Book of Abstracts

Workshop on Modelling of Brain Activity

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Contents

1 Stephen Coombes: Modelling Brain Waves

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In this talk I will explore the way in which synaptically coupled neural networks may generate and maintain travelling waves of activity. Although these models are inherently non-local, a combination of mathematical approaches (predominantly drawn from non-smooth dynamical systems) means that we are now in a position to address fundamental questions about the effects of intrinsic ionic currents, synaptic processing, and anatomical connectivity on travelling waves in neural tissue. I will present a number of examples from both one and two dimensions, focusing on the contributions of axonal delays, adaptation, refractoriness, and slow hyper-polarisation activated currents, to brain waves seen in the cortex, thalamus, and hippocampus. I will also endeavour to explain the functional relevance of such waves and how in some instances they may subserve natural computation.

2 Alberto Pérez: Phase Response Curves in Epilepsy

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In [1], researchers show that epileptic dynamics shows a phasic dependency which can either facilitate or prevent seizure attacks. This phasic dependency can be studied through the Phase Response Curves (PRCs). Indeed, PRCs indicate which is the relationship between the phase at which a cycle is perturbed and the consequent phase shift.

This talk has two-fold scope. First part of the talk will be devoted to explain basic concepts of dynamical systems theory. Then, in the second part, we illustrate how these mathematical concepts can be used to gain insight in a biological motivated question. In particular we will show preliminary results of the computation PRCs of a reduced 2D slow-fast model capturing dynamics in [1].

[1] Loss of neuronal network resilience precedes seizures and determines the ictogenic nature of interictal synaptic perturbations WC Chang, J Kudlacek, J Hlinka, J Chvojka, M Hadrava, V Kumpost, ... Nature neuroscience, 2018, 21 (12), 1742

3 Helmut Schmidt: Oscillations in networks of spiking neurons and their role in memory tasks

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Oscillations are ubiquitous in the brain and often correlate with distinct cognitive tasks. Nonetheless, their role in shaping network dynamics, and hence in driving behavior during such tasks is poorly understood. I will present some recent findings on the role of oscillatory drive in network dynamics related to cognitive processing in simple working memory, and memory recall tasks. Bistable neuronal networks are able to sustain working memory by virtue of external stimuli switching between stable states. In larger networks, multiple stable patterns can merge through changes in synaptic strength – the mechanism of long-term memory formation. Slow oscillations, in the delta and theta band, are effective in activating network states associated with memory recall by virtue of the system sweeping through a saddle-node bifurcation. On the other hand, faster oscillations, in the beta range, can serve to clear memory states by resonantly driving transient bouts of spike synchrony which destabilize the activity. To systematically describe the network activity and its bifurcation structure, a set of exact mean-field equations for networks of quadratic integrate-and-fire neurons is used.

4 Pavel Sanda: Bidirectional oscillatory interactions during NREM sleep

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The dialogue between cortex and hippocampus is known to be crucial for sleep dependent consolidation of long lasting memories. During slow wave sleep, memory replay depends on slow oscillation (SO) and spindles in the (neo)cortex and sharp wave-ripple complexes (SWR) in the hippocampus. However, the mechanisms underlying interaction of these rhythms are poorly understood. Here, we examined the interaction between cortical SOs and hippocampal SWRs in a computational model of the hippocampo-cortico-thalamic network and compared the results with human intracranial recordings during sleep. We observed that ripple occurrence peaked following the onset of SO (Down-to-Up-state transition) and that cortical input to hippocampus was crucial to maintain this relationship. Ripples influenced the spatiotemporal structure of cortical SO and duration of the Up/Down-states. In particular, ripples were capable of synchronizing Up-to-Down state transition events across the cortical network. Slow waves had a tendency to initiate at cortical locations receiving hippocampal ripples, and these "initiators" were able to influence sequential reactivation within cortical Up states. We concluded that during slow wave sleep, hippocampus and neocortex maintain a complex interaction, where SOs bias the onset of ripples, while ripples influence the spatiotemporal pattern of SOs.

5 Oscar Gonzáles: Biophysical origin of resting-state infraslow fluctuations in brain networks

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Resting-state infraslow (0.01-0.2 Hz) brain activity is observed in fMRI, EEG, and local field potential recordings. These fluctuations were found to be correlated across brain regions and are thought to reflect neuronal activity fluctuations between functionally connected areas of the brain. Resting-state infra-slow brain activity fluctuations are observed across various cognitive and disease brain states. Although resting-state fluctuations have received a great deal of interest over the past few years, the underlying biophysical mechanisms are not well understood. Using computational modeling, we show that spontaneous resting-state fluctuations arise from dynamic ion concentrations and are influenced by the Na+/K+ pump, glial K+ buffering, and AMPA/GABA synaptic currents. These findings provide insights into the biophysical mechanisms underlying generation of this phenomenon and may lead to better understanding of how different cognitive or disease states influence resting-state activity.

