TwentySecond Annual Computational Neuroscience Meeting CNS*2013

Workshop on

Relevance of Synaptic Plasticity for Multistable Behaviour in Neural Systems

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Organizers:

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Description of workshop content

Fluctuating spontaneous activity has been observed in several areas of the brain. In particular, irregular oscillations among more synchronized and less synchronized states appear in the hyppocampus during slow-wave sleep and quiet wakefulness, due to the massive endogenous activation of large neuronal populations. Furthermore, abnormal synchronization processes characterize several neurological diseases. For instance, under healthy conditions particular neuronal populations located in the thalamus and the basal ganglia fire in an uncorrelated manner. In contrast, abnormal synchronization of these neuronal populations causes Parkinsonian resting tremor.

Recent computational studies have revealed that synaptic plasticity is a fundamental ingredient to ensure multistability in neuronal circuits. In particular, spike timing dependent plasticity (STDP) appears to play a crucial role in promoting the coexistence of states with different level of synchrony.

These studies can be extremely useful for the understanding of mechanisms of memory consolidation in the neocortex as well as for the development of new Deep Brain stimulation techniques.

This workshop aims to provide a forum to discuss the relevance of plasticity for the emergence of multistable dynamical behaviours in neuronal populations . The main focus of the workshop will be to understand the relevance of novel numerical findings in the field of computational neuroscience followed by a frank and open discussion with experimental neuroscientists.

Program

09:30 – 10:00	**Quasisynchronous behavior in a random network with short-term plasticity** Stefano Luccioli, Firenze, Italy
10:00 – 10:30	**The role of intrinsic plasticity for multistable behavior** Claudius Gros, Frankfurt, Germany
10:30 – 11:00	**Coffee Break**
11:00 – 11:30	**Spatio-temporal Irregularity and Multi-stability in Balanced Networks with Short-term Synaptic Plasticity** Gianluigi Mongillo, Paris, France
11:30 – 12:00	**Heterosynaptic plasticity prevents runaway synaptic dynamics** Maxim Bazhenov, Riverside, USA
12:00 – 12:30	**Sisyphus Effect in neural networks with Plasticity** Alessandro Torcini, Firenze, Italy
12:30 – 14:00	**Lunch break**
14:00 – 14:30	**Self-organized noise resistance of oscillatory neural networks with spike timing-dependent plasticity** Oleksandr Popovych, Juelich, Germany
14:30 – 15:00	**A neuro-mechanical model of forward, backward and sideward stepping** Sylvia Daun-Gruhn , Cologne, Germany
15:00 – 15:30	**Plasticity, neuronal synchrony and multi-stability in the human thalamus** Rowshanak Hashemiyoon, Pittsburgh, USA
15:30 – 16:00	**Coffee Break**
16:00 – 16:30	**Coordinated reset neuromodulation for deep brain stimulation neurotechnology and pre-clinical results** Christian Hauptmann, Juelich, Germany
16:30 – 17:00	**Impact of acoustic coordinated reset neuromodulation on effective connectivity within a neural tinnitus network** Alexander Silchenko, Juelich, Germany

Abstracts

Quasisynchronous behavior in a random network with short-term plasticity

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We investigate the occurrence of quasisynchronous events in a random network of excitatory leaky integrate and-fire neurons equipped with short-term plasticity. The dynamics is analyzed by monitoring both the evolution of global synaptic variables and, on a microscopic ground, the interspike intervals of the individual neurons. We find that quasisynchronous events are the result of a mixture of synchronized and unsynchronized motion, analogously to the emergence of synchronization in the Kuramoto model. In the present context, disorder is due to the random structure of the network and thereby vanishes for a diverging network size N (i.e., in the thermodynamic limit), when statistical fluctuations become negligible. Remarkably, the fraction of asynchronous neurons remains strictly larger than zero for arbitrarily large N. This is due to the presence of a robust homoclinic cycle in the self-generated synchronous dynamics. The nontrivial large-N behavior is confirmed by the anomalous scaling of the maximum Lyapunov exponent, which is strictly positive in a finite network and decreases as N - 0.27.

