to a coherent view of behavioural memory. Neither approach has alone been successful in establishing firm links between molecules and behaviour. The main focus of the activity of the Centre is on the intermediate level of analysis, namely the level of networks of neurons that together encode and store information that can be recalled at a later time.

The Norwegian Centres of Excellence

The CBM is one of thirteen Centres of Excellence (CoE) established by the Research Council of Norway in 2002. The centres were selected after an evaluation by international experts who assessed a large number of applications from highly qualified candidates. Three of these centres were located in Trondheim and the NTNU community.

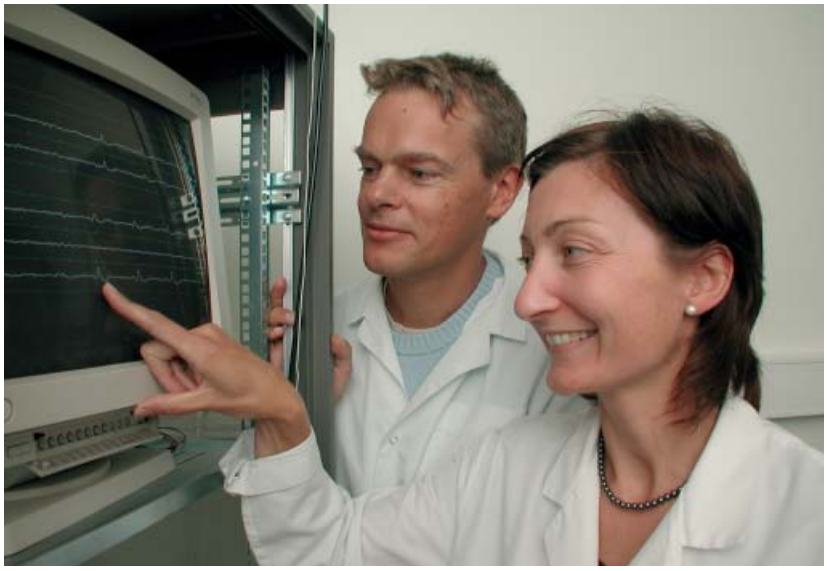
The intention of the CoE Scheme is to bring more researchers and research groups up to a high international standard. The Norwegian Minister of Education and Research, Kristin Clemet, has stressed that the centres will be given the time and resources to engage in long-term research in their areas. The Minister has also emphasised that the Centres will not be required to produce immediate results, but that their ultimate ambition should be research of Nobel Prize level.

Milestones in 2003

In the course of 2003 the CBM has made considerable progress in understanding the function of the major network stages of the hippocampus when it comes to generating memory. The Centre has also made great progress in understanding the relations between the hippocampus and areas of the cerebral cortex that lie in front of the hippocampus, thereby contributing to the understanding of the hippocampal-neocortical interactions responsible for long-term storage of memory. Several of these discoveries result directly from newly established collaborations with the visiting professors of the Centre. These and other research milestones are described in detail on pages 9–12 of this Annual Report. An important objective of the CoE system is to build up new teaching and recruitment provision within selected areas. In the autumn of 2003, NTNU and the CBM therefore established new educational provision for students with bachelor's degrees in such subjects as psychology, medicine, physics or biology, who can take a master's degree in interdisciplinary neuroscience. In the long term it may be relevant to develop this course of study further into a national master's degree in co-operation with other universities.

The hippocampus: **Memories are made of this**

The human memory contains memories of one's first kiss, the way to one's job, the PIN code of one's credit card, and a great deal more. Researchers at the Centre for the Biology of Memory (CBM) are working full-time to extend the boundaries of our knowledge of memory, with the focus on the little hippocampus fold of the cerebral cortex.



The Professors Edvard Moser and May-Britt Moser are the directors of the Centre for the Biology of Memory (CBM).

The hippocampus is absolutely crucial to the capacity possessed by human beings and all other mammals to store sensory impressions in the form of memory traces, and it is therefore also central to the memory research being conducted at the CBM. "The hippocampus is in evolutionary terms an older part of the cerebral cortex. Its function in the brain of mammals may in part be compared with the internal memory in a modern computer," say the CBM's director and co-director, Professor Edvard Moser and Professor May-Britt Moser. They add that the comparison should not be taken too far, but computer technology has at least given us a vocabulary that makes it easier to describe the brain and the memory processes.

One girl, one boy
Some grief, some joy
Memories are made of this

DEAN MARTIN, 1956

The point of departure is that both the brain and the computer retrieve and process information, and store information that may be retrieved again later. The hippocampus can be compared with the internal memory of the computer in the sense that this structure receives sensory impressions that are processed before being sent on in the form of electrical signals to different parts of the cerebral cortex ("the hard disk") where they are stored more permanently. It is however important to bear in mind that the hippocampus too can store memories and sensory impressions for a relatively long period of time.

After processing in the hippocampus, memory about location is stored in one area of the cerebral cortex, individual objects and items in another, emotional content in a third, and so on – and the sum of all the stored impressions acting in concert constitutes a memory. The computer, incidentally, stores information practically instantaneously, but permanent storage in the brain involves repeated events and can take a long time.

"The current theory, which has most certainly not been proven, is that the hippocampus maintains connections between the different storage structures in the cerebral cortex for a period of time after a group of sensory impressions has been stored. But after a certain time, perhaps as long as several years, the memories will have become so permanent that they don't need the connection through the hippocampus in order to be maintained," explains Professor Edvard Moser.

The researchers at the CBM are now investigating in great detail how these processes occur, inter alia by measuring the electrical activity in nerve cells in the hippocampus of rats. The electrical activity can be measured with the use of micro-thin electrodes that are introduced into the hippocampus. The electrodes can register the activity of up to approximately 100 individual cells at the same time. This makes it possible to obtain information that is found only in the collective signal patterns of the cells and not in their individual activity.

Better treatment for memory loss

The CBM is a basic research centre with long-term funding from the Norwegian Research Council, so the Mosers and their colleagues do not need to think about immediate practical applications or short-term profitability. Nevertheless, their research does afford great possibilities in this area.

"One of our objectives is to learn more about how normal memory functions, and that's a prerequisite for understanding what happens when memory fails. So we believe that in the long term our research will be able to contribute to more effective treatment for Alzheimer's disease and other forms of memory loss. Incidentally such disorders may become a growing problem in Norway and many other countries in the years ahead, as both the average life expectancy and the proportion of elderly people in the population increase. Aging generally leads to some decline in memory, but in addition approximately 10 per cent of the population over the age of roughly 60-70 are affected by a pathological loss of memory," says May-Britt Moser.

At the same time she stresses that there are enormous individual variations,

and the individual can do a great deal to maintain his or her memory. The point is that the brain is like a muscle: it gets stronger when it is used.

The digital brain

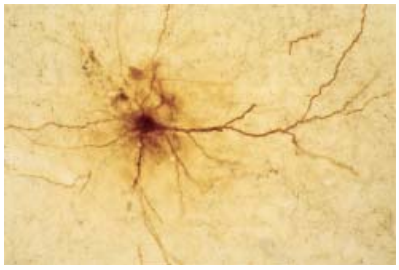
But let us take a closer look at the parallels between the brain and the computer. While the computer processes and stores information in the binary number system – which only recognises the values "0" and "1" – the nerve cells of the brain transport information in the form of electrical action potentials, which also in principle can only have the value "0" or "1".

"There are no half action potentials, just as the computer doesn't operate with "half" digital numbers," Professor Moser explains.

The action potentials cannot normally pass directly from one nerve cell to another, but they can nevertheless be transferred indirectly. When the action potential arrives at a synapse (the point of contact between two nerve cells), it may cause the secretion of molecules that are called *neurotransmitters*, and these can activate postsynaptic receptors. This triggers the passage of ionic currents across the postsynaptic membrane. Together with signals from other synapses, the currents may give rise to new action potentials in the postsynaptic cell that are then passed further. There are strong and weak synapses, in the sense that they make it easy or difficult for such a signal to be generated.

Specific patterns of action potentials can lead to the synthesis of proteins that permanently change the strength of the synapse. The current theory is that these synaptic changes, which remain distributed in the cerebral cortex, constitute the physical and chemical basis of memory. This is a parallel to the fact that the computer needs a certain number of bits to encode a piece of information.

