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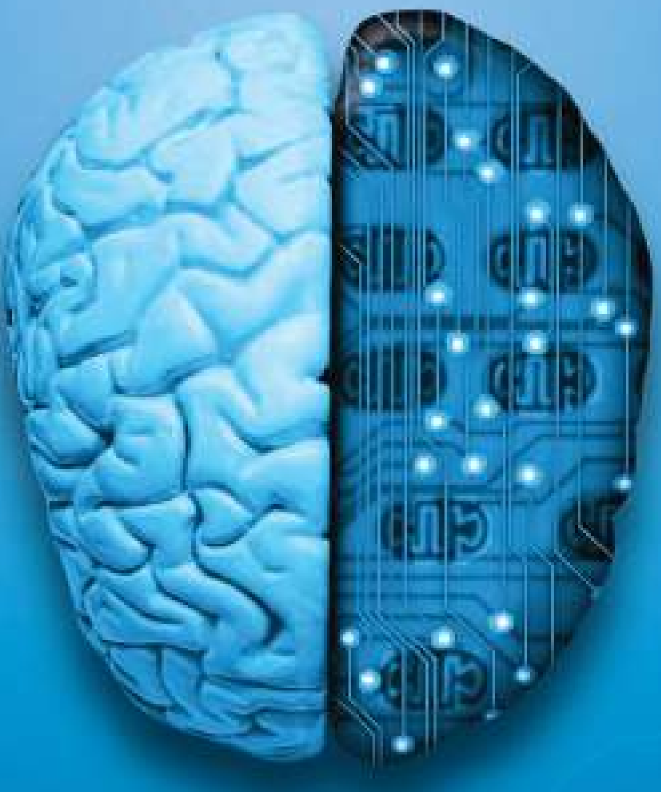
# Computational Neuroscience

## National Bernstein Network Computational Neuroscience



Dear reader,

Every second, billions of nerve impulses buzz through our brain. But how do they give rise to our thoughts and emotions, sensations and memories? This question is one of the great scientific challenges of our time. Within the Bernstein Network Computational Neuroscience we try to find answers to this, and related questions, by combining neurobiological experiments, computer-based data analysis, mathematical modeling and numerical simulation.

Since 2004, the German Federal Ministry of Education and Research (BMBF) has supported the new research field Computational Neuroscience through the funding initiative “National Bernstein Network Computational Neuroscience”. Within the last few years, the network has grown substantially, and currently comprises more than 200 research groups, some of which were only set up in the last years.

Bernstein Centers and Bernstein Groups are devoted to basic research in Computational Neuroscience. Their permanent integration into the host universities and newly established faculty positions with tenure provide the basis for a sustainable development of our young research field. Embedded into these lively scientific environments, Bernstein Award winners can start their own independent groups. The Bernstein Foci advance technological and medical applications. Finally, Bernstein Collaborations and international programs connect the network not only within Germany but also worldwide.

This brochure offers an insight into our research. Along eight broader themes, we outline the network’s research fields by presenting examples of our work. We hope that this tour will convey to you some of the fascination of these research topics, the enthusiasm of the scientists and the exciting future prospects of brain research. Of course, this brochure can show you only a minute fraction of what we do. We therefore invite you to find out more about latest research news and interesting activities on our website (www.nncn.de).

In the past few years, the Bernstein Network has successfully established itself in the international scientific community. At the same time, the network has managed to link Bernstein projects at each site with ongoing and new focus areas in teaching and research, which has also greatly benefited various projects of the German Excellence Initiative. This broad base allows excellent support for junior researchers. It is most important, however, that the research initiated by the BMBF can be maintained at the participating universities and research institutions on a long-term basis and at a high scientific level and intensity. As our research and its technological applications —including “brain-computer interfaces”—raise issues of great social relevance, alongside our scientific work we will continuously seek a dialogue with the public. Our ultimate hope is that, together, we will succeed in achieving a better understanding of mind and brain.

Prof. Andreas Herz
*Spokesman of the Project Committee*
*Bernstein Network Computational Neuroscience*

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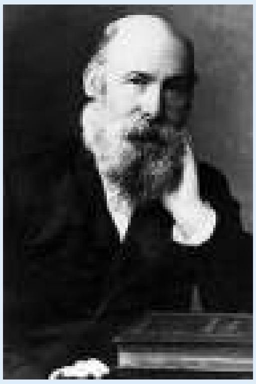
# CONTENTS

# What is Computational Neuroscience?

**The brain** is probably the most complex structure that evolution has produced. Billions of nerve cells, linked by trillions of connections, process enormous amounts of information within a split second. Although recent decades have seen significant progress in our understanding of the cellular and molecular basis of brain function, we are still far from a deep understanding of complex cognitive capacities such as perception, learning and action.

**Computational Neuroscience** can make an important contribution to this endeavor. Its interdisciplinary approach combines the expertise of mathematicians, physicists, biologists, physicians, psychologists, computer scientists and engineers. This allows hypotheses to be rephrased in mathematical terms that can be simulated and tested in the computer. Computer simulation is a modern form of "thought experiment" that is essential for the quest to understand such complex structures as the human brain.

**For medicine and technology,** Computational Neuroscience offers an enormous innovation potential. Processes in neurological diseases, for example in epilepsy, are emulated on the computer. In these simulations, hypotheses on their origin as well as approaches to their diagnosis and therapy can be tested. In conjunction with information technology, this opens up new horizons for applications. Already, neuronal implants offer deaf people access to acoustic perception. Thought controlled artificial limbs are being tested in the clinic. Intelligent computer systems and autonomous robots will make future life easier, both in sickness and in health.



**Julius Bernstein**
**(1839–1917)**

As early as 1902, when barely any households were connected to the electricity supply and electric light was a luxury, Julius Bernstein (1839–1917) postulated a mechanism that explained how electric stimuli spread along the membranes of nerve cells. Bernstein's "membrane theory" was the first ever physicochemical explanation of electric events in biology and the first quantitative theory in electrophysiology. Of course, at the time, Bernstein could not even dream of the opportunities afforded by modern computers. Nevertheless, with his mathematical description of neuronal processes, he paved the way for computer modelling of complex brain processes. In recognition of this seminal research, the German Federal Ministry of Education and Research has chosen to name their Computational Neuroscience funding initiative after Julius Bernstein.

# The Bernstein Network

**Having recognized the potential** of the new research field Computational Neuroscience at a very early stage, in 2004 the German Federal Ministry of Education and Research (BMBF) launched the funding initiative “National Bernstein Network Computational Neuroscience”. Its objective is to sustainably establish this discipline in Germany and to explore its perspectives for innovation. Within the framework of the Federal Government’s High-Tech Strategy, the National Bernstein Network is currently supported with a total funding volume of around 156 million euros.

**The network provides** a new quality of integration and interconnection of expertise in the theoretical and experimental neurosciences in Germany, it expands them and links them internationally. Across Germany, the network comprises more than 200 research groups at over 20 locations. The participating research groups are located at universities and other research institutes (Fraunhofer, Helmholtz, Leibniz, and Max Planck Institutes). The integration of collaboration partners in industry fosters the translation of research results into practical applications. The network offers a variety of study programs and training opportunities for young scientists, high-profile research projects and attractive career prospects. A central coordination site supports the network’s activities and works to enhance visibility, communication and synergy effects.

**David Willshaw**
*University of Edinburgh, UK*
*Representative for the United Kingdom in the International Neuroinformatics Coordinating Facility (INCF)*

“The Bernstein Network has established Germany as the European leader in Computational Neuroscience, a field of research that is now recognized as an essential part of the multidisciplinary research activity in the neurosciences.

Researchers in the Bernstein Network have built profitable connections with partners in industry and clinics, forming a basis for innovations in many future key areas of science, medicine, commerce and technology.”

**Larry Abbott**
*Columbia University New York, USA*

“The German Bernstein Network has played a major role in the explosive worldwide growth of Computational Neuroscience.

By assembling an impressive group of internationally recognized researchers and young scholars, and through its unique structure and scientific activities, the Bernstein Network has made major contributions to our understanding of neural circuitry and cognitive functions and is set to play a leading role in this area for years to come.”

# Bernstein Centers

**Six "Bernstein Centers for Computational Neuroscience"** (BCCN) form the core of the Bernstein Network. In 2004, the BMBF initially provided 40 million euros for the centers, and extended this funding in a second round in 2010 by another 43 million euros.

**As structural cores,** the Bernstein Centers establish the discipline Computational Neuroscience at the respective locations in a sustainable fashion. Supporting this objective, 14 new professorships in the area of Computational Neuroscience were or are being created at the centers, which are initially financed by the BMBF and subsequently permanently maintained by the respective states. As their academic teaching activities are integrated into the educational portfolio of the host universities, the centers significantly contribute to the discipline's dissemination and development.

**The centers unite** a critical mass of experimental and theoretical expertise, focusing on research areas of international relevance. At the core of the centers' scientific interests are fundamental questions about the function and information processing of the brain—from single cells up to whole networks.


Berlin

The **BCCN Berlin** addresses the question: "How is it possible that we can respond to sensory stimuli with millisecond precision, given that the neuronal processing elements—synapses, neurons, small and large networks—vary tremendously in their responses to the same stimulus?" Using mathematical models, neurophysiological recordings and imaging techniques, the scientists investigate the computing steps of the brain at the level of individual cells and whole networks.


Göttingen

The **BCCN Göttingen** studies the dynamics and adaptivity of neuronal circuits in the brain. Mathematical models and computer simulations, combined with cutting edge experimental techniques, are employed to discover how the brain's functionality and adaptivity emerge from the collective interplay of its parts. The center investigates cooperative processes from the subcellular level to the level of neuronal networks and up to interacting brain areas and cognitive functions. The research projects also lay the foundations for the development of novel neuroprostheses.


Heidelberg–Mannheim

The **BCCN Heidelberg–Mannheim** examines the relationships between genetic risk factors for psychiatric disorders, the resulting network dynamics and their influence on cognition and behavior. Computer models are developed in order to gain a deeper understanding of how specific molecular and neuronal processes could lead to psychiatric disorders, such as schizophrenia and depression. The results may be used to identify novel pharmacological interventions ('in silico-neuropharmacology').

Our perception is not simply a copy of the sensory stimuli we receive, but an abstract interpretation of the world. Complex processing mechanisms, which combine the information of the sensory stimuli with specific prior knowledge about the physical properties of the world, enable this interpretation. At the BCCN Tübingen, scientists from different disciplines work together to explore the neural basis of these inference processes in the brain.


Tübingen

"How are space and time represented in neural systems?" This is the research topic of the **BCCN Munich**. Neural representations are investigated using modern experimental methods, computer-based modeling and theoretical analyses of various sensory modalities (acoustic, vestibular, visual). The center aims at, inter alia, a better understanding of age-related deficits in spatial cognition and the identification of new therapeutic avenues to reduce these deficits. Some of the projects are also concerned with the development of technical assistive systems.


Munich

The brain enables us to actively interact with our environment. Speed, fault-tolerance, adaptivity and creativity characterize normal brain function, guaranteeing that we successfully master our daily lives. Dynamics are an outstanding feature of the brain at each level of observation. The **BCCN Freiburg** aims to improve our understanding of these dynamics regarding the underlying mechanisms, inter-relations and functional role, and explore the application of new insights and techniques to outstanding questions in biomedicine and neurotechnology.


Freiburg

**As an example** for the long-term transformation of the initial BMBF funding into an independent research structure, the BCF (Bernstein Center Freiburg) was recently established as an independent Research Center at the University of Freiburg. The BCF integrates all research projects in Computational Neuroscience and Neurotechnology funded by the BMBF or other third party funding sources. Moreover, it implements and manages all teaching and training activities in this interdisciplinary research area.

# Bernstein Award

**Actively promoting** particularly talented young scientists is of crucial importance for the sustainable establishment of the young discipline Computational Neuroscience in Germany. To this end, in 2006 the BMBF launched the annual "Bernstein Award for Computational Neuroscience". It offers excellent young researchers from all over the world the best conditions for establishing an independent research group at a German research institution and pursuing their outstanding research ideas as full members of the Bernstein Network. The prize is valued at up to 1.25 million euros over the course of five years.

**Combining theoretical** and experimental approaches, the awardees investigate a variety of research questions.

**Matthias Bethge**[6, 35] examines how the brain encodes visual information and separates relevant and irrelevant information.

**Jan Benda**[5, 36] focuses on the role of neuronal variability for signal processing in sensory systems.

"How do dynamic cellular processes influence information processing?" **Susanne Schreiber**[1, 15, 37] is trying to find out.

