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COMPUTATIONAL NEUROSCIENCE AND THE HYBRID BRAIN

FREIBURG IM BREISGAU, 12 - 14 OCTOBER 2015

Photo: Martin Pyka

Lecture Hall, Institute of Biology I, Hauptstr. 1

Organized by

Ulrich Egert, Stefan Rotter, Carsten Mehring and Ad Aertsen

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Conference Dinner
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79098 Freiburg im Breisgau

Science Jam
Bernstein Center Freiburg
Hansastraße 9a
79104 Freiburg im Breisgau

Hotel
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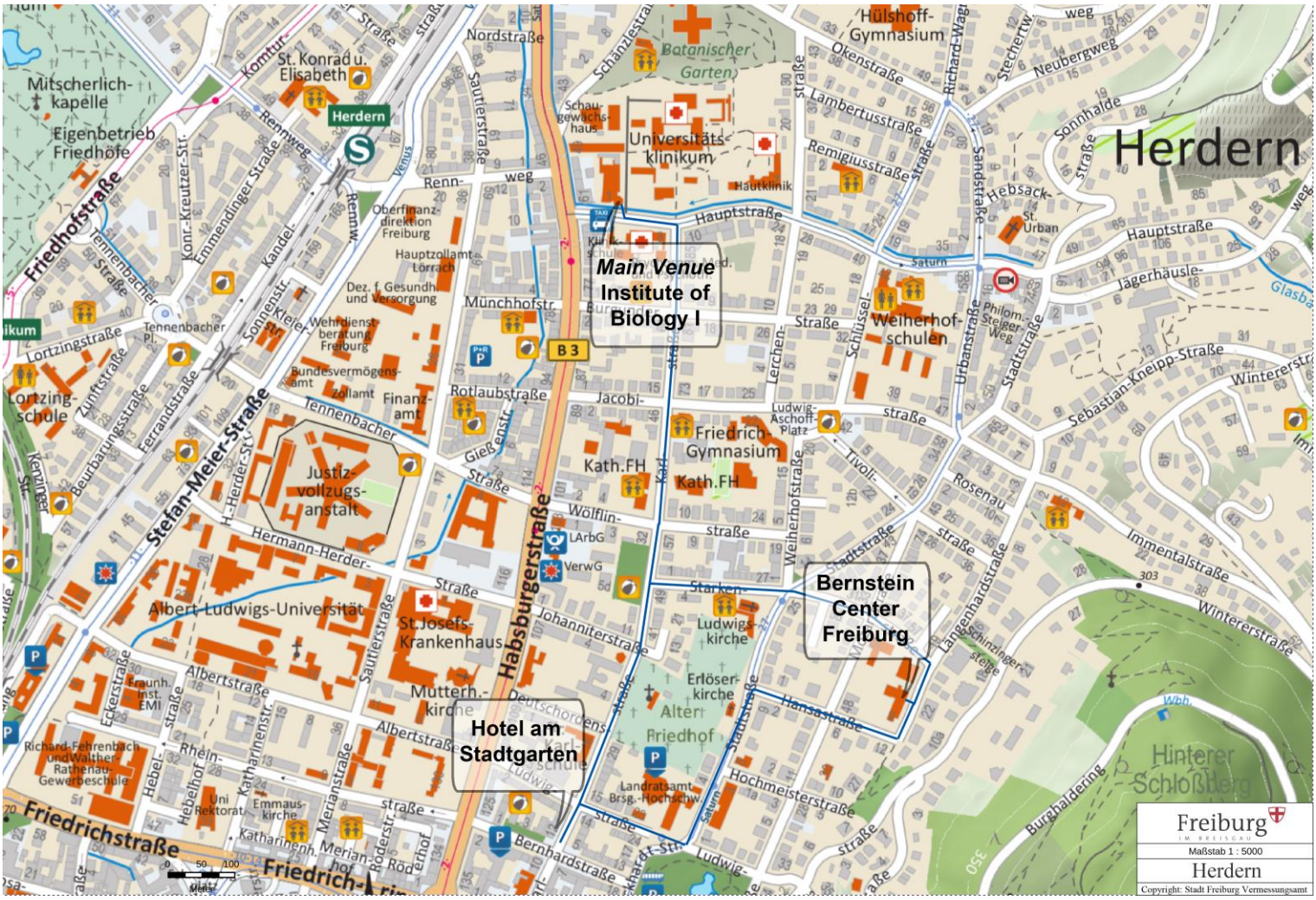
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Mon 12/10		Tue 13/10		Wed 14/10	
9:00	Registration		**Session IV – Plasticity**		**Session VII – Carl-Zeiss Kick-Off**
9:20	Welcome Ulrich Egert		**Chair: Carsten Mehring**		**Chair: Stefan Rotter**
				9:30	Welcome Stefan Rotter
	Session I – Control & Learning	9:00	Claudia Clopath		
	Chair: Ulrich Egert	9:30	Josef Bischofberger	10:10	Klaus Herberger
9:30	Carsten Mehring	10:00	Romain Goutagny		
10:00	Philip Sabes			10:25	Margit Zacharias
		10:30	*Coffee Break*		
10:30	*Coffee Break*			10:40	*Coffee Break*
		11:00	Poster Session		
10:50	Aaron Batista			11:10	Robert Schmidt
11:20	Robert van Beers	12:00	*Lunch*	11:40	Tom Tetzlaff
11:50	Ioannis Vlachos			12:10	Torfi Sigurdsson
			Session V – Epilepsy		
12:20	*Lunch*		**Chair: Arvind Kumar**	12:40	*Lunch*
		13:30	John Huguenard		
		14:00	Carola Haas		**Session VIII – Circuitry and Function**
	Session II – Networks of Networks	14:30	Christopher Kim		**Chair: Ad Aertsen**
	Chair: Stefan Rotter	15:00	Antje Kilias	14:00	Andreas Lüthi
14:00	Arvind Kumar	15:30	*Coffee Break*	14:30	Martin Angelhuber
14:30	Samora Okujeni			15:00	Philippe Isope
15:00	Gaute Einevoll		**Session VI – Rehabilitation**		
				15:30	Closing Remarks Ulrich Egert
15:30	*Coffee Break*		**Chair: Arvind Kumar**		
		16:00	Surjo Soekadar		
	Session III – Neurotechnology	16:30	Diljit Singh Kajal	16:00	*Get Together BCF Workshop*
	Chair: Ulrich Egert				
			Outreach/Ethics		
16:00	Andreas Hierlemann	17:00	Oliver Müller		
16:30	Thomas Stieglitz				
17:00	Jürgen Hennig	19:00	*Evening Event: Science Jam at BCF (Special Edition)* Fingerfood and drinks will be served from 18.30 See map for instructions		
19:00	*Conference Dinner at "Haus zur Lieben Hand"* See map for instructions				

