Recent Publications
New non-invasive method for brain research – Mapping movements in the brain – Embedded nerve cells hold the key to brain activity

Meet the Scientist
Ilka Diester – Andrea Huber Brösamle

News and Events
Personalia – Bernstein Award 2012 – New call for Bernstein Award 2014 – Animal use in biomedical research – New BCOS head – New call for D-J collaborations
New non-invasive method for brain research

Electric brain stimulation has successfully been used in the treatment of neurological and psychiatric disorders for many decades. However, it remains widely unclear what precisely happens when electric currents are applied to the human brain: Stimulation-dependent interferences impeded reliable direct recording and reconstruction of the brain’s electrical activity. Now, neuroscientists at the Bernstein Focus: Neurotechnology Freiburg-Tübingen and the University of Tübingen became the first to record neuromagnetic activity in the millisecond-by-millisecond range while the brain of a human subject was under electric current stimulation.

The newly developed non-invasive method allows the assessment of the direct stimulation effects on the neuromagnetic activity of the human brain. This is achieved by using specific mathematical algorithms and stimulation electrodes that let neuromagnetic fields—which arise during brain activity—pass undistorted. Previously applied methodologies were only able to indirectly measure neuronal activity during electrical brain stimulation, and therefore were imprecise. This was accomplished, for example, by quantification of blood oxygenation or changes in the cerebral blood flow.

This new method now allows us to resolve many basic research questions related to functionalities of the brain. Thus, the Tübingen neuroscientists expect, for example, important insights regarding the role of brain oscillations. A close link between changes in electrical brain oscillations and disorder-related behavior became identified rather early after their discovery in the 1920s of the last century. However, the exact relationship remains largely unknown.

Mapping real-life movements in the brain

Whether we run to catch a bus or reach for a pen: Activities that involve the use of muscles are related to very specific areas in the brain. Traditionally, their exact location has only been determined through electrical stimulation or unnatural, experimental tasks. A team of scientists in Freiburg has now succeeded for the first time in mapping the brain’s surface using measurements of everyday movements.

Attributing abilities to specific brain regions and identifying pathological areas is especially important in the treatment of epilepsy patients, as severe cases require removal of neural tissue. Until now, such “mapping” involved stimulating individual regions of the brain’s surface with electric currents and observing the reaction or sensation. Alternatively, patients were asked to perform the same movements again and again until the physicians isolated the corresponding patterns in brain activity. However, these methods required the patient to cooperate and to provide detailed answers to the physicians’ questions. This is a prerequisite that small children or patients with impaired mental abilities can hardly meet, and hence there is a need for other strategies.

Scientists from the group of Tonio Ball at the Cluster of Excellence “BrainLinks-BrainTools” and the Bernstein Center at the University of Freiburg report in the current issue of NeuroImage that the brain’s natural activity during everyday movements can also be used to reliably identify the regions responsible for arm and leg movements. The researchers examined data from epilepsy patients who had electrodes implanted under their skull prior to surgery. Using video recordings, the team captured the spontaneous movements of their patients, searching for concurrent signals of a certain frequency in the data gathered on the surface of the brain. They succeeded in creating a map of the brain’s surface for arm and leg movements that is as accurate as those created through established experimental methods.

A big hope for the team of researchers is also to gain new insights into the control of movements in the brain, as their method allows them to explore all manner of behaviors and is no longer limited to experimental conditions. Last but not least, the scientists explain that this new method of analyzing signals from the brain will contribute to the development of brain-machine interfaces that are suitable for daily use.

Text: Gunnar Grah / Bernstein Center Freiburg (mod.)

Embedded nerve cells hold the key to control brain activity

Understanding complex systems such as the brains of mammals: Arvind Kumar and colleagues from the Bernstein Center and the Cluster of Excellence “BrainLinks-BrainTools” at the University of Freiburg present a new view on brain function. Much of today’s brain research follows an approach that has been in use for decades: An area of the brain is either silenced or augmented in its activity, and the resulting effects in other parts of the brain—or in the whole organ—are measured. While this approach is very successful in understanding how the brain processes input from our senses, a team of scientists from Freiburg argues that it is too simple when trying to understand other brain regions.