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The role of intrinsic plasticity for multistable behavior

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The brain disposes of several regulative mechanisms in order to stabilize distinct working regimes. On the highest level dynamical regimes suitable for distinct cognitive tasks are selected via diffusive control, mediated by neuromodulators such as Dopamine, Seretonin etc (Gros, 2010). On a local level two distinct adaption processes are known, synaptic plasticity describing the effectiveness of inter-neural information exchange and intrinsic plasticity regulating the response of individual neurons upon stimulation. Both adaption processes may work together in creating two possible types of multi-stabilities, either in terms of dynamical regime (chaos, intermittent bursting, synchronized firing, ..) selection or as transient state dynamics (Gros, 2007/2009) within a given dynamical state. Here we discuss the role of intrinsic plasticity for stabilizing multistable dynamics.

It is reasonable to assume that a neuron may try to adapt its intrinsic parameters, like threshold and gain, in order to achieve a firing-rate statistics maximizing information content in terms of Shannon's information entropy. Minimization of this objective function leads to slow adaption of the neurons intrinsic parameters which lead to several

types of multi-stabilities for the fast dynamics, the neural firing rate. For networks of rate encoding neurons we show that chaotic, intermittent bursting and synchronized regimes may be stabilized (Markovic & Gros, 2010/2012). We furthermore show that intrinsic adaption may transiently stabilize dynamical states corresponding to neural memories in terms of attractor ruins, with the overall dynamics corresponding to continuous latching transitions from one memory to the next.

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Spatio-temporal Irregularity and Multi-stability in Balanced Networks with Short-term Synaptic Plasticity

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Joint work with Carl van Vreeswijk and David Hansel

In physiological conditions, cortical dynamics exhibits significant spatio-temporal irregularity. Spike trains are characterized by high coefficient of variations and exponential-like distributions of inter-spike intervals. Distributions of average emission rates are right skewed and long tailed, with rates ranging from below 1Hz to several tens of Hz. This pattern of activity does not depend on the cortical region, on the behavioral state nor on the conditions of activation of the network. Theoretical studies, supported by experimental results, indicates that spatio-temporal irregularity is a signature of a basic mode of operation of local cortical circuits: dynamical balance of excitation and inhibition. Theory also predicts, however, that networks operating in such a regime would respond linearly to external inputs. This poses a serious problem for neurophysiologically-based models of computation for, in those models, computation relies to a large extent on non-linearities. The problem is especially severe for the attractor framework, where computation relies on the network being able to exhibit multiple, steady states of activity, and within which important computations, as short-term memory and decision making, have been modeled. By which mechanisms could non-linearity and multi-stability be restored in networks working in the balanced regime? We have investigated the possibility that non-linearity in the balanced regime be provided by short-term synaptic plasticity (STP). We have shown that balanced networks with STP do indeed exhibit a bi-stable regime, where a non-zero, low rate state coexists with an high-rate state of activity. In both states, the patterns of network activity exhibit

significant spatio-temporal irregularity, consistently with experiment. In this scenario, bi-stability is achieved by a change in the levels of (self-generated) synaptic noise, rather than by changes in the mean drive. Importantly, the bi-stable regime achieved by this mechanism is tolerant to significant levels of spatio-temporal irregularity in the patterns of network activity. These results highlight a new functional role for STP, and lay the groundwork for a principled understanding of functional/computational implications of the balanced regime.

Heterosynaptic plasticity prevents runaway synaptic dynamics

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Spike-timing dependent plasticity (STDP) and other conventional Hebbian-type plasticity rules are prone to produce runaway dynamics of synaptic weights. Once potentiated, a synapse would have higher probability to lead to spikes and thus to be further potentiated, but once depressed, a synapse would tend to be further depressed. The runaway synaptic dynamics can be prevented by precisely balancing STDP rules for potentiation and depression, however, experimental evidence shows a great variety of potentiation and depression windows and magnitudes. Here we show that modifications of synapses to layer 2/3 pyramidal neurons from rat visual and auditory cortices in slices can be induced by intracellular tetanization: bursts of postsynaptic spikes without presynaptic stimulation. Induction of these heterosynaptic changes depended on the rise of intracellular calcium, and their direction and magnitude correlated with initial state of release mechanisms. We suggested that this type of plasticity serves as a mechanism that stabilizes the distribution of synaptic weights and prevents their runaway dynamics. To test this hypothesis, we developed a cortical neuron model implementing both homosynaptic (STDP) and heterosynaptic plasticity with properties matching the experimental data. We found that heterosynaptic plasticity effectively prevented runaway dynamics for the tested range of STDP and input parameters. Synaptic weights, although shifted from the original, remained normally distributed and non-saturated. Our study presents a biophysically constrained model of how the interaction of different forms of plasticity Hebbian and heterosynaptic may prevent runaway synaptic dynamics and keep synaptic weights unsaturated and thus capable of further plastic changes and formation of new memories.