Monday, 12 October 2015

09:00 Registration at Main Venue

09:20 - 09:30 Welcome
Ulrich Egert

Session I – Control & Learning
Chair: Ulrich Egert

09:30 - 10:00 Skill Learning and Control of Supernumerary Movement Effectors
Carsten Mehring, University of Freiburg, Germany

10:00 - 10:30 A Learning-Based Approach to Artificial Sensory Feedback
Philip N. Sabes, University of California, USA

10:30 - 10:50 *Coffee Break*

10:50 - 11:20 Learning about Learning with Brain-Computer Interfaces
Aaron Batista, University of Pittsburgh, USA

11:20 - 11:50 Retention of Motor Adaptation
Robert van Beers, University of Amsterdam, The Netherlands

11:50 - 12:20 Control of Pathological Brain Activity in Spatially Extended Models
Ioannis Vlachos, University of Freiburg, Germany

12:20 - 14:00 *Lunch* (Main Venue)

Session II – Networks of Networks
Chair: Stefan Rotter

14:00 - 14:30 To Go or Not: Basal Ganglia Dynamics Underlying Brain Function and Dysfunction
Arvind Kumar, KTH Royal Institute of Technology, Stockholm, Sweden

14:30 - 15:00 Relations Between Network Structure and Activity Dynamics
in Developing Neuronal Networks
Samora Okujeni, University of Freiburg, Germany

15:00 - 15:30 What can the Local Field Potential (LFP) Tell Us About Cortical Network Activity?
Gaute Einevoll, Norwegian University of Life Sciences (UMB), Aas, Norway

15:30 - 16:00 *Coffee Break*

Session III – Neurotechnology
Chair: Ulrich Egert

16:00 - 16:30 Highly Integrated CMOS Microsystems to Interface with Neurons at Subcellular Resolution
Andreas Hierlemann, ETH Zürich, Switzerland

16:30 - 17:00 Neural Implants for Mice and Men
Thomas Stieglitz, Universtity of Freiburg, Germany

17:00 - 17:30 Observation of Neuronal Networks and Connectivity with MRI
Jürgen Hennig, University Medical Center Freiburg, Germany

19:00 Conference *Dinner* (at “Haus zur Lieben Hand”, see map)

Tuesday, 13 October 2015

Session IV – Plasticity
Chair: Carsten Mehring

09:00 - 09:30 Emergence of Functional Connections in Neural Networks with Synaptic Plasticity
Claudia Clopath, Imperial College London, UK

09:30 - 10:00 Bidirectional GABAergic Control of AP Firing in Newly Generated Young Hippocampal Granule Cells
Josef Bischofberger, University of Basel, Switzerland

10:00 - 10:30 Theta-Gamma Coupling Modulation in the Hippocampus During Spatial Memory Processing
Romain Goutagny, University of Strasbourg, France

10:30 - 11:00 *Coffee Break*

11:00 - 12:00 Poster Session

12:00 - 13:30 *Lunch* (at Main Venue)

Session V – Epilepsy
Chair: Arvind Kumar

13:30 - 14:00 Epilepsy and Brain-Machine Interface
John Huguenard, Stanford University, USA

14:00 - 14:30 Synaptic Plasticity and Reorganisation in Temporal Lobe Epilepsy
Carola Haas, University of Freiburg, Germany

14:30 - 15:00 Altered Network Dynamics in a Computational Model of Mesial Temporal Lobe Epilepsy
Christopher Kim, University of Freiburg, Germany

15:00 - 15:30 The Hippocampal Clock in a Mesial Temporal Lobe Epilepsy Model
Antje Kilias, University of Freiburg, Germany

15:30 - 16:00 *Coffee Break*

Session VI – Rehabilitation
Chair: Arvind Kumar

16:00 - 16:30 Hybrid Brain/Neural Computer Interaction (BNCI) in Neurorehabilitation: From Bench to Bedside and Beyond
Surjo Soekadar, University of Tübingen, Germany

16:30 - 17:00 Changing local brain activity and global network communication by means of BCI training
Diljit Singh Kajal, University Hospital Tübingen, Germany

Outreach/Ethics

17:00 - 17:30 Ethical Aspects of Neurotechnology & New Perspectives in Public Outreach
Oliver Müller, University of Freiburg, Germany

19:00 *Evening Event: Science Jam at BCF*
(Special Edition)
Fingerfood and drinks will be served from 18:30
at Bernstein Center Freiburg (see map)