“The traditional approach reduces the brain’s enormous complexity by defining relatively arbitrary subunits”, Kumar and his colleagues explain. For this abstraction to work, information must flow in one direction only. But this is not what happens in the brain, which is a complex network of smaller sub-networks that allows feedback to preceding units. Even for a network of ten units, unraveling each unit’s function would require more than 100,000 individual experimental setups—an impossible task.

Perhaps, the main question in understanding the brain is not so much how a particular area affects the activity of others, but rather how exactly brain activity can be changed from one state to another”, Kumar states. For this purpose, the neuroscientists introduced a new quality of nerve cells: their embeddedness. This is a measure for the role that a neuron plays within a network. It combines data about where a nerve cell receives information from, where it connects to, and how much it contributes to the whole network. The researchers combine this idea with the insight that already a limited number of elements within a network can control its overall behavior. Concentrating on the so-called “driving neurons” promises that even manipulating only a small number of nerve cells will provide new insight into the dynamics within the whole network. The team from Freiburg hopes that this will open new perspectives on understanding the brain, its function – and dysfunction.


Recent Publications

For a network of five elements, the combinations to be tested to ascertain each unit’s effect are already 52 (shown as orbiting symbols). Hence, this traditional way to investigate brain function is useless in most cases.

Text: Gunnar Grah / Bernstein Center Freiburg (mod.)
Ilka Diester

“And now we deactivate this brain area here for a short period of time,” says Ilka Diester, “and watch how the neighboring area will respond to its failure,” as she keenly studies the monitor displaying the neuronal impulses recorded from the second brain region. In her research, Ilka Diester deals with the question of how the motor cortex encodes movements. She is particularly interested in sensorimotor circuits: What information does the motor cortex receive? To which other brain areas does it itself send signals? And what happens if these motor circuits are disrupted—are there stabilization mechanisms by which the brain can cope with small damages? Using theoretical models and experiments, Ilka Diester will pursue these questions in a project supported by the Bernstein Award. Since July 2013, she has been a laureate of the 2012 Bernstein Award.

In her research approach, Diester combines two important experimental tools of neuroscience: optogenetics and electrophysiology. By optogenetic interventions, she induces specific perturbations in a local area of the motor cortex to temporarily activate or deactivate it. At the same time, she records the nerve cell activity in a remote motor area and observes the impact of the silencing or the overactivation of the first brain region on the second. How does area 2 react when area 1 is modulated—does it immediately try to counteract to compensate for the change of neuronal activity? “The results will allow us to deduce which robust mechanisms the motor cortex has to counterbalance small damages in the short term,” Diester says.

Born in Finland and raised in small towns in Sweden and in Northern Germany, Ilka Diester moved to Berlin to study biology. As a young student, she attended the math lectures of Andreas Herz (nowadays speaker of the Bernstein Project Committee and coordinator of the Bernstein Center Munich)—who inspired her enthusiasm for neuroscience. Apart from that, Diester developed two additional main scientific interests over the course of her undergraduate studies: genetics and computer science. Already early on, she realized that she wanted to work on a medically relevant topic. After her thesis on a genetic disease, she completed a PhD in the group of Andreas Nieder at the Hertie Institute for Clinical Brain Research in Tübingen. In her doctoral thesis, she investigated how neurons in the prefrontal and parietal cortex encode cognitive categories—such as numerical values—using in vivo electrophysiology. At that time, she realized the importance of basic research for medical progress. “Only when we understand the working principles of the brain, will we be able to detect faulty processes and develop new therapies,” says Diester.

In 2008, Ilka Diester moved to Stanford University in the United States. There, she had the opportunity to do a combined postdoc in two scientific groups, and hence to integrate her two scientific backgrounds in genetics and neuroscience. In the lab of Karl Deisseroth, she first came into contact with optogenetics. This method merges genetic and optical techniques to stimulate specific types of nerve cells or circuits with light. For this purpose, light-sensitive membrane proteins are built in the cell membranes of neurons by means of genetic vectors. As a consequence, the nerve cells become light sensitive: whenever they come in contact with light of a specific wavelength, they change their firing behavior. Depending on the type of the inserted membrane
protein, the neuron is activated or deactivated for the duration of stimulation and can thus be literally “turned on or off”. In the Deisseroth lab, Ilka Diester also learned how to combine optogenetics with behavior and electrophysiology to investigate specific neuronal circuits.

