Bernstein Centers for Computational Neuroscience

BCCN Newsletter

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10/2006

Quantitative fluorescence microscopy at the push of a button

Scientists from Göttingen develop new methods for the quantitative analysis of molecular processes.

For about the last two decades, scientists have been using ‘imaging technologies’ to visualize molecular processes in living tissue with the aid of fluorescent dyes. By applying calcium-binding dyes to slices, for example, an increase of calcium ions can be observed in nerve cells when they emit action potentials. Exact quantitative statements, however, have not been possible up to now. With the help of computer-assisted methods, Detlev Schild, professor for physiology at the University of Göttingen, and his co-worker Tsai-Wen Chen have now succeeded in exactly quantifying molecular processes in living tissue.

A large problem in deriving quantitative data from fluorescence staining is the so-called ‘background staining’ – fluorescent dye that binds non-specifically to the tissue, or reflections in the lenses. In addition, quantitative signal measurements are disturbed by irregularities in the fluorescence signal and in the amplifier, known as ‘noise’. The background signal is generally determined by measuring the fluorescence in a part of the tissue that, according to theoretical considerations, should not produce a specific signal. This method is laborious and quite inaccurate.

Schild and Chen therefore looked for an alternative way to determine the background which would not rely on measurements in neighbouring regions. The specific signal, for example the calcium concentration, changes with the activity of the cell, whereas the background signal does not. ‘We used this temporal information in fluorescence to determine the background,’ explains Schild.

Fluorescence is measured at different positions within the ‘region of interest’ (ROI) - the region of a cell or a tissue in which the researchers wish to investigate the calcium metabolism. The exact fluorescence values at the different positions in the ROI will always differ slightly from each other. However, the ROI is selected so that the dynamic change of the specific signal is the same at all measured positions. Based on the temporal change of fluorescence at the different positions, both the background signal and the noise can then be eliminated.

The method will be widely applicable. In order to gain an exact understanding of how a cell interprets signals or the mechanisms by which cells communicate with one another, the quantification of molecular data is essential. With the method developed by Chen and Schild, quantitative data can now be determined not only very accurately, but also very quickly. ‘Microscope manufacturers can now integrate our method into their software, so that the background can automatically be subtracted at the push of a button,’ suggests Schild.

Source: Chen, T-W., Lin, B-J., Brunner, E., Schild, D. (2006). In-situ background estimation in quantitative fluorescence imaging. Biophysics Journal 90(7):2534-47

Why can fever cause seizures?

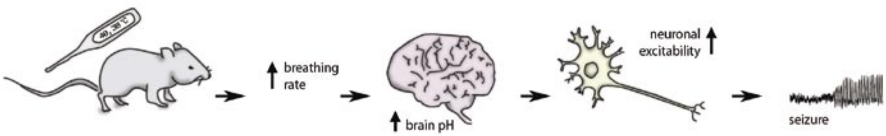
Scientists from Berlin and Helsinki found the cause of febrile seizures in rats, suggesting new therapeutic approaches

Three to fourteen percent all of children in the age of six months to six years who experience high fever develop 'febrile seizures' - the child's entire body or individual limbs twitch and the eyes roll. Seizures are created in the brain when large numbers of nerve cells discharge simultaneously. Sebastian Schuchmann, scientist at the Charité, and Dietmar Schmitz, member of the BCCN Berlin, in co-operation with a research team from Finland, have now shed light on the cause of such febrile seizures. Children with a temperature frequently exhibit accelerated breathing. Due to that, the blood concentration of oxygen and carbon dioxide changes, leading to an increase in pH - that is, the blood becomes more alkaline. In rat experiments, Schuchmann and colleagues have now shown that this respiration-induced increase in blood pH causes seizures. Their results offer important indications for possible therapies.

Febrile seizures have been investigated in rats for quite some time now. In the first few days after their birth, rats are placed in a very warm environment, such that their body temperature rises, much like in human fevers, and seizures are induced. The consequences of febrile seizures in rats have already been investigated in great detail – however, very little has been discovered about their causes. Up to now, one could only speculate about why young rats are inclined to developing febrile seizures. Now, the scientists from Berlin and Helsinki have found an answer to that question.

A neural circuit in the brain controls the breathing rhythm and thereby regulates various physiological parameters. On the one hand, controlling the breathing rhythm keeps the blood concentrations of oxygen and carbon dioxide constant. On the other hand, respiration plays a substantial role in regulating body temperature. In children – and young rats – this mechanism is not fully developed yet. When challenged by a sudden rise in body temperature, it does not react optimally. Respiration is accelerated in order to cool the body, but this happens at the expense of the optimal blood concentrations of oxygen and carbon dioxide. The blood pH value rises.