Wednesday, 14 October 2015

Session VII – Carl-Zeiss Kick-Off
Chair: Stefan Rotter

09:30 - 10:10 Welcome/Talk
Computational Neuroscience of Brain Disease:
Neuronal Mechanisms of Brain Function and Dysfunction
Stefan Rotter, University of Freiburg, Germany

10:10 - 10:25 Only Knowledge can shape the future
in a manner that is responsible and beneficial to life
Klaus Herberger, Carl-Zeiss-Foundation, Stuttgart, Germany

10:25 - 10:40 *Margit Zacharias*, Vice-President for Innovation and Technology Transfer, University of Freiburg, Germany

10:40 - 11:10 *Coffee Break*

11:10 - 11:40 A Two-Step Model of Action Suppression Based on Basal Ganglia Neurophysiology
Robert Schmidt, University of Freiburg, Germany

11:40 - 12:10 Effect of Alzheimer's Disease on the Dynamics and
Computational Performance of Recurrent Neural Networks
Tom Tetzlaff, Jülich Research Center, Germany

12:10 - 12:40 Neural Circuit Dysfunction in Psychiatric Disease: Insights from Animal Models
Torfi Sigurdsson, Goethe University Frankfurt, Germany

12:40 - 14:00 *Lunch* (at Main Venue)

Session VIII – Circuitry and Function
Chair: Ad Aertsen

14:00 - 14:30 Deconstructing fear
Andreas Lüthi, Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

14:30 - 15:00 The Central Amygdala in Fear Learning and Anxiety - A Modeling Perspective
Martin Angelhuber, University of Freiburg, Germany

15:00 - 15:30 Understanding Operational Rules for the Modular Information Processing
in the Cerebellum
Philippe Isope, University of Strasbourg, France

15:30 - 16:00 Closing Remarks
Ulrich Egert

16:00 *Get Together*
BCF Workshop

ABSTRACTS
IN ALPHABETICAL ORDER

The Central Amygdala in Fear Learning and Anxiety

A Modeling Perspective

Martin Angelhuber

Bernstein Center Freiburg, University of Freiburg, Germany

Classical fear conditioning is one of the most powerful models to study the neuronal substrates of associative learning and can provide important insights into the emergence of anxiety disorders. Recent experimental studies have revealed an inhibitory microcircuit in the central amygdala (CEA), which is essential for the acquisition and expression of conditioned fear. During fear conditioning distinct CEA subpopulations acquire phasic responses to the conditioned stimulus and change their baseline firing rates. Notably, these changes in baseline firing rate correlate with fear generalization. While acquisition of the phasic responses can be attributed to synaptic plasticity on the afferent connections, it has been shown, that the changes in baseline firing can be linked to subpopulation-specific modulation of tonic inhibition, mediated by extrasynaptic GABA-receptors.

In this talk I show how a modeling approach can shed further light on the roles of these two types of plasticity and their effect on fear generalization. Specifically I will address the effect of tonic conductance changes on the processing of incoming stimuli in the CEA network. Corroborating experimental observations, the model suggests that tonic inhibition controls fear generalization and, together with experimental data relating fear generalization to anxiety, the results indicate the central amygdala may act as a link between fear learning and the emergence of anxiety.

Learning about Learning with Brain-Computer Interfaces

Aaron Batista

SMILE: Sensory Motor Integration Laboratory and Engineering, Department of Bioengineering, University of Pittsburgh, USA

Although originally envisioned as a therapeutic device, brain-computer interfaces (BCI) have proven to have great value as a tool in basic neuroscience. In particular, they enable unprecedented access to the neural mechanisms of motor skill learning, because in a BCI setting, we know all the neurons that control behavior directly, and we can design the mapping from neural activity to behavior. We leverage these unique aspects of BCI control to probe the mechanisms of learning among populations of neurons. There are different classes of BCI mappings: some of which are relatively easy to learn to control, and others which can be learned only after several days of practice. This raises the intriguing possibility that the neural mechanisms used to learn in those two contexts are quite different: fast BCI learning may be facilitated by the cerebellum, and slow BCI learning may require the basal ganglia.

Retention of Motor Adaptation

Robert van Beers

MOVE Research Institute Amsterdam, Department of Human Movement Sciences, VU University Amsterdam, The Netherlands

Motor adaptation is a motor system's response to a change in the environment, such as a perturbation of the visual feedback about one's movements. Many experimental studies have focused on the factors determining how fast subjects adapt to a perturbation, and how fast they readapt upon reexposure to a perturbation. This has led to a range of computational models that can explain many aspects of motor adaptation.

A less studied aspect of motor adaptation is retention, or how well adaptation is retained after the perturbation is removed. Here we studied how scaling the visual feedback about motor errors during adaptation affects retention of motor adaptation. Subjects reached to visual targets in eight directions from a fixed start location. They adapted to a visuomotor rotation, in which the visual feedback about their finger location was rotated by 30 deg about the start location. Moreover, the error in the movement direction with respect to the required direction was multiplied by a gain factor to determine the displayed finger position. We tested four groups of subjects with gains of 1/3, 2/3, 1 and 4/3. The results show that subjects in all groups adapted to the perturbation, although the group with gain 1/3 adapted less than the other groups.

To measure retention, subjects produced 200 error-clamp trials after adaptation. In these trials they always received visual feedback that suggested that they moved in the correct direction. In this phase, the level of adaptation decreased in all groups. However, the extent of this decrease differed between groups, with the smaller gains having better retention than the larger gains. This result is not predicted by any of the existing models for motor adaptation. We conclude that downscaling of the feedback about movement errors facilitates retention of motor adaptation. Downscaling of errors may therefore be a useful technique for movement rehabilitation following brain injury or stroke. However, the computational origin of this effect remains to be determined.