The biological memory is both creative and constructive, in the sense that it is the whole time subject to change in the light of new information. This means that the memory of mammals cannot be compared to a video recording with exact depiction of what happened – it is rather a matter of a processed version from a very imaginative director. But that is another story.



A nerve cell can be compared to a tree with roots and branches, where the tips of each root and branch end in a synapse with connections to another nerve cell.

Recall mirrors learning

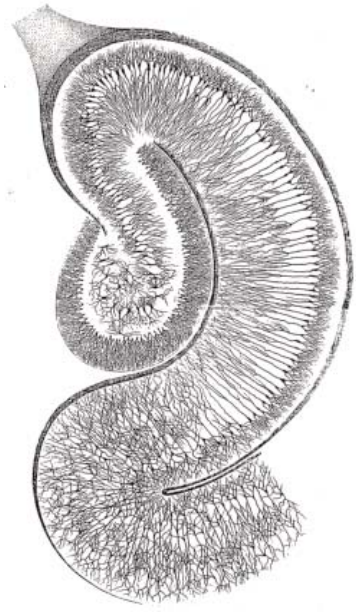
"Even though we know a lot about action potentials, synapses and proteins, there's still a long way to go before we understand what really happens during learning and the storing of memories. So one of our great goals is to learn more about how the concerted activity in groups of nerve cells contains information. Among other things, we believe that the cells that are active when something is being learnt, are reactivated when something is recalled. But this still remains to be proven," says Edvard Moser.

The hippocampus consists of a number of sub-units, and the researchers at the CBM are now in the midst of a massive undertaking to learn more about the processes that take place in the different stations. They will also be studying the connections between the stations of the hippocampus and the rest of the cerebral cortex, inter alia with a view to finding out more about how the long-term memory can gradually become more independent of the "internal memory" in the hippocampus.

People with defective hippocampi lose the capacity to remember new experiences, while older memories – like childhood memories – may often remain intact. "This gives strength to the theory that the permanent storage of memories takes place in the cerebral cortex, while the memories in the hippocampus are lost or deleted sooner or later. The hippocampus is after all a relatively small structure with limited capacity," says May-Britt Moser.

Discovered a new memory circuit

On 12 June 2002 the Norwegian Research Council decided that a Centre of Excellence in the field of the biology of memory should be established at NTNU's Medico-technological Research Centre. Just about a week later members of the Centre announced in the journal Science that they had discovered a new memory-supporting circuit in the brain (Brun, Otnæss, Molden, Steffenach, Witter, Moser and Moser, 2002). It had been previously known that information from the external cerebral cortex could follow two different routes into the hippocampus. The discovery was that the two routes provide for different functions. Only the one route is necessary for the recall of memories, while both routes can provide for recognition.



The hippocampus takes its name from the Latin word for a seahorse, because the structure has roughly the same shape as the tail of this tiny fish. In humans the hippocampus is the same size as a thumb. *(Cross section through the hippocampus drawn by Camillo Golgi. Image from his Opera Omnia, courtesy of Marina Bentivoglio, Univ. of Verona.)*

Laying the ground for international research co-operation

In the course of its first year of operation, research results from the CBM have been received with great interest in international communities. It has also been noticed that the Centre's structure and organisation are eminently suited to international research co-operation.

The presentations of research projects at the CBM during the Annual Meeting of the Society for Neurosciences (SFN) in New Orleans were received with great interest. Hill-Aina Steffenach in discussion with Professor Robert Sloviter of the University of Arizona, and Menno Witter of CBM.

The CBM has a desire to be innovative both within research and in the organisation of research. The way in which international research co-operation often takes place is that large projects are divided up into subprojects that are carried out separately in different research institutions in several countries, but the CBM is among the few international research centres that provide researchers from a number of subject fields – such as mathematics, anatomy, physiology and psychology – with the opportunity to really work together and plan and perform experiments. The international researchers co-operating with the CBM see this form of organisation as both fruitful and inspiring, and they thereby contribute to giving the Centre the possibility of setting about some of the most important unsolved problems within memory research. In the course of 2003 the CBM researchers have presented both research results and on-going projects on several occasions. In November, Edvard and May-Britt Moser, together with six post-doctoral students and research fellows, presented a selection of on-going research projects during the Annual Meeting of the Society for Neurosciences (SFN) in New Orleans, and were received with very great interest. The SFN is the world's largest and most important organisation for brain researchers, with 34,000 members, of whom as many as 28,000 were present in New Orleans.

Richard Morris

Richard Morris is Professor of Neuroscience at the University of Edinburgh. He is also Adjunct Professor of Psychology at the Norwegian University of Science and Technology and Life Sciences Coordinator for the Office of Science and Technology's Foresight Project on Cognitive Systems. Professor Morris has also served as the Director of the Centre for Neuroscience and is a past Chairman of the Brain Research Association (now BNA) and Department of Neuroscience.

The focus of Professor Morris' research is the function and neural mechanisms of the hippocampal formation.

Making collaboration straightforward

"The CBM provides an institutional framework that makes collaboration straightforward. This means that we can perform important research without applying for small individual grants with detailed description of each project. There aren't many international research centres that offer this possibility," says Richard Morris, who is Professor of Neuroscience at the University of Edinburgh.

Carol Barnes, a professor at the University of Arizona at Tucson and incoming President of the SFN, agrees. "The CBM gives us the possibility to spend a significant amount of time actually interacting in the laboratories. The CBM has affiliated to itself a number of researchers from abroad who come together as a group at least once a year, in addition to the fact that we also travel to Norway individually from time to time. It would be impossible to have the same kind of opportunity for focused attention to research without the structure that

The researchers at the Centre for the Biology of Memory (CBM) are working to extend the boundaries of our knowledge of memory.

The animal unit at the CBM was built in 2001 and satisfies the requirements of a modern rodent unit as recommended in the European Convention.

The researchers at the CBM must be able to master a large number of different tasks, like the construction of electrodes to register the activity of the brain.

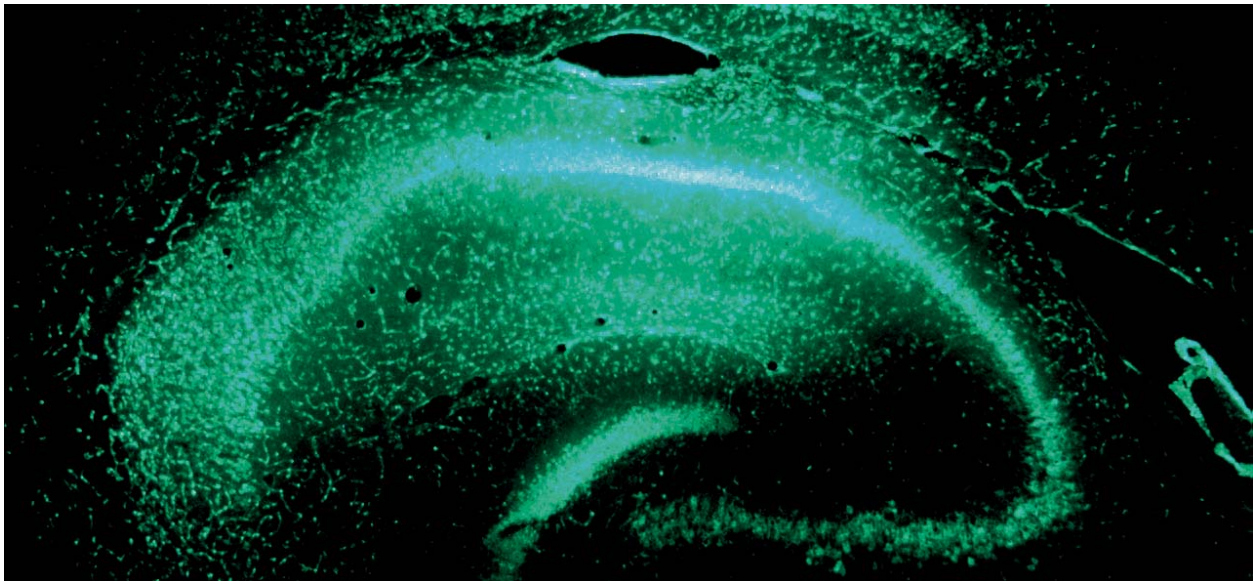
the centre provides," says Professor Barnes.