It is well known that an increased pH value makes neurons more excitable. If neurons fire uncontrollably and synchronously, a seizure can be induced. Schuchmann and his colleagues showed in their rat experiments that the increased blood pH value caused by accelerated respiration can indeed elicit convulsions. Accordingly, seizures could be terminated by increasing the content of carbon dioxide in the breathing air, leading to a decrease in blood pH. This result of Schuchmann and colleagues suggests a new approach for the therapy of febrile seizures. It remains to be shown whether this therapy also works in humans.



Schematic illustration of the events that can lead to ferbile seizures in young rats.

Source: Schuchmann, S.*, Schmitz, D.* et al. (2006). Experimental febrile seizures are precipitated by a hyperthermia-induced respiratory alkalosis. Nat Med. Jul;12(7):817-23. * equal contribution

Fastest biped walking robot

Göttingens RunBot breaks world record in speed walking

A structure of two legs held by a horizontal bar, 23 cm in height, controlled by a simple program – this structure is the world record holder in robot speed walking, at least relative to its body size. With 3.5 leg lengths per second, RunBot is more than twice as fast as the previous title holder in the discipline, MIT's 'Spring Flamingo.' RunBot was developed by Florentin Wörgötter, scientist at the University of Göttingen and at Göttingen's Bernstein Center, in collaboration with his colleagues, Bernd Porr (Glasgow) and Tao Geng (Stirling).

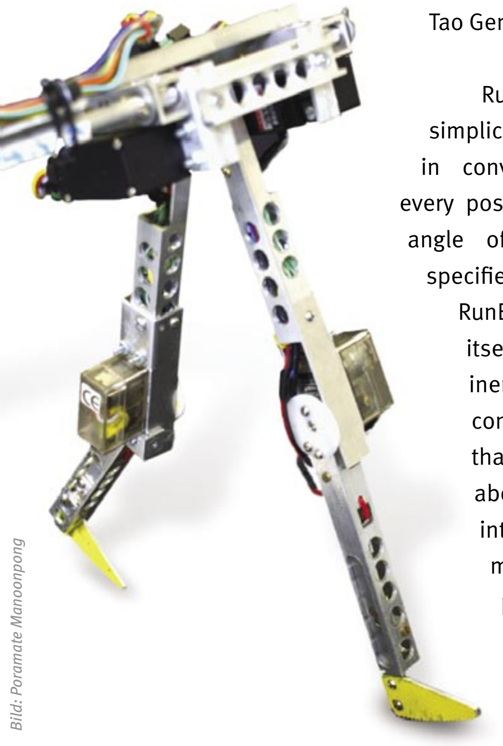


Bild: Poramate Manoonpong

RunBot's success is built upon simplicity and dynamics. Whereas in conventional industrial robots, every position of their feet and every angle of their joints is precisely specified by the control program, RunBot basically walks by itself, driven by gravitation and inertia of its limbs. Its gait is controlled by a simple program that reflects the activity of about 20 'neurons' and only interferes with the flow of the movement at a few selected points. As soon as the robot moves its thigh forward, up to a defined angle, the knee receives a signal to stretch. As soon as the foot contacts the ground, the joints of the hip and knee of the supporting leg receive a signal to bend and the weight is shifted to the free leg. RunBot's gait is a reflex movement – every motion segment triggers the next one.

The simplicity of movement control, however, is not the only factor that makes the RunBot run fast, although it is an important prerequisite. RunBot has another feature which is also crucial for its unprecedented walking performance: it can learn. A mathematical algorithm furnishes the robot with the ability to autonomously optimize its movement program to achieve maximum walking speed. The algorithm systematically varies the flexion angle of its joints and the velocity of the leg swinging forward. If the new parameters increase walking speed, they are taken as the starting point for further movement modifications. As the robot's gait is driven by only a few parameters, RunBot learns quickly. Once the 'learning program' is started, RunBot approaches maximal walking speed within a few minutes.

Conventional industrial robots do not learn. Every movement they perform has to be programmed in detail, and every modification of their behavior can only be achieved through an adjustment of the program. If robots achieve the ability to learn, complex tasks can be accomplished with substantially less programming effort. At the moment, RunBot is a specialist in its learning abilities – it can learn to walk fast. In the future, it will also learn to solve other tasks, such as climbing stairways or navigating in uneven terrain.

Source: Geng, T., Porr, B., Wörgötter, F. (2006). Fast Biped Walking with a Sensor-driven Neuronal Controller and Real-time Online Learning. International Journal of Robotics Research 25 (3).

