Bernstein Center for Computational Neuroscience Berlin

Research results of the BCCN Freiburg presented at:

bccn freiburg

BCCN Symposium 2006

Information:

The second Bernstein Symposium took place from October 1-3, 2006 at the Institute of Anatomy, Charité, in the direct neighborhood of the future Berlin Bernstein Center's building. Around 130 scientist of all four Bernstein Centers participated and discussed their recent findings and results together with invited international scientists.

"Variability and Precision", "Dynamic", "Adaptivity" und "Space-Time" – were the four session topics. The centers' research focuses on topics like how human beings process visual or acoustic information, how they plan their movements, how they develop a sense of time and its use for orientation in space. Additionally research results of clinical or technological applications like automatic speech recognition, prediction of epileptic seizures were presented.

A highlight of the symposium was the award of the first Bernstein Prize to Mathias Bethge by the BMBF represented by MD Dr. Peter Lange.

When:

Oct 01, 2006 – Oct 03, 2006

Where:

Charite Campus Mitte,
Center of Anatomy,
Berlin

Pictures (19)

CHARITÉ

Freie Universität Berlin

Fraunhofer Institut Rechnerarchitektur und Softwaretechnik

MDC Max-Delbrück-Centrum für Molekulare Medizin Berlin-Buch

HUMBOLDT-UNIVERSITÄT ZU BERLIN

GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

Network De-Synchronization Precedes Epileptic Events

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Abstract Although Mesial Temporal Lobe Epilepsy (MTLE) is among the most common forms of partial epilepsies, processes involved in seizure generation are still fairly unknown. Due to the pharmacoresistance of MTLE, treatment is limited to surgical resection of large brain areas and thus advance in less invasive therapies is urgently needed. Therefore, it is essential to understand the role of the interaction of sclerotic areas with presumably healthy areas in the initiation of epileptiform events. We employed a model for MTLE in mice with histological changes mimicking human hippocampal sclerosis to study synchronization processes between the two hippocampi. We found that epileptiform activity not only involves the ipsilateral sclerotic hippocampus but also the contralateral, histologically unchanged hippocampus. Additionally, we could show that phase synchronization between the two hippocampi changes not only at the onset of epileptiform events but already several seconds before. This suggests that brain areas outside the sclerotic hippocampus, here the contralateral hippocampus, are involved in generation of epileptiform events in MTLE and inspires further diagnostic investigation on the interaction of the epileptic focus with healthy brain areas in humans.

Dynamics of Spatially Structured Networks: Implication for Synfire Activity and Firing Rates

Arvind Kumar[1], Stefan Rotter[2], Ad Aertsen[1]

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no abstract available

Time Scale Dependence of Neuronal Correlations

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Abstract Neural activity is measured and processed at various signal levels (e.g. spike counts, synaptic currents, membrane potentials, LFP, EEG). Here, we consider linearly filtered spike signals and point out that correlations among these data depend both on the spike train auto/cross-correlation structure and the filter properties (e.g. bin size, synaptic time constants). Thus, the strength of interaction between neurons can be effectively controlled by the neuronal filter characteristics and by the marginal statistics of individual spike trains. For common-input systems (networks) we further show that filter properties and the common-input strength (network connectivity) can be extracted from measured correlation functions.

How Input Correlations Shape Population Activity in Recurrent Cortical Networks

Birgit Kriener[1], Tom Tetzlaff[1], Ad Aertsen[1], Markus Diesmann[2], Stefan Rotter[3]

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Abstract The complex dynamics of balanced random networks of excitatory and inhibitory integrate-and-fire neurons has been extensively studied (van Vreeswijk & Sompolinsky, 1996; Brunel, 2000). The activity of large neuronal populations was successfully characterized using a mean field approach. In the inhibition dominated regime, a network state was predicted which is characterized by asynchronous global dynamics, while individual neurons fire irregularly in a Poisson-like fashion. Numerical simulations of networks in this regime, however, display transient synchronizations which induce a much higher variance of the population activity than predicted by the mean field model. Previously, such phenomena were attributed to finite size effects, which would become negligible for very large networks.

Here we show that the predictions of mean field theory are quite precise already for relatively small networks, provided the synaptic couplings are fully consistent with the mean field assumptions. However, in networks composed of two types of neurons which are either excitatory or inhibitory (a direct reflection of Dale's law), correlations induced by common input are no longer negligible. We demonstrate that these correlations are indeed responsible for the synchrony observed in the simulations that were not accounted for in previous theories. We further derive a simple linear two-population rate model, which correctly describes the qualitative features of the population power spectrum in the asynchronous-irregular regime. However, it is not the delayed interaction between two antagonistic neuronal populations, but rather the correlations induced by common input that were ignored so far, which are responsible for the emergence of population synchrony in that regime.

