Parallel Session

Neuroscience II

PATIENT-SPECIFIC MODELING OF CORTICAL SPREADING DEPRESSION

Julia M. Kroos

jkroos@bcamath.org

BCAM - Basque Center for Applied Mathematics, Bilbao, Spain

Keywords: Migraine, Cortical Spreading Depression, PDE-ODE coupled systems, Finite elements.

Migraine is a common disease in present day population and 30% of the migraine patients suffer from migraine aura, perceptual disturbances preceding the typical headache. Cortical Spreading Depression (CSD), a depolarisation wave that originates in the visual cortex and propagates across the cortex to the peripheral areas, has been deemed as a correlate of visual aura by several studies. Until now little is known about the origin of this phenomenon, and curative treatments are unspecific and cause severe side effects.

However, the complex and highly individual characteristics of the brain cortex suggest that the geometry might have a significant impact in supporting or contrasting the propagation of CSD. Accurate patient-specific computational models are thus fundamental to cope with the high variability in cortical geometries among individuals, but also with the conduction anisotropy induced in a given cortex by the complex neuronal organisation in the grey matter.

We introduce a reaction-diffusion model for the extracellular potassium concentration on a personalized brain geometry, obtained from MRI imaging, to study the role of the geometry in shaping CSD. Patient-specific conductivity tensors are derived locally from Diffusion Tensor Imaging (DTI) data and provide detailed information about the anisotropy and the electrical conductivity properties of the cortical tissue. Additionally, we introduce a multiscale PDE-ODE model that couples the propagation of the depolarisation wave associated to CSD with a detailed electrophysiological model for the neuronal activity to capture both macroscopic and microscopic dynamics.

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MODELLING TRANSIENT TRAITS OF CORTEX FORMATION: THE IMPORTANCE OF EVOLVING CELL DIVISION STRATEGIES

Noemi Picco

picco@maths.ox.ac.uk

Mathematical Institute, University of Oxford, Radcliffe Observatory Quarter, Woodstock Road, Oxford OX2 6GG, UK

Joint work with Fernando García-Moreno (Achucarro Basque Center for Neuroscience), Thomas Woolley (Cardiff University), Zoltán Molnár (University of Oxford) and Philip Maini (University of Oxford).

Keywords: Neurogenesis, Transient differentiation dynamics.

The brain is the most complicated organ of any animal, formed and sculpted over 500 million years of evolution. The cerebral cortex is the folded grey matter that forms the outside of the brain, and is the seat of higher cognitive function.

Many factors influence how neurogenesis in the cortex differs between species, including the types of neurons and neural progenitor cells, the different ways in which they proliferate and differentiate, and the length of the process. Critically, to fully understand the development of the cortex we are faced with the challenge of understanding the temporal changes in cell division strategy. Combining mathematical modelling and experimental observations we incorporate these different factors to model development and evolution of the mammalian cortex.

A key determinant of the neuronal production is the modulation of proliferative (self-amplifying) and differentiative (neurogenic) divisions. We propose a new ordinary differential equation model that incorporates our hypothesised temporal changes in the propensity of different cell division types. By analysing this model, we identify a developmental programme that is consistent with the temporal pattern of neuronal output in the cortex of different species. Additionally, we highlight the current limitations in the interpretation of model predictions, due to the limited data currently available and identify a specific need for experimental quantifications.

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SYNCHRONIZATION PATTERNS, BIFURCATIONS AND CONTROL STRATEGIES IN CENTRAL PATTERN GENERATORS

Roberto Barrio

rbarrio@unizar.es

Applied Mathematics department, University of Zaragoza, Zaragoza, Spain

Joint work with Á. Lozano (Centro Universitario de la Defensa, Zaragoza, Spain), M. Rodríguez (Centro Universitario de la Defensa, Zaragoza, Spain) and S. Serrano (University of Zaragoza, Zaragoza, Spain).