Sisyphus Effect in neural networks with Plasticity

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The collective dynamics of excitatory pulse coupled neurons with spike-timing dependent plasticity is studied. The introduction of spike-timing dependent plasticity induces persistent irregular oscillations between strongly and weakly synchronized states, reminiscent of brain activity during slow-wave sleep. We explain the oscillations by a

mechanism, the Sisyphus Effect, caused by a continuous feedback between the synaptic adjustments and the coherence in the neural firing. Due to this effect, the synaptic weights have oscillating equilibrium values, and this prevents the system from relaxing into a stationary macroscopic state.

Acknowledgements

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Self-organized noise resistance of oscillatory neural networks with spike timing-dependent plasticity

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Joint work with Serhiy Yanchuk and Peter A. Tass

It is known that synchronization in oscillatory networks can be destroyed by independent noise. One might thus expect that such a random noise stimulation can be a powerful tool for desynchronizing synchronized neural populations. We here show that for oscillatory neural networks with adaptive synaptic weights governed by spike timing-dependent plasticity (STDP) intriguingly the opposite is true. In fact, we reveal that independent noise has a constructive effect on the collective dynamics of oscillatory neural ensembles with STDP. According to experimental results, the synaptic coupling strength among neurons is potentiated or depressed depending on whether the firing of the pre-synaptic neuron advances or follows that of the post-synaptic neuron, respectively. We found that the mean synaptic coupling of the neural ensembles increases with the noise intensity, and there is an optimal noise, where the amount of synaptic coupling gets maximal in a resonance-like manner as found for the stochastic or coherence resonances, although the mechanism in our case is different. This leads to a noise-induced self-organization of the coupling topology, which effectively counteracts the desynchronizing impact of independent noise over a wide range of the noise intensity. This phenomenon essentially relies on the presence of STDP. Our results suggest a possible mechanism of how the brain may counteract external perturbations and noise in order to preserve the existing level of neural synchrony and bridge the transition from information coding by precise spiking times to variable and imperfect spike timing. Furthermore, our results show that independent noise can by no means be considered as an effective method for desynchronization of oscillatory neural networks with STDP. Given the attempts to counteract neural synchrony underlying tinnitus with noisers and maskers, our findings may even have clinical relevance and contribute to a deeper understanding of why the maskers and noisers have a limited efficacy in counteracting tinnitus.

A neuro-mechanical model of forward, backward and sideward stepping

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Joint work with Sascha Knops and Tibor Istvan Toth

The mechanism underlying the generation of stepping has been the object of intensive studies. Stepping involves the coordinated movement of different leg joints and is, in the case of insects, produced by antagonistic muscle pairs. In the stick insect, the coordinated actions of three such antagonistic muscle pairs produce leg movements and determine the stepping pattern of the limb. The activity of the muscles is controlled by the nervous system as a whole and more specifically by local neuronal networks for each muscle pair. While many basic properties of these control mechanisms have been uncovered, some important details of their interactions in various physiological conditions have so far remained unknown. We have created a neuro-mechanical model of the coupled three joint control system of the stick insects middle leg to unravel details of the neuronal and mechanical mechanisms driving a stepping single leg in situations other than forward walking [1,2]. The model can generate forward, backward, or sideward stepping. Using the model, it is, because of it's detailed biological description, possible to make detailed suggestions as to how rhythmic stepping might be generated by the central pattern generators of the local neuronal networks, how this activity might be transmitted to the corresponding motoneurons, and how the latter might control the activity of the related muscles. The entirety of these processes yields the coordinated interaction between neuronal and mechanical parts of the system. Moreover, based on experimental findings which state that only the activity of the muscles which move the leg forward and backward is reversed during backwards walking, we hypothesize a mechanism by which motoneuron activity could be modified by a premotor network and suggest that this mechanism might serve as a basis for fast adaptive behaviour, like switches between forward and backward stepping, which occur, for example, during curve walking, and especially sharp turning, of insects.