Both Carol Barnes and Richard Morris had been co-operating with Edvard and May-Britt Moser for a number of years before the CBM was established, and both had their first contact with Norway through the strong research community around Professors Per Andersen, Terje Lømo and Theodor Blackstad at the University of Oslo. They share this background with several other core members of the CBM, including Bruce McNaughton, Ole Paulsen, May-Britt Moser and Edvard Moser. Indeed, Norway has in fact had a strong position within neurophysiology and brain research ever since Per Andersen's research group laid much of the foundation for the subject at the end of the 1970s, among other things by describing the fundamental principles of how the hippocampus functions. Professor Lømo made one of the most fundamental discoveries in the biology of memory, namely that the connections between nerve cells can be strengthened through a process that is called long-term potentiation, as early as his student days.

Developments at breakneck speed

"The study of memory has developed strongly from being mostly anecdotal or observational 20-30 years ago, until today, when we can actually perform rigorous studies of the mechanisms that form the biological basis of memory. The CBM is one of very few research centres that is expressly devoted to the study of memory, and organised in such a way as to bring together international scientists with an interest in the biology of memory to cooperate on projects. The creation of this centre was very timely, useful and interesting," says Richard Morris.

Professor Morris points out that the research at the CBM is considered as being ambitious in the subject communities. "The CBM is working on the transition from being able to record from just one cell at a time in the brain



An important CBM aim is to identify functions of cell populations in the hippocampus. The picture shows hippocampal cells stained by fluorescent tracer injection in the CA1 subfield.

Carol Barnes

Carol Barnes is a professor of psychology and neurology at the University of Arizona in Tucson. Professor Barnes is also president elect of the Society for Neuroscience (SFN), the world's largest organization of scientists devoted to the study of the brain, with a total of 34,000 members.

Dr. Barnes' research interests involve the delineation of brain changes during late ontogeny (senescence) and the functional consequences of these changes on information processing and memory in older organisms. The major emphasis of the research in her lab has been an examination of the relationship between neurological change in the hippocampal formation of old rats and the accompanying decline of spatial learning-memory performance.

Carol Barnes joined the UA in 1990 and became a co-founder of the Arizona Research Laboratories Division of Neural Systems, Memory and Aging, a dedicated research unit for the study of brain mechanisms of learning and their changes with age, from the molecular to the behavioral levels.

of an animal, to attempting to record from a large number of cells at once. This is an important step forward, because we believe that an individual memory doesn't reside in an individual cell. On the contrary, we believe that memory is distributed across a very large number of cells, at a very large number of different synaptic connections. The transition to studying a large number of cells at once is challenging because we should be thinking very carefully about what kind of conclusions you can draw from such experiments. But I'm not in any doubt that this is the right way ahead," says Professor Morris.

The visiting professors

Carol Barnes and Richard Morris belong to the CBM's group of altogether seven visiting professors from the USA, Germany, the United Kingdom, Italy and the Netherlands. Professor Barnes has a special interest in brain systems and how they age.

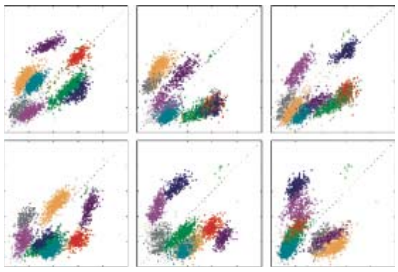
"The understanding of memory is fundamental and important as a phenomenon in itself, but also if you want to treat impairments of memory, both in normal aging and in diseased states. Edvard and May-Britt Moser have brought together a very strong group of researchers at the CBM, and have excellent possibilities of carrying on the proud Norwegian traditions in this field. The CBM is making good progress in terms of understanding important aspects of memory at the physical level, and they have strong behavioural and computational components as well," says Professor Barnes.

Richard Morris' contribution to the research at the CBM is focused on the biochemistry around the different memory processes. "We're trying to take advantage of the developing knowledge about how different kinds of neurotransmitters operate at the synaptic connections in memory areas like the hippocampus, in order to actually explore the impact of altering that chemistry in a real learning and memory task. That may also provide a route to new insight in what happens when memory processes go wrong in the aging or diseased brain," he points out.

New dimensions in memory research

For many years memory researchers have known that there is a connection between *where* the rat is and which nerve cells in the hippocampus are active. The CBM researchers are now working along a new dimension to find the connection between specific nerve cells and *what* the rat is doing.

"The firing of cells in the hippocampus is so place-specific that we can look at the electrical signals from them and find out where in the room the rats are with an accuracy of roughly three centimetres. In other words, a clear connection has been established between the localisation of the rats and which nerve cells are active. But now we're trying to give this knowledge a new dimension by letting the rats search for different types of food in mazes while we observe the activity in the hippocampus. By doing this we can perhaps find a connection between *what* the rats are doing and which cells are active," explains Associate Professor Robert Biegler. The project is a collaboration between his group and the core team at CBM.



By means of advanced mathematical calculations the diffuse electrical signals that reach the electrodes can be traced back to individual cells in the hippocampus. The different colours represent different cells, which can be separated from one another by means of a clustering algorithm written by Sturla Molden, Cand. Scient., who is a Ph.D. student at the CBM.

The holy grail of memory research

But the CBM researchers' ambition is to extend the experiment along yet another dimension: the time axis. If they manage to find a connection between the activity in the hippocampus cells and *where* the rat is, *what* the rat is doing and *when* it does something, they will have come a long way in the direction of discovering the equivalent of the "Holy Grail" in memory research. "There are many indications that a special pattern of activity in the hippocampus is associated with a specific memory. But no scientific article has yet been published confirming this connection," Paulo Girão, a Ph.D. student, points out.

Frode Tuvnes, Robert Biegler and Paulo Girão train rats to find food in a radial maze with 12 arms 80 cm in length. At the end of each arm there is a food bowl, but the rat must go right down to the bowl to find out whether there really is food in it. "The rats don't want to waste time by going into an arm where they've been already. To save time, they have to remember which arm they've visited. They do that quite well," says Professor Biegler.

The rats first spend three to four weeks with one training session per day to learn the task, before having a number of micro-thin electrodes implanted in their hippocampus. These electrodes make it possible to observe which nerve cells are active by watching a computer screen. By means of advanced mathematical calculations and specially developed software, the diffuse electrical signals that reach the electrodes can be traced back to individual cells in the hippocampus. "In other words, we're not only looking at behaviour, but at the connection between behaviour and the way in which information is stored and organised in the brain," says Frode Tuvnes.

Custard is the favourite

The researchers place three different types of food in the maze: custard, ordinary rice and rice with a touch of honey. In this way the researchers can find out whether the activity in the nerve cells in the hippocampus correlates with the type of food the rats expect to find at the end of the arm. The rats' favourite food, incidentally, is custard, with honeyed rice as number two.

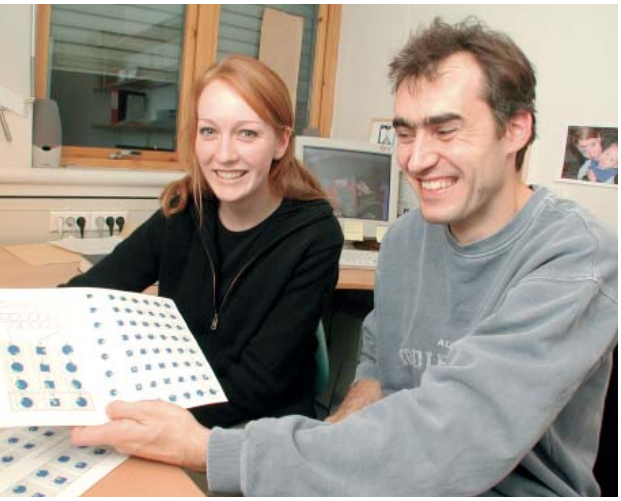
Frode Tuvnes, Paulo Girão and Robert Biegler train rats to search for food in a radial maze with arms 80 cm in length. After three to four weeks of training the rats have learnt what kind of food there is at the end of each arm, and this is something the researchers can use to explore new dimensions in animal memory.