"Among the many factors that influence our daily decisions, which are the most important parameters?" This question is being addressed by **Jan Gläscher**[38].

**Udo Ernst**[20, 39] examines how factors such as prior knowledge and context influence information processing in the visual system.

*Bernstein Awardees (from left):*
*Jan Benda (2007), Susanne Schreiber (2008), Matthias Bethge (2006).*

*Bernstein Awardee 2009: Jan Gläscher*

*Bernstein Awardee 2010: Udo Ernst*

# Bernstein Partners

**The funding measure** “Bernstein Partners” was established in 2007 in order to make full use of the existing knowledge in Germany to establish the young discipline Computational Neuroscience and to expand the spectrum of topics. It includes the establishment of five Bernstein Groups, funded by a total of 5 million euros, and eleven Bernstein Collaborations, supported by another 7.5 million euros.

**The “Bernstein Groups”** are additional structural cores that are smaller than the Bernstein Centers and focus their regional experimental and theoretical skills on more narrowly defined topics.

Information processing occurs on multiple scales within our brain—from the molecular level up to the interaction of multiple brain regions. By aid of mathematical models, scientists of the **Bernstein Group Heidelberg** investigate the subcellular and cellular mechanisms of signal processing in neurons and reconstruct the anatomy of single cells. On this basis, they build highly detailed simulations of the behavior of single cells and small neuronal networks.

All cognitive capacities are ultimately based on the activity of individual nerve cells, which either “fire” or remain silent. This neuronal activity reflects not only sensory stimulation and top-down regulation, but also exhibits substantial spontaneous fluctuations. The influence of this variability on neuronal responses and on cognitive function is explored by the **Bernstein Group Magdeburg**.

Incoming stimuli are also highly variable. We are nevertheless able to recognize faces or objects, regardless of the situation, lighting conditions or many other factors. Researchers of the **Bernstein Group Bremen** examine the foundations of this surprising adaptivity in the visual system.

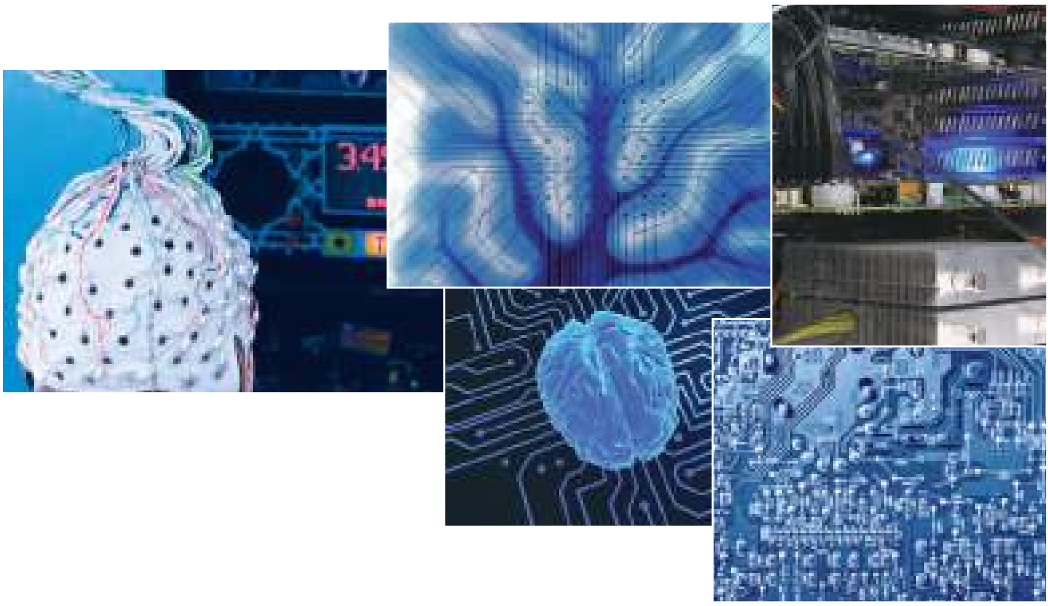
A theoretical framework of the **Bernstein Group Bochum** explains higher brain functions as a result of the spatial and temporal activity patterns of neural networks. The theoretical models are formulated based on a range of experimental data.

Pain is a complex process. Members of the **Bernstein Group Jena** develop time-varying analysis methods and models to improve the investigation of interactions between brain regions during pain processing. Many areas of Computational Neuroscience can benefit from these methodological developments.

**The “Bernstein Collaborations”** connect Bernstein Centers with individual research groups distributed all over Germany that contribute important expertise for tightly focused collaborative projects.

**Project titles and locations:**

- Action Potential Encoding *(Bochum / Göttingen)*
- Movement Associated Activation *(Tübingen / Freiburg)*
- Memory Network *(Gießen / Tübingen / Berlin)*
- Information Encoding *(Göttingen / Munich)*
- Neuronal Synchronization *(Rostock / Freiburg)*
- Neurovascular Coupling *(Tübingen / Berlin)*
- Network Simulation *(Heidelberg / Munich)*
- Olfactory Coding *(Constance / Berlin)*
- Physiology and Imaging *(Erlangen–Nuremberg / Berlin / Magdeburg)*
- Transcranial Stimulation *(Kassel / Göttingen / Ilmenau)*
- Temporal Precision *(Aachen / Berlin)*



# Bernstein Focus: Neurotechnology

**The funding measure** "Bernstein Focus: Neurotechnology" (BFNT) aims at narrowing the gap between basic research and technological applications. Since 2008, research along these lines has been supported at five different locations with a total of 34 million euros.

**Besides a high regional** focus of neuroscientific and technological capacities, close collaboration with leading industry partners is an essential part of the concept. A total of eight professorships were established within the Bernstein Focus: Neurotechnology. They will be permanently maintained by the individual states.

**Advances in the neurosciences** increasingly allow principles from biology and information theory to be used for innovative solutions in a range of different areas such as biomedicine, information technology and robotics. The projects of the Bernstein Focus: Neurotechnology undertake important steps towards this goal.

The goal of the **BFNT Berlin** is to systematically develop non-invasive techniques of 'brain reading' in order to support human-machine interactions. Both resolution and usability are to be optimized. This research could, for example, be employed in the field of telecommunications. An understanding of the neural processes that cope with disturbances in speech signals can be used to optimize technical systems and to improve quality. In addition, the technique could be applied in driver assistance systems, contributing to improving traffic safety. The sustainable establishment of this field is supported by a dedicated chair in neurotechnology.

At the **BFNT Göttingen,** scientists work on the development of feedback loops between neuronal and technical systems in which biological and technical components are closely interconnected: the neuronal system influences the technical device, which in turn sends information back to the neuronal system. Central fields of application include diagnosis, treatment and rehabilitation of neuronal deficits and control of prostheses. This research approach also includes the application of optical and electrical stimulation and imaging.

Developing neuroprostheses is the objective of the **BFNT Freiburg–Tübingen**. Electrical and chemical signals in the brain will be used to control devices that will one day assist stroke patients or counteract seizures in epilepsy patients. To this end, scientists in Freiburg and Tübingen study interfaces between technical devices and neuronal networks, develop methods to extract information from neuronal signals (e. g. for brain-computer interfaces and explore strategies for the stimulation of neuronal networks.

Our ability to visually perceive our environment is for most of us both natural and indispensable. For computers, the perception and recognition process is still a big hurdle. The **BFNT Frankfurt** plans to develop an artificial vision system that can learn autonomously and assembles itself from basic functional elements. Such systems could be applied in robots, in driver assistance systems, or in traffic control.

# Bernstein Focus: Neuronal Basis of Learning

**The "Bernstein Focus: Neuronal Basis of Learning"** expands the Network's scope by application-oriented collaborative projects in the innovation field of learning. Since 2009, the BMBF has supported eight collaborations by this funding measure, with a total of 16 million euros.

**Our ability to remember** glues our lives together—over short as well as long time periods. We know where we are and what we have just done thanks to our short-term memory. The fact that we remember our childhood and long gone events is due to long-term memory. Every event that we memorize changes our brain a little and leaves its traces. Every person's brain is slightly different and structured by personal experiences and a variety of learning processes.

**The projects in this Bernstein Focus** tackle a wide range of questions, such as: What changes occur in individual nerve cells during conditioning? How do birds learn complex songs and how can our brain distinguish the different songs? What processes occur when we make decisions? Which architecture does a neuronal network need to have in order to be able to learn autonomously?

**To tackle these different aspects** of learning, researchers from the experimental sciences work in close cooperation with experts in theoretical neurobiology. Results from basic research are translated into clinical applications. As soon as the causes and effects of different brain activities have been understood, this knowledge can be used for developing new therapies, for example, for stroke and dementia patients.

**Also in the field of** technology, innovative applications can be expected. Plugged into mathematical formulas, biological insights can be used for the development of modern computer systems. Further fields of possible applications range from driver assistance systems to autonomously acting robots that explore their environments and adapt their actions accordingly.

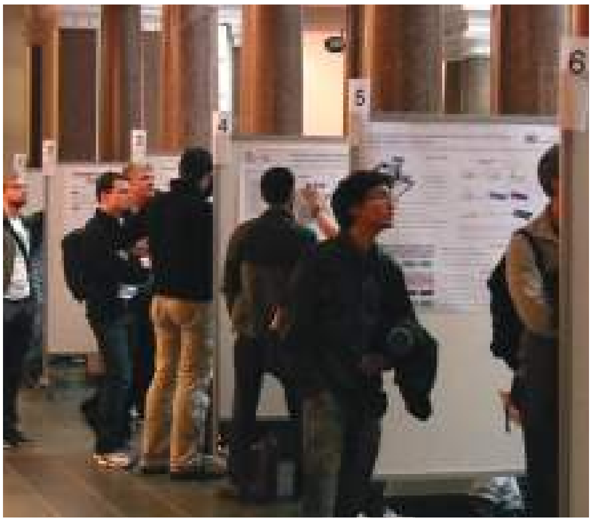
**Project titles and locations:**

- Memory in Decision Making
  *(Berlin / Freiburg / Würzburg)*
- Complex Human Learning *(Hamburg / Berlin)*
- Ephemeral Memory *(Martinsried / Munich / Constance)*
- Learning Behavioral Models *(Bochum / Lauffen)*
- Plasticity of Neural Dynamics *(Martinsried / Munich)*
- Sequence Learning
  *(Bochum / Berlin / Bremen / Oldenburg)*
- Visual Learning *(Jena / Göttingen)*
- State Dependencies of Learning
  *(Berlin / Bochum / Lübeck / Leipzig)*

# Bernstein Conference

**Just like the brain** itself, a research network lives through the diversity and richness of its connections. A central communication hub is the annual “Bernstein Conference”. Starting from a mainly internal forum, it has grown into a full-blown international conference, offering plenty of opportunities for intensive scientific exchange and for establishing contacts to Bernstein members and other national and international scientists. Worldwide leading experts are invited as speakers. Taking place at annually changing network locations, the Bernstein Conference also provides the framework for the annual Bernstein Award prize ceremony.

**The conference is followed** by a symposium organized by the Bernstein Network’s students. It offers the young researchers opportunities to present their work, exchange ideas in a relaxed atmosphere and establish personal contacts to the distinguished invited speakers.





# Training the Next Generation

**Ambitious research needs** well-qualified scientists. For this reason, the members of the Bernstein Network are involved in a variety of study programs and continuing education courses, from the undergraduate level to master and doctoral programs and special courses for advanced scholars.

**In addition to a PhD program,** the Bernstein Center Berlin developed the first Master's degree in Computational Neuroscience in cooperation with Berlin's Technische Universität, Freie Universität, Humboldt Universität, and Charité.

**Interview with**
**Klaus Obermayer** [1, 7, 17, 27, 41]
*Technische Universität Berlin*
*Coordinator of Germany's first Master's program in Computational Neuroscience*

**Who is the target group of your study programs?**

We focus on students both from theoretically and from experimentally oriented disciplines. Students of mathematics, physics or computer science can learn to apply their knowledge to neurobiology. On the other hand, biologists, physicians and psychologists are introduced to the necessary theoretical knowledge. This interdisciplinary approach is very beneficial for all participants. Applicants to the Master's program need a first degree, i. e., a Bachelor's or Diploma degree. For the PhD program, a Master or Diploma degree is required.

