Book of Abstracts

Workshop on Prediction in Complex Networked Systems: Focus on Epilepsy

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Contents

1 Petr Marusič: Classification of epileptic phenomena

Charles University, Prague, Czech Republic

Clinical perspective of epileptic seizures and epilepsies as network phenomena will be presented. The network concept has impact not only for better understanding of pathophysiology of focal epilepsy but also for clinical practice, particularly for epilepsy surgery.A concept of epileptic zones remains of high clinical relevance in presurgical evaluation of refractory epilepsy patients and in resection planning. Recent advances in understanding how each of the epileptic zones is functionally organized strengthened the importance of the network concept.

2 Klaus Lehnertz: Seizure Prediction: from preliminary observations to implanted systems; what's next?

Department of Epileptology; Helmholtz Institute for Radiation and Nuclear Physics; Interdisciplinary Center for Complex Systems, University of Bonn, Bonn, Germany

The field of seizure prediction aims at identifying precursors of epileptic seizures from brain dynamics or other physiological observables to advance understanding of mechanisms underlying seizure generation as well as to improve therapeutic possibilities and thus, the quality of life of people with epilepsy. In this talk, I will provide an overview of the progress that has been made in the field: from preliminary descriptions of pre-seizure phenomena in the 1990s to the recent development of implantable seizure prediction and prevention systems. I will also highlight shortcomings of recent approaches as well as unsolved issues and will discuss possible research directions that may help to find better solutions.

3 Milan Paluš: Estimating connectivity from time series

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Complex systems consisting of many interacting elements or (sub)systems are described as complex networks. Frequently the structure of such systems is not known, however, the dynamics or temporal evolution of system components can be observed and recorded as time series. Then experimentally observed networks of such interacting systems are inferred from recorded multivariate time series by evaluating a statistical measure of dependence, usually the crosscorrelation coefficient, mutual information, or some measure of synchronization. Measures of causality are used for inference of directed networks. The steps of this process can be recognized as the estimation of a connectivity measure, followed by proper statistical testing of its significance. The latter step helps us to infer the existence of a link. The following step can be the evaluation of a strength of a link, which might not be always well defined. We will define some measures useful for estimating connectivity in brain networks and demonstrate the necessity of proper testing of their statistical significance.

4 Christian Meisel: From neurons to networks: bifurcations, phase transitions and critical slowing down in neural systems

Harvard Medical School, Boston, USA

Over the recent years it has become apparent that the concept of phase transitions applies to a much wider class of systems than those classically considered in physics. Second order phase transitions, where, upon gradually changing one parameter, a system rapidly changes its qualitative behavior, are ubiquitously observed in systems composed of many interacting units.

In this talk we will discuss evidence for such dynamical transitions at multiple scales in the human brain, and how a better understanding of them can provide insights at multiple levels, from the information integration in neurons and cortical networks to the onset of epileptic seizures and monitoring of excitability levels for optimized antiepileptic drug treatment.

First, we will review the recently uncovered scaling laws related to critical slowing down, i.e. a system's tendency to recover more slowly near a bifurcation. Next, we will discuss experiments demonstrating critical slowing down and its precise scaling laws in individual neuron activity.

Finally, we will discuss evidence from reduced cortical cultures, 2-photon imaging and human recordings that also cortical network activity resides in the vicinity of a critical transition with implications for information processing and sleep. We will talk about how the concept of critical slowing down provides valuable metrics to assess epileptic seizure risk and affords more objective ways to monitor cortical excitability in patients with epilepsy. Together, these results indicate critical transition theory as an interesting framework for brain function that links structure, dynamics and function across different scales.

5 Wessel Woldman: Dynamic network properties derived from resting-state EEG in the context of epilepsy

University of Exeter, Exeter, UK

It is still unclear how brain network properties determine seizure onset in people with epilepsy, how they differ for different types of seizures, or how network properties can be described in a clinically-useful manner. Understanding network properties would cast light on seizure-generating mechanisms. We derived functional brain networks from segments of 20s (background) scalp EEG (N=116), which were then integrated with a dynamical description of the brain using a Kuramoto-model. In this talk, I will show how specific properties of these dynamic network models can be used to quantify seizure likelihood and onset patterns in a simple computational framework.