Meanwhile, in the group of Krishna She-noy, she dealt with the development of neuroprosthetics and deepened her knowledge of dynamic systems theory, as applied to the motor system. Diester found her stay at Stanford extremely motivating: “The local motto seems to be ‘the sky is the limit’—as long as you bring the right skills and capabilities, only you yourself are your limiting factor. With a strong will and working hard, you can achieve anything you want there.” During this period, Ilka Diester managed to establish optogenetic techniques in the motor system of non-human primates for the first time. At that time, this method had only previously been applied in rodents.

With a clearly defined research field of her own—the combination of optogenetics and neuroprosthetics—the neurobiologist returned to Germany in 2011. At the Ernst Strüngmann Institute in Cooperation with the Max Planck Society in Frankfurt, Diester built up her junior research group. Together with her lab members, she examines the fundamentals of sensorimotor circuits in rodents and rhesus monkeys. As described above, on the one hand she is interested in which robust mechanisms the motor cortex has to react to minor failures that may occur, for example, as a result of a stroke. On the other hand, Diester examines similarities and differences of optogenetic and electrical stimulation: The motor cortex seems to respond much more sensitively to electrical than to light stimulation. For her work, she received the Boehringer Ingelheim FENS Award last year, and this year, a Starting Grant by the European Research Council.

By means of the Bernstein Award grant, Ilka Diester will now further deepen the theoretical aspects of her work and will increasingly make use of computer models. Hereby, she hopes to be able to analyze her experimental data even more thoroughly—and to find out in detail how neural networks readjust if a certain component is silenced or overactivated. The long-term goal of Diester’s research is to gain a solid understanding of the motor cortex circuits, which is a prerequisite for developing neural prostheses. For example, it is conceivable that one could develop an electrically controlled prosthesis with which the patient receives feedback on tactile information. Until now, human subjects must solely rely on visual information when lifting a glass by a controlled robot arm. A built-in sensor in the fingertip of the prosthesis could inform the brain via optogenetic techniques that the hand needs to grasp firmer to prevent the water glass from slipping. “This would be an example of how optogenetics could be applied in daily life,” Diester says. “However, these prospects still lie in the far future. We are working on the way to get there,” she says and takes a critical look at the monitor, showing the nerve cell responses.
Andrea Huber Brösamle

Diploma thesis at Roche, PhD thesis at the Swiss Federal Institute of Technology (ETH) Zurich, postdoctoral fellow at The Johns Hopkins University—Andrea Huber Brösamle’s resume demonstrates a first class scientific career. Until recently, she was an independent research group leader at the Helmholtz Zentrum München, where she investigated the molecular basis of neural plasticity and regeneration of adult nerve fibers. Since September 15, 2013 she has been the head of the Bernstein Coordination Site (BCOS).

“I knew that I wanted to work in the life science field very early on,” Andrea Huber Brösamle says. Growing up near Basel, she came in contact with the pharmaceutical companies based there at a young age. Following her interest, the Swiss native studied biology with an emphasis in biochemistry at the University of Basel. She completed her diploma thesis in preclinical pharmaceutical research, analyzing the molecular basis of Alzheimer’s disease. During a car journey, she listened to a radio feature about Martin Schwab, her future PhD supervisor. “When I heard about his search for regeneration strategies of paraplegia, I knew, ‘This is what I want to do.’” She sent him a letter, describing why she had to do a doctorate in his lab—and for the following years she joined his lab at the Institute for Brain Research at ETH Zurich.

Her focus was Nogo-A, a neurite growth inhibitor that prevents nerve fibers from regenerating after injury to the spinal cord. For her findings on how this growth inhibitor can be neutralized by antibodies, Huber Brösamle was awarded the medal for an outstanding doctoral thesis at ETH Zurich. In 2002, she was further awarded the “Outstanding Young Investigator Award” from the International Campaign to Cure Paralysis for her research.

The biologist completed her postdoctoral studies in the group of Alex Kolodkin at the Department of Neuroscience, The Johns Hopkins Medical School in Baltimore, USA. “During that time, I took one step back in ontogenesis for my research,” Andrea Huber Brösamle says. “I was interested in how nerve fibers develop directed growth and which factors lead this process.” Applying tracing methods in mice and chicken embryos, she studied the molecular markers which ensure that nerve fibers find their way from the central nervous system to the limbs and thus ensure the correct development of the motor system. The neuroscientist is especially grateful for the scientific freedom she experienced during this time. Thanks to postdoctoral scholarships from the Swiss National Foundation and the Christopher Reeve Foundation, she could fully concentrate on her own research, and develop new ideas and also take on higher risk research.