The objective is to find out how information is grouped in populations of nerve cells in the hippocampus: Is it the same nerve cells that encode information for each of the three types of food/events?

The three researchers are particularly concerned with the moment when the rat is in the centre of the maze deciding which arm to explore. It is important that the arms of the maze are sufficiently long – otherwise the rats may just as well take a walk to see whether any food is lying there. "They only use their memory if it's too much effort to look for the food," comments Associate Professor Biegler.

"We hope that this research can shed new light on human memory, because there are many features in common between the memories of all mammals. A lot of the biochemistry of the memory is common to the whole animal kingdom," he explains.

Some like similarities **and others like differences**



The post-doctoral research fellows, Jill Leutgeb and Stefan Leutgeb, are investigating how one part of the hippocampus picks up differences, while another part is concerned with similarities.

The hippocampus consists of a number of sub-departments with different functions that have hitherto been largely very poorly mapped. The CBM researchers, Jill and Stefan Leutgeb, see signs that nerve cells in one sub-department express patterns and features that are common to different learning contexts, while another sub-department is concerned with finding the differences and making them as great as possible.

Earlier experiments have shown that the nerve cells in the hippocampus of a rat in an enclosure with which it is familiar, "fire" place-specific signals. This may be interpreted as meaning that the hippocampus contains a kind of map of areas in which the rat has learnt to find its way about. The Leutgebs' research suggests that the rats use the two hippocampal areas CA3 and CA1 differentially when they store and retrieve memories.

"The nerve cells that are active in CA3 in a special enclosure in our laboratory are completely mute in other enclosures. Conversely, it appears that most of those cells in CA1 that are active in a special enclosure are also active in enclosures that are similar. This gives support to a hypothesis that CA1 preserves similar features, while CA3 looks for differences and magnifies them," says Jill Leutgeb.

"The sub-departments of the hippocampus are different both anatomically and functionally. CA3, for example, appears to be a sort of "data processor" with the capacity to compare incoming information with patterns that have already been stored," adds Stefan Leutgeb.

CA3 is a unique structure in that it has what are called *recurrent connections*, i.e. the nerve cells there have an unusually large number of connections to other nerve cells in the same area. While the probability that a typical nerve cell in the cerebral cortex will have a connection to another randomly selected cell is less than 0.01 per cent, the probability that a CA3 cell has a connection to another CA3 cell is as high as 4 per cent. The large number of connections is no doubt very useful when CA3 is to compare new sensory impressions with stored memory traces.

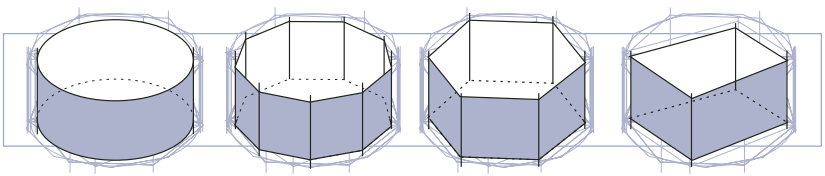
How the hippocampus sorts the impressions

A series of experiments conducted by Jill and Stefan Leutgeb in collaboration with members of the centre, including the Italian theoretical physicist Alessandro Treves, suggest that the CA3 cells preserve differences in sensory impressions by means of a phenomenon called *orthogonalisation* or *pattern separation*. These researchers have done calculations on this and determined that different "maps" are stored in such different ways as at all possible in the nerve cells of CA3. Thus it is probably easier for the rat to distinguish similar but different sensory impressions from one another, which is necessary to prevent memory interference. "This is a pioneering discovery that shows among other things why it's important to have an interdisciplinary staff at the Centre," Professor Edvard Moser points out.

The separation of impressions and memory

It is extremely important for the CBM researchers to be able to draw a distinction between the electrical activity in the hippocampus that is due to sensory impressions, and the activity that has to do with memory. Together with three of the Visiting Professors (McNaughton, Barnes and Treves), the CBM team has hatched out an ingenious experiment to document this difference: They release the rats into enclosures that gradually change shape from square to circular (or vice versa), and monitor the nerve cells in the hippocampus to see when they switch over from signalling "square" to "circular". If the firing of cells in the hippocampus changes gradually from "square" to "circle", and at the same point in the transition irrespective of whether the experiment began with a square or circular enclosure, this suggests that the nerve cells are first and foremost triggered by sensory impressions. But if the Leutgebs find nerve cells in which the activity patterns are displaced, this may mean that the observed firing is also steered by the animal's memory.

"We believe that CA3 in the hippocampus functions in such a way that a limited number of incoming sensory impressions are enough to activate impressions that are stored in the memory. In this way the whole memory of an earlier experience can be activated. This phenomenon is called *pattern completion*, and we hope that these experiments are going to teach us more about this mechanism," say Jill and Stefan Leutgeb.



An important CBM experiment is to release the rats into an enclosure that gradually changes shape from square to circular (or vice versa). This experiment can help the researchers to distinguish between hippocampal activity that is due to sensory impressions from activity that is due to memory processes (Illustration: Haagen Waade, CBM).

Fear and space in the hippocampus

The hippocampus is a relatively small structure with a limited number of nerve cells, but it nevertheless consists of several sub-departments with different structures and functions. Hill-Aina Steffenach and Kirsten Kjelstrup are two of the CBM researchers who want to know more about what goes on in the sub-departments of the hippocampus and its immediate vicinity.

"It's not certain that we'll ever get right to the bottom of things in our understanding of how the memory works. The task can perhaps be compared to a computer programme that understands itself – there's no such thing yet! But it's obvious we can get much farther than where we are today," says Kirsten Kjelstrup, a medical student who is working for a Ph.D.

The heads of the CBM, Edvard and May-Britt Moser, have previously published results showing that rats to a great extent use the *dorsal* part of the hippocampus – the part that turns towards the animal's spine – for spatial orientation. The corresponding part of the hippocampus is also active in humans – and other mammals – trying to get their bearings by means of memory.

Ph.D. students Hill-Aina Steffenach and Kirsten Kjelstrup are mapping the sub-departments of the hippocampus and entorhinal cortex.

The seat of fear is the belly side

Kirsten Kjelstrup and Hill-Aina Steffenach, both research fellows at CBM, participate in experiments aiming to find out more about the division of labour internally in the hippocampus, and between the hippocampus and the entorhinal cortex. Kirsten Kjelstrup has gone hunting for the division of labour between the *ventral* and the *dorsal* parts of the hippocampus, while Hill-Aina Steffenach is investigating corresponding anatomical differences in the *entorhinal cortex*. The terms dorsal and ventral are, incidentally, more precise than words like front/back or upper/lower, which do not provide good comparisons between mammals given that some are four-legged and others two-legged.

"The information from sensory impressions goes through the entorhinal cortex before it arrives at the hippocampus, and studies carried out by Visiting Professor Menno Witter and his colleagues show that the entorhinal cortex consists of multiple overlapping bands. The lateral band of the entorhinal cortex has connections to the dorsal part of the hippocampus, which has to do with spatial orientation. The medial band of the entorhinal cortex has instead connections to the ventral part of the hippocampus, which plays a part in controlling the rats' fear reactions. If a rat feels unsafe, we may see changes in the activity of both the medial entorhinal cortex and the ventral hippocampus," says Steffenach.

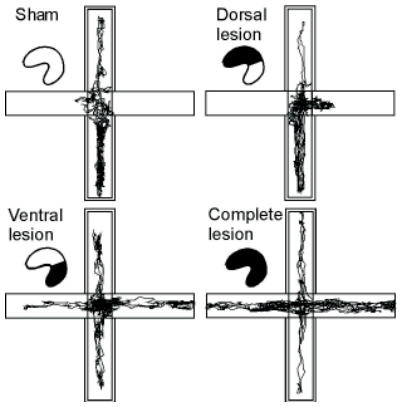
The entorhinal cortex also has an intermediate area that appears to have nerve connections to more intermediate and dorsal parts of the hippocampus.

Corridors and diving boards

Kjelstrup and Steffenach have done experiments in which the rats are released into a four-arm maze, in which two arms have high walls and are perceived as safe corridors for the rat, while the other two arms lack walls and give a feeling of being on a "diving board" when the rat creeps out onto them.