6 Abigail Cocks: Understanding Sensory Induced Hallucinations: from Neural Fields to Amplitude Equations

Explorations of visual hallucinations, such as in [1], show that annular rings with a background flicker can induce visual hallucinations in humans that take the form of radial fan shapes and vice versa. The well-known retino-cortical map tells us that the corresponding patterns of neural activity in the primary visual cortex for rings and arms in the retina are orthogonal stripe patterns. The implication is that cortical forcing by spatially periodic input can excite orthogonal modes of neural activity. To understand this phenomena, we adapt the work of [2] that shows how spatial forcing of the planar Swift-Hohenberg PDE model along one spatial axis can lead to the excitation of a pattern in the perpendicular direction. By utilising a weakly nonlinear multiple-scales analysis for a non-local neural field model with spatial forcing we determine the relevant amplitude equations for understanding pattern formation. In turn we use these to uncover the parameter regimes which favour the excitation of patterns orthogonal to sensory drive, and thus shed light on the original psycho-physical observations in [1].

[1] V. A. Billock and B. H. Tsou. Neural interactions between flicker-induced self-organized visual hallucinations and physical stimuli. Proceedings of the National Academy of Sciences, 104(20) 8490-8495, 2007.

[2] R. Manor, A. Hagberg, and E. Meron. Wavenumber locking and pattern formation in spatially forced systems. New Journal of Physics, 11(6):63016, 2009.

7 Gorka Zamora-López: Model-based graph theory: a new framework to study whole-brain connectivity (and beyond)

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The use of graph theory has been essential in the past two decades to investigate brain connectivity. However, classical graph theory comes with several limitations which have restricted – and often obscured – the interpretation of results on real applications. A much ignored aspect is that graph metrics are derived assuming a dynamical model on how information propagates, which is kept away from the eyes of the users. Besides, this assumption does not often match the characteristics of the real systems studied.

Here, we propose a generalization of graph theory where the underlying dynamical model is explicit and tunable. It allows to redefine graph metrics such that both the link weights and the temporal evolution of the network become a natural characteristic of the analysis. We apply this formalism to study brain connectivity from fMRI at rest and during task. Model parameters are inferred by estimating effective connectivity, thus tuning the analysis to the particular system at hand. The framework allows to identify novel features of the information flow in the network, e.g., differentiated input and output roles of structural hubs, and identifying a time-scale separation between 'early' and 'late' integration motifs.

8 Viktor Sip: Modelling seizure propagation in epileptic brain networks

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Surgical interventions in epileptic patients aimed at the removal of the epileptogenic zone have success rates at only 60-70% [1]. This failure can be partly attributed to the insufficient spatial sampling by the implanted intracranial electrodes during the clinical evaluation, leading to the incomplete picture of the seizure propagation patterns in the regions that are not directly observed.

Utilizing the partial observations of the seizure evolution in the brain network complemented by the assumption that the epileptic seizure propagates along the structural connections [2] that can be estimated from the diffusion-weighed MRI, we aim to infer if and when are the hidden regions recruited in the seizure. To this end we use a data-driven model of seizure recruitment and propagation across a weighted network. The simple dynamical model is enriched by strong nonlinearity caused by the discontinuous changes of the node states from normal to seizing state. For the inversion of this model we adopt the Bayesian inference framework, and we infer the parameters of the model by the Hamiltonian Monte Carlo method [3] using the Stan software [4].

Results of the computational experiments with the synthetic data generated by the same model show that the quality of the inference results depend on the number of observed nodes and on the connection strength. The precision of the inferred onset times

increases with the number of observed nodes and with the strength of the network effects, while the capacity of the model to infer the excitabilities of the hidden nodes is limited in all studied cases. If our assumptions are fulfilled in the real epileptic seizures, these results indicate that the state of the hidden nodes during the seizure might be inferred from the incomplete observations.

[1] Bulacio, J. C.; Jehi, L.; Wong, C.; Gonzalez-Martinez, J.; Kotagal, P.; Nair, D.; Najm, I. & Bingaman, W. (2012). Long-term seizure outcome after resective surgery in patients evaluated with intracranial electrodes. Epilepsia, Wiley, 53, 1722-1730.