Hertie Senior Research Professorship to Thomas Brandt

To preserve creative minds in the field of neurosciences after the age of retirement, the Hertie-Foundation has established the "Senior-Forschungsprofessur" (Senior Research Professorship). Thomas Brandt, 63, Director of the Neurological Department at the University Hospital Großhadern in Munich and member of the Bernstein Center for Computational Neuroscience, is the first laureate. The award was presented by Annette Schavan, Federal Minister of Education and Research, at the award ceremony at the Ludwig Maximilians University in Munich on July 15, 2006.

The "Hertie-Senior-Forschungsprofessur" is an unprecedented funding measure which will serve as a model and trigger a debate which is long overdue, regarding the demographic structure of our society. How do we handle the capacity and experience of scientists above the age of 65 in Germany? Is a civil service law, which impedes research activity above this age, still appropriate? Composers, poets, painters – effectively all people in creative professions continue to be inventive and productive until high age. But this privilege is refused to scientists, who need to be affiliated to a university to continue their career. They will take all their experience with them into retirement or emigrate to foreign countries, where they can continue their research.

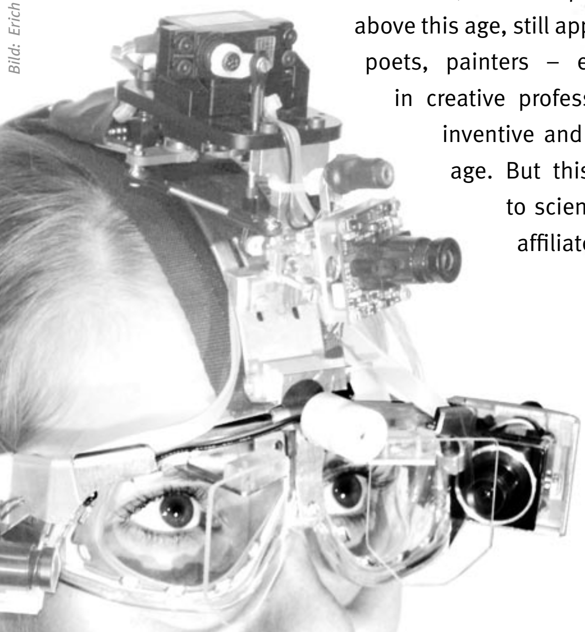


Bild: Erich Schneider

Brandt and colleagues developed a head mounted camera controlled by the eye movement

The goal of the Hertie-Senior-Forschungsprofessur is to preserve the potential of researchers approaching retirement for a longer period of time. The laureate is obliged to retract from all non-honorary responsibilities to fully concentrate on research tasks. Thereby, the former professor position is liberated for young scientific staff.

The research professorship is not only a model in funding policies; it is an honor in the very first place. Brandt belongs to the leading scientists worldwide in the field of balance disorders. He has investigated the causes of the Benign Paroxysomal Positional Vertigo, the most prevalent balance disorder, and developed therapeutic measures. In addition, Brandt was the first to describe the Phobic Postural Vertigo, the second most prevalent balance disorder.

Using imaging techniques to visualize brain activity, Brandt investigated how the vestibular and the visual system are adjusted to each other. In order to keep a clear vision even if our head is moving, our brain compensates every movement of the head with an eye movement in the opposite direction – if the head turns right, the eyes automatically move left. How this works, why a disturbance of this interplay on a swaying boat leads to motion sickness, or why one has the illusion to move when observing a moving train are also questions addressed by Brandt's research.

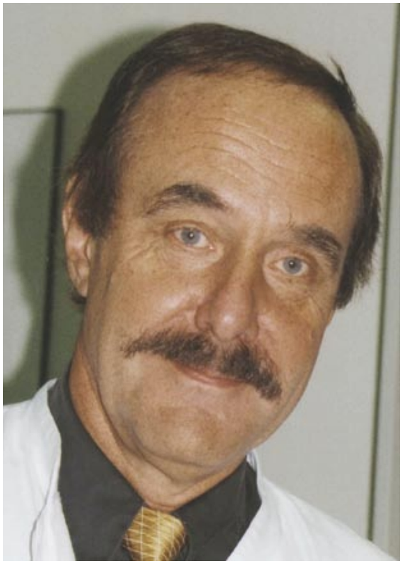
Meet the Scientist

Prof. Dr. med. Dr. h.c. Thomas Brandt, FRCP

1943	born in Dessau
1964 - 1969	Medical sudies
1971 - 1976	Department of Neurology and Clinical Neurophysiology, University of Freiburg
1976 - 1984	Director of the Neurological Clinic with Department of Clinical Neurophysiology, Alfried Krupp Hospital, Essen
since 1984	Chairman of Neurology, University of Munich
	Director of Department of Neurology, Klinikum Grosshadern, Munich