But if the researchers inject drugs that knock out parts of the hippocampus, something thrilling takes place. "Those rats that have lesions in the dorsal part of the hippocampus stay in the safe corridors, while the rats with ventral lesions on the other hand run about unconcernedly all over the place – on the diving boards too. Incidentally the same thing happens if the rats are given Valium! This suggests that the fear response is dependent on the ventral hippocampus and disappears when this part of the structure isn't functioning," says Kirsten Kjelstrup.

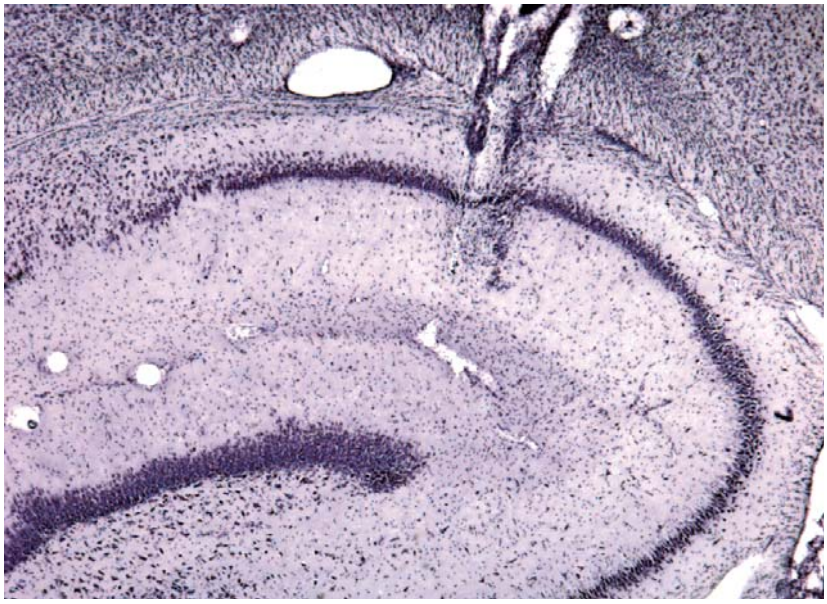
The four-arm maze has two arms that are felt to be safe on account of the walls, while the other two are open and are perceived as "diving boards" when the rats walk on them.



A rat with lesions in the dorsal hippocampus (above right) keeps to the safe part of the maze, while a rat with lesions in the ventral hippocampus or the whole hippocampus just as easily walks out onto the diving board. This experiment suggests that the rats' fear reaction depends on the ventral part, which is closer to the belly.

Memory in the forecourt of the hippocampus

It has been known since the 1950's that the hippocampus plays a central role for the memory of mammals. The researchers Marianne Fyhn and Vegard Heimly Brun are now testing new hypotheses that elements of the processing of memory begin as early as the entrance to the hippocampus, in the structure that is called the entorhinal cortex.



When the CBM researchers are to investigate the activity in the nerve cells in the hippocampus and the entorhinal cortex, they use specially developed equipment with micro-thin electrodes that can be placed with an accuracy of a 1/100th part of a millimetre at the cells that are to be investigated. The electrodes are so sensitive that they can register the electrical activity in a number of individual cells at the same time.

"All information that's to enter the hippocampus first goes through the *entorhinal cortex*, and we're now working on the basis of a hypothesis that this structure is more important than had been believed over the past 30 years. We've already seen results to suggest that a part of the processing in the hippocampus actually begins as early as in this 'forecourt'", say the research fellows, Marianne Fyhn and Vegard Heimly Brun. They are in the process of performing a series of joint experiments between the core group at CBM and Visiting Professors Menno P. Witter and Alessandro Treves.

When the CBM researchers are to investigate the activity in the nerve cells in the hippocampus and the entorhinal cortex, they use specially developed equipment with micro-thin electrodes that can be placed with an accuracy of a 1/100th part of a millimetre at the cells that are to be investigated. The electrodes are so sensitive that they can register the electrical activity in a number of individual cells at the same time.

Cand. Scient. Marianne Fyhn and medical student Vegard Heimly Brun, who both are working for a Ph.D., are studying the nerve cells in the entorhinal cortex, which is a kind of port of entry to the "internal memory" in the hippocampus.

The hippocampus contains a "map"

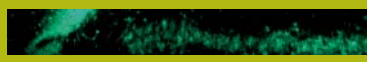
The rats are first trained to find food in enclosures that may for example be square or circular, placed in rooms with different characteristics on the walls. Earlier experiments have shown that a rat that is placed in a new enclosure develops a sort of map as it becomes familiar with the new surroundings. The map means that specific groups of nerve cells "fire" an electrical signal at specific points in the enclosure.

"The same group of cells in the hippocampus of the same rat always fire when the rat is in the same place. We've seen that this place-specific firing is stable over several days, and this suggests that the firing has great information value," say Fyhn and Heimly Brun.

The rats also manage to distinguish between different enclosures in the same room. If a rat is moved from a circular enclosure to a square one, the pattern of firing cells in the hippocampus is radically altered. This phenomenon is called *remapping*. But at the same time it appears that the firing pattern in the entorhinal cortex is not changed to the same extent. This may suggest that the hippocampus is important for the rats' capacity to distinguish between inputs that resemble one another, while the structures in front of the hippocampus in the entorhinal cortex express instead the features in common between different environments. The capacity of the hippocampus to distinguish between environments and episodes that resemble one another is probably crucial to recalling memories without mixing them up. This function is particularly important when memories must be *recalled*, and perhaps less decisive when only *recognition* is required.

Incidentally recognition corresponds to a multiple-choice task that involves choosing the right answer from a list of alternatives, while recall is a matter of finding the right answer without any tips in advance. It appears that recall requires activity in the hippocampus, while the entorhinal cortex and bordering structures can, under some circumstances, manage some types of recognition.

Scientific publications in 2003



Moser team:

MOSER, E.I. (2003)
Interneurons take charge. *Nature*, **421**, 797-799.

MOSER, E.I. & MOSER, M.-B. (2003)
One-shot memory in hippocampal CA3 neurons. *Neuron*, **38**, 147-148.

TUVNES, F.A., STEFFENACH, H.-A., MURISON, R., MOSER, M.-B. & MOSER, E.I. (2003)
Selective hippocampal lesions do not increase adrenocortical activity. *Journal of Neuroscience*, **23**, 4345-4354.

MORRIS, R.G.M., MOSER, E.I., RIEDEL, G., MARTIN, S.J., SANDIN, J., DAY, M. & O'CARROLL, C. (2003)
Elements of a neurobiological theory of the hippocampus: the role of activity-dependent synaptic plasticity in memory. *Philosophical Transactions of the Royal Society, Biological Sciences*, **358**, 773-786.

TUVNES, F.A., MOSER, M.-B. AND MOSER, E.I. (2003)
Lesions of ventral hippocampus impair avoidance of, but not escape from, potentially threatening stimuli. *Society for Neuroscience Abstracts* **29**, 91.10.

STEFFENACH, H.-A., WITTER, M.P., MOSER, E.I. AND MOSER, M.-B. (2003)
Impaired retention of spatial memory after lesions of a dorsolateral strip of the entorhinal cortex. *Society for Neuroscience Abstracts* **29**, 91.8.

KJELSTRUP, K.G., LEUTGEB, S., WITTER, M.P., MOSER, E.I. AND MOSER, M.-B. (2003)
CA3 pyramidal cells in the ventral one-third of the hippocampus are not spatially modulated. *Society for Neuroscience Abstracts* **29**, 91.7.

FYHN, M., WITTER, M.P., MOSER, M.-B. AND MOSER, E.I. (2003)
Decorrelation of spatial input from entorhinal cortex in dentate gyrus and hippocampus. *Society for Neuroscience Abstracts* **29**, 91.6.

OTNÆSS, M.K., FYHN, T.H., TUVNES, F.A., MOLDEN, S., MOSER, E.I. AND MOSER, M.-B. (2003)
Does the hippocampus contribute to simple non-spatial associations? *Society for Neuroscience Abstracts* **29**, 91.9.

LEUTGEB, S., KJELSTRUP, K., TREVES, A., MOSER, M.-B. AND MOSER, E.I. (2003)
Differential representation of context in hippocampal areas CA3 and CA1. *Society for Neuroscience Abstracts* **29**, 91.5.