[2] Proix, T.; Bartolomei, F.; Guye, M. & Jirsa, V. K. (2017). Individual brain structure and modelling predict seizure propagation. Brain, Oxford University Press (OUP), 140, 641-654.

[3] Betancourt, M. A. (2018). Conceptual Introduction to Hamiltonian Monte Carlo. arXiv:1701.02434v2.

[4] Carpenter, B.; Gelman, A.; Hoffman, M. D.; Lee, D.; Goodrich, B.; Betancourt, M.; Brubaker, M.; Guo, J.; Li, P. & Riddell, A. (2017). Stan: A Probabilistic Programming Language Journal of Statistical Software, Foundation for Open Access Statistic, 76.

9 Oscar Gonzáles: Ionic and synaptic mechanisms of seizure generation and epileptogenesis

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The biophysical mechanisms underlying epileptogenesis and the generation of seizures remain to be better understood. Among many factors triggering epileptogenesis are traumatic brain injury breaking normal synaptic homeostasis and genetic mutations disrupting ionic concentration homeostasis. Impairments in these mechanisms, as seen in various brain diseases, may push the brain network to a pathological state characterized by increased susceptibility to unprovoked seizures. In this talk I will review our recent computational studies exploring the roles of ionic concentration dynamics in the generation, maintenance, and termination of seizures. I will further discuss how ionic and synaptic homeostatic mechanisms may give rise to conditions which prime brain networks to exhibit recurrent spontaneous seizures and epilepsy.

10 Stephen Coombes: Mathematical modelling of large-scale brain dynamics

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The tools of dynamical systems theory are having an increasing impact on our understanding of patterns of neural activity. In this talk I will describe how to build tractable

tissue level models that maintain a strong link with biophysical reality. These models typically take the form of nonlinear integro-differential equations. Their non-local nature has led to the development of a set of analytical and numerical tools for the study of waves, bumps and patterns, based around natural extensions of those used for local differential equation models. By way of illustration I will show how such models and methods of analysis can shed light on the emergence of spatially distinct frequency specific MEG networks from one underlying structural connectome.

11 Jonathan Hadida: Modelling and Optimisation of Large-Scale Biophysical Networks

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Biophysical network models formulate the evolution of neuronal activity as large systems of differential equations. These equations usually involve interpretable quantities (e.g. membrane potentials), and come with many parameters controlling important aspects of the network structure (e.g. the strength of connections), or of the dynamics (e.g. the local balance of excitation / inhibition). Crucially, these equations can be used to generate synthetic data (i.e. computer simulations), which can be compared to empirical data using several quantitative features (e.g. functional connectivity, spectral contents, etc.). In this context, model-fitting consists in estimating values for all parameters in order to maximise the similarity between simulated and empirical features.

In practice, this maximisation problem is extremely difficult for two main reasons: i) because analytic gradients are not available (the effects of parameters on the final similarity score is not analytically tractable); and ii) because simulations of whole-brain activity are computationaly costly. Such problems are knows as "expensive black-box" problems in the optimisation jargon, and Bayesian optimisation methods are designed specifically to address these challenges.

In this talk, I will present my research on these topics, using resting-state MEG dynamics as a target activity, and discuss results obtained for model-fits with non-uniform parameterisations of the cortex (i.e. allowing different regions to have different local parameters).

12 Martin Gajdos: Simulation of noise in BOLD fMRI

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Synthetic fMRI data are useful in many applications of neuroscience research, e.g. in testing and validation of methods developed for fMRI data processing and inference. Important part of synthetic fMRI data is noise. Although many studies use white noise, this approach could be too simplistic. In this work, we introduce a tool for generation of realistic BOLD fMRI noise based on properties observed in real datasets. The simulated

noise consists particularly of noise caused by movements of subject's head (NMSH), noise caused by breathing and heartbeats (NBH) and 1/f noise (NF).

13 Helmut Schmidt: Ephaptic coupling modulates axonal transmission delays

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Axonal connections are widely regarded as faithful transmitters of neuronal signals with fixed delays. The reasoning behind this is that extra-cellular potentials caused by action potentials travelling along axons are too small to have an effect on other axons. Here I demonstrate that although the extra-cellular potential generated by a single action potential is only a few microvolts, the collective extra-cellular potential generated by volleys of action potentials can reach several millivolts. As a consequence, the resulting change in the axonal membrane potentials can considerably alter the velocity of action potentials, and therefore affect axonal transmission delays between brain areas.