Bidirectional GABAergic Control of AP Firing in Newly Generated Young Hippocampal Granule Cells

Josef Bischofberger

Stefanie Heigele, Sebastien Sultan, and Nicolas Toni

Department of Biomedicine, FB Psychology, University of Basel, Switzerland

The hippocampus is one of the few regions in the adult mammalian brain, where new neurons can be generated thorough life. The first synaptic contacts of the newly generated young granule cells are formed by local GABAergic interneurons, which are crucial for activity dependent survival and functional maturation of the young neurons between 1-3 weeks post mitosis. However, it is still absolutely unclear, whether activation of GABAergic synapses might generate action potential (AP) firing or whether shunting inhibition might predominate. We performed whole-cell patch-clamp recordings from newborn granule cells in acute brain slices of the adult mouse hippocampus. Whereas glutamatergic synaptic inputs always remained subthreshold in the young newborn neurons, we have found that activation of GABAergic synaptic inputs depolarized young neurons and reliably evoked APs. Furthermore, pairing of subthreshold EPSPs or somatic current injection with brief bursts of GABAergic inputs revealed efficient GABAergic excitation at conductances of about ~1.5 nS. Stronger GABAergic inputs effectively blocked AP firing via shunting inhibition, which might be important to protect the young cells from over excitation. Taken together, GABAergic synaptic inputs in newly generated young granule cells can dynamically support either AP generation or shunting inhibition dependent on hippocampal network activity.

Emergence of Functional Connections in Neural Networks with Synaptic Plasticity

Claudia Clopath

Bioengineering Department, Imperial College London, UK

Animals have the fascinating ability to learn to adapt to their environment, as well as memorize experiences. My core research interest lies in synaptic plasticity, that is, how the strength of synapses between neurons changes, which is believed to be the key neural mechanism involved in learning and memory. More precisely, I design models of plasticity across different time scales, synapse types and brain regions, in order to explain the phenomenology, and built plastic artificial neuronal networks in order to study the role and function of plasticity. In this talk, I will focus on the development of functional subnetworks of excitatory and inhibitory neurons.

What can the Local Field Potential (LFP) tell us about Cortical Network Activity?

Gaute Einevoll

Department of Mathematical Sciences and Technology, Norwegian University of Life Sciences (UMB), Norway

Even though the LFP has been measured for more than half a century, the interpretation of the recorded data has so far largely been qualitative. The biophysical origin of the signal is well understood, and several modeling studies have explored the link between neuron and network activity. However, the computation of LFP from network activity has until now been too cumbersome and computer-intensive to allow for practical exploration of the links between different types of network dynamics and the resulting LFP. Thus validation of candidate cortical network models against measured LFP data has essentially been absent.

In collaboration with researchers in Juelich, our group has recently the developed a hybrid LFP modeling scheme combining the efficiency of simplified point-neuron network models with the biophysical principles underlying LFP generation by multicompartment neurons. In the seminar, example results from applying the the scheme to a full-scale cortical network model for a one square millimeter patch of primary visual cortex (the so called Potjans-Diesmann model) will be presented. The results demonstrate that the laminar LFP distribution depends strongly on, e.g., network state and external synaptic inputs, suggesting that LFP recorded in vivo indeed can be used to probe network activity and distinguish between candidate network models.

Theta-Gamma Coupling Modulation in the Hippocampus during Spatial Memory Processing

Romain Goutagny

Team NCG: Neurobiology of Cognitive Decline, University of Strasbourg, France

Spatial reference memory in rodents represents a unique opportunity to study brain mechanisms responsible for encoding, storage and retrieval of a memory and is precociously altered in neuropsychiatric diseases such as Alzheimer's disease. Even though its reliance on hippocampal networks has long been established, the precise computations performed by different hippocampal subfields during spatial learning is still not clear. To fulfill this gap, we recorded local field potentials in behaving mice using a newly designed appetitive version of the Barnes maze and showed that dentate gyrus networks, but not CA1 networks, exhibit a transient learning-dependent increase in theta-gamma coupling specifically at the vicinity of the target area in the maze. Since this type of activity is altered early in animal models of neuropsychiatric disorders, these results might explain the early cognitive deficits present in such diseases.

Synaptic Plasticity and Reorganisation in Temporal Lobe Epilepsy

Carola Haas

Experimental Epilepsy Research group, Department of Neurosurgery, Medical Faculty, University of Freiburg, Germany

Mesial temporal lobe epilepsy (MTLE) is the most common form of epilepsy in adults. In MTLE, seizures originate from the meso-limbic network in which the entorhinal-hippocampal loop holds a key function. Aberrant wiring among neurons in the hippocampus is critically involved in the generation of limbic seizures. Little is known, however, whether and how the entorhinal input influences epileptic activity originating from the hippocampus. In the present study we investigated structural and functional alterations of entorhinal input onto dentate granule cells in epileptic mice. We anterogradely traced the medial perforant path (MPP), assessed its connectivity with dentate granule cells and examined the functional alterations in the intrahippocampal kainate mouse model of MTLE. We show by high-resolution confocal imaging and subsequent 3D reconstruction that medial perforant path fibers establish more contacts with newly-formed postsynaptic spines in chronic epilepsy.