BRUN, V.H., LEUTGEB, S., WU, H.Q., SCHWARCZ, R.,WITTER, M.P., MOSER, M.-B. AND MOSER, E.I. (2003)
Place representation in CA1 after selective lesions of entorhinal cortex layer III. *Society for Neuroscience Abstracts* **29**, 91.4.

LEUTGEB, J.K., FREY, J.U. & BEHNISCH, T. (2003)
LTP in cultured hippocampal-entorhinal cortex slices from young adult (P25-30) rats. *J. Neurosci. Methods* **130**, 19-32.

LOPEZ-BENDITO G, LUJAN R, SHIGEMOTO R, GANTER P, PAULSEN O AND MOLNAR Z (2003)
Blockade of GABAB receptors alters the tangential migration of cortical neurons. *Cerebral Cortex* **13**, 932-942.

SARGOLINI, F., ROULLET, P., OLIVERIO, A. & MELE, A. (2003)
Effects of intra-accumbens focal administrations of glutamate antagonists on object recognition memory in mice. *Behavioural Brain Research*, **138**, 153-163.

SARGOLINI, F., FLORIAN, C., OLIVERIO, A., MELE, A. AND ROULLET, P. (2003)
Differential involvement of NMDA and AMPA receptors within the nucleus accumbens in consolidation of information necessary for place navigation and guidance strategy in mice. *Learning and Memory* **10**, 285-292.

Carol A. Barnes:

ERICKSON, C.A. AND BARNES, C.A. (2003)
The neurobiology of memory changes in normal aging. *Experimental Gerontology*, **38**, 61-69.

ROSENZWEIG, E.S. AND BARNES, C.A. (2003)
Impact of aging on hippocampal function: plasticity, network dynamics, and cognition. *Progress in Neurobiology*, **69**, 143-179.

BARNES, C.A. (2003)
Long-term potentiation and the ageing brain. *Philosophical Transactions of the Royal Society of London, Series B*, **358**, 765-772.

MCNAUGHTON, B. L., BARNES, C. A., BATTAGLIA, F. P., BOWER, M. R., COWEN, S. L., EKSTROM, A. D., GERRARD, J. L., HOFFMAN, K. L., HOUSTON, F. P., ARTEN, Y., LIPA, P., PENNARTZ, C. M. A., SUTHERLAND, G. R. (2003)
Off-line reprocessing of recent memory and its role in memory consolidation: a progress report. In: *Sleep and Brain Plasticity* (P. Maquet, C. Smith and B. Stickgold eds.), Oxford: Oxford University Press.

ROSENZWEIG, E.S., REDISH, A.D., MCNAUGHTON, B.L., AND BARNES, C.A. (2003)
Hippocampal map realignment and spatial learning. *Nature Neuroscience*, **6**, 609-615.

LIN, G., ADIGA, U., OLSON, K., GUZOWSKI, J.F., BARNES, C.A. AND ROYSAM, B. (2003)
A hybrid 3-D watershed algorithm incorporating gradient cues and object models for automatic segmentation of nuclei in confocal image stacks. *Cytometry*, Part A, **56A**: 23-36.

BARNES, C.A. (2003)
Long-term potentiation and the ageing brain. In: T.V.P. Bliss, G.L. Collingridge and R.G.M. Morris (Eds.) *Long-Term Potentiation: Enhancing Neuroscience for 30 years*, Oxford University Press: United Kingdom.

Bruce L. McNaugthon:

MCNAUGHTON, B.L. (2003)
Long-term potentiation, cooperativity, and Hebb's cell assemblies: a personal history. *Philosophical Transactions of the Royal Society of London, Series B*, **358**, 629-634.

MCNAUGHTON, B.L. (2003)
Long-term potentiation, cooperativity, and Hebb's cell assemblies: a personal history. In: T.V.P. Bliss, G.L. Collingridge and R.G.M. Morris (Eds.) *Long-Term Potentiation: Enhancing Neuroscience for 30 years*, Oxford University Press: United Kingdom.

ROSENZWEIG, E.S., REDISH, A.D., MCNAUGHTON, B.L., AND BARNES, C.A. (2003)
Hippocampal map realignment and spatial learning. *Nature Neuroscience*, **6**, 609-615.

MCNAUGHTON, B.L., BARNES, C.A., BATTAGLIA, F.P., BOWER, M.R., COWEN, S.L., EKSTROM, A.D., GERRARD, J.L., HOFFMAN, K.L., HOUSTON, P.F., KARTEN, Y., LIPA, P., PENNARTZ, C.M.A., AND SUTHERLAND, G.R. (2003)
Off-line reprocessing of recent memory and its role in memory consolidation: A progress report. In: P. Maguet, C. Smith and B. Stickgold (Eds.) *Sleep and Brain Plasticity*. Oxford University Press: United Kingdom.

NITZ, D. & MCNAUGHTON, B.L. (2003)
Differential modulation of CA1 and dentate gyrus interneurons during exploration of novel environments. *Journal of Neurophysiology*, EPub 1 Oct.

Randolf Menzel:

EISENHARDT D, FRIEDRICH A, STOLLHOFF N, MÜLLER U, KRESS H, AND MENZEL R. (2003)
The AmCREB gene is an ortholog of the mammalian CREB/CREM family of transcription factors and encodes several splice variants in the honeybee brain. *Insect Molecular Biology* **12**, 373-382.

GIURFA M AND MENZEL R. (2003)
Biology of Adaptation and Learning, in Part I Biology and Behaviour of Adaptation and Learning. In Kühn R, Menzel R, Menzel W, Ratsch U, Richter MM, and Stamatescu I-O, editors. *Adaptivity and Learning: An Interdisciplinary Debate*. Berlin Heidelberg New York: Springer-Verlag. p 7-9.

GIURFA M AND MENZEL R. (2003)
Human spatial representation derived from a honeybee compass. *Trends Cogn Sci* **7**, 59-60.

MENZEL R. (2003)
Creating Presence by Bridging Between the Past and the Future: the Role of Learning and Memory for the Organization of Life, in Part I Biology and Behaviour of Adaptation and Learning. In Kühn R, Menzel R, Menzel W, Ratsch U, Richter MM, and Stamatescu I-O, editors. Adaptivity and Learning: An Interdisciplinary Debate. Berlin Heidelberg New York: Springer-Verlag. p 59-70.

MENZEL R. (2003)
Invertebrate Learning: Associative Learning and Memory Processing in Bees. In Byrne JH, editor. *Learning and Memory Second Edition- A revised and updated edition of Encyclopedia of Learning and Memory*. Farmington Hills, MI: Macmillan. p 273-277.

MENZEL R. (2003)
In Squire LR, editor. *The History of Neuroscience in Autobiography - Vol. 4*. Amsterdam: Elsevier. p 452-484.

RILEY JR, SMITH AD, STACH S, REYNOLDS DR, STOLLHOFF N, BRANDT R, SCHAUPP F, AND MENZEL R. (2003)
The Automatic Pilot of Honeybees. *Proceedings of the Royal Society of London DOI: 10.1098/rspb.2003.2542.*

ROHLFING T, BRANDT R, MENZEL R, AND MAURER CR, JR. (2003)
Segmentation of Three-Dimensional Images Using Non-Rigid Registration: Methods and Validation with application to Confocal Microscopy Images of Bee Brains. In Sonka M and Fitzpatrick JM, editors. *Medical Imaging: Image Processing, Vol. 5032 of Proceedings of the SPIE*, February 2003. p 363-374.

SANDOZ JC, GALIZIA CG, AND MENZEL R. (2003)
Side-specific olfactory conditioning leads to more specific odor representation between sides but not within sides in the honeybee antennal lobes. *Neuroscience* **120**,1137-1148.

SCHRÖTER U AND MENZEL R. (2003)
A New Ascending sensory tract to the calyces of the honeybee mushroom body, the subesophageal-calycal tract. *Journal of Comparative Neurology* **465**,168-178.

Richard Morris:

MORRIS RGM (2003)
Long-term potentiation and memory. *Philosophical Transactions of the Royal Society*, London, B., **358**, 643-647.