Honours and Memberships (selekted)

1999	Betty David Koetser Memorial Price for Brain Research, Zürich
2000	Bárány Gold Medal 2000, Uppsala
2000	Doktor Robert Pfleger-Preis 2000, Bamberg
since 1998	Neurological chief editor „Nervenarzt“
1992 - 2001	Section Editor „Journal of Vestibular Research“
since 2001	Joint Editor in Chief „Journal of Neurology“



Investigating the mechanisms of eye movement also brought Brandt to the idea of developing, together with a team of engineers, a head mounted camera which is controlled by the eye movements of its carrier, so that it records from his perspective. Compensatory eye movements prevent image blurring and shaking, even if the carrier moves his head.

For the Hertie-Senior-Forschungsprofessur, Brandt will resign from his position as director of the Neurological Department at the University Hospital, giving up the extra income through payments of privately insured patients. To him, this tradeoff is worthwhile. “I can achieve more in research,” says Brandt, “my research group is not destined to break up. In contrast, we will continue in 2007 with new drive.” Brandt can now rid the bonds of administrative work and can fully concentrate on his creative potential.

The first BCCN Summer School in Munich

The first 'BCCN Summer School' of the Bernstein Center for Computational Neuroscience in Munich took place from July 20-22 in Herrsching on the Ammersee. The majority of the twenty participants came from different research institutions in Munich.

The topic of the 2006 Summer School was motion detection. In all classes of the animal kingdom, special neuronal circuits in the visual, vestibular and auditory system cater specifically for motion detection. Such mechanisms are essential for survival in the wild, for tracking prey and for identifying danger. However, observation of the environment is only one aspect of motion detection – when the animal itself moves, the environment passes by its eye. In order to be able to orientate itself in space, an animal must be able to set the movements, which its eye observes, against information about its own motion from its equilibratory system.

In five talks by group leaders and advanced postdocs from the BCCN Munich and one guest scientist, the participants in the Summer School were able to learn how the eye, ear and organ of equilibrium contribute to motion detection and how they interact while doing so. The talks were followed by presentations by the participating doctoral students and lively discussion. Thus, the young scientists were not only able to gain a good insight into a central topic of the Bernstein Center in Munich, they were also able to practice their communication skills in talks and discussions.

In the coming years a BCCN Summer School, dealing with varying topics from the field of computational neuroscience, will take place every summer. The organizers hope that with this concept they will, in the future, be able to attract participants from the Bernstein Centers in Berlin, Freiburg and Göttingen in order to increase communication between these centers and their doctoral students.

Further information:
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Advanced Course in Arcachon

The 11th 'Advanced Course in Computational Neuroscience' took place in Arcachon (France) from August 7th to September 1st under the directorship of Ad Aertsen (BCCN Freiburg) and his colleagues Peter Dayan (UK), Israel Nelken (Israel) and Nicolas Brunel (France). Further members of the teaching faculty included Marc-Oliver Gewaltig, Markus Diesmann and Stefan Rotter from the BCCN Freiburg.

The Advanced Course is an annual event aimed at graduate students and postdocs from across the whole discipline of Computational Neuroscience. Through a mixture of lectures, tutorials, and work on a personal project, the students are introduced to the central ideas and methods of the field, simultaneously addressing several levels of neural organization, from subcellular processes to operations of the brain. The participants immensely profit from the informal contact with the faculty and each other, paving the way for future collaborations and career opportunities.

Further information:
http://www.neuroinf.org/courses/EUCOURSE/EU06/courses.shtml
Application deadline for next course: March 2007

Flavio Fröhlich

Birgit Kriener

International student exchange programs with the BCCNs

The Bernstein Centers are supporting exchange of students and researchers with other leading centers in the world and are encouraging students to take part in advanced courses and summer schools. Different Bernstein Centers have started formal exchange cooperations with renowned institutions and plan further alliances with other locations. For instance, the Freiburg Center has recently closed formal agreements with the Interdisciplinary Center for Neural Computation (ICNC), Hebrew University (Jerusalem, Israel) and the Graduate Program in Computational Neurobiology, University of California (San Diego, USA). Here, two of the first exchange students describe how they profited from this exchange.

Visit from the West...

I am a graduate student in the Computational Neurobiology PhD program at the University of California, San Diego. This summer I had the great privilege to visit the Bernstein Centers for Computational Neuroscience. I spent two very exciting weeks interacting with research groups at the Centers in Munich, Freiburg, and Göttingen. During a typical day, I would visit laboratories and meet with graduate students, postdocs, and professors to discuss science. I found it very refreshing to also talk about scientific questions not directly related to my own research. Experiencing the breadth of questions addressed with computational and theoretical techniques helped me to better understand the key factors leading to successful computational neuroscience research.