**What are the motivations with which students apply to your programs?**

The motivations are as diverse as the entire discipline. Some want to understand how the brain functions, from the perspective of biology or computer science. For many of them, clinical research and biomedical technology are interesting fields of work. Finally, there are some students, coming from more technical disciplines, who want to do research in the areas of artificial intelligence or autonomous robotic systems.

**How are the two programs structured?**

In both cases, students require solid math skills. In the first year of the Master's degree, the basics of Computational Neuroscience are taught. That comprises modeling neuronal systems and higher brain functions, analysis of neuronal data and machine learning. In the second, more research-oriented year, the students perform three scientific projects in the experimental and theoretical areas, and finally carry out their Master's thesis.

PhD students start by acquiring specific scientific foundations through advanced courses. Over the following semesters, they can expand their scientific spectrum by attending further courses in Berlin or elsewhere.

**The programs have been operating for several years already. Where do the graduates end up?**

Most of those who have completed the Master Program want to continue with a PhD. Also after the PhD, the vast majority remain in academia. Some graduates were able to gain a foothold in basic research departments in industry.

**How do educational efforts contribute to Computational Neuroscience?**

Study programs allow us to attract highly qualified students from all over the world. The growing number of applicants for our Master and PhD programs reflects their increasing attractiveness. The study programs contribute to Germany's position as one of the world's leading countries in this discipline. I am convinced that, in the future, industry and research will find more and more applications for the methods and models of Computational Neuroscience. This will also increase the need for outstanding graduates.

# Internationalization

**Modern science does not** stop at national borders. Members of the Bernstein Network maintain a variety of worldwide contacts to other leading scientists and centers for Computational Neuroscience. Scientific exchange is fostered by international collaborations and exchange programs (e. g. with the US-American Sloan-Swartz Centers for Theoretical Neurobiology).

In a series of bilateral workshops, organized in collaboration with the corresponding national funding agencies, it was possible to increase contacts to countries that are especially active in Computational Neuroscience and explore the potential for further cooperation. Such workshops have already resulted in funding agreements with the USA and Japan, and in a dedicated bilateral German–US-American funding measure in Computational Neuroscience (see below).

**Hirsh Cohen**

*Science Director, Swartz Foundation, USA*

“We at the Sloan-Swartz-Centers program have been very fortunate to be able to share with the Bernstein Centers some of the superb talent that we are all now seeing come into the field of Computational Neuroscience through our annual exchange of young people. And through this and many other means we are sharing the excitement of this fast moving, growing and vastly important new science.”

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## German–US-American Collaborations

**In the joint** transnational funding initiative “Germany–USA Collaborations in Computational Neuroscience”, the BMBF, the National Science Foundation (NSF) and the National Institutes of Health (NIH) support scientific exchange and collaboration in Computational Neuroscience since 2010. In a first funding round, 1.7 million euros were made available on the German and the US-American side, respectively. Additional funding rounds are intended to continuously intensify German–US-American cooperation. The following projects are already being funded:

- Berlin–Cambridge: Role of Astrocytes in Cortical Information Processing
- Freiburg–Cambridge: Integration of Bottom-Up and Top-Down Signals in Visual Recognition
- Lübeck–New York: Effects of Weak Applied Currents on Memory Consolidation during Sleep
- Mannheim–Los Angeles: Persistent Activity in the Entorhinal Cortex In Vivo
- Munich–San Diego: Hippocampal Representation of Auditory and Spatial Sequences

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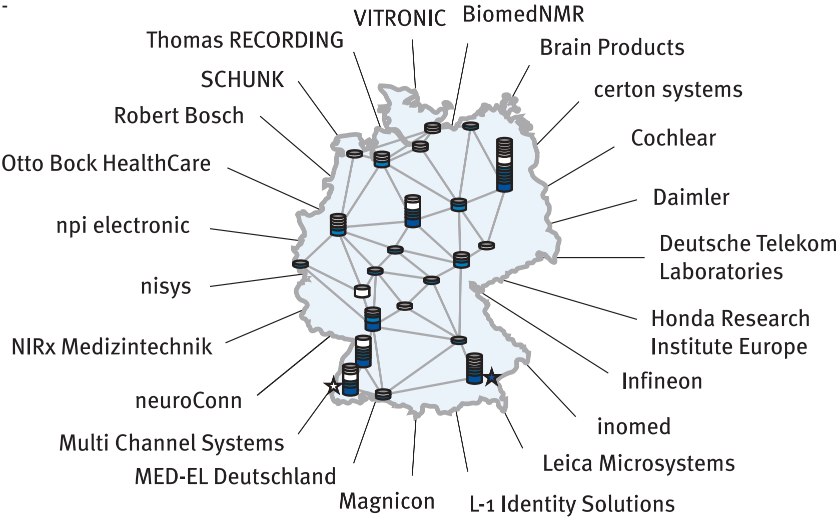
## German INCF Node (G-Node)

**Scientific advances** in the neurosciences can be accelerated significantly by the exchange of methods and the development of standards. To this end, the International Neuroinformatics Coordinating Facility (INCF) was founded in 2005 on the recommendation of a working group of the Organisation for Economic Cooperation and Development (OECD). It currently has 16 member countries worldwide, with Germany being a founding member. As an international platform, INCF supports the exchange of data, models and analysis tools and supports the standardization process. The German INCF node in Munich (G-Node) has been financed by the BMBF since 2008, with a funding volume of approximately 2 million euros. As an integral part of the Bernstein Network, the node serves as a central connection point to the global network of the INCF.

G-Node supports national and global collaborations between experimental and theoretical neuroscientists by supplying open-source infrastructure for data access, storage and analysis, tailored to the needs and requests of individual researchers. G-Node extends the teaching and training activities in the Bernstein Network in the areas of method development and data analysis.

# Collaborations with Industry

**Computational Neuroscience** offers an enormous potential for technological applications that exploit the principles of neuronal processes. Members of the Bernstein Network work in close cooperation with over 20 industry partners from various areas, ranging from information technology and electronics through suppliers for lab and medical equipment up to telecommunications and automotive industry. These collaborations facilitate and accelerate knowledge transfer between academia and economy. Additionally, in joint workshops and bilateral meetings with participants from academia and industry, specific topics are identified in which new applications appear to be especially promising.



# Bernstein Association for Computational Neuroscience

**The public has** high expectations from the field of neuroscience. Since Computational Neuroscience is an extraordinarily complex research area, special efforts are required to convey its research topics, results, and their implications to science and society.

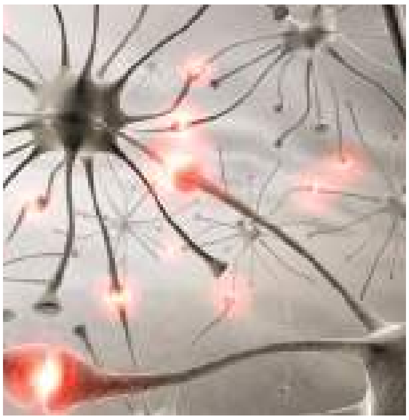
**The Bernstein Association for Computational Neuroscience,** founded in 2009, takes up this task. Its objective is to promote research and training in Computational Neuroscience in Germany and communicate the research themes to the general public. As a nonprofit organization, it operates on the basis of donations and membership fees.

**With the internationally** advertised “Brains for Brains Award”, the Bernstein Association offers young researchers from all over the world a unique opportunity to get to know the scientific landscape in Germany, to present their work to the scientific audience of the Bernstein Conference and to establish personal contacts with local experts.

Bernstein
Association for
Computational Neuroscience

# The Brain's Code

**The brain is** the most complex information processing system that evolution has produced. With our senses we perceive the world, we interpret what we see and hear, we think and plan our actions. A system can only receive, store and process information if it has a "language", an internal representation of the messages into which it encodes the information. The brain, too, has such a code. Neurons transmit information in the form of electrical signals, known as action potentials or spikes. Every bit of information is encoded in the spatial and temporal patterns of spikes. But what does this neural "Morse code" look like in detail? Many scientists across the world are working on cracking this mystery.



*A single nerve cell simultaneously communicates with up to 10,000 other cells.*

**In some neurons,** researchers found, the number of spikes emitted in a certain period of time is what counts. Some sensory cells operate on this principle—the louder a sound or the brighter a light, the higher the frequency with which they emit their spikes. Neurons that innervate muscles also use such a "rate code". The faster their spike frequency, the stronger the muscle's contraction. However, a rate code is only one possibility for transmitting information.

**Often, the exact timing** of the pulses is also of great importance. For example, this is the case in sound localization, studied by researchers around Benedikt Grothe[5, 16] and Hermann Wagner[29]. An acoustic signal reaches the ear directed towards the sound source slightly earlier than the opposite ear, resulting in a binaural time difference. Neurons can measure binaural time differences of less than one hundred microseconds—which probably is one of the brain's most accurate mechanisms. Their average spike rates depend on the binaural time difference: if two signals arrive simultaneously, their rate is maximal. With increasing time differences, their spike rate decreases. Thus, the neurons act as very precise coincidence detectors. This processing mechanism apparently arose independently twice in evolution: in mammals and in birds.

**To measure the exact timing** of a given nerve cell's activity in relation to other cells, neuronal oscillations —synchronous activity patterns of neuron populations— can be used as reference signals. Many neurons have a "self-resonance"—a kind of favorite frequency at which they prefer to discharge and thus send out signals to their target cells. However, since they are interconnected in complex networks, in which each neuron responds to its neighbors, a common rhythm develops. This process is comparable to the synchronization of applause after a concert. Various scientists in the Bernstein Network investigate how these oscillations are produced, applying multidisciplinary approaches including computer simulations (see "Computer Models of the Brain", p. 21). One research theme of Marlene Bartos[2], Peter Jonas[2], Hannah Monyer[4, 21] and Susanne Schreiber[1, 15, 37] is to examine the role played by inhibitory neurons (neurons that inhibit other cells instead of exciting them) in the generation of such oscillations and how they contribute to information coding. Joint oscillations of many neurons are a common phenomenon. Neuronal oscillations can also be measured during sleep. It is currently assumed that they are relevant in memory formation. For instance, they play an important role in spatial memory.

**A further function** of neuronal oscillations was first theoretically formulated by Christoph von der Malsburg[8] and later on supported by the research of Wolf Singer[8]. Oscillations, according to their theory, contribute to binding together the distributed activities of the brain. In visual perception, for example, different features of an object —its color, shape and motion—are processed in different areas of the visual cortex. The researchers hypothesize that synchronous neuronal activity in these different areas accounts for our perception of a multi-faceted object as a whole.

**“Prominent critics have argued that free will must be an illusion, for the simple reason that neural dynamics are based on deterministic laws. However, this reasoning is not correct. Thermal noise causes random variability at all levels of the brain, consequently, thinking and decision-making processes are never fully predetermined. This insight itself does not explain free will, and should not be misunderstood as doing so, but it indicates that the argument put forward by supporters of ‘Neural Determinism’ does not stand up to scientific scrutiny.”**

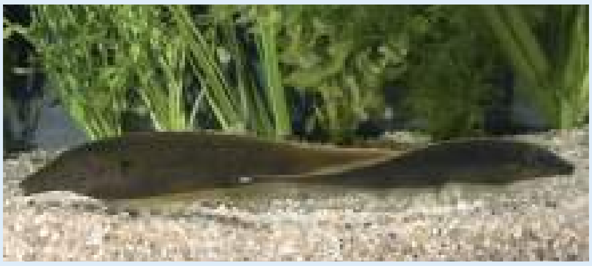
*Andreas Herz* [1, 5, 14, 25, 40]

**For a long time** it was thought that a given neuronal network could either faithfully transmit the rate of nerve impulses or maintain their exact timing, but not both simultaneously. However, recent neuronal network simulations by Ad Aertsen [2, 9], Arvind Kumar [2] and Stefan Rotter [2, 9] have shown that under certain, well-understood conditions, both kinds of information transfer are indeed possible in one and the same network. This finding significantly expands a basic model of neuronal signal propagation.

**Besides the neuronal mechanisms** of signal transmission, researchers are facing another big puzzle. In contrast to conventional assumptions, nerve cells do not behave in a simple, stereotyped stimulus-response pattern. A given stimulus can sometimes elicit a neuronal response and sometimes fail to do so. Up until now, it was assumed that this “unreliability” is compensated by the fact that many cells work simultaneously, averaging out such “errors”. But new experiments have shown that even the activity of a single cell can have an influence on an animal’s behavior (see interview with Michael Brecht, p. 20). Another assumption is that the neuronal “noise” could regulate the neuronal sensitivity or the synchrony of whole networks. Finding out which additional functions are hidden within the signal fireworks of the brain is still a major challenge for the Bernstein Network’s scientists.