After a five-year stay in the States, where her two children were born, Andrea Huber Brösamle moved with her family to Germany in 2006. At the Institute of Developmental Genetics, Helmholtz Zentrum München, she established her own independent research group. Here, she had the opportunity to combine her previous research interests and integrate further techniques, such as electrophysiological recordings and genomic analyses. Her main scientific interest lies in neuronal plasticity and regeneration: Can damage during embryonic development of the motor system be compensated after birth? “Not only guidance cues
are important to form a correct neuronal circuit, but also sub-
stances that hold the nerve fibers together,” Huber Brösamle
explains. If these molecules are missing, the process will end in
faulty connections. In her investigations, Huber Brösamle found
that there is a sensitive period right after birth. During this sta-
ge, intensive training may correct small perturbances. However,
this period does not last forever: After a short time, certain mo-
lecules close this window. If treatment in this period is missed,
a relatively healthy organism may compensate the faulty circuits
for some time. Yet, if additional factors—such as age—add up, it
becomes more and more likely that the damage becomes open-
ly visible. “Therefore, in my opinion, research on degenerative
diseases should increasingly look also at developmental pro-
cesses,” the neurobiologist says.

Why does she—being a successful researcher—want to leave
her scientific career? “We are experiencing an extremely exciting
time in the development of public research. Thematically orga-
nized networks are becoming increasingly important,” Andrea
Huber Brösmale replies. “I am thrilled to be able to shape this
development in neuroscience—the area of my interest.” During
the course of her scientific career, the aspect of making science
possible grew increasingly stronger. Still in the US, she actively
worked for the Consortium for Amyotrophic Lateral Sclerosis
(ALS) research. Her commitment in the field of science manage-
dent did not expire after that: She has been working as a re-
viewer for national and international research agencies and was
elected member of the scientific technical council of Helmholtz
Zentrum München. “I was particularly fascinated by the diffe-
rences between institutions such as the ETH Zurich or The Johns
Hopkins University, which are basically determined by the ori-
etation of their research personalities, and program-oriented
institutions such as Helmholtz, which is primarily funded by the
Federal Ministry of Education and Research,” Huber Brösamle
explains.

To further deepen her second main interest, Andrea Huber
Brösamle completed a two year extra-occupational training at
the Helmholtz Management Academy in St. Gallen, where she
graduated with a Masters in Management in 2010. Here, she
learned the basics of finance and dealing with media in addi-
tion to various management areas, such as innovation manage-
ment. In her master thesis, she focused on the topic of definition
of goals in science and evaluation of scientists. As a longtime
member of international research associations—such as the
European Neuroscience Institute Network and the Internatio-
nal Research Consortium on Spinal Cord Injury—Andrea Huber
Brösamle has also personally noticed the importance that an
administration follows the needs of researchers—which is an
experience that will also be useful for the coordination of the
Bernstein Network.

Regarding the Bernstein Network, Andrea Huber Brösamle
especially appreciates how the numerous and diverse areas of
the individual research labs are brought together in the field of
computational neuroscience. She is looking forward to working
for the network. For her start in the BCOS, she is planning a tour
through Germany to visit the various Bernstein sites: “I am very
excited to meet all the people and hear about their projects in the
Bernstein Network.”
**Personalia**

**Niels Birbaumer** (BFNT Freiburg-Tübingen, University of Tübingen) received the Aristotle Prize 2013 of the “European Federation of Psychologists’ Associations” (efpa). The prize is awarded to European psychologists who have made a distinguished contribution to psychology. Furthermore, he has been appointed as Senior Professor at the University of Tübingen. The professorship allows distinguished professors to continue their association with the university at a high level with all rights of petition of an active professor.


[www.nncn.de/nachrichten-en/seniorprofessurbirbaumer](http://www.nncn.de/nachrichten-en/seniorprofessurbirbaumer)

**Ilka Diester** (BPCN 2012, Ernst Strüngmann Institute, Frankfurt) received a Starting Grant by the European Research Council (ERC) for her project “Optogenetic dissection of motor cortex dynamics and pathways.”