I was impressed by the seamless fashion in which experimental and computational neuroscience research is integrated to form very promising and exciting interdisciplinary projects at the Bernstein Centers. Not only did I learn about new techniques and results, but I also made many new friends. I would like to encourage my fellow PhD students on both sides of the ocean to consider an exchange visit as a highly rewarding and excellent opportunity to extend scientific horizons.

- Flavio Fröhlich

...and going to Far-East

I'm a graduate student in the PhD program of the Bernstein Center for Computational Neuroscience Freiburg. My PhD project is concerned with the impact of network coupling structure on the ongoing dynamics of local cortical networks. This summer I had the opportunity to join the Summer Program of RIKEN BSI in Tokyo as an intern in Prof. Fukai's lab. His lab is interested in very similar questions I am. At the BSI nearly every branch of neuroscience is represented, and it was a great experience to be able to discuss my work with the BSI researchers (see photo).

People there are very aware of the German efforts to establish cooperations in the field of computational neuroscience and are extremely supportive of these ideas. I had a great time and got much input for future work. I hope this contact with the BSI will strengthen and allow other BCCN students to take part in this exchenge, even beyond the annual Summer Program.

- Birgit Kriener

Flavio Fröhlich does his PhD research in the laboratory of T. Sejnowski at The Salk Institute for Biological Studies.
Birgit Kriener does her PhD under the supervision of Stefan Rotter, Ad Aertsen and Markus Diesmann at the BCCN Freiburg.

A united move to RIKEN

Two Principal Investigators of the BCCNs Berlin and Freiburg accept appointments as Unit Leaders at RIKEN Brain Science Institute

Starting in September 2006, Sonja Grün (Berlin) and Markus Diesmann (Freiburg), both founding members of the BCCNs, will continue their research as Unit Leaders at the renowned RIKEN Brain Science Institute in Tokyo, Japan. The upcoming RIKEN Newsletter will publish an interview with the couple. Here we quote from that interview:

‘In September, two new research units will join the theoretical research groups at RIKEN Brain Science Institute. In addition to conducting experiments, the presence of the units promises to be a new social experiment for RIKEN -a change that could influence science management and open doors for researching couples. These units might also catalyse more interaction between experimental and theoretical laboratories within RIKEN BSI with exciting results. These new units, you see, are, like their unit leaders, a couple: partners in research.

Husband and wife team, Markus Diesmann and Sonja Grün, are German scientists with a passion for theoretical brain science. The pair was working in separate institutes in different parts of Germany. According to Markus, they want to “understand thinking, to find out how we solve problems.” Moreover, they wanted to do it together. RIKEN BSI offered them a way to do that. …’

Despite their moving, Diesmann and Grün will maintain responsibility for their respective BCCN projects, thereby also strengthening the bonds between the BCCNs and RIKEN.

Personalia in brief

Klaus-Robert Müller has accepted a W3 professorship for Machine Learning at the Technische Universität Berlin. His work is concerned with theoretical concepts and algorithms for machine learning and signal processing and their practical application to real world data analysis problems. Müller so far held a joint professorship between the University of Potsdam and the Fraunhofer-Institute for Computer Architecture and Software Technology and he will keep his Fraunhofer affiliation.

Sonja Grün and **Markus Diesmann** will join the RIKEN Brain Science Institute (Tokyo) as Unit Leaders in the Computational Neurosciences (see article at the left).

Thomas Brandt is the first laureate of the newly established ‘Senior-Forschungsprofessur’ (Senior Research Professorship) of the Hertie Foundation. The Senior Research Professorship is a funding measure to preserve the capacity and experience of scientists after the age of retirement (see pages 5 and 6).

Markus Diesmann and Sonja Grün

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Impress

Published by:
Bernstein Centers for Computational Neuroscience
Berlin – Freiburg – Göttingen – Munich
http://www.bernstein-centers.de

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Layout:
newmediamen, Berlin / Dr. Katrin Weigmann

Print: Elch Graphics, Berlin

The Bernstein Centers for Computational Neuroscience are funded by the Federal Ministry of Education and Research (BMBF) and are a central element of the "National Network Computational Neuroscience". The aim of the funding measure is to concentrate scientific expertise in Germany and to promote the clinical and technological applications of theoretical insights in the field of neuroscience.

Cover image: The head mounted camera is controlled by the eye movements of its carrier, so that it records from his perspective (see pages 5-6)

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