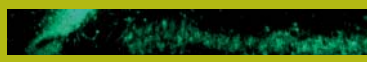
MORRIS RGM, MOSER EI, RIEDEL G, MARTIN SJ, SANDIN J, DAY M, AND O'CARROLL C (2003)
Elements of a neurobiological theory of the hippocampus: the role of activity-dependent synaptic plasticity in memory. *Philosophical Transactions of the Royal Society*, London, B., **358**, 773-786.

MORRIS RGM AND DAY M (2003)
Places and Flavours: one-trial paired-associate learning as a model of episodic-like memory in the rat. In *"Limbic and Association Cortical Systems - Basic, Clinical and Computational Aspects*, Eds. Ono, T., Matsumoto, G., Llinas, RR, Berthoz, A, Norgren, R, Nishijo, H, and Tamura, R. Elsevier Science.

DAY M, LANGSTON R, AND MORRIS RGM (2003)
Glutamate receptor mediated encoding and retrieval of paired-associate learning. *Nature*, **424**: 205-209.

KENWARD M, MORRIS RGM, AND TARRASSENKO L (2003)
Neural connections that compute. *Trends Neurosci.*, **26**: 393-394.

MORRIS RGM AND FILLENZ M (EDS) (2003)
Neuroscience: Science of the Brain. Booklet (56 pp) prepared for young students. British Neuroscience Association and European Dana Alliance for the Brain.



Ole Paulsen:

LOPEZ-BENDITO G, LUJAN R, SHIGEMOTO R, GANTER P, PAULSEN O AND MOLNAR Z (2003)
Blockade of GABAB receptors alters the tangential migration of cortical neurons. *Cerebral Cortex* **13**, 932-942.

MEREDITH RM, FLOYER-LEA AM AND PAULSEN O (2004)
Maturation of LTP induction rules in rodent hippocampus: Tole of GABAergic inhibition. *J Neurosci*, **23**, 11142-11146.

Alessandro Treves:

TREVES A (2003)
Computational constraints that may have favoured the lamination of sensory cortex. *Journal of Computational Neuroscience*, **14**, 271- 282.

ROUDI Y AND TREVES A (2003)
Disappearance of spurious states in analog associative memories. *Physical Review*, **E 67,** art. 041906.

MONTAGNINI A AND TREVES A (2003)
The evolution of mammalian cortex: from lamination to arealization. *Brain Research Bulletin*, **60**, 387-393.

TREVES A (2003)
A machine for learning and memory. In E Frauenfelder and F Santoianni, editors, Mind, *Learning and Knowledge in Educational Contexts*, pages 135-143, London. Cambridge Scholars Press.

TREVES A (2003)
The evolution of mammalian cortical networks: Computational advantages. In V Capasso, editor, *Mathematical Modelling & Computing in Biology and Medicine, 5th ESMTB Conference 2002*, pages 148-153, Grenoble. European Society for Mathematical and Theoretical Biology.

Menno Witter:

KLOOSTERMAN F, WITTER MP, VAN HAEFTEN T (2003)
Topographical and laminar organization of subicular projections to the parahippocampal region of the rat. *J. Comp. Neurol* **455**, 156-171

VAN DER WERF YD, WITTER MP, JOLLES J, UYLINGS HBM (2003)
Contributions of thalamic nuclei to memory functioning. *Cortex* **39**, 1047-1062

VAN DER WERF YD, SCHELTENS PH, LINDEBOOM J, WITTER MP, UYLINGS HBM, JOLLES J (2003)
Deficits of memory, executive functioning and attention following infarction in the thalamus; a study of 22 cases with localised lesions. *Neuropsychol*. **41**, 1330-1344

KAJIWARA R, TAKASHIMA I, MIMURA Y, WITTER MP, IIJIMA T (2003)
Amygdala input promotes the spread of excitatory neural activity from the perirhinal cortex to the entorhinal-hippocampal neurocircuit. *J. Neurphysiol* **89**, 2176-2184.

KEUKER JIH, ROCHFORD CDP, WITTER MP, FUCHS E (2003)
A cytoarchitectonic study of the hippocampal formation of the Tree Shrew (Tupaia belangeri). *J. Chem Neuroanat*. **26**, 1-15

WOUTERLOOD FG, BÖCKERS T, WITTER MP (2003)
Synaptic contacts between identified neurons visualized in the confocal laser-scanning microscope. Neuroanatomical tracing combined with immunofluorescence detection of postsynaptic density proteins and target neuron-markers. *J Neurosci Meth* **128**, 129-142

TOLNER EA, VAN VLIET EA, HOLTMAAT AJGD, ARONICA E, WITTER MP, LOPES DA SILVA FH, GORTER JA (2003)
GAP-43 mRNA and protein expression in the hippocampus and parahippocampal region during the course of epileptogenesis in rats. *Eur. J. Neurosci*. **17**, 2369-2380

KLOOSTERMAN F, VAN HAEFTEN T, WITTER MP, LOPES DA SILVA F (2003)
Electrophysiological characterization of interlaminar entorhinal connections: an essential link for re-entrance in the hippocampal-entorhinal system. *Eur. J. Neurosci*. **18**,1-16.

WITTER MP (2003)
Organization of cortico-hippocampal networks in rats related to learning and memory. *Int. Congr Ser. 2644*. Elsevier B.V.

WITTER MP, AMARAL DG (2004)
The Hippocampal Region. In: *The Rat Brain*. G. Paxinos (Ed.). Academic Press 3rd edition.

GROENEWEGEN HJ, WITTER MP (2004)
The Thalamus In: *The Rat Brain*. G. Paxinos (Ed.). Academic Press 3rd edition.

Robert Biegler:

BIEGLER, R. (2003)
Reading cognitive and other maps: How to avoid getting buried in thought. In K.J. Jeffery (Ed) *The Neurobiology of Spatial Behaviour*, Oxford Univerity Press, Oxford.

Hanna Mustaparta:

BICHAO, H., BORG-KARLSON, A.-K., ARAUJO, J. AND MUSTAPARTA, H. (2003)
Identification of plant odours activating receptor neurones in the weevil *Pissodes notatus* (Colepotera, Curculionidae). *J Comp Physiol A* **189**, 203-212.

STRANDEN M, LIBLIKAS I, KÖNIG WA, ALMAAS TJ, BORG-KARLSON A.-K., AND MUSTAPARTA H (2003)
(-)-Germacrene D receptor neurones in three species of heliothine moths: structure-activity relationships. *J Comp Physiol A* **189**, 563-577.

STRANDEN M., RØSTELIEN T., LIBLIKAS I., ALMAAS T. J., BORG-KARLSON, A.-K. AND MUSTAPARTA, H. (2003)
Receptor neurones in three heliothine moths responding to floral and inducible plant volatiles. *Chemoecology* **13**, 143-154.

Report from the Board for 2003

The most important goal for the Centre for the Biology of Memory in 2003, which was the Centre's first whole year of operation, was to establish the activity and build it up to be fully operational. The management of the Centre performed this task to the full satisfaction of the Board. In the course of the year the Centre lived up to expectations with respect to both administrative development and scientific results.

In 2002 the Norwegian Research Council nominated 13 Centres of Excellence (CoE) after a comprehensive and thorough process, in which 129 research communities competed. The CoE system is one of several measures intended to raise the level of quality of Norwegian research, and it means that specially selected groups of researchers receive long-term funding to engage in basic research of top-class international standard. The Centre for the Biology of Memory and two other CoE units at NTNU were inaugurated by Kristin Clemet, the Minister of Education and Research, at a ceremony on 18 November 2002.

The Board of the Centre for the Biology of Memory had two meetings in the course of 2003 with a total of 17 items of business to be transacted. In addition to its work on establishing the actual Centre, the Board discussed the establishment of a Master's Degree course and a Ph.D. programme in neuroscience, involving a number of subject communities at NTNU. The Master's Degree course was started in the autumn of 2003. Work is in progress to develop this course of study into a national Master's Degree course in co-operation with other universities.