Immunohistochemical identification of pre- and postsynaptic elements indicated that these contacts are functionally mature synaptic contacts. On the ultrastructural level both compartments of medial perforant path synapses were increased in size and complexity, reminiscent of long-term potentiation-related morphogenesis. Finally, we assessed the functional consequences of synaptic remodeling in acute slices and found that medial perforant path-mediated excitatory postsynaptic responses were enhanced. Altogether we provide first evidence that new excitatory synapses are formed within the termination zone of fibers originating from the entorhinal cortex. These synapses exhibit ultrastructural and functional properties similar to those elicited by long-term synaptic potentiation. Our data suggest that remodeling of entorhinal input increases the excitatory drive to the dentate gyrus and thereby contributes to the generation of epileptic seizures.

Observation of Neuronal Networks and Connectivity with MRI

Jürgen Hennig

Medical Physics, Department of Radiology, University Medical Center Freiburg, Germany

MRI offers the opportunity for non-invasive in vivo observation of the brain and to study both the functional as well as the morphological connectivity of brain regions on a macroscopic level. New methods for functional fMRI allow not only a static mapping of functional areas, but also to observe the spatio-temporal dynamics of brain activity. Of special current interest are observations of correlated activity across different brain regions measured by resting state fMRI. A number of highly reproducible networks including the default mode network, but also networks associated with somatosensory and other functional areas have been identified and modulations of resting state networks have been observed under various physiological and pathological conditions. The future challenge will be to integrate the information gained from such long range interactions with the network activities at smaller scales- from the network activity in functional units like the hippocampus down to the level of single functional units.

Only Knowledge can Shape the Future in a Manner that is Responsible and Beneficial to Life

Klaus Herberger

Carl- Zeiss- Stiftung, Ministerium für Wissenschaft, Forschung und Kunst Baden-Württemberg, Stuttgart, Germany

It is the task of research in all areas of life to serve this purpose. Inspired by this idea, physicist Ernst Abbe founded the Carl Zeiss Foundation 125 years ago. The dividends paid out by its member companies ZEISS and SCHOTT from their earnings lay the basis for the Foundation to fulfill this objective. The focus is placed on cultivating up-and-coming young scientists and promoting research structures in fields of science that are of major relevance for future developments. With its specialist expertise in neuronal networks, the Bernstein Center in Freiburg is being sponsored by the Carl Zeiss Foundation for four years in order to raise the diagnosis and therapy of brain diseases to a new level.

Highly Integrated CMOS Microsystems to Interface with Neurons at Subcellular Resolution

Andreas Hierlemann

Department Biosystems Science and Engineering, ETH Zurich, Basel, Switzerland

To understand, how functions and characteristics of neuronal networks arise from the concerted interactions of the involved neurons, it is necessary to have methods that allow for interacting with neuronal functional subunits and ensembles - somas, axons, dendrites, single neurons, and entire networks - at high spatiotemporal resolution and in real time. Here, we demonstrate how CMOS high-density microelectrode array systems, featuring several thousands of electrodes at densities of more than 3’000 electrodes per mm2, can be used to record from or stimulate potentially any individual neuron or subcellular compartment on the CMOS chip.

Epilepsy and Brain-Machine Interface

John Huguenard

Neurology & Neurological Sciences, Stanford University, USA

Modern neuroscience has produced many recent technological advances that are rapidly impacting the development of novel treatment modalities. Advances in signal detection, sensitization of neurons, and light delivery into the brain of experimental animals are converging to allow for early detection of seizures and rapid termination via optogenetic methods. Our work has shown that identification of network nodes involved in seizure propagation, followed by viral based gene therapy to render neurons within such nodes sensitive to light, and finally with real time detection of seizure or pre-seizure network state, together produce a system for real time optogenetic control in epilepsy arising from cortical injury. More recently we have shown that novel opsins that don't just increase or decrease activity in network nodes, but switch their firing state from bursting to tonic firing, can be very effective in blocking seizures in genetic epilepsy models. We are at the leading edge of this technology and further work will require careful identification of critical network nodes, optimization of gene therapy approaches and seizure

Understanding Operational Rules for the Modular Information Processing in the Cerebellum

Philippe Isope

Institut des Neurosciences Cellulaires et Integratives CNRS UPR, Strasbourg, France

To understand the progressive emergence of complex functions at the molecular level, it is essential to bridge the gap between global brain function and molecular neuroscience. Fortunately, the brain is modular: neuronal networks of the cerebral cortex are organized in local circuits or modules that serve different functions in specific brain regions, from the forebrain to the spinal cord. A given cortical area is composed of many functional modules that allow a parallel processing of incoming information. One major challenge of current neuroscience is to unravel the operational modes of these modules or 'microcircuits' (Grillner et al., 2005).

The cerebellum plays a major role in the control and learning of skilled movements. Recent evidence has demonstrated that the cerebellar cortex plays a role in the precise timing of individual components of the motor program and is involved in the synchronization of cerebello-thalamo-cortical oscillations observed during motor tasks. To understand, and ultimately manipulate, the integrative role of the cerebellum in the motor circuit its input/output transformation needs to be elucidated. Although the cellular organization of the cerebellar cortex looks homogeneous across lobules and folia, anatomical and molecular data have shown that the cerebellum is also organized in modules. Functional studies have demonstrated that task-related modules can be identified and selectively modified. The organization of the basic microcircuit of the cerebellar cortex is now well described; however rules governing how incoming information is channeled through the microcircuitry and how the specific processing of one given input is carried out by the microcircuit are still poorly understood. Furthermore, the functional connectivity within and across individual modules has not yet been characterized. I will present our recent findings that can shed light to these fundamental questions.