## Mating males throw females off the beat

Nerve cells can code information in several ways: in their firing rate or in the exact time points at which they emit their action potentials, for example with respect to the oscillations of a whole network. Jan Benda [5, 36] has now discovered a further variant of temporal coding. In this case, the question is not: “To what extent does an individual neuron deviate from the oscillation?”, but: “How synchronously does the entire group of neurons oscillate?” Such a “synchronization code” is used by the electro-receptors of weakly electric fish. When a male fish encounters a female, he sends out courtship signals. The signals interfere with the synchronous oscillation of the electro-receptor neurons of the female, with the result that they fire less synchronously. However, if a male fish meets another male, aggression signals are exchanged. The effect of these signals is that electro-receptor neurons increase the synchronicity of their firing. This shows that the synchronicity of neuronal responses contains important information about the fish’s environment. Accidental fluctuations in the electric signals of the brain—known as background noise—gain particular importance in view of such synchronization codes. The intensity of the background noise affects the synchronization of the neurons. “So far, background noise has generally been regarded as an unavoidable disturbance inherent to the system. However, it is also possible that the processing characteristics of a neuron are tuned by adjusting the noise level,” explains Benda [5, 36].



*Weakly electric fishes generate an electric field, which is used for orientation and communication.*

**Interview with Michael Brecht** [1, 15]
*Humboldt Universität zu Berlin*
*Coordinator of the Bernstein*
*Center Berlin*

**How does reverse physiology work?**

We stimulate individual cells in an animal's brain by electrodes and then measure the changes in behavior. This enables us to examine the influence that individual cells exert, for example, in a sensory detection task. In comparison to classical neurophysiology, in which you typically present a stimulus to an animal and then measure the neural responses, this is a kind of "reverse" approach.

**How big is the influence of an individual cell, given the background of neuronal noise?**

Very big. We can clearly elicit movements by stimulating just one single cell. It was previously believed that the brain can only achieve precision by averaging over the activities of many cells. In my opinion, our experiments refute this hypothesis. We believe that the brain works much more precisely than previously assumed. How it achieves this is not really understood yet.

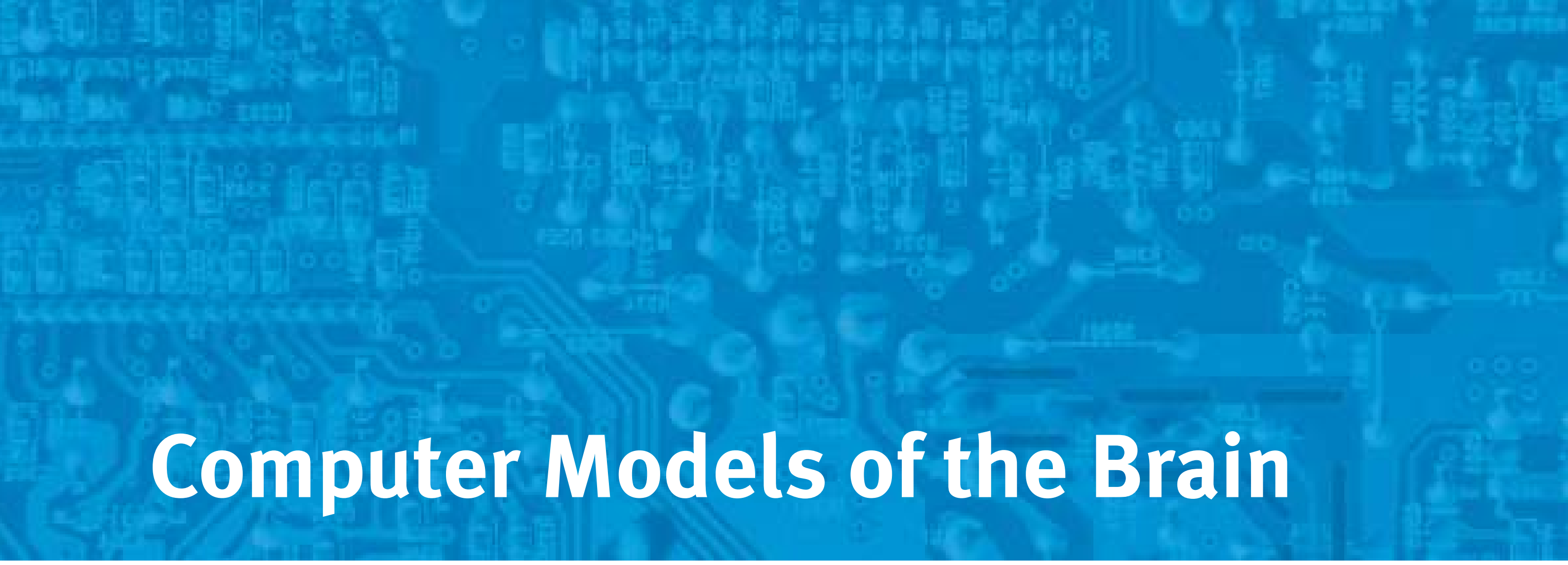
**Is neuronal variability actually poorly understood neural activity rather than real noise?**

The opinions on this question vary greatly among scientists. But I believe this is actually true. Otherwise, it would really be impossible to elicit a behavioral effect by exciting one single cell.

## Beat keepers in the brain help to boost memory

When billions of nerve cells exchange information, often a common rhythmic activity pattern emerges. Neurons that inhibit, rather than activate, other cells contribute greatly to the generation of these network oscillations. It is known that these cells play a central role in memory formation and information processing. Marlene Bartos [2] and British colleagues switched off the output of fast inhibitory neurons in the hippocampus of mice. This part of the brain is the seat of spatial and working memory. The animals initially showed no behavioral changes. However, when animals needed an intact spatial working memory to find their way in a maze, they showed deficits and made significantly more errors than healthy animals. Bartos [2] and colleagues concluded that inhibitory neurons are especially important for working memory. A reduction in working memory is also observed in schizophrenic patients. So far, their deficits were primarily suspected in the cerebral cortex. The new results now indicate that an altered function of fast inhibitory neurons in the hippocampus may also be involved in this disease.

*Inhibitory neurons keep the beat in the brain and play an important role in memory formation and behavior.*

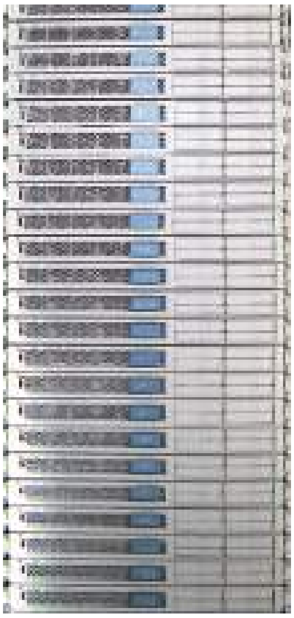


# Computer Models of the Brain

**Complex systems** such as the climate, the stock market and our brain are hard to understand. Intuition and simple reasoning fail when we want to deduce the whole system's behavior with all its myriad interactions. Mathematical models and computer simulations are very helpful for deducing causal connections and testing hypotheses about individual aspects. They apply rules that determine the interactions between different system parameters, such as humidity, wind speed and temperature in the climate example. On this basis, they make predictions (e. g., the weather forecast for the next days) and illustrate dependencies between different parameters.

**Neurobiological experiments** examine many aspects of neuronal processing and interactions. Based on these results, researchers formulate mathematical rules and models—either with paper and pencil, or with computer simulations. These are put to work testing detailed questions such as: Which processes between nerve cells are of particular significance for signal transmission? How can a nerve cell process thousands of input impulses in parallel? Which types of computations can a particular neuronal network execute? The tools of modern computer technology enable scientists to investigate cell and network models of enormous complexity and biological realism.

**The basic building blocks** of the nervous system are neurons. They transmit signals in the form of electrical impulses, called action potentials or spikes. In 1952, Alan Lloyd Hodgkin and Andrew Fielding Huxley formulated a mathematical model that explains the origin and transmission of spikes in squid axons. This model forms the basis of many current brain simulations and has long been assumed to apply equally to all animals. However, a few years ago, Maxim Volgushev[32] and Fred Wolf[3, 10, 12, 32] showed, on the basis of high-precision measurements, that spike generation in the mammalian brain is both faster and more variable than predicted by the former theory. They developed a modified model that is compatible with the new findings and suggests subtle differences in the molecular mechanisms of spike generation compared to the original model.



*Even modern computer clusters work several hours to simulate few minutes of neuronal activity.*

**At the contact points,** or synapses, between two neurons, the electrical impulse is converted into a chemical signal. The upstream neuron releases transmitter substances that are detected by the downstream neuron. This transduction process opens up many possibilities for regulating the transmission of impulses. The intensity of the receiving neuron's stimulation depends strongly on the history of the respective synapse's activity. Erwin Neher[3, 10] showed experimentally and by modeling why the strength of synapses depends on the number of impulses that arrived within a short period of time. This "short-term plasticity" enables us both to react very quickly and to respond differently, depending on context.

**In many neuronal** disorders such as depression or Parkinson's disease, the release of neurotransmitters is impaired. Gabriel Wittum[8, 21] und Andreas Draguhn[4, 21] analyze, which effects this has on signal processing and how adverse effects can be mitigated by medication, applying, amongst other methods, computer models.

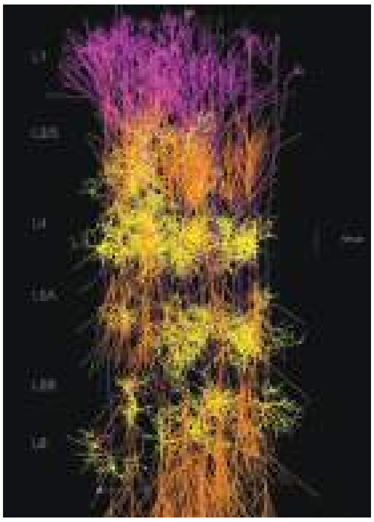
**Mathematical models** also allow neuronal processes to be studied at several levels, from molecular interactions up to communication in very large neuronal networks. The critical decision when creating such simulations is determining the right balance between detail and abstraction. The optimum in this tradeoff entirely depends on the biological question. Ad Aertsen[2, 9], Markus Diesmann[2, 9], Abigail Morrison[2] and Stefan Rotter[2, 9] use a computer cluster to simulate networks of more than 100,000 neurons, each with 10,000 synaptic contacts—mimicking several cubic millimeters of cortex. The system takes several hours to simulate a few minutes of neuronal activity, including biological details like synaptic plasticity, the presumed neuronal basis of learning (see "Learning and Memory", p. 30). In addition to the electrical activity within the nerve cells, Peter Bastian[4, 34], Andreas Draguhn[4, 21]

**"Whenever the brain receives sensory input, processes it or remembers, it processes information which is encoded in sequences of action potentials in multiple nerve cells. To what extent, though, does the impulse sequence depend on the particular network structure of the brain, or even on the exact properties of individual nerve cells and their connections? Adequate models of network dynamics are needed to investigate such questions."**

*Ad Aertsen* [2, 9]

and Stefan Lang[4] also simulate the transmission of electric fields in the intercellular space. In this way, they hope to gain a better understanding of the origin of electrical signals which can be recorded from outside, for instance by electroencephalography (EEG).

**The prediction** of a phenomenon of neuronal dynamics which, in different systems, is known as self-organized criticality, is also possible due to mathematical models. For instance, when trickling sand on top of a pile, many sand grains simply remain in place. Often, however, smaller or larger avalanches are formed by the toppling grains. Similar behavior was predicted and experimentally observed in neural systems, where small spontaneous activations can trigger avalanches of neuronal activity. If the effect is produced by the system itself and if it extends over a large bandwidth, it represents a form of self-organized criticality. Theo Geisel[3, 10], Michael Herrmann[3, 10] and Anna Levina[3] explain the avalanche dynamics by self-regulating mechanisms at the synaptic level and interpret its functional role in the following way: by producing scale-invariant activity patterns, even when idle, the brain can maintain a state in which it remains sensitive to stimuli of very different intensities. In this way, weak stimuli are not missed, while stronger ones still cause an adequate response.