Keywords: Neuron model, Central Pattern Generators, Bifurcations.

The study of the synchronization patterns that control biological processes has become a growing discipline [6]. Some of them are believed to play a crucial role in the emergence of pathological rhythmic brain activity in different diseases, like Parkinson's disease. On the other hand, small networks of neurons model central pattern generators (CPG) that control insect locomotion [1, 4]. In this work, we study small CPGs (6-neuron model) for insect locomotion where each neuron follows the Hodgkin-Huxley like model of Ghigliazza-Holmes [4]. A first key point is the development of a detailed "roadmap" that provides an exhaustive information [2] about the dynamics of a single neuron. Such information shades light on the effect of varying a parameter. This helps us to identify locomotive properties determined by individual neurons or by whole network.

By using suitable symmetry reductions, the basic 6-neuron model can be reduced to a 3-cell model [1, 4]. Therefore, a detailed bifurcation analysis of a 3-neuron model [6] is relevant. With a suitable combination of short and weak global inhibitory and excitatory stimuli over the network, we can switch between different stable patterns in small neuron networks (in our case a 3-neuron network). We develop a systematic study [5] showing and explaining the effects of applying the pulses at different moments. Moreover, we apply the technique on a completely symmetric network and on a slightly perturbed one (a more realistic situation). The approach of using global stimuli, as in the case of applying a current or a chemical substance to all the network, allows one to avoid undesirable synchronization patterns with nonaggressive stimuli. Also, the use of the roadmaps reveals [2, 3] the existence of heteroclinic cycles between saddle fixed points (FP) and invariant circles (IC) in a 3-cell CPG network. Such a cycle underlies a robust jiggling behavior in bursting synchronization [3].

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ALFRED: AUTOMATED IMAGE ANALYSIS OF MICROTUBULE NETWORKS IN NERVE CELLS

Beatriz Costa-Gomes

beatriz.costagomes@manchester.ac.uk

Faculty of Biology, Medicine and Health, University of Manchester
A.3051, Michael Smith Building, Oxford Road, M13 9PL, United Kingdom

Joint work with Simon Pearce, Matthias Heil and Andreas Prokop from the University of Manchester.

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Our bodies are electrically wired by axons, the up-to-a-meter long, cable-like protrusions of nerve cells. Axons have to be maintained for a lifetime, but 50% are lost during ageing and even more in neurodegenerative diseases. The axons' backbones are formed by parallel bundles of filamentous tubular polymers, called microtubules (MTs), which run along axons. In ageing and certain forms of neurodegeneration, MTs tend to lose their bundled organisation and take on dynamic curled conformations, usually occurring in axonal swellings.

One key challenge for studying of this phenomenon, is the retrieval of reliable quantitative information about axonal MT organisation in different genetic or experimental conditions. For this, we developed ALFRED[1], a MATLAB application combining newly developed and existing algorithms derived from bioimaging analysis and bioinformatics, which we apply to fluorescence images in order to objectively compare phenotypes between different biological conditions, giving a more precise and user-independent analysis. Images are initially virtualised using a "vesselness" algorithm, commonly used to analyse vascular networks [1], followed by skeletonisation. These two steps allow the identification of the MTs present in the image, which can be further analysed. From the identified MTs, we can extract important properties independent of image resolution, such as their curvatures (via a newly developed polynomial fitting algorithm), straightness (via Hough transformations), and further important values such as fibre lengths are extracted via graph theory algorithms.

In its current version, the parameters computed by ALFRED allow us to clearly distinguish between images that a human would classify as being distinct. We are now working on the refinement of parameter extraction to improve data quality and sampling speed, as well as the analysis and interpretation to identify the most informative parameters and understand how they translate into MT behaviours. In the future, ALFRED-generated data from biological samples are intended to be used for the development of a multi-scale mathematical model describing axonal MT behaviours in health and pathology.

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[1] Advanced Labelling, Fitting, Recognition & Enhancement of Data

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