The Hippocampal Clock in a Mesial Temporal Lobe Epilepsy Model

Antje Kilias

Bernstein Center Freiburg, University of Freiburg, Germany

Theta band oscillations dominate rodent EEG signal during active exploration and REM sleep and are considered as the basis of spatial navigation and sequential learning. In epileptic mice EEG signals alternate between pathological hallmarks and putatively normal network oscillations. While the generation of epileptiform activity is still not fully understood, origin of theta band activity in the healthy hippocampus has been studied intensively. Therefore, investigating alterations of theta rhythm in epileptic brains can reveal changes in the underlying network structure or cross-structural coupling that allow for the emergence of seizures. We found local as well as overall changes of the frequency, power and coupling of theta band activity in the epileptic hippocampal formation. Surprisingly this perturbation of the rhythm is restricted to the network level. Individual neuronal firing probability is still modulated by theta as known in the healthy hippocampus.

Altered Network Dynamics in a Computational Model of Mesial Temporal Lobe Epilepsy

Christopher Kim

Bernstein Center Freiburg, University of Freiburg, Freiburg, Germany

Characteristics of mesial temporal lobe epilepsy include death of inhibitory cells and increased excitation due to mossy fiber sprouting. We consider a computational model, where an excitatory-inhibitory network is innervated by an additional excitatory population. We discuss how the excitatory innervation give rise to rate instability and interleaving of asynchronous and oscillatory states.

To Go or Not: Basal Ganglia Dynamics Underlying Brain Function and Dysfunction

Arvind Kumar

Computational Biology, School of Computer Science and Communication, KTH, Royal Institute of Technology, Stockholm, Sweden

Basal ganglia (BG) play a crucial role in several motor and cognitive function. Accordingly, chemical and/or structural changes in one or more of BG nuclei result in major brain disorders like Parkinson's disease, Huntington's disease etc. Recent data experimental data suggests that some of the brain diseases that involve BG dysfunction are also manifested at level of changes in the dynamical states of neuronal activity in one or more BG nuclei.

In my talk I will describe the recent progress in modelling and understanding the origin of various dynamical states within the BG nuclei. Our models provide novel insights about link between the network dynamics and brain function/dysfunction involving the BG. First, given the recurrent connectivity structure, striatum function can be modeled as a threshold detector and sets the stage for go and no-go decisions. Second, PD can be understood as a change in operating point in the striatum instead of a bifurcation in the sub thalamic nucleus and globus pallidus networks, as is commonly assumed. I will also show how neuromodulators such as dopamine influence the local dynamics as well as the inter-nuclei interactions resulting in a disease related activity dynamics. Finally, I will discuss how such computational models of brain diseases could help us develop novel therapeutic measures.

Deconstructing Fear

Andreas Lüthi

Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

Classical fear conditioning is one of the most powerful models for studying the neuronal substrates of associative learning and for investigating how plasticity in defined neuronal circuits causes behavioral changes. In animals and humans, the amygdala is a key brain structure within a larger neuronal network mediating the acquisition, expression and extinction of fear memories. In unraveling the substrates of fear conditioning and extinction, the major focus has been on the study of plasticity at excitatory synapses. However, little is known about how fear memories are encoded at the neuronal population level. In my presentation, I will show recent work on population coding in BLA. Moreover, I will describe how switches in the activity between distinct types of amygdala output pathways mediate the selection and rapid adaptation of defensive behavior.

Skill Learning and Control of Supernumerary Movement Effectors

Carsten Mehring

Neurobiology and Neurotechnology, University of Freiburg, Freiburg, Germany

In this talk I will discuss two recent studies from our lab related to human motor control:

(1) Acquisition of motor skill is a difficult and controversial topic that remains poorly understood. Recent research on motor learning has been mostly focused on motor adaptation following a visuomotor or a force perturbation. We investigated motor skill learning using a new path tracking task, where subjects had to track various curved paths as fast as possible, in the absence of any external perturbations. We found that subjects become better with practice, even for novel untrained paths. Most importantly we found that with higher tracking skill subjects took a longer chunk of the future path into account when computing the control policy for the upcoming movement segment. These findings demonstrate that subjects increase their planning horizon with skill, in analogy to model predictive control theory.

(2) Can BCIs be used to control non-body objects in addition and independent to movements of the subject's own limbs? Such concurrent control may be especially challenging when the neural signals controlling the BCI and the neural signals controlling the movements of the natural limbs stem from the same brain area and therefore may interfere. Here we investigate whether subjects can learn to dissociate the competing neural activities and use them for concurrent control of a BCI and contralateral limb movement. We present results from human ECoG studies where the channel over motor cortex most highly activated by finger movements was used for BCI control while subjects simultaneously and independently controlled the movements of their finger. We examine whether the concurrent control is accompanied by motor cortical reorganisation allowing for distinct cortical sites responding primarily to the BCI and less to movement behaviour.

Ethical Aspects of Neurotechnology & New Perspectives in Public Outreach

Oliver Müller

Philosophisches Seminar and Cluster of Exzellence BrainLinks-BrainTools, University of Freiburg, Freiburg, Germany

Technological interventions in the brain raise ethical questions. The identity and personality of patients might be modified by these interventions. Furthermore, 'merging' humans and machines might change basic normative concepts such as agency and responsibility. These potential expansions require both an ethical assessment and a dialogue with the public, as citizens might be concerned about these new possibilities. In this talk, I first want to identify the most relevant ethical questions, in order to sketch a normative framework for the ethical assessment of neurotechnologies such as deep brain stimulation. Secondly, I will present a new model for participatory activities in the field of public outreach that is connected to the awareness of the ethical implications – against the background that philosophers have to leave the ivory tower, at least sometimes.