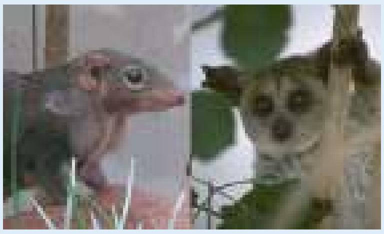
*Three-dimensional reconstruction of a cortical column, an important functional unit of about one millimeter width in the cortex.*

**How can our brain** be active, even if no external stimulus is presented, for example, when we dwell on our thoughts? In large networks, where each neuron is connected with many others, Stefan Rotter[2, 9] observed for the first time that neuronal activity was maintained over a long period of time, even without continuous external stimulus. The network was engaged entirely with itself. Could this kind of behavior be the substrate of our thoughts and memories?

**From the basics** of hearing or seeing to the emergence of memory and to the action of drugs—computer models can help to explore theories and test hypotheses on a variety of questions. Translating neurophysiologic processes into computer software also offers new avenues for technological developments (see "Spare Parts for the Brain", p. 33 and "Robots of the Future", p. 36).

## Self-organization instead of environment and genes

A scientific team including Fred Wolf[3, 10, 12, 32] and Siegrid Löwel[10, 12, 32] recently discovered that the brains of ferrets, tree shrews, and bush babies show a surprising similarity in their visual cortex: in each of these species, the arrangement of nerve cells preferring bars of the same orientation followed a common design. Neither early influences of the environment nor genetics could explain these findings. Using a mathematical model, however, the scientists could precisely predict the observed brain architectures. The model describes how self-organized neuronal circuits emerge in the brain. These new findings support the fundamental role of self-organization during brain development. A familiar example for self-organization is the so-called brazil-nut-effect: the biggest nuts are usually found on top of the granola. Models of self-organization can also explain physical processes like dune formation and are applied to traffic jam analysis and to organization of work flow in big groups.

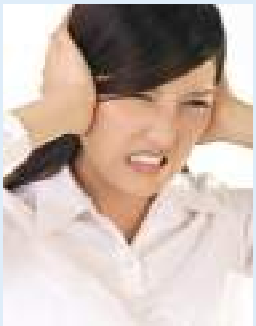


*Visual cortical organization in tree shrews (left) and bush babies is amazingly similar.*

## Eye movements in the mathematical model

When we observe a moving car, we have to adjust the speed of our eyes carefully in order to track the object. Two brain areas, receiving their information through parallel pathways, are involved in the control of such pursuit movements. Stefan Glasauer[5] and colleagues created a computer model that captures the main biological interconnections. The model was able to pursue a moving object. More than this: “For the first time, we have been able to explain the individual roles of the anatomical parallel processing pathways,” says Glasauer[5]. They showed that one area calculates basic speed, while the other mainly computes acceleration. The model was confirmed in experiments, in which one of the two areas was switched off for a few seconds by transcranial magnetic stimulation (TMS).

## Ringing simulations



Tinnitus—loud music, an explosion or simply too much stress can cause permanent ringing in the ears. According to estimates, tinnitus affects about five to ten percent of the population. But how is tinnitus generated? The auditory nerve transfers acoustic information from the inner ear to the first processing stage of the brain, the cochlear nucleus. This nucleus acts as an amplifier: when auditory nerve fibers are not very active, for example as a result of hearing loss, the amplifier increases the signal. But the auditory nerve is also active without stimulation. After hearing loss, this neuronal noise is over-amplified, leading to phantom sounds, similar to those that occur when a stereo system is turned on at full volume without putting a CD in it. Using computer models, Richard Kempter[1, 15, 29] and Roland Schaette[1] have elucidated this relation between tinnitus and neuronal gain. “Our studies are designed to understand the basic relationship between hearing loss and tinnitus,” explains Kempter[1, 15, 29]. From these findings, new therapeutic measures can be derived. “Our hope is that exposure to appropriate acoustic signals in the right frequency range can decrease the hyperactivity caused by hearing loss,” says Kempter[1, 15, 29].

# Understanding Neurological Diseases

**Perception, memory, emotions.** We generally take these abilities for granted and use them daily, trusting in their correctness and adequacy. It is only when problems occur in these basic functions that we become aware of what a healthy brain accomplishes every day. For a long time already, depression, schizophrenia and Alzheimer's disease are widespread diseases. In industrialized nations, the costs of neurological and psychiatric diseases amount to about a third of the total health expenditure.

**Over the last decades,** research on neurological disorders has provided detailed insights into their causes and effects. With ongoing progress in genome analysis, researchers are identifying increasing numbers of gene variants that are more abundant in patients with certain neurological diseases than in healthy people. These genes are called "risk genes". Certain diseases can be attributed to alterations in neuronal transmitter release or to disturbed functioning of certain ion channels. Imaging techniques are allowing more and more detailed investigations of disease-related brain changes, from cellular structures up to entire brain areas (see "A Glimpse into the Brain", p. 28). But how do the different hierarchical levels—genes, cells, and brain areas—affect each other? How do different gene variants influence cognition and behavior? A mechanistic understanding of these questions is still basically lacking, although it would be of utmost clinical significance.

**Computational Neuroscience** can make important contributions to this problem. Theoretical models can pinpoint links between genetic predispositions and cognitive functions or pathological changes. The interdisciplinary research approach, facilitating research on several levels of hierarchy, is of particular importance in this context.

**In computer models,** Peter Bastian[4,34] and Daniel Durstewitz[4] simulate altered neuronal network activity caused by psychiatric diseases like schizophrenia or depression. In a first step, they create a realistic picture of the altered network behavior in form of a computational model. Then, the parameter configurations of the model can be systematically explored for their ability to re-establish a "healthy operating regime". In this sense, they try to invert the transition from a healthy into a psychiatric mode. Since these simulations are done in computers that use silicon chips, this new research direction has been coined "in silico neuropharmacology" (see interview with Daniel Durstewitz, p. 25).

**But models** are only as good as the data from which they were derived. Therefore, detailed experimental investigations remain an indispensable research element. Among others, Hilmar Bading[4,21] and Hannah Monyer[4,21] work towards a deeper understanding of how genetics and neuronal activities influence each other.

## Learning after stroke

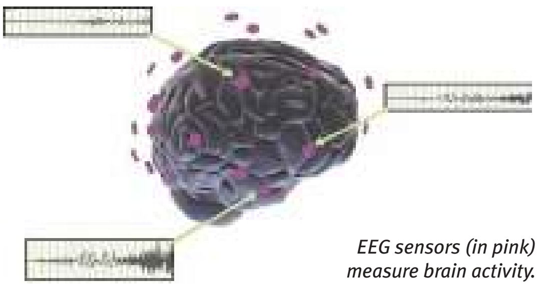
In Germany alone, every year around 200,000 people suffer from stroke. More than two thirds of the patients sustain permanent damage. Much of what was previously normal—walking, talking, eating—must be learned again. However, many patients do not fully recover all their previous capabilities. Siegrid Löwel[10,12,32] investigates why learning after stroke is so difficult and how it can be promoted. "We know from our own investigations that even brain regions that were not directly affected lose their plasticity," says Löwel[10,12,32]. With experiments in mice, the researchers want to clarify which non-local control mechanisms are responsible for the interaction between distant brain areas. The combination of two imaging methods (optical recording and 2-photon microscopy) shall provide new insights into the underlying neuronal processes.

**Epilepsy research** likewise profits from the potential of Computational Neuroscience. Ulrich Egert[2,9], Michael Frotscher[2] and Carola Haas[2] investigate neuronal processes of epilepsy in the hippocampus. Based on histological analyses, extracellular recordings and computer simulations of the hippocampus, they analyze both the formation and the propagation of epileptic activities. A better understanding of these processes can result in the development of new therapeutic strategies.

**Already today, the findings** and new analysis tools of Computational Neuroscience contribute significantly to a better understanding of neurological diseases. Based on these insights, new approaches for therapies can be developed. In addition to clinical applications, the study of neurological deficits also offers opportunities for a better understanding of neuronal processes in the healthy brain.

## Predicting epileptic seizures

Epilepsy is one of Germany's most common neurological disorders. In a significant proportion of patients, presently available antiepileptic drugs are not sufficiently effective. Andreas Schulze-Bonhage[2,9,42] and Jens Timmer[2] are developing a method by which seizures may be predicted. Using EEG measurements, typical excitation patterns are identified, triggering an alarm. "So far, these measurements are not sensitive enough to predict all seizures correctly," says Hinnerk Feldwisch-Drentrup[2]. To improve prediction accuracy, huge EEG databases are evaluated worldwide. The ultimate objective of this approach is to alert patients reliably and in real time of an upcoming seizure, allowing them to avoid dangerous situations, or, even better, stop a seizure by taking a fast-acting medication. Alternatively, the application of appropriate deep brain stimulation (see "Spare Parts for the Brain", p. 33) could bring the brain's activity back on track.



*EEG sensors (in pink) measure brain activity.*

**Interview with Daniel Durstewitz**[4]
*Central Institute for Mental Health, Mannheim, Coordinator of the Bernstein Center Heidelberg-Mannheim*

**Which role do single genes play in the development of neurological disorders?**

In recent years, a number of risk genes have been identified for many psychiatric diseases like schizophrenia or depression. These genes tend to differ in healthy people and psychiatric patients. Central questions of our work are how these gene variants affect neuronal information processing, and how this may explain the observed effects on cognition and behavior. Computational Neuroscience offers important tools and approaches to study these relationships.

**What is "in silico neuropharmacology"?**

By this label we refer to the study of neuropharmacological effects via computer simulations. In this approach, neuronal networks, described at a biophysical level by various parameters, are simulated on the computer, where these networks are characterized by biophysical parameter configurations and dynamical behavior typical for particular psychiatric conditions, like schizophrenia for example. These computer simulations allow the assessment, in a relatively short time, of different parameter configurations for their ability to restore normal functionality in a psychiatrically ill brain.

**Certain steps of drug development are also called "in silico development". What is the difference to your approach?**

In drug development, the aim is to optimize the chemical structure of an active pharmaceutical ingredient. Our approach, however, is situated on a completely different level, namely at the level of neuronal networks and structures. Our goal is to reach a better understanding of psychiatric diseases via computer simulations of such neural systems. We also hope that these computer simulations will then enable us to infer new cocktails of pharmacological agents that might be best suited for treating certain psychiatric conditions.

# Perceiving is more than Seeing

**Man is a visual** being. But how does our brain construct objects, faces and entire landscapes from the electromagnetic waves of light? How does the two-dimensional retinal image of the world give rise to our three-dimensional perception? And how do we decide where to direct our attention?

**The retina already** provides the first contribution to information processing: rather than just individual pixels, it also conveys more abstract information about the properties of edges, color contrast and motion to the brain. For instance, Tim Gollisch[5] examines how individual retinal cells respond to differences in light intensity and how they process pictures by interaction with their neighbors.

**In the brain itself,** more complex visual properties are analyzed. Thanks to intensive basic research, we are now beginning to understand how the brain processes, for instance, shapes and motion patterns. But this does not yet explain how we perceive. Only through correct interpretation we can attribute a meaning to colors and shapes. We perceive what we see by putting objects into a context and linking them to our experience. We can grasp an object even if we have never seen it before—for example, an abstract image or sculpture. Computers still cannot do any of this. “Machines can only recognize a very limited object class about which they have acquired detailed previous knowledge. We try to understand the principles of shape analysis, so that, one day, computers will be able to interpret images from a broad range of subjects,” says Matthias Bethge[6, 35].

**“There is no machine** that recognizes objects equally well as a human,” states Felix Wichmann[1, 6, 7]. By applying models of machine learning, he expands the repertoire of methods in cognitive research. For example, by comparing hundreds of images of different faces, a computer learns to recognize regularities. “The advantage of this approach is that I can disassemble the machine afterwards and look inside,” says Wichmann[1, 6, 7]. If we similarly understand the underlying principle in humans, we could in turn equip computers with this capability and use them for identification or sorting tasks.

**Only a fraction** of all the information that hits the retina reaches our perception. This is due to the fact that higher neuronal functions, such as attention, act back onto early processing steps. Stefan Treue[3, 10] and his team found evidence for such processes in primates. In the truest sense of the word, attention sharpens our senses—we mainly see what is important to us (see interview with Stefan Treue, p. 27). The movements of our eyes can reveal the focus of our attention. With the aid of technical devices that measure and analyze eye movements, scientists can investigate attention under natural conditions. The neuronal basis of attention and the interactions between different brain areas during attentional control are also relevant from a medical point of view, for instance, for the development of effective diagnostics and treatments for attention deficit disorders.