Acknowledgements

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Plasticity, neuronal synchrony and multi-stability in the human thalamus

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The brain is an assembly of neurons constantly in flux. Episodes of coordinated activity are thought to be a fundamental mechanism underlying various processes and functions. One such example is illustrated by the synchronization of activity expressed as oscillations, which have been associated with a wide variety of behaviors from the sensory and motor system to decision making and consciousness itself. It is no wonder then that aberrent rhythms have been associated with a range of neurological as well as neuropsychiatric disorders. The use of targeted electrical stimulation to push a system from a pathologically hypersynchronized to an appropriately synchronized state has been reported in many disorders such as Parkinsons disease, tinnitus, and epilepsy. However, in Tourette syndrome subjects receiving deep brain stimulation (DBS) therapy, the opposite effect has been observed, where the stable state is pushed from pathological hyposynchrony to a more coordinated state [1]. This occurs in a nonlinear fashion with multiple stable states appearing over time correlated with different levels of neuronal synchrony. While various theories exist concerning the mechanism of action of DBS, the prominent theory is that of a neuromodulatory effect [2]. Degree of neuromodulation and synaptic drive are known to allow the occurrence of switching between multiple stable states. The effect of DBS on pathophysiological molecular and cellular elements which control spike-timing dependent plasticity is explored.

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Coordinated reset neuromodulation for deep brain stimulation neurotechnology and pre-clinical results

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Joint work with Peter A. Tass

In the past decade deep brain stimulation (DBS) - the application of electrical stimulation to specific target structures via implanted depth electrodes - has become the standard treatment for medically refractory Parkinsons disease and essential tremor.

These diseases are characterized by pathological synchronized neuronal activity in particular brain areas. Coordinated reset neuromodulation a stimulation technique developed using a model-based approach- intends to specifically counteract excessive neuronal synchronization and to induce a cumulative unlearning of pathological synaptic connectivity and neuronal synchrony [1-3]. To enable the pre-clinical and clinical investigation of coordinated reset neuromodulation we developed a dedicated implantable pulse generator capable. We present the device and first pre-clinical results obtained with CR in MPTP treated non-human primates, a well established animal model of Parkinsons disease [4]. The pre-clinical results will be compared with our findings from computer simulations.

Acknowledgements

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Impact of acoustic coordinated reset neuromodulation on effective connectivity within a neural tinnitus network

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Joint work with Ilya Adamchic, Christian Hauptmann and Peter A. Tass

Chronic subjective tinnitus is an auditory phantom sensation, which evolves as a consequence of damage to the peripheral auditory system and causes characteristic changes of brain activity in the central auditory system. In a prospective, randomized, single blind, placebo-controlled clinical trial, we used acoustic coordinated reset (CR) neuromodulation to specifically counteract subjective chronic tonal tinnitus by means of desynchronization of tinnitus related neuronal synchrony. CR treatment was safe and well-tolerated and resulted in a significant decrease of symptoms, as measured by clinical scores, as well as in significant changes in the oscillatory brain activity [1]. A mechanism, underlying the perception of a phantom sound, is likely to include the imbalance in communication between auditory and non-auditory brain areas. The objective of the present study was to analyze whether CR neuromodulation caused an alteration of the

effective connectivity in a tinnitus related network of localized EEG brain sources.EEG recordings were performed at baseline and after 12 weeks of CR therapy in 28 patients with bilateral chronic tinnitus and in a control group of healthy subjects.

To increase the signal-to-noise ratio, we focused on a subgroup of good responders, which is characterized by the substantial reduction in clinical scores after 12 weeks. To determine which connections matter, we performed a BESA source reconstruction in the following predefined regions of interest: temporal and frontal areas, parietal cortex, and anterior and posterior cingulate cortex. To that network we applied a data-driven approach, combining empirical mode decomposition and partial directed coherence analysis [2], in patients with bilateral tinnitus before and after 12 weeks of CR therapy as well as in healthy controls. Dynamic causal modeling (DCM) was used to infer about the types of interactions, which were altered by CR neuromodulation. Prior to CR therapy and compared to the healthy controls, the good responders showed a significantly increased connectivity between the left primary auditory cortex and the posterior cingulate cortex in the gamma and delta bands together with a significantly decreased effective connectivity between the right primary auditory cortex and the dorsolateral prefrontal cortex in the alpha band. After 12 weeks of CR therapy most of the pathological interactions were gone, so that the connectivity patterns of good responders and healthy controls became statistically indistinguishable. Our DCM results show that CR therapy specifically counteracted the imbalance of excitation and inhibition. CR therapy significantly weakened the excitatory connection between posterior cingulate cortex and primary auditory cortex and significantly strengthened inhibitory connections between auditory cortices and the dorsolateral prefrontal cortex [3].

References

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