[www.nncn.de/nachrichten-en/diesterercstartinggrant](http://www.nncn.de/nachrichten-en/diesterercstartinggrant)

**Jens Frahm** (BCCN and BFNT Göttingen, Biomedizinische NMR Forschungs GmbH at the MPI for Biophysical Chemistry, Göttingen) received this year’s science prize of the Stifterverband für die Deutsche Wissenschaft (Donors’ Association for the Promotion of the Sciences and the Humanities) for his pioneering work in the field of magnetic resonance imaging (MRI).


**Theo Geisel** (BCCN and BFNT Göttingen, MPI for Dynamics and Self-Organization, University of Göttingen) was elected regular member of the mathematical-physical class of the Göttingen Academy of Sciences and Humanities.

[www.nncn.de/nachrichten-en/theogeistelaademy](http://www.nncn.de/nachrichten-en/theogeistelaademy)

**Onur Güntürkün** (BNFL sequence learning, Ruhr-Universität Bochum) was elected to the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) Senate for the field psychology. With his election to the Senate, he is at the same time appointed to the Joint Committee of the DFG.

[www.nncn.de/nachrichten-en/guentuerkundfgsenat](http://www.nncn.de/nachrichten-en/guentuerkundfgsenat)

**Wolfgang Keil** (BCCN Göttingen, MPI for Dynamics and Self-Organization, Göttingen) has been awarded the Otto Hahn Medal of the Max Planck Society in recognition of his outstanding doctoral thesis that was supervised by **Fred Wolf** (BCCN and BFNT Göttingen, BFNL visual learning, BCOL action potential encoding, MPI for Dynamics and Self-Organization).

[www.nncn.de/nachrichten-en/ottohahnmedaillekeil](http://www.nncn.de/nachrichten-en/ottohahnmedaillekeil)

**Jakob Macke** (BCCN Tübingen, MPI for Biological Cybernetics, Tübingen) was invited to join the Junge Akademie at the Berlin-Brandenburg Academy of Sciences and Humanities and the German National Academy of Sciences Leopoldina.

[www.nncn.de/nachrichten-en/jakobmackejungeakademie](http://www.nncn.de/nachrichten-en/jakobmackejungeakademie)

**Eberhart Zrenner** (BCCN Tübingen, University of Tübingen) has been appointed as Senior Professor at the University of Tübingen. He will now continue his projects on new therapies in ophthalmology, foster the development of young scientists and supervise the special clinic for inherited retinal degenerations for another five years.

[www.nncn.de/nachrichten-en/seniorprofessurzrenner](http://www.nncn.de/nachrichten-en/seniorprofessurzrenner)
Ilka Diester receives Bernstein Award 2012

Ilka Diester was honored with the Bernstein Award 2012 on July 9, 2013. The award was conferred by Dr. Christiane Buchholz at the Federal Ministry of Education and Research (BMBF). Using the prize, endowed with up to 1.25 Mio €, Ilka Diester will expand her research group at Ernst Strüngmann Institute for Neuroscience in collaboration with the Max-Planck Society in Frankfurt. The reason for reallocating the award was that Tim Vogels—original winner of the Bernstein Award 2012—has pursued a career opportunity outside Germany and thus cannot make use of the BMBF funding (see also meet the scientist).

www.nncn.de/nachrichten-en/bernsteinpreisdiester

Public discussion: Animal use in biomedical Research

For the Bernstein Network’s research, animal experiments in many cases are still indispensable. Thus, many Bernstein Network members actively engage in the public discourse on animal experimentation in biomedical research. On June 24, 2013, a public discussion that illustrated the necessity of animal use in biomedical research from various perspectives was held at the Werner Reichardt Centre for Integrative Neuroscience (CIN) at the University of Tübingen. The following Bernstein Network members participated in the discussion: Stefan Treue (BCCN and BFNT Göttingen, German Primate Center Göttingen), Andreas Nieder, Peter Thier, and Eberhart Zrenner (all three BCCN Tübingen, University of Tübingen).

www.nncn.de/nachrichten-en/cingespraech240613

New call for proposals: Bernstein Award 2014

In 2014, the German Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF) intends to confer the ninth annual Bernstein Award to an excellent young scientist with outstanding research ideas in the field of Computational Neuroscience. The “Bernstein Award for Computational Neuroscience” is endowed with up to 1.25 Mio € for a period of five years, and allows young scientists from all nations to establish an independent research group at a German university or research institution. Application deadline for the year 2014 is April 15, 2014.