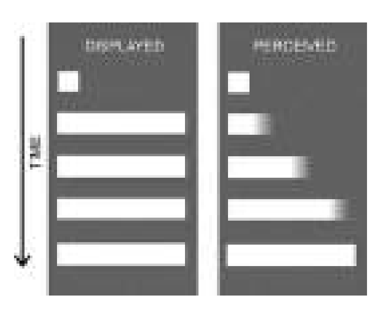
*The EyeSeeCam, developed in collaboration with Stefan Glasauer[5], records eye and head movements and uses this information to steer a camera sitting at the side of the device. In this way, the experimenter can “see through the subject’s eyes”.*

**How does the brain manage** to respond so quickly and reliably to visual impressions? How does it recognize objects viewed from different perspectives and how does it fill in the missing image information when objects are partially blocked? How does it combine information on color and shape of an object? The list of questions about the visual system seems endless. The brain has acquired an impressive set of tools to deal with all these complex tasks. Deciphering how this visual toolkit functions is the aim of many scientists of the Bernstein Network.

*Eyesight test for mice. Just as we spontaneously follow a moving train with our eyes, mice track a moving pattern of stripes with reflexive head movements. Using these tracking movements, scientists like Siegrid Löwel[10, 12, 32] can determine which stripe width the mouse can still react to, that is, the visual acuity it has in this test.*

## Neurons alert their neighbors

When a short bar appears on a screen, rapidly followed by a long one, it looks to us as if the short bar "grows" into the long one, thus producing an illusory motion. In fact, however, we might be witnessing the process of how the brain prepares for upcoming events. Presentation of the short bar not only activates those visual cortical neurons that are responsible for perceiving the short bar, but also leads to a gradual pre-activation of the neighboring cells representing more distant locations. Usually, this spreading activation remains unnoticed, since it remains below perceptual threshold. But if the pre-activated cortical cells are then stimulated by the long bar, they reach their firing threshold much faster. A wave of activity builds up, hence the bar seems to grow. Using computer simulations, Dirk Jancke[19] and his team could explain how neighborhood activation and inhibition interact with each other on the population level during this process. In this way, they revealed a mechanism that could play an important role in the perception of moving objects, as it shortens neuronal processing times.



*When a long bar appears shortly after a short one, the short bar seems to grow. The reason is that neurons pre-activate their cortical neighbor cells, allowing them to react more quickly.*

**Interview with Stefan Treue**[3, 10]
*Director of the German*
*Primate Center, Göttingen*

**Where does attention arise?**

Today, it is commonly assumed that a network of areas in the frontal and parietal cortex is responsible for the allocation of attention. Directing attention is the result of weighing various parameters: particularly salient items in our environment, information about the current situation and our acquired experiences and memories—all these issues come into play.

**Does our perception change by attention?**

Without attention, our perception provides us only with a rough sketch of our environment. But if we focus our attention on certain aspects, our perception gets more rapid, more accurate, and more sensitive to small changes. That also implies that different observers may have very different perceptions of a given situation, because each of them directs his attention to other details.

**Can we focus on several properties of an object (e. g. color, shape, motion) at a time?**

In contrast to "classical" multi-tasking, we do not have to divide our attention between the different features of an object. Rather, an automatic process seems to spread our attention to all aspects of the object, even if we concentrate only on one particular feature. This observation is commonly assumed to indicate that we jointly represent the different attributes of an object, and therefore will always attend to the object as a whole.

# A Glimpse into the Brain

**Modern imaging techniques** offer unique insights into the brain and its activity, without having to intervene in any way. This enables us to tackle questions that cannot be answered in animal experiments. What is consciousness? How do pain and consciousness interact? How and when are decisions generated? With various techniques, a dream of many scientists is coming true: watching the brain at work.

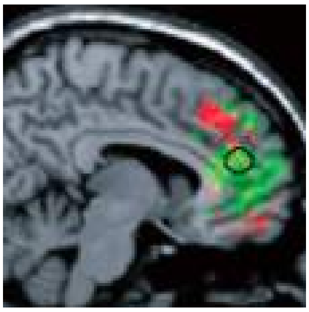
**Exact anatomical mappings of** the intact brain have been provided by computer tomography (CT) and magnetic resonance imaging (MRI), which have been of great value for research and the clinics for decades. However, these techniques cannot trace the structural connections that carry the communication within and across cortical areas. This restriction is overcome by diffusion tensor imaging (DTI). This method measures the motion of water molecules and its directional dependence. As water can move more freely and therefore faster along nerve fibers rather than perpendicular to them, the orientation of fiber bundles can be determined. As Jens Frahm[3,10] and Jürgen Hennig[9], among others, could show, DTI is a valuable tool for basic as well as clinical research, in presurgical planning and for the further understanding of neurological disorders such as schizophrenia and Alzheimer's disease.

*Magnetic resonance imaging scanner*

**The great mysteries** of the brain are hidden within its neuronal activity. Over 80 years ago, the invention of electroencephalography (EEG) enabled scientists for the first time to get a handle on cognitive processes in the brain. Synchronous activity of many nerve cells creates an electric field that can be measured by sensors on the scalp. Thus, EEG provides a "real time" representation of parts of the brain's activity. Scientists of the Bernstein Network use this technique for predicting epileptic seizures (see "Understanding Neurological Diseases", p.24) and for developing neuro-feedback therapies that, for example, help children with attention disorders to control their hyperactivity. Due to its relatively low technical requirements, the EEG is also well suited for controlling brain-computer interfaces (see "Spare Parts for the Brain", p. 33).

**With the advent of** functional magnetic resonance imaging (fMRI), detailed spatial representations of brain activity have become possible. Down to a millimeter, fMRI measures alterations of the blood oxygenation level, which serves as a good parameter for corresponding changes in neuronal activity. To determine the location and extent of changes in brain activity, however, careful mathematical analysis is essential. Conventional approaches only examine changes at single points in space (voxels) that occur independently from changes at other locations. Often, however, the neuronal changes that are associated with a thought or a perception are not clearly restricted to a single area. "We are looking for spatially distributed activation patterns that are characteristic for certain mental states," John-Dylan Haynes[1,7] explains his approach, that is based on the highly developed analytical methods of Computational Neuroscience. In this way, Haynes[1,7] could show that decisions mature in the brain well before they are consciously perceived.

**How does the brain process** information about other people's decisions? How does this knowledge influence individual choices? Combining fMRI measurements and computer models, Jan Gläscher[38] explores the impact of social influences on the neuronal basis of decision-making. What happens if we regret our choice? Together with Christian Büchel[17], Gläscher[38] also investigates the role of the orbitofrontal cortex, an important evaluative center of the brain. Such studies tell us much about human behavior and hidden motivations. But they also serve as a basis for therapeutic approaches for people whose evaluation and decision processes are disturbed, for instance, in depression or in obsessive-compulsive disorders.



*Where do intentions develop? fMRI indirectly measures the neuronal activity by their oxygen consumption. Regions marked in green code covered intentions before they are carried out. Regions marked in red code intentions that are currently executed. The fine-grained activity patterns differ depending on intention.*

*Diffusion tensor imaging allows tracking the fiber bundles that connect various areas in the two hemispheres.*

## Optogenetics — Making the brain "see"

When we say that something dawns on us, we use this as a mere metaphor for the process of understanding. But for a few years, scientists are actually able to make neurons sensitive to light. Ernst Bamberg[10], together with colleagues from botany and biophysics, isolated a membrane protein from a protozoal green alga: channelrhodopsin. Using methods from modern genetics, he transferred the protein into the membrane of nerve cells. When exposed to light, the membrane-channel opens, leading to an activation of the nerve cell. In the meantime, other proteins have been found that react to different colors of light or that do not activate but rather inhibit nerve cells upon illumination. This opens up far-reaching possibilities: By simply shining light on them, nerve cells can be switched on or off. In this way, the functions of single cells or brain areas can be studied and new intervention approaches for neurological diseases can be tested. The development of this promising method shows how basic research provides groundbreaking impulses for both applied and clinical neuroscience.

## Pain in the brain

Even though it is your fingers or your foot that hurts—the neuronal response that lets us get aware of the pain occurs in the brain. The sensation of pain arises from a typical pattern of neuronal activity, in which several brain areas are involved. Scientists around Jens Haueisen[22], Wolfgang Miltner[22], Jürgen Reichenbach[22] and Herbert Witte[22] examine this "neuromatrix of pain". The researchers use functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and magnetoencephalography (MEG), to investigate the brain's reaction to mild pain stimuli, both in healthy subjects and in subjects with acute or chronic pain. To adequately evaluate the complex brain response, the scientists work on improving the mathematical analysis methods for fMRI, EEG and MEG. A better understanding of the neuronal basis of pain will provide a basis for improving long-term treatment of pain patients.

**Interview with John-Dylan Haynes**[1, 7]
*Charité, Professor for "Theory and Analysis of Large-Scale Brain Signals" at the Bernstein Center Berlin*

**The media are keenly interested in neuroscientific imaging techniques. Why is that?**

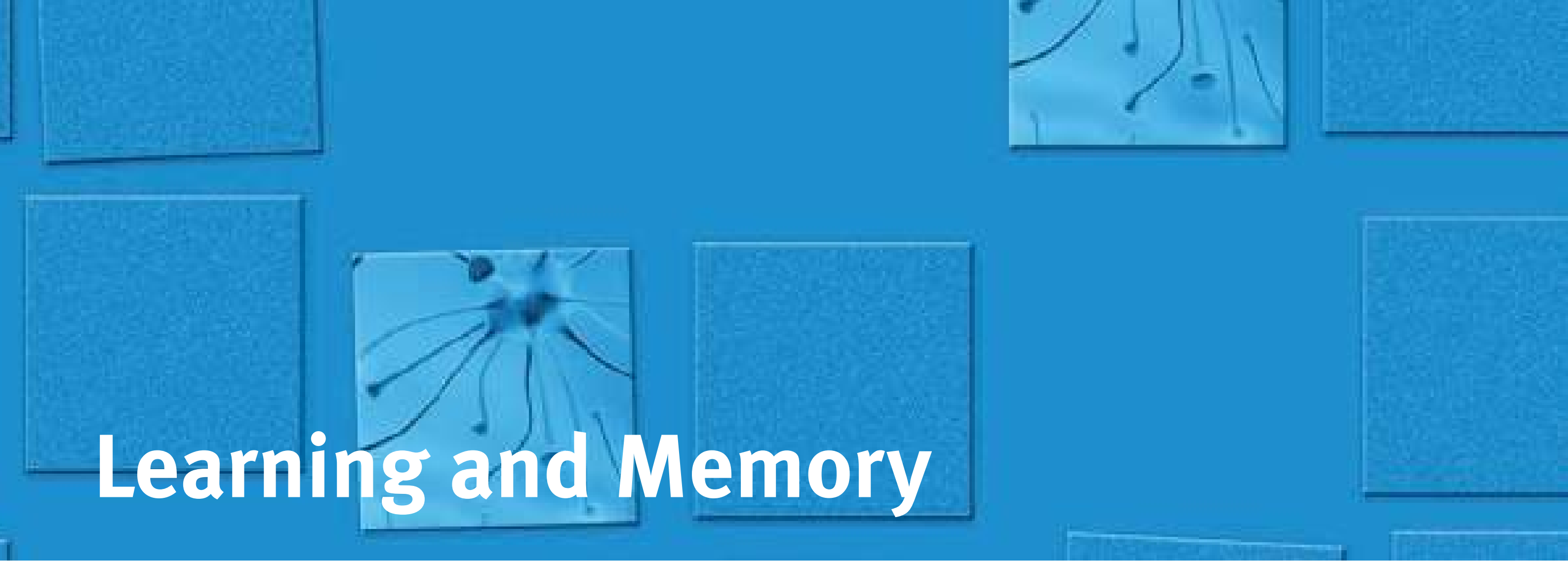
Every day we interact with people and can at best guess what is going on in their minds. To get insight into the other's thoughts is an old dream of mankind—or perhaps a nightmare. Now this dream is put onto a scientific basis, and evidence is accumulating that it might indeed one day become true. I think that these prospects elicit an ambivalent fascination. On the one hand, they make you curious and open up promising possibilities—on the other hand, they create discomfort.

**How close are we today to the oft-alluded to "mind reading"?**

We cannot read just any thought from the brain. This would need kind of a dictionary, listing all thoughts and their corresponding brain activity. The diversity of all possible thoughts puts fundamental limits to this approach. But within these limits, we can indeed investigate crucial elements of thinking and decision-making.

**A U.S. company claims to be able to do lie-detection based on fMRI. Would you trust them?**

Basically, I think it should be possible to tell whether someone is lying or not. But this would require data on the activity patterns that occur during lying under realistic conditions. As far as I know, no one has these data and will not get them any time soon.