Spatio-Temporal Structure of Spontaneous State Transitions in the Neocortex in vivo

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Abstract Spontaneous state transitions of neocortical activity, as observed during slow-wave sleep or under certain anesthetics, are characterized by fast changes between epochs of intense network activity (up-states), and silent periods, where spiking activity is virtually absent (down-states). In single cells, up-states are characterized by massive synaptic input, leading to a strongly fluctuating, depolarized membrane potential, while in down-states, the membrane potential shows only few fluctuations at a hyperpolarized level. The strong synchronization between cells during this kind of activity is reflected in population signals, such as the local field potential and the EEG. Waves of synchronized activity have been demonstrated to travel from varying initiation points over the human cortex during slow-wave sleep. In animal experiments it was shown that only a small, time-varying fraction of the cells in a given cortical volume takes part in the oscillatory activity. We investigated the spatio-temporal structure of slow-wave activity in vivo in the rat neocortex under ketamine/xylazine anesthesia, combining extracellular recordings with up to 12 electrodes with one simultaneous intracellular recording, which was used to detect state transitions. Triggered on these, we extracted multiple episodes of spike activity from the extracellular electrodes and determined the state transition for each of the individual electrodes from the averaged episodes. The emerging spatio-temporal pattern was then tested for pattern consistency and variability across repeated activity waves employing single trial rate estimates. We found that in most recordings there was considerable variability with respect to the precise spatio-temporal structure of activity waves. However, in many cases a preferred direction of activity spread could be identified during limited recording periods. This indicates that under ketamine/xylazine anesthesia, activity waves may travel in a stereotypic manner over the neocortical tissue. Such stereotypic patterns of activity might lead to selective strengthening of active synapses, linking slow-wave activity to learning-related phenomena like memory consolidation during slow-wave sleep.

Grid Computing in Computational Neuroscience

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Abstract We show how the established grid computing framework used by Particle Physics has been locally adapted to the needs of Computational Neuroscience at the BCCN Freiburg and how this could be extended on a national or global scale. Computing resources could then be used like electric power, produced in sufficient amounts at some sites and distributed by a global grid structure to where it is actually needed. This provides the opportunity for using resources more efficiently than previously possible and to carry out numerical research of hitherto in the field of computational neuroscience unpreceded scale. In order to practically explore the new concepts we have locally implemented the required hard and software infrastructure and formally established the virtual domain "CNS".

Predicting Epileptic Seizures: An Evaluation of Two Prediction Methods Based on Long-Term Intracranial EEG Recordings

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Abstract Purpose: Concerning the predictability of epileptic seizures, recent work has shown that methods from nonlinear dynamics can be used to analyze neurophysiological recordings for detection of preseizure changes. When utilizing these methods for seizure prediction it is crucial to assess their prediction performance on long-term EEG data, including tests for statistical significance.

Methods: A bivariate phase synchronization index and the univariate "Dynamical Similarity Index" were adapted for seizure prediction (Mormann et al. Physica D 2000;144:358-369 and Le Van Quyen et al. NeuroReport 1999;10:2149-2155). Based on the seizure prediction characteristic (Winterhalder et al. Epilepsy Behav 2003;4:318-325) and a long-term intracranial EEG database with continuous recordings of 14 patients for up to 14 days (mean 7.5) including 330 seizures we performed an analysis with prediction windows up to 4 hours. All results have been validated by a statistical test procedure (Schelter et al, Chaos 2006; 16: 013108).

Results: When using the phase synchronization index for seizure prediction significant prediction performance could be observed for 10 patients with a mean sensitivity of 48.1% ranging from 38.1% to 66.7%, for a maximum false prediction rate of 0.15 false predictions per hour. Results for the dynamical similarity index were significant for 7 patients with a mean sensitivity of 47.1%.

Conclusions: The investigated univariate and bivariate analysis techniques have shown similar performance in predicting epileptic seizures. Both methods have achieved statistical significant prediction performance on long-term EEG data with considerable inter-patient variability.

Learning the Functional Connectivity in Neuronal Cultures

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Abstract Discovering the functional connectivity and modelling the dynamics of neuronal networks is essential to understand neural information processing. In the current work, we focus on neuronal cultures, which are small living networks in a closed system. We present a machine learning approach, which constructs the functional connectivity map of a neuronal culture based on multiple spike trains of its spontaneous activity recorded by Multi-Electrode-Arrays (MEA). The spike train of an electrode is modelled as a point process, where the rate depends on the finite spike history of all electrodes. For a similar model, Chornoboy et al. presented a maximum likelihood approach for learning the parameters offline. To capture the network plasticity, however, we follow a steepest descent approach, which naturally allows for online learning. A ROC curve analysis of our experiments shows that this online approach predicts the upcoming spiking activity well.