In addition the Board took up matters relating inter alia to:
- the Board's terms of reference
- scientific reports
- accounts and budget
- the room situation
- contracts of employment
- a visit from the Centre's Advisory Board in 2005

Arnstein Finset, *Chairman of the Board*
Vigdis Moe Skarstein
Gunnar Bovim
Jan Morten Dyrstad

Trondheim, 21 January 2004

Operating accounts 2003 *(Årsregnskap)*

Income *(Inntekter)*	**Accounts** *(Regnskap)*	**Budget** *(Budsjett)*
Grants *(Bevilgninger)*		
Norwegian Centre of Excellence *(SFF)*		6 000 000
Other external projects (*Andre eksterne prosjekt)* **Note 1**		4 419 000
The Portuguese Ministry of Science and Technology		489 000
Contribution from the Norwegian University of Science and Technology *(Bevilgning fra NTNU)*		
S/O funding *(S/O-midler)*		1 196 000
Patch-clamp unit *(Patch-clamp-enhet)*		1 575 000
Operational grant *(Driftsbevilgning)*		1 333 333
Salaries *(Lønnsmidler)*		2 014 000
Other benefits *(Naturalytelse)* **Note 2**		3 847 106
Total income *(Sum inntekter)*		20 873 439
Expenses *(Utgifter)*		
Net personnel costs (including social benefits) **Note 3**	9 078 782	
(Netto faste lønnsmidler inkl sosiale kostnader)		
Scientific equipment *(Vitenskapelig utstyr)* **Note 4**	2 422 371	
Laboratory consumables *(Drift av laboratoriet)*	2 554 815	
Travel expenses *(Reise- og oppholdskostnader)*	652 922	
Other expenses *(Naturalytelse)*	3 847 106	
Profit transferred to 2004 *(Resultat overført til 2004)*	2 317 443	
Total expenses *(Sum utgifter)*	20 873 439	

Who's who at **The Centre for the Biology of Memory**

Note 1 – Other external projects
Grants from:
- Fifth framework programme of the European Community (2000-03)
- From the Research Council of Norway:
- Medicine and Health Programme Grant (2000-05)
- Strategic University Programme in Neuroscience (2000-03)
- Visiting Professorship to Richard Morris (2000-03)

Bevilgninger fra:
- *EUs 5. rammeprogram (2000-03)*
- *Fra Norges forskningsråd:*
- *MH-gruppe*
- *Strategisk Universitetsprogram (SUP)*
- *Gjesteprofessorat Richard Morris*

Note 2 – Other benefits
Server operations and backup, rooms and general operation, compensation for the use of administrative services.
Drift og backup av server, areal og drift, bruk av sentrale tjenester

Note 3 – Net personell costs
Indirect expenses from the CoE-grant amount to NOK 1 199 147. NOK 749 443 of this sum is re-directed as equity.
Indirekte kostnader beregnet av SFF-bevilgningen utgjør kr 1 199 147. Av dette er kr 749 443 tilbakeført som egenandel til prosjektet.

Note 4 – Scientific equipment
The sum includes patch-clamp unit, 2 Neuralynx data acquisition systems
Beløpet inkluderer patch-clamp enhet, 2 Neuralynx dataacquisition-systemer

The Board:

Professor **Arnstein Finset,** *University of Oslo (chairman)*

Vigdis Moe Skarstein, *University Director, NTNU (2003)*

Associate Professor **Julie Feilberg,** *ProRector, NTNU (from 2004-01-01)*

Professor **Gunnar Bovim,** *Dean, Faculty of Medicine, NTNU*

Associate Professor **Jan Morten Dyrstad,** *Dean, Faculty of Social Science and Technology management, NTNU*

The Advisory Board:

Professor **Larry Squire,** *University of California San Diego, USA (chairman)*
Professor **Terry Sejnowski,** *Howard Hughes Med Inst, Salk Institute, San Diego, USA*
Professor **Erin Schuman,** *California Institute of Technology, Los Angeles, USA*
Professor **Earl Miller,** *Massachusetts Institute of Technology, Boston, USA*

Directors

Edvard I. Moser, *Professor and director*

May-Britt Moser, *Professor and co-director*

Visiting professors

Carol Barnes, *Professor University of Arizona, USA*

Bruce McNaughton, *Professor University of Arizona, USA*

Randolf Menzel, *Professor Free University of Berlin*

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

Ole Paulsen, *Professor Oxford University, UK*

Alessandro Treves, *Professor International School for Advanced Studies, Italy*

Menno P. Witter, *Professor Free University of Amsterdam, Netherlands*

Research fellows

Stefan Leutgeb,
Post-doc

Jill Leutgeb,
Post-doc

Paul Ganter,
Post-doc

Francesca Sargolini,
Post-doc

Junior Research Fellows

Sturla Molden,
Cand. scient./Ph.D. student

Hill-Aina Steffenach,
Cand. scient./Ph.D. student

Frode A. Tuvnes,
Cand. scient./Ph.D. student

Mona Kolstø Otnæss,
Cand. polit./Ph.D. student

Kirsten Gjerstad Kjelstrup,
Stud. med./Ph.D. student

Vegard Heimly Brun,
Stud. med./Ph.D. student

Marianne Fyhn,
Cand. scient./Ph.D. student

Paulo Girão,
Ph.D. student

Torkel Hafting Fyhn,
Ph.D. student

Stig Hollup,
Cand. polit./Ph.D. student

Katrine Hauglund,
Ph.D. student.

Project students

Sunniva Steine,
Stud. med.

Thomas Smedsrud,
Stud. med.

Master students

Tora Bonnevie

Wenche Langfjord

Lisa Nielsen

Kamilla Medås

Trygve Solstad

Technical team

Ingvild Hammer,
Bioengineer

Kyrre Haugen,
Histology technician

Klaus Jenssen,
Electronics engineer

Raymond Skjerpeng,
Programmer

Haagen Waade,
Computer engineer

Ingunn E. Bakken,
Senior executive officer

Knut S. Grøn,
Animal technician (part-time)

Ingolf Hanssen,
Veterinary (part-time)

Roy Ulriksen,
Jack-of-all-trades (part-time)

Espen Sjulstad,
Electrode wirer (part-time)

Bjørn Håvard Solem,
Electronics technician (part-time)

Associated members

Robert Biegler,
Associate professor NTNU, Norway (DSCN 3038)

Hanna Mustaparta,
Professor NTNU, Norway

Boleslaw Srebro,
Visiting Associate professor, Master Study in Neuroscience

Gerit Pfuhl,
master student

Approvals

Animal experimentation in Norway is regulated through the Norwegian Animal Welfare Act and the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes.

Permission for performing experiments has been granted by the National Animal Research Authority. This authority has also inspected and accepted the animal unit of the Department of Psychology. The animal unit was built in 2001 and satisfies the requirements of a modern rodent unit as recommended in the European Convention. The licenses are valid for rats and mice.

Relations with the surrounding neuroscience community

Both NTNU and the Research Council have encouraged the Centre to establish relations with the surrounding local neuroscience community. The Centre is partly associated with the Department of Psychology at the Faculty of Social Science and Technology Management. Moreover, two research groups (Robert Biegler, Department of Psychology, Faculty of Social Sciences and Technology Management), and Hanna Mustaparta (Department of Biology, Faculty of Natural Sciences and Technology,) are interacting closely with the Centre, with their laboratories next to those of the core group. Their research supports the core activity of the Centre. These two groups are in receipt of a share of the CoE support. Their relationship to the CBM will be re-evaluated on the occasion of the mid-way evaluation in 2006.

The Biegler group has developed tasks that distinguish differences in how much various species of birds remember from differences in how long or accurately they remember. The Mustaparta group has long experience with olfactory mechanisms in an insect antennal lobe preparation. They are collaborating with visiting professor Randolf Menzel, who is working on spike ensemble activity in insects, complementing the proposed research in the mammalian hippocampus.

Animal keepers and brain researchers

The researchers at the CBM must be able to master a large number of different tasks. In addition to the important work of studying the memory processes in the rats' brains, the researchers must among other things train them to perform such tasks as finding food in enclosures of different shapes. The rats can also be trained to find their way about in different mazes, or in pools of water with hidden escape platforms.

The researchers must also construct the electrodes that are to register the activity of the brain and analyse the results. In addition the CBM has a staff of electrical engineers and technicians who are in charge of more specialised tasks, as well as its own keepers.

The CBM uses hooded rats that have been specially bred for their calm temperament that means they are happy in laboratory surroundings. Effective learning is dependent on the fact that the rats are not subject to stress or disorders.

NTNU

Annual Report 2003
Centre for the Biology of Memory

NTNU
Norwegian University of Science
and Technology