6 Timothée Proix: Spatiotemporal modeling of seizure propagation and termination in human focal epilepsy

University of Geneva, Geneva, Switzerland

Seizures can spread and terminate across brain regions via a rich diversity of spatiotemporal patterns. While the seizure onset area is usually invariant across seizures for an individual patient, the source of the traveling spike-and-wave discharges (2-3 Hz) during seizures can either remain stationary at the seizure onset area, or move with the slower propagating ictal wavefront. Additionally, although most focal seizures terminate quasi-synchronously across brain regions, some evolve into separate ictal clusters and terminate asynchronously. We introduce an unifying perspective based on a new neural field model of epileptic seizure dynamics. Two main mechanisms, namely the co-existence of wave propagation in excitable media and coupled-oscillator dynamics, together with the interaction of multiple time scales, account for the reported diversity. We confirm our predictions using seizures recorded from people with pharmacologically resistant epilepsy. Our results contribute toward patient-specific seizure modeling.

7 Thorsten Rings: Tackling indirect directional couplings in large networks: Partial or non-partial?

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We investigate the relative merit of partialized and non-partialized time-series analysis techniques for inferring directional couplings in complex networks of weakly interacting dynamical systems from multivariate data in the presence of indirect directional couplings. We show that particularly in larger networks partialization does not provide information about directional couplings extending the information gained with a non-partialized approach.

8 Přemysl Jiruška: Understanding the complex nature of ictogenesis

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How seizures emerge from the abnormal dynamics of neural networks within the epileptogenic tissue remains an enigma. Recent studies demonstrate that to advance our understanding of ictogenesis requires detailed information about the epilepsy dynamics at multiple temporal scales. Seizure onset represents the product of the interaction between the process of a transition to seizure, long-term fluctuations in seizure susceptibility, epileptogenesis and disease progression. Approaching the ictogenesis from the complex perspective is a crucial prerequisite for the identification of the causal mechanisms and ideal targets to effectively control the seizure emergence.

9 Rob Wykes: Insights on seizure dynamics and post-ictal cortical spreading depressions (CSD) obtained from in vivo calcium imaging in awake rodents

University College London, London, UK

To image cortical sensory responses and epileptiform discharges we expressed fluorescent calcium indicators (either GCaMP3 or GCaMP6) in excitatory neurons. We first mapped the retinotopic organisation of visual areas as a proxy to the functional connectivity of the visual cortex. Calcium indicator fluorescence yielded high-quality maps of retinotopy in primary visual cortex (V1) and higher visual areas. Focal seizures were evoked in the visual cortex by direct administration of chemoconvulants into V1. We combined widefield calcium imaging, LFP recordings and behavioural measures in awake mice to characterise the correlates of interictal and ictal events across areas of the visual cortex. GCaMP fluorescence revealed that interictal discharges were confined to the focus (V1 area) and triggered standing waves of activation in synaptically connected territories. However trains of polyspikes (ictal events) resulted in a traveling wave of activation originating in the V1 focus. These travelling waves spread in a retinotopic fashion both across lateral connections, recruiting V1 territories, and across long-range connections, starting secondary foci in higher visual areas. We demonstrate a strong correlation between the spatio-temporal dynamics of epileptic manifestations and the functional connectivity of the focus.

Seizures propagated at ~ 0.5 mm/s. Approximately 25% of seizures were followed by a Ca^{2+} wave that spreads at a much slower velocity typical of CSD ($\sim$ 3 - 5 mm/min), and was followed by an undershoot implying electrical silence. Interestingly, the CSD-like wave started at a site distinct from the seizure focus (and remote from the site of application of the chemoconvulsant), and the depolarisation spread radially, with no relation to the functional organisation of the cortex.

We have developed in vivo imaging approaches that allow concurrent recordings of seizures and CSD in awake animals. We are currently applying this method to record spontaneous seizures and post-ictal CSD in several mouse models of epilepsy.