Patterned Substrates – Adding Structure to in vitro Neuronal Networks

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Abstract In culture, dissociated neurons tend to form haphazard networks and become spontaneously active within a couple of days in vitro. Within a week, network activity changes from rare single spikes towards frequent synchronized bursts, the mature state of activity for this type of network. Although interesting as a type of generic networks, dissociated cultures are limited in that no defined hierarchical structure or connectivity is formed. Microengineering, however, enables the design of culture substrates with cell-adhesive and cell-repellent regions, allowing restricted adhesion of neurons and possibly directed outgrowth of neurites. This opens a possibility to design networks with defined connectivity statistics. Such networks are of interest since they display very basic features of neuronal circuits and computational properties that can also be matched to simulations of neuronal networks. In this project, we present an approach to modulate the connectivity probabilities of neurons in the network through micropatterned substrates. Tissue from the prefrontal cortex of neonatal rats was dissociated and cultured on glass coverslips. The substrate surfaces were patterned with polyethylene imine (PEI) and polydimethyl acrylamide (PDMAAm), with PEI printed onto PDMAAm. We can show that cell somata and neurite outgrowth is limited to the adhesive PEI patterns and repelled from PDMAAm regions, thereby limiting the direction and distance across which neurons can connect. In combination with electrophysiological measurements, e.g. with microelectrode array or single cell recordings, and with simulations modeling networks with comparable connectivity statistics, our approach will enable investigations on structure-function dependencies in simple neuronal networks.

Synaptic Activation of Hippocampal Mossy Cells is Reduced in Reeler Mice

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Abstract Development alterations of cortical structures can cause increased propensity for epilepsy. In Reeler mutant mice migration defects during development result in an altered lamination of the hippocampus and the dentate gyrus. To test whether these alterations can support epileptogenesis, we have investigated morphological and physiological properties as well as synaptic activation of mossy cells, neurons that provide excitatory feed-back within the dentate networks. Analysis of the morphology of intracellularly-filled mossy cells in acute slices of reeler mice revealed that the dendrites extend aberrantly into the molecular layer and receive synaptic input from putative perforant path axon terminals. Consistent with this observation, extracellular stimulation in the molecular layer revealed monosynaptic excitatory response in the neurons during the whole-cell patch-clamp recordings. Despite this aberrant excitatory input, mossy cells show a reduction in their synaptic activation compared to wild type mice. In reeler mossy cells strong GABAA receptor-mediated inhibition contained excitation. Blockade of inhibition resulted in a dramatic increase in the excitability of mossy cells in both wild-type and reeler slices, but no spontaneous seizure activity was observed. Thus our data show that developmental alteration do not result in an enhanced, but rather a lowered excitability of mossy cells and the dentate circuits of the reeler mouse. (Supported by the DFG: SFB 505 and TR-3)

How Input Correlations Shape Population Activity in Recurrent Cortical Networks

Birgit Kriener[1], Tom Tetzlaff[1], Ad Aertsen[1], Markus Diesmann[2], Stefan Rotter[3]

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Abstract The complex dynamics of balanced random networks of excitatory and inhibitory integrate-and-fire neurons has been extensively studied (van Vreeswijk & Sompolinsky, 1996; Brunel, 2000). The activity of large neuronal populations was successfully characterized using a mean field approach. In the inhibition dominated regime, a network state was predicted which is characterized by asynchronous global dynamics, while individual neurons fire irregularly in a Poisson-like fashion. Numerical simulations of networks in this regime, however, display transient synchronizations which induce a much higher variance of the population activity than predicted by the mean field model. Previously, such phenomena were attributed to finite size effects, which would become negligible for very large networks.

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Reinforcement Learning in Spiking Neural Networks

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Abstract Computationally powerful reinforcement learning algorithms have been developed in the context of machine learning (Sutton98). There is experimental evidence based on the work of Schultz and his colleagues (Schultz97, Schultz98) that our brain also uses reinforcement learning algorithms, but it is still unclear how these algorithms could be implemented by a biological neuronal system. Here we demonstrate how a reinforcement learning algorithm for a non-trivial task can be transferred to a neural network of spiking integrate-and-fire neurons, in which the value function and policy are represented by synaptic weights and adapted via local synaptic plasticity rules.