Relations Between Network Structure and Activity Dynamics in Developing Neuronal Networks

Samora Okujeni

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Neuronal morphology and eventually the connectivity of neuronal networks are shaped by neuronal interactions that regulate axonal and dendritic growth as well as synaptogenesis. The emergence of stereotypical connectivity patterns, such as clustered horizontal connectivity in the cortex, e.g., depends on spontaneous activity that typically consists of synchronized network discharges during development. Recent modelling studies indicate that clustered connectivity promotes spontaneous activity, in turn, suggesting that both features may coevolve during development on the basis of activity-dependent structural plasticity. To address this, we manipulated activity-dependent structural plasticity in cultured networks of cortical neurons by chronic inhibition of protein kinase C (PKC), which regulates cytoskeletal polymerization processes in response to synaptic activity. Similar as in vivo, clustered connectivity and synchronous bursting activity likewise develop in cultured networks. We show that chronic inhibition of PKC leads to the formation of more homogeneous network structure with reduced clustering of neurons and neurites. Interestingly, the homogeneous networks are less spontaneously active and produce far less complex activity patterns. The emergence of clustered connectivity may thus play a crucial role for the regulation of spontaneous activity dynamics in developing networks and vice versa.

Computational Neuroscience of Brain Disease: Neuronal Mechanisms of Brain Function and Dysfunction

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Computational techniques in brain research have become an important complement to purely experimental and purely theoretical approaches, giving rise to a whole new field at the interface between experiment and theory. In fact, new insight into the functioning of neurons and networks gained by the analysis of computational models has not only shaped our perspective on empirical data, but in some cases also left a lasting impact on the design of new experiments and novel experimental protocols, has given rise to the development of new neurotechnology, and has also influenced the ongoing evolution of brain theory. The notion of "balance between excitation and inhibition" is an excellent example, where theoretical arguments and numerical methods played an essential role in the establishment of a new and by now very influential neuroscientific paradigm. So is "synaptic plasticity", which was originally postulated as a hypothetical mechanism underlying learning and memory, based on essentially theoretical considerations.

Surprisingly, Computational Neuroscience has so far not found broad applications related to diseases of the brain. Neither are the methods of Computational Neuroscience part of regular clinical practice, e.g. by supporting the diagnostic process, or by simulating and possibly predicting results and side effects of therapeutic intervention. We believe, however, that our young discipline has a huge potential in this direction as it typically addresses the mechanisms of brain function – and, therefore, also of brain dysfunction – at the level of neurons, networks and integrated neural systems. And it is precisely these neuronal mechanisms that the diagnosis and treatment of brain disorders need to address!

With funds generously provided by the Carl Zeiss Foundation, we have now begun to establish the necessary research infrastructure supporting this new research direction of "Computational Neuroscience of Brain Disease". We are confident this will enable us to contribute novel insights and innovative methods resulting from our research.

A Learning-Based Approach to Artificial Sensory Feedback

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Learning plays a central role in the integration of spatial information for movement control, allowing for both the development of multisensory spatial processing and the ongoing maintenance of accurate "state estimation". We have shown how a simple network model can learn de novo to perform the multisensory spatial computations needed for statistically optimal movement control. In this model, learning is accomplished by an unsupervised, Hebbian-like learning rule, driven only by the common statistics of the network inputs, e.g., by spatiotemporal correlations between sensory modalities. Motivated by these observations, we demonstrated experimentally that correlated sensory inputs do drive de novo multisensory learning in a real sensorimotor task. Animals were first trained to perform a reaching task under the guidance of visual feedback. They were then exposed to a novel, artificial feedback signal in the form of a non-biomimetic pattern of multi-electrode intracortical microstimulation (ICMS). After training with correlated visual and ICMS feedback, the animals were able to perform precise movements with the artificial signal alone. Furthermore, they combine the ICMS signal with vision in a statistically optimal fashion, as would be done for two natural stimuli. These results suggests a new route to studying multisensory processing in the brain. They also point the way to a novel learning-based approach to artificial somatosensory feedback for brain-machine interfaces

A Two-Step Model of Action Suppression Based on Basal Ganglia Neurophysiology

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Classic basal ganglia models describe the globus pallidus (GP) as a homogeneous structure that relays information from the striatum to the subthalamic nucleus and the substantia nigra pars reticulata. In contrast to this, recently discovered arkypallidal neurons ("Arky") in GP provide vast inhibitory back-projections to the striatum. Therefore, GP might strongly shape the output of the striatum in both normal and pathological behavior, e.g. by spreading beta oscillations in Parkinson's disease. To identify functional roles of Arky neurons, we investigated the activity patterns of Arky and other GP neurons during a Stop signal task, which requires the abrupt cancellation of an imminent action. We first establish that Arky neurons can be identified through their distinctive firing properties across the natural sleep/wake cycle. We then show that, unlike other sets of basal ganglia neurons, an Arky subpopulation responds strongly and selectively to Stop cues. The timing of this Stop response corresponds closely to the suppression of developing Go-related activity in striatum. Our results support a two-step model of action suppression, whereby actions-in-preparation are first paused via a subthalamic-nigral pathway, then canceled via the selective GABAergic Arky projections to striatum.

Neural Circuit Dysfunction in Psychiatric Disease: Insights from Animal Models

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There is general agreement that psychiatric diseases such as schizophrenia, autism and depression will ultimately be understood as neural circuit disorders. Yet despite decades of research, exactly how neural circuit abnormalities give rise to psychiatric illness remains poorly understood. Efforts to further our understanding will likely benefit from studying animal models of psychiatric disease, which allow the impact of etiological factors on neural circuit function to be investigated in detail. In this talk, I will discuss the general strategies for using animal models to investigate neural circuit dysfunction in psychiatric disease. I will also describe our own work examining how genetic mutations that predispose to schizophrenia disrupt long-range functional connectivity and sensory processing in the brain.