# Learning and Memory

**Each person has** his or her own life story. Experiences shape us—or rather, our brain. For ages, people have been wondering what "substance" our memories are made of. In the meantime, neuroscientists have shed first light on this puzzle.

**No matter whether we are thinking, calculating** or listening to music—our brain is always highly active. Information is passed along between cells in the form of electrical impulses. Where two neurons get in contact, at the synapse, the electrical signal is converted into a chemical one. Transmitter substances are released from the upstream cell and promote or inhibit the formation of new electrical impulses in the downstream neuron. This process sounds complicated, but it is of utmost importance, since this is where learning takes place.

**This signal transmission process** can alter the properties of a synapse: the amount of available transmitters may vary, as well as the likelihood of repeated release. Also, the ability of the downstream nerve cell to respond to the chemical signal can be modulated. Already in 1949, the psychologist Donald Hebb formulated what was later named the "Hebbian" rule: If neuron A repeatedly takes part in exciting neuron B, the contact from A to B is strengthened.

**Only many years** later, scientists found out that this Hebbian strengthening depends on the precise difference in time with which the two neurons fire. The shorter the time when neuron A fires before neuron B, the more an excitatory synaptic link from A to B is strengthened. Conversely, if neuron B fires shortly before neuron A, the connection from A to B is weakened. Scientists around Leo van Hemmen[5] for the first time formulated this temporal relation in mathematical terms. This principle, later called "Spike-Timing-Dependent Plasticity" (STDP), is today an indispensable concept of Computational Neuroscience. Van Hemmen[5] and colleagues have also shown that STDP allows for the emergence of complex connectivities. The amazing accuracy of neuronal sensory systems with which, for example, owls and snakes detect their prey solely on the basis of acoustic information, is probably only possible thanks to STDP.

**Basic features** of many behavioral patterns, such as singing in songbirds, are inherited. But these rough genetic presets must be optimized by learning and practicing. In birds, the brain areas that are involved in this process are partially known already: one signal pathway continuously varies the song, while the other one provides positive feedback if the song was improved. This strengthens those neuronal connections that are responsible for better song variations. Onur Güntürkün[13] wants to find out whether this system is also involved in motor learning of other animals.

**"Don't go to bed** without being able to say that you have learned something today," once said Georg Christoph Lichtenberg (1742–1799), German writer and professor of experimental physics. Here, the scholar was wrong, because even during sleep, memories are consolidated. Information to be rescued from oblivion must be sent from the "working memory" in the hippocampus to the cerebral cortex for long-term memory. Short, synchronous network oscillations in the hippocampus are particularly observed during sleep. Scientists at the Bernstein Network investigate how these oscillations might emerge. Uwe Heinemann[1, 15] and colleagues have shown that long-term changes in synaptic activity are one underlying mechanism for the emergence of oscillations.

**"Learning happens** constantly and at different time scales," Petra Ritter[15] says. Together with Richard Kempter[1, 15, 29], she examines how oscillations and learning processes relate to each other. Such findings could be used to support learning processes, for instance in stroke patients that have to relearn many everyday abilities.

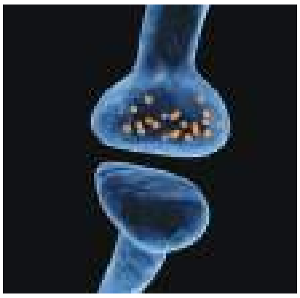
**The question of how we learn** is also of high interest for developing modern computer systems and robots. For quite some time, engineers have been inspired by biological models, for example by learning in infants (see "Robots of the Future", p. 36). Learning systems are far more flexible and error tolerant than completely pre-programmed systems. This is of essential importance whenever artificial systems act in a natural surrounding, since anticipating all eventualities is just impossible. The capacity of learning is also especially important wherever man and machine communicate or interact. If learning will enable machines

**"Quite a lot is already known about cellular learning processes: if we learn something, the strength of some synapses, i. e. the connections between neurons, is changed. However, how do we recall the information that was stored in this way in a synapse? What influence do these changes have on the activity of the brain, such that we can remember what we have learned? These questions are at the center of our research."**

*Christian Leibold*[5, 16, 45]

to capture human instructions faster and more accurately, this will be a tremendous advantage, for example, for the control of neuroprosthetic communication systems.

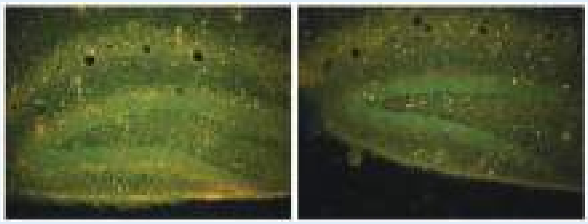
**Over the last decades,** many questions regarding our capacity to learn and remember have been solved already. But we are still far away from a deep understanding of how exactly and which memories are stored, and how they are subsequently read out correctly.



*At the contact points between neurons, information is transmitted through signalling molecules that are stored in vesicles (orange).*

## New cells in the brain— sometimes less is more

Our brain is on the horns of a dilemma: long-term storage versus adaptation and learning. The precise development of new neuronal connections can be studied in the hippocampus. In this area, new cells emerge throughout life and must be integrated into the network. The hippocampus is the mediator between short-and long-term memory. Markus Butz[3] and colleagues examined what happens if too many cells develop in this region. The researchers raised gerbils in isolation. As a result, the cell density in the hippocampus increased. However, the reorganisation of neuronal connections, which is highly important for learning, was much less than usual. When the researchers reduced the rate of cell division by medication, the cell density in the hippocampus decreased and the interactions between neurons became stronger. The researchers explained the apparent contradiction between cell density and intensity of reconstruction in a mathematical model: as too many cells compete for incoming stimuli, no cell gets enough input for real integration. Some cells in the model increased their input signals by recurrent wiring. Such recurrent feedback could also play a role in the formation of epilepsy.



*Reorganizational processes in the hippocampus, indicated by bright spots. Animals reared in isolation (right) show significantly decreased reorganization rate as compared to normal animals.*

## Fear can hardly be unlearned

Fear is an important safeguard of our body. By putting us on alert, it ensures quick responses. Dangerous situations are stored very effectively in our memory, and they can influence our behavior for a long time. Even fears that we thought to be long gone can reoccur in a particular situation. The reason may be that the fear was not deleted, but only masked. This is what Ioannis Vlachos[2], Arvind Kumar[2] and Ad Aertsen[2, 9] believe. The amygdala, an evolutionarily very old part of the brain is responsible for fear learning processes. In a computer simulation, the researchers rebuilt part of this structure. One group of cells activated the anxiety behavior, another suppressed that fear. When the influence of the latter group became smaller, for example by changing the context, the fear suddenly returned. This finding may be of particular significance for the therapy of anxiety disorders.

## Bees learn sweet scents

How successful bees are in their search for food largely depends on their ability to detect nectar-rich flowers from a distance, by identifying their scent. Martin Strube-Bloss[1, 11], Martin Nawrot[1, 2, 11] and Randolf Menzel[1, 11, 28], trained bees on five different scents, one of which was rewarded by a sugar solution. To investigate the neuronal basis of memory processes, they measured the activity of individual neurons in a brain region that was considered a candidate location for memory processes. The measurements revealed that certain cells weren't active during learning itself, but rather three hours after the learning phase. This suggests that these cells are essential for mid-term memory. Such memory consolidation at later times is an important process in the brain, which now will be reproduced in computer models.

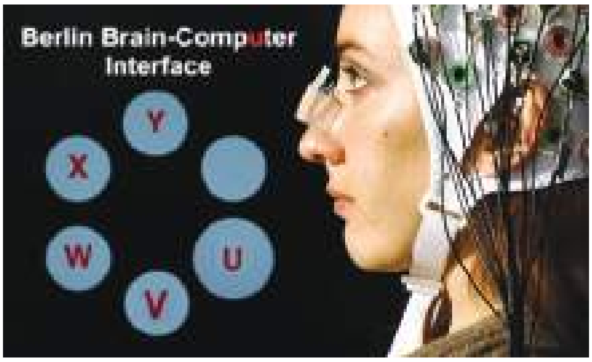
*When it senses the "right" scent, the bee extends its proboscis to collect the sugar solution.*

# Spare Parts for the Brain

**Modern prostheses** do not have much in common with former wooden peg legs. High-tech arm and leg prostheses, directly controlled by the brain, are coming within reach. Computer systems can already be controlled by the mere “power of thoughts”. Tiny retinal implants are developed that enable blind people to have some visual perception, and inconspicuous cochlear implants let deaf people hear again.

**Accidents or diseases** can interrupt the transmission of brain signals to the muscles. This is, for example, the case in paraplegia, in which legs and often also arms remain permanently paralyzed. Also a number of neurological diseases affect voluntary muscle control. In the final stage of neurodegenerative diseases like amyotrophic lateral sclerosis (ALS), patients enter the so-called “locked-in” state. Although fully conscious, they cannot move and communicate any more—they are completely isolated from the outside world. Various members of the Bernstein Network are working on the development of so-called “Brain-Computer Interfaces” (BCI) that read out brain activity and use it for controlling technical devices or communication systems.

**Brain activity** can, in principle, be measured in two different ways, invasively and non-invasively. Non-invasive procedures such as electroencephalography (EEG) are relatively easy to handle and risk-free because they do not require any surgical procedures. Electrodes on the scalp measure the electric fields generated by brain activity and send the data to a computer (see “A Glimpse into the Brain”, p. 28). By voluntarily producing certain brain signals, technical devices like computer cursors or even pinball machines can be controlled. Such systems usually apply a simple control principle: In a training session, the computer learns to differentiate between brain activities that are evoked, for example, by the imagination of movements of the right or left hand, respectively. These are then associated to control signals, for example for moving a cursor to the right or to the left. Using the EEG technique, also driver-assistant systems for cars and planes are explored that measure the driver’s state of alertness and raise an alarm in case of microsleep attacks. Through the skull, however, the excitation patterns of the brain are blurred, just like looking through a frosted glass. Due to this fact, EEG methods will probably stay limited to devices that distinguish between a small set of predefined actions.



*“Mental typewriter”, developed by Klaus-Robert Müller [1, 7, 24], Gabriel Curio [1, 7], and Benjamin Blankertz [7]. On the monitor, letters appear in quick succession. The subject concentrates on the next letter he / she wants to write. When it appears, a specific form of activity can be discerned in the EEG, and this letter becomes selected. Typing velocity with this kind of device can reach about a word per minute.*

**Precise control** of a prosthetic arm requires more accurate techniques that are, in the truest sense of the word, closer to the brain. During invasive procedures, hair-thin electrodes are introduced a few millimeters into the pain-insensitive brain, where they can directly measure the electrical activities of multiple single neurons or neuron groups. From this neuronal activity, details of an imagined movement, say, grasping an object, can be reconstructed, and direct control signals for an arm prosthesis can be generated. In animal experiments, such brain-controlled devices have already been tested successfully. But invasive procedures also have their challenges: Healthy tissue is beeing destroyed, and immune reactions can lead to inflammation and can interfere with the function of the implant. Therefore, Carsten Mehring [2, 9, 31], Tonio Ball [2, 9], Jörn Rickert [9] and Ad Aertsen [2, 9] apply an alternative method, in which the sensors are placed between the skull and the surface of the brain, without penetrating the brain itself. This semi-invasive procedure is called electrocorticography (ECoG). “We are looking for an optimal compromise between fully-invasive and non-invasive methods,” says Mehring [2, 9, 31]. “It will certainly take some more time until brain-machine interfaces are used routinely. The proof-of-principle, however, has already been provided,” explains the physicist.

**Great successes** have been achieved in the field of neuroprosthetics over the last decades. A great variety of different technologies has become available that can

*With the aid of a cochlear implant, a deaf person can hear, despite defective sensory cells of the inner ear. The outer part of the prosthesis processes sound information and sends signals to the implant, which in turn electrically stimulates the intact auditory nerve at various positions of the cochlea, leading to an acoustic perception.*

re-establish the flow of information between the brain and the sensory organs or the muscles. In order to develop implants that integrate into the complex neuronal clockwork of the brain itself, the brain's function with its multiple feedback loops needs to be understood much more thoroughly. And even this is not enough: "The brain is a highly plastic organ that constantly changes through learning and adaptation," says Ulrich Egert [2, 9]. "Therefore, neuronal implants must have the ability to adapt to changing conditions, which means that they must independently adjust to changing signal quality, perform quality checks and do troubleshooting." A lot of further research needs to be done in the field of man-computer interaction.