Can We Differentiate Spike Co-ordination from Rate Co-variation?

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Abstract The question, whether correlations observed in neuronal spiking data are only an artifact of rate co-variations, or if neurons use internal mechanisms of spike co-ordination has been the topic of a long and lively debate. To gain insight into statistical differences between rate co-variance and spike coordination we study models of correlated Poisson processes that implement the above mentioned mechanisms. Parameters are the mean firing rate, the time scale and the degree of correlation. Analytical derivations of the correlation functions and the predictors reveal obvious differences between the models, implying that, theoretically and with knowledge about the underlying model, a differentiation between rate co-variation and spike co-ordination can be made.

However, if data generated based on these models are analyzed with the aim to identify the model class a given data set belongs to, we face considerable limitations. A crucial point for the differentiation is the correct estimation of the predictor, which in turn relies on a reliable estimation of the time dependent firing rate, which for particularly short time scales appears to be extremely difficult. We conclude that, even though there is an objective theoretical difference between rate co-variation and spike co-ordination, an identification of the origin of correlation in a real data might not always be possible.

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Time Scale Dependence of Neuronal Correlations

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Abstract Neural activity is measured and processed at various signal levels (e.g. spike counts, synaptic currents, membrane potentials, LFP, EEG). Here, we consider linearly filtered spike signals and point out that correlations among these data depend both on the spike train auto/cross-correlation structure and the filter properties (e.g. bin size, synaptic time constants). Thus, the strength of interaction between neurons can be effectively controlled by the neuronal filter characteristics and by the marginal statistics of individual spike trains. For common-input systems (networks) we further show that filter properties and the common-input strength (network connectivity) can be extracted from measured correlation functions.

Anatomy–Based Network Models of Cortex and their Statistical Analysis

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Abstract Most current studies of cortical network dynamics assume completely random wiring, a very practical but presumably too simplistic approach. The network structure of cortex is much more complicated, in particular, it comprises both local and long-range connections, and special features like patchy projections.

In this study we investigated and compared several alternative network architectures which may lead to more realistic cortical network models. First, in order to enable distance dependent connectivity, we assumed an embedding of all neurons in space, reflecting the geometry of dendrites and axons. To assess the influence of the spatial embedding on network topology we considered both randomly positioned nodes and regular lattices. The wiring comprised local and non-local connections in various compositions. The parameters of all models were arranged to span the full continuum from local/regular to completely random connectivity.

Second, we employed the framework of stochastic graph theory to define a set of characteristic network properties. For example, we analyzed the degree distribution, clustering coefficient and average shortest path length of our networks, as well as the spectrum of eigenvalues and the locality of the eigenfunctions of the corresponding adjacency matrices. This enabled us to quantitatively study the impact of statistical neuro-anatomical knowledge, andto compare our enriched cortical network models to other well-known types of abstract graphs, e.g. small-world networks.

In a comparative study of these models we show that the global graph-theoretic properties of the resulting networks may be vastly different. Especially, the abundance of non-local connections is a crucial point, potentially leading to dramatic changes in network topology. In addition, the modalities of the spatial embedding are important as they strongly influence the variance of degrees across the network.

In conclusion, we began to identify a set of parameters that characterize large networks like the neocortex as an integrated system, helping to better interpret neuro-anatomical data, and to develop new network models sub-serving the understanding of cortical function.

Online Interaction with in–vitro Neuronal Networks

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Abstract Random ex-vivo neuronal networks allow investigations of neuronal function and network formation at the population level. After one week in-vitro, cultured neuronal networks are dominated by synchronized bursts, which may play a role in synaptic plasticity processes and in some ways resemble, e.g., seizure discharges in epilepsy. Our primary goal is to achieve a dissociation or reduced amount of bursting activity in the network. For this purpose, we have established an activity-controlled feedback system for neuronal networks grown on microelectrode arrays (MEAs). This is used to interact with the networks via electrical stimulation, e.g. to interfere with population bursts or to define stimuli for a specific network state. With a LINUX based setup we are able to implement various feedback paradigms, such as single/multi-site, real-time/delayed and linear/non-linear feedback. Extracellular electrical activity from primary cultures of rat neocortical cells is recorded from up to 60 channels and processed online as raw or spike data. Features of the activity (e.g. spike rate or burst frequency) are then extracted online to control a stimulus generator connected to the MEA system, which enables stimulation at any of the electrodes. Additionally, the MEA setup is coupled with a perfusion system inside a dry incubator, allowing continuous medium exchange and long-term recordings with minimal handling interference. With this approach, we aim at dynamic control of neuronal activity in cultured neuronal networks.