10 Jaroslav Hlinka: Occam's razor and modeling of complex brain network phenomena

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In the talk we shall highlight the general challenge of dealing with complex data by applying complex analysis approaches, and ask whether and how is this relevant to epilepsy research. Brain dynamics naturally constitute one of the archetypal complex systems showing a plethora of rich emergent phenomena. To understand the mechanisms behind the observed properties, computational modeling and advanced data analysis approaches are increasingly adopted. However, the complexity of the applied approaches may lead into a new set of problems, related to the ambiguity of the appropriate interpretation of the analysis or modeling results. In such cases, it may be suitable to apply the general heuristic principle of parsimony, sometimes called Occam's razor. In this contribution we shall demonstrate, how some rich and complex properties of brain dynamics and connectivity structure can be explained from relatively simple principles and models (including low-dimensional nonlinearity or even linear stochastic dynamics), and at the same time which aspects remain to be explained by some richer model. The specific examples include the small-world property of brain connectivity networks, the temporal properties of of brain states and the dual role of perturbations on the epileptic seizure activity. We shall open discussion on which (and how) some complex data and model observations can be linked to some fundamental underlying phenomena.

11 Piotr Suffczynski: Do seizures start via critical transitions? Evidence from models, rodents and humans

Department of Biomedical Physics, Institute of Experimental Physics, University of Warsaw, Warsaw, Poland

Complex dynamical systems may exhibit sudden large-scale deviations from their normal behaviour, termed critical transitions. As a system approaches a tipping point, its dynamics should exhibit critical slowing down phenomenon that should be measurable. We tested this prediction in computational model generating different types of dynamical transitions, LFP signals in animal model of epilepsy and intracranial EEG recordings from epileptic patients. In modelled time series trends in predictors before transitions were in agreement with a general theory of critical transitions. In epileptic rats around 65% of seizures were preceded by critical slowing down, while in human patients only 8% of subjects exhibited early warning signs of critical transition. It suggests that in general, seizure onset in humans does not exhibit typical signatures of critical transition. The discrepancies between theoretical and animal models and data from epileptic patients indicate that complexity may be a fundamental issue when transferring theoretical concepts to complex systems such as the human brain.

12 Yujiang Wang: The micro-spatial-temporal dynamics underlying epileptic seizure onset

Newcastle University, Newcastle, UK

Using spatio-temporal computational models of cortical tissue, I will highlight the perspective that the dynamics of epileptic seizures observed on the EEG may have several dynamic spatio-temporal mechanisms underpinning them. I will show how this perspective may help us understand different focal seizure onset patterns, and their implications for epilepsy treatment. I will also demonstrate in a hands-on tutorial how to simulate these kinds of micro-spatial-temporal dynamic, and how they could be further explored to make useful predictions in the context of epilepsy treatment.

13 Levin Kuhlmann: Seizure Prediction – Post-NeuroVista trial developments and future challenges

University of Melbourne, Melbourne, Australia

In 2013 the Melbourne group completed the first-in-man trial of an implanted seizure prediction device (NeuroVista trial) that was the first study to demonstrate the feasibility of seizure prediction with long-term human data. However, improvements in seizure prediction performance are still needed to make seizure prediction clinically and commercially viable. This talk will summarise developments from the Melbourne group since the time of the trial, demonstrating how improvements in seizure prediction performance have been achieved with the trial dataset through Bayesian forecasting, deep learning, international crowdsourcing and benchmarking of algorithms (Epilepsyecosystem.org), and ensembling techniques. Future challenges will be highlighted to describe how the field could achieve further improvements in seizure prediction performance through future trials with other wearable and implantable devices and a deeper understanding of the preictal and proictal states.

14 Helmut Schmidt: The role of axons in seizure initiation

Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

In this talk I present the hypothesis that axonal connections between brain areas could be a potential generator of epileptiform activity. This hypothesis is based on the fact that axons, and in particular nodes of Ranvier in myelinated axons, have Na^+ channel densities of up to three orders of magnitude higher than the soma. Further, recent electrophysiological results have revealed that the threshold for action potential initiation is significantly lower in axons than at the soma. Whilst this ensures fast signal transmission in the healthy brain, epilepsy-related channelopathies may push the system into a regime where perturbations (e.g. channel noise) can tip the dynamics and initiate random action potentials that no longer serve to process signals, but rather create and propagate activity that is detrimental to the organism.

In short, axonal connections may not simply be the passive links between the nodes of the epileptic network, but rather be the active elements in epileptogenesis.

15 Timo Bröhl: Important edges in functional networks prior to extreme events

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We investigate importance of edges in coupled oscillator networks that are capable of self-generating and self-terminating extreme events. We address the question whether changes of importance of edges carry predictive information of an upcoming extreme event.