## Towards visual prostheses

An about 40-year-old man reads his name and recognizes two spelling errors. Nothing unusual, except he had gone blind many years ago. Miikka owes his new ability to see to a three by three millimeter chip that was implanted behind his retina. Eberhart Zrenner [6] and his team, in cooperation with Retina Implant AG, developed this visual prosthesis, that is equipped with 1500 light sensors, amplifiers and electrodes. After the loss of photoreceptors, the prosthesis takes over their function and detects light of different intensities. The information is converted into electrical signals, conveyed to the neurons of the inner retinal layers and then processed by the nervous system. Until now, 18 patients have been implanted with such subretinal implants and are using them at home or outdoors. Electricity is supplied by a small coil under the skin behind the ear. Some of the treated patients are able to recognize different shades of grey, large moving objects, and also items of daily life such as knives, forks, cups, hands of clocks, door handles, etc. The technology still has to be tested and developed further, but a major step towards a visual prosthesis has been achieved.

*Although he is blind due to the disease retinitis pigmentosa, a retinal implant allows the patient Miikka to read his name. He even identifies two spelling errors.*

**Interview with Oliver Müller**[9]
*University of Freiburg*
*Head of the junior research group "The relevance of human nature in biomedical ethics" at the Institute of History of Medicine*

**Have the insights of modern neuroscience changed our idea of man?**

I don't think that they have induced fundamental changes. However, some neuroscientists, journalists and politicians apparently would like to change our idea of man and redefine the basis of our identity and morality, by claiming that the "ego" and our freedom are mere illusions. Already Karl Jaspers called these all too fast conclusions "brain mythologies". That was in 1913 …

**Does a neuroprosthesis intervene into the wearer's identity?**

Identity and self-conception are initially constituted by the person's own biography, and for a prosthetic user, this certainly includes the prosthesis. The technology also changes the reality of life, it interferes with conscious processes, and it promises a control and domination of these processes. This will change the identity of the patient.

**Is this alarming in itself?**

No, it is not necessarily bad–good therapeutic success changes the reality of life, too. But one has to very closely watch any changes in consciousness and personality. Dangerous opportunities for manipulation may arise. By the way, one may also invert the perspective: man becomes part of a machine, he adapts to the implanted technology.

**Neuro-enhancement aims at optimizing brain performance. Where could such efforts in neuroprosthetics lead?**

In neuroprosthetics, the question of improvement is raised in a special way: It is about generating optimized hybrid beings between man and machine, about changing a man into a working or fighting machine, about cyborgization.

**Do we have to fear such "cyborgs" in the near future?**

This is a very unlikely future scenario. Nevertheless, the discussion about cyborgization contains important aspects, because in the end, it is always about the limits of technology, about what we consider to be "human". It would be ethically highly problematic if we would not heal people anymore, but adapt them neurotechnologically to commercialization processes, and thereby marginalize other aspects such as sociability or religiosity.

## "Pacemakers" for the brain

For a number of neurological disorders, the pathophysiological mechanisms within the brain are partly known, as, for example, in Parkinson's disease. But in a significant proportion of patients, the usual drugs do not work, or not any more. In such cases, deep brain stimulation can be a way out. In this technology, thin electrodes are introduced into specific brain regions. Connected to a battery implanted into the chest, these so called "brain pacemakers" send electrical stimuli that excite or inhibit the targeted region. The modulation of neuronal activity aims at restoring neuronal function. Marcos Tatagiba[9] and Alireza Gharabaghi[9] successfully employ this method in patients suffering from Parkinson's disease or other forms of tremor. Applications of this technique to other neurological diseases such as epilepsy are currently being tested.

*For deep brain stimulation, thin electrodes are implanted into the pain-insensitive brain.*

# Robots of the Future

**Each simple, everyday gesture** is an enormous achievement of the brain. Even when simply pouring ourselves a glass of water, we have to coordinate the movements of dozens of muscles, react to the swashing water and visually estimate how much water there is still to pour. For a long time, engineers tried to pre-program all these operations step by step. But such an approach not only is extremely laborious, but also highly error-prone. Every slight change in conditions results in a failure of the program. Therefore, scientists are now using a different strategy: they make robots learn. Various learning methods are being explored.

**Already by trial and error,** robots can develop successful behavioral strategies. Scientists in the group of Florentin Wörgötter[3, 10] have built one of the world's fastest walking robots that incorporates this learning style. The mechanical biped varies the settings of individual leg movements at random. If this increases the walking speed, the machine remembers the current settings and repeats the procedure. One objective of this line of research in the Bernstein Network is to better understand learning processes. To test whether one has understood a given learning principle, it is translated into mathematical equations. The scientists then use these to program a robot. Based on its behavior, a number of questions can be answered: How fast does the robot learn? Does it really learn what it is supposed to learn? Psychological learning models such as reinforcement learning can also be tested in these machines. In addition, these experiments serve to refine the methods by which robots are supplied with different patterns of action—be it for orientation, grasping or for the interpretation of information. Such capabilities would allow robots to independently find their way or to perform certain actions on demand.

**Humans not only learn** by trial and error, but also by imitation and instruction. Until robots are able to apply such learning behaviors, they will have to be especially improved in one capacity: the interpretation and processing of sensory information. "So far, robots have to be hand-fed with carefully prepared information," describes Christoph von der Malsburg[8] of the constraints of current systems. In the worst case, such information is already outdated when the system is completed. Therefore, von der Malsburg[8] and colleagues choose a different approach: "Our models are children, who autonomously learn to see by exploring their visual environment," explains Jochen Triesch[8].

**The ultimate goal** of various research projects in the Bernstein Network is to develop robots that explore their environment and learn to ascribe meanings to objects. Like curious toddlers, they would "play" with objects and draw conclusions from them. Thus, they should be able to learn that an object can look very different when viewed from different perspectives, that a cup can be filled with something, or that a cylinder can be rolled when placed on its side. Artificial vision systems have a wide range of application fields—from security technologies, where they are already applied today, over quality control in industrial production to automated navigation and control, such as in self-steering vehicles. When robots succeed to learn by playing, as children do, they have performed a great developmental step towards autonomy.

**Truly autonomous service robots,** however, are still far from becoming reality. "Right now, we still have to step in with our oil cans and screwdrivers every once in a while," says Florentin Wörgötter[3, 10]. The time that it will take until we can build completely autonomous machines should be used for developing an ethical framework on the use of autonomous machines.

*"RunBot" is one of the fastest biped robots in the world.*

**Interview with Florentin Wörgötter**[3, 10]
*University of Göttingen*
*Coordinator of the Bernstein Focus:*
*Neurotechnology, Göttingen*

**Is it true that your robots learn to serve drinks?**

No, unfortunately we have not reached this goal yet. But we are working on self-learning systems. To teach a robot how to pour a glass of water, I have two options: either I pre-program the entire movement sequence. Or I provide the robot with the ability to learn.

**What is the challenge here?**

To be able to learn from a human, the robot has to detect and interpret his or her movements correctly. Then, this knowledge must be translated into the right action. This constitutes the learning difficulty. Nowadays, a robot succeeds in pouring a drink after ten attempts. Much like a small child, it has to learn to control the momentum of its movement so that it doesn't spill anything. This isn't easy.

**What are such robots good for?**

First of all, robots are models. Like computer models, they serve to investigate a particular question, for example: How is biped walking controlled? But also, how do we learn movement patterns? Computer simulations can provide us with important information on this. But if I want to know how my model behaves in the real world, with unexpected shadows or on a sloped floor, robots teach me much more. I can never incorporate all possible and unanticipated environmental influences into a computer model.

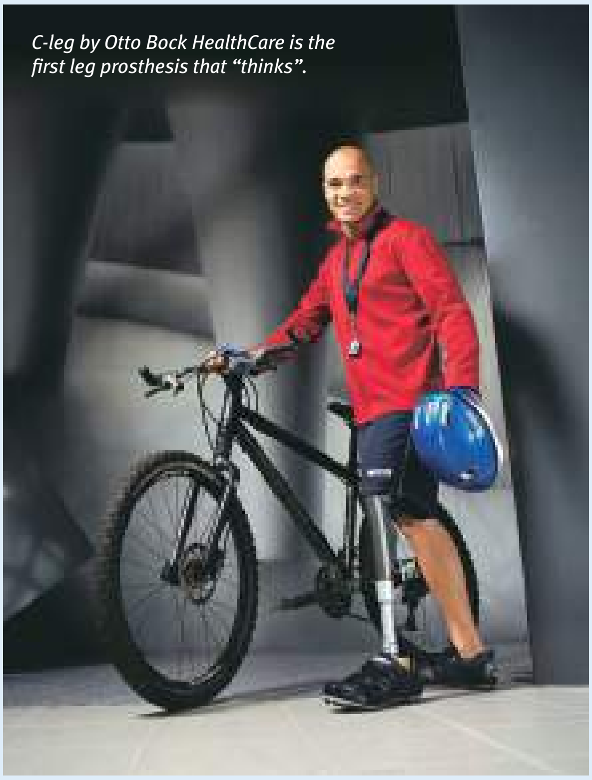
**Are there also practical applications for these systems?**

Absolutely. These findings are very important for the development of so-called orthoses, external supportive elements for joints. In the future, they are meant to support people with muscle atrophy or even partially paralyzed patients and to enable them to walk. Having built a robot that walks on two legs and keeps its balance, I can use this knowledge for controlling such an orthosis. Since the orthosis will have to be adjusted to every patient's specific needs, I can use the robot to test different patient-adapted scenarios and adjust the orthosis' control correspondingly.

## Chaos get robots on the move

Simple movements such as reflex-based walking and breathing are regulated by the interplay of few neurons in the brain or spinal cord. This efficient circuitry can also be used for controlling walking in robots. So far, however, the machines were limited to one single gait and could not adapt to changing circumstances. Now, Silke Steingrube[3], Poramate Manoonpong[3], Marc Timme[3], and Florentin Wörgötter[3, 10] have developed a six-legged robot that alters its gait pattern depending on the environment. Its secret is to exploit a method of so-called "chaos control". Initially, the minute control network produces a chaotic activity pattern of leg movements. Simple sensor-induced signals can transform this into a periodic pattern that determines the gait. Depending on need, different patterns—and thus different gaits—are produced. This allows the hexapod to efficiently climb slopes and free itself after a leg got stuck in a hole. A learning mechanism enables the robot to immediately switch to the optimal gait when a given situation reoccurs.

*The leg movements of this hexapod are controlled by chaos-control.*


*C-leg by Otto Bock HealthCare is the first leg prosthesis that "thinks".*

## The walking prosthesis that adapts to movements

More than ten years ago, the medical technology company Otto Bock HealthCare[3, 10] developed the first artificial leg that "thinks". A sensor in the base plate detects the walking phase of the patient and transmits this information to the prosthesis' knee joint, which locks or unlocks correspondingly. This mechanism greatly facilitates walking. Based on the findings of the project "RunBot", Florentin Wörgötter[3, 10] and colleagues are, in cooperation with Otto Bock HealthCare[3, 10], developing improved walking prostheses and ortheses. The walking robot serves as an important model. By manipulating the robot with weights, the scientists can predict how the prosthesis will respond to a heavier body weight, or to intense strain. Using the information from various sensors, the prosthesis additionally adapts to its owner's walking behavior and is able to —to some degree—predict movement patterns, including climbing stairs or sitting down.

*The robot "iuro" interprets gestures and spoken hints by passers-by to find its way.*

## Robot asks for the way

Just arrived at a foreign city and don't have a map? No problem, helpful passers-by will guide you by explanations or gestures. This simple and efficient strategy should also enable modern robots to navigate in a foreign environment. Kolja Kühnlenz[5], in collaboration with colleagues, designed a robot that autonomously finds its way through the city. Unlike traditional approaches, the robot does not have GPS or maps, but rather talks to passers-by. It records spoken instructions via a microphone, and gestures by a camera. Lasers scan the surroundings and alert it of obstacles. The robot currently is still larger than a refrigerator and can cross the road only with the help of an assistant. Regardless, it is able to get oriented in a complex environment, which is a key feature for robots on their way to autonomy.

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### 43 Lübeck—New York: Effects of Weak Applied Currents on Memory Consolidation during Sleep

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### 44 Mannheim—Los Angeles: Persistent Activity in the Entorhinal Cortex In Vivo

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### 45 Munich—San Diego: Hippocampal Representation of Auditory and Spatial Sequences

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