www.nncn.de/nachrichten-en/bpcn2014
Andrea Huber Brösamle new head of BCOS

Since September 15, 2013, Andrea Huber Brösamle is the new head of the Bernstein Coordination Site (BCOS). Following her studies in biology at the University of Basel, Andrea Huber Brösamle investigated neuronal growth factors for her PhD at the Brain Research Institute of the Swiss Federal Institute of Technology (Eidgenössische Technische Hochschule, ETH) and the University of Zurich. After a post-doctoral research stay at The Johns Hopkins Medical School in Baltimore, USA, she joined the Institute of Developmental Genetics at the Helmholtz Zentrum München in 2006 and headed a research group on the cellular and molecular mechanisms of the development and plasticity of neuronal circuits (see also meet the scientist).

Simone Cardoso de Oliveira left BCOS on April 30, 2013, to take on a new professional challenge within the Cluster of Excellence “BrainLinks-BrainTools” in Freiburg.

The Bernstein Coordination Site supports the scientists of the Bernstein Network in their joint activities and serves as a link between the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF), the Project Management Agency—part of the German Aerospace Center (Projektträger im Deutschen Zentrum für Luft- und Raumfahrt, PT-DLR)—and the network partners. In the years to come, a particular challenge will be the long-term establishment of the Bernstein Network and its institutional consolidation. With her neuroscientific background, extensive management training (St. Gallen) and broad experience at various leading research institutions, Andrea Huber Brösamle is ideally suited for these tasks.

New call for German - Japanese collaborations in CNS

New proposals for German–Japanese collaborations are solicited within the funding measure “Germany–Japan Collaboration in Computational Neuroscience”. The transnational initiative for supporting collaborative research between Germany and Japan is jointly funded by the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF), the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) and the Japan Science and Technology Agency (JST). Deadline for applications is September 30, 2013.

www.nncn.de/nachrichten-en/djcooperationen
## Upcoming Events

<table>
<thead>
<tr>
<th>Date</th>
<th>Title</th>
<th>Organization</th>
<th>URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sept. 2-6, 2013, Göttingen</td>
<td>11th Summer Course on Computational Neuroscience (hosted by BCCN Göttingen)</td>
<td>M. Puelma-Touzel, A. Palmigiano, D. Hofmann</td>
<td><a href="www.bccn-goettingen.de/events/cns-course">www.bccn-goettingen.de/events/cns-course</a></td>
</tr>
<tr>
<td>Sept. 29 Okt. 2, 2013, Kloster Heiligkreuztal</td>
<td>Tübingen Summer School: Neuroenhancement</td>
<td>Forum Scientarium and Werner Reichardt Centre for Integrative Neuroscience (CIN), University of Tübingen</td>
<td><a href="www.forum-scientiarum.uni-tuebingen.de/tiss">www.forum-scientiarum.uni-tuebingen.de/tiss</a></td>
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<tr>
<td>Oct. 6-11, 2013, Freiburg</td>
<td>BCF/NWG Course: Analysis and Models in Neurophysiology</td>
<td>S. Rotter, U. Egert, A. Aertsen, J. Kirsch (all Bernstein Center Freiburg), S. Grü (BCCN Berlin, D-J Collaboration)</td>
<td><a href="www.bcf.uni-freiburg.de/events/conferences-workshops/20131006-nwgcourse">www.bcf.uni-freiburg.de/events/conferences-workshops/20131006-nwgcourse</a></td>
</tr>
<tr>
<td>Oct. 17-19, 2013, Göttingen</td>
<td>Conference on Physics of Biological and Complex Systems for early career researchers and PhD students</td>
<td>Doctoral students of the IMPRS for Physics of Biological and Complex Systems including students of the Bernstein Center Göttingen</td>
<td><a href="www.thirdinfinity.mpg.de">www.thirdinfinity.mpg.de</a></td>
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The Bernstein Network

Chairman of the Bernstein Project Committee: Andreas Herz

The National Bernstein Network Computational Neuroscience (NNCN) is a funding initiative of the Federal Ministry of Education and Research (BMBF). Established in 2004, it has the aim of structurally interconnecting and developing German capacities in the new scientific discipline of computational neuroscience and, to date, consists of more than 200 research groups. The network is named after the German physiologist Julius Bernstein (1835–1917).

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