Changing local brain activity and global network communication by means of BCI training

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Brain computer interfaces (BCI) have not only been applied to control devices by brain activation but also to modulate brain function using neurofeedback training. In my presentation, I will provide two examples for neurofeedback-induced changes of motor function using local brain activity and global network communication signals. The first example demonstrates rehabilitation training in hemiparetic chronic stroke patients. During the training, magnetic brain activity was recorded from primary motor cortex using magnetoencephalography (MEG). Patients were requested to voluntarily increase or decrease the motor cortex activity in the lesioned hemisphere. Feedback was provided by moving the patients' hand passively depending upon whether they successfully generated the requested activity. Results show that the training is capable of re-establishing cortical motor control in hemiparetic stroke patients. In the second example, we used functional connectivity between left and right primary motor cortex as feedback signal in order to train subjects to synchronize and desynchronize both motor regions. Results demonstrate that learned voluntary control of interhemispheric coupling can be learned and directly affects motor performance in healthy subjects. While increased interhemispheric synchronicity caused the deterioration of performance in a bimanual tapping task, decreased coupling resulted in higher tapping speed. …

Hybrid Brain/Neural Computer Interaction (BNCI) in Neurorehabilitation: From Bench to Bedside and Beyond

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Clinical brain-machine interfaces (BMIs) are rapidly advancing as versatile tools to restitute and restore body and brain functions, e.g. to control robots or prosthetic devices after paralysis or to foster neuroplasticity in neurorehabilitation, e.g. in severe stroke, spinal cord injury or traumatic brain injury. After impressive proof-of-principle demonstrations of implantable and non-invasive BMI systems, integration of this technology into patients' everyday life represents a major challenge for the coming years. While broader application of implantable BMIs will depend on reliability, safety and long-term stability of these systems, recent advances in sensor technology, bio-signal fusion and integration of context information in non-invasive hybrid brain/neural computer interaction (BNCI) systems could significantly improve these systems' capacity to assist in daily-life activities and increase efficacy of neurorehabilitation by fostering generalization of learned skills from clinical environments to the patients' everyday life.

Neural Implants for Mice and Men

Thomas Stieglitz

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Neural implants serve as fundamental tools in the neurosciences to investigate the electrical activity of single cells up to networks, correlate behavior to it and identify pathophysiological changes in disease models. A kind of toolsbox of devices is available for a large variety of questions in preclinical studies. If neural implants are transferred into clinical applications in humans, not only functionality has to be guaranteed but also strong safety aspects have to be considered. Even though many application scenarios have been proposed for neural implants from a research point of view only few success stories have been written with respect to economic success and market penetration. Cochlea implants as sensory neural prostheses, spinal cord stimulators to treat pain and incontinence, deep brain stimulators to modulate movement disorders in Parkinson's disease and vagal nerve stimulators to decrease the seizure frequencies in epilepsy are most prominent applications, however, for less than a million patients worldwide, even though the costs of brain related diseases in Europe extends the cumulative costs of cancer and cardiovascular diseases.

This talk will give a comprehensive overview of neural implants for preclinical investigations in neurosciences including electrical recording and stimulation of nerve cells and networks, tools for optogenetics and multimodal probes. In addition, challenges of stability and reliability will be discussed that arise in translational research when novel concepts are transferred into human clinical trials. Examples cover brain-machine interfaces of miniaturized implants in the central nervous system and peripheral nerve interfaces to deliver sensory feedback in hand prosthesis control after amputation.

Effect of Alzheimer's Disease on the Dynamics and Computational Performance of Recurrent Neural Networks

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High-level brain function such as memory, classification or reasoning can be realized by means of recurrent networks of simplified model neurons. In Alzheimer's Disease (AD), the impairment of such functions is clearly correlated to synapse loss. So far, the mechanisms underlying this correlation are only poorly understood. Here, we investigate how the loss of excitatory synapses in sparsely connected random networks of spiking excitatory and inhibitory neurons alters their dynamical and computational characteristics. We find that the loss of excitatory synapses on excitatory neurons lowers the network's sensitivity to small perturbations of time-varying inputs, reduces its ability to discriminate and improves its generalization capability. A full recovery of the network performance can be achieved by firing-rate homeostasis, implemented by an up-scaling of the remaining excitatory-excitatory synapses. By studying the stability of the linearized network dynamics, we show how homeostasis can simultaneously maintain the network's firing rate, sensitivity to small perturbations and computational performance.

Control of Pathological Brain Activity in Spatially Extended Models

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There is a growing interest in developing novel brain stimulation methods to control disease-related aberrant neural activity and to address basic neuroscience questions. Conventional methods for manipulating brain activity rely on open-loop approaches that are in many respects inferior to closed-loop protocols. Previously we showed that a conceptually simple and effective closed-loop method for the control of pathological oscillations in spiking neural networks is delayed feedback control (DFC). Here we consider the more realistic scenario of spatially extended systems, which are able to capture the rich dynamical patterns that are observed in the brain. We study the stability of these systems and focus on the emergence of spatio-temporal patterns via Hopf and/or Turing bifurcations. We then demonstrate that incorporation of a spatial control term in the DFC protocol is sufficient to control the onset of these instabilities and to steer the activity of the system in any preferred direction. Our results contribute to a better understanding of the effects of closed-loop control in realistic models of neural activity and, therefore, pave the way for the development of novel and more efficient brain stimulation tools.

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