

MINISYMPOSIUM

MATHEMATICAL NEUROSCIENCE

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Minisymposium Keywords: Neuroscience, Stochastic processes, Dynamical Systems, Bursting, Brain disorders.

Mathematics has a long history of application in Biology, as exemplified by the activities of the ESMTB. Well recognised sub-fields of Mathematical Biology have emerged in areas ranging from ecology to cancer. In the same way that biological and clinical understanding has progressed with the use of mathematics in these areas, so too may it advance the field of neuroscience, such as in the diagnosis and treatment of disorders, including epilepsy and schizophrenia, which are accompanied by differences in brain dynamics. Compared to some other areas of Mathematical Biology, the field of Mathematical Neuroscience is in its infancy. This mini-symposium will introduce some of the challenges and hot-topics in this field and show how these can be tackled using techniques drawn from a wide variety of mathematical disciplines including stochastic processes, dynamical systems theory, and machine learning. The first talk by Susanne Ditlevsen will provide a perspective talk suitable for newcomers, as well as showcase the use of stochastic processes for understanding the spiking behaviour of neural networks and inferring visual processes. Subsequent talks will focus on applications to brain disorders and understanding neural rhythms. Krasimira Tsaneva-Atanasova will talk about the challenge of developing bio-markers for schizophrenia, making use of dynamical systems techniques for the analysis of human movement. The third talk by Elif Ersöz will show how the theory of canards can be used to great effect in understanding mixed-mode oscillations that are ubiquitous in brain rhythms. The fourth talk by Forrester will discuss synchronisation patterns elicited by Transcranial Magnetic Stimulation, with application in depression. The aim of this mini-symposium is to raise the profile of Mathematical Neuroscience within the ESMTB community, and encourage more Mathematical Biologists to contribute to this exciting field.

Minisymposium: Mathematical Neuroscience

INFERRING VISUAL PROCESSING IN THE BRAIN

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Joint work with Kang Li (University of Copenhagen), Claus Bundesen (University of Copenhagen), Søren Kyllingsbæk (University of Copenhagen), Stefan Treue (Goettingen University), Vladislav Kozyrev (Cognitive Neuroscience Laboratory Goettingen)

Keywords: Spike trains, Visual attention, Probability-mixing, Statistical modeling of neurobiological data, Serial and parallel processing of visual stimuli.

A fundamental question concerning the way the visual world is represented in our brain is how cortical cells respond when their classical receptive fields contain more than a single stimulus object. It is a statistically challenging problem how to infer such behavior and distinguish between different explanatory models from neurobiological data. Particular challenges are that data are partially observed, highly noisy and autocorrelated. A standard way to deal with noisy data is to average over trials. In this talk I will argue that this might blur or entirely remove essential characteristics and mechanisms, which are fundamental for understanding brain function. For a single cell, two opposing models have been proposed in the literature. In the response-averaging model [15], the firing rate of the cell to a pair of stimulus objects is a weighted average of the firing rates to the individual objects. By contrast, in the probability-mixing model [1], the cell responds to the pair of objects as if only one of the objects was present in any given trial. I will compare the abilities of the two models to account for spike trains recorded from single cells in the middle temporal visual area of rhesus monkeys, using point process techniques. The results support the probability-mixing model [8].

The next natural question to ask is how a population of neurons responds to multiple stimuli. This is related to a long debated question in psychology of whether the processing mechanism in visual search is serial or parallel [2]. I will present some measures to distinguish between the different processing mechanisms, and suggest different models that can account for simultaneously recorded spike trains in prefrontal cortex of rhesus monkeys while processing task-relevant visual displays [9]. I will discuss how the different models offer different underlying assumptions on how the brain works.

Minisymposium: Mathematical Neuroscience

INDIVIDUAL MOTOR SIGNATURES AND SOCIO-MOTOR BIOMARKERS IN SCHIZOPHRENIA

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Keywords: Action-perception, Human movement, Mathematical modelling, Statistical analysis, Computational psychiatry.

Human movement has been studied for decades, and dynamic laws of motion that are common to all humans have been derived. Yet, every individual moves differently from everyone else (faster/slower, harder/smooth, etc.). We propose an index of such variability, namely an individual motor signature (IMS) able to capture the subtle differences in the way each of us moves. We show that the IMS of a person is time-invariant and that it significantly differs from those of other individuals [13]. Furthermore, in an effort to establish reliable indicators of schizophrenia we have developed a method that could detect deficits in movement and social interactions, both characteristics of the disorder. We asked people to perform movements alone, and to mirror the movements of a computer avatar or a humanoid robot. Using mathematical modelling and statistical learning techniques we were able to distinguish people with schizophrenia from healthy participants with accuracy and specificity slightly better than clinical interviews and comparable to tests based on much more expensive neuroimaging methods [14]. This methodology could help with diagnosis of schizophrenia and other related psychiatric conditions such as psychosis and potentially to also monitor patients' responses to therapeutic treatment.

Minisymposium: Mathematical Neuroscience

CANARD MEDIATED MIXED-MODE BURSTING OSCILLATIONS IN A RATE MODEL

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Keywords: Canard solutions, Mixed-mode bursting oscillations, Spontaneous activity, Activity-dependent depression, Network plasticity.

The term “mixed-mode oscillations” (MMOs) is used to describe the dynamics that combine small-amplitude oscillations and large-amplitude oscillations. MMOs arise in multiple-timescale systems with at least two slow variables and a folded critical manifold [3]. The pivotal role of the folded singularities and associated canard structures in shaping these complex dynamics has been identified in many models of biological rhythms. Mixed-mode bursting oscillations (MMBOs) can appear in four-dimensional (4D) systems with two slow and two fast variables as a combination of folded-node type dynamics following fast oscillations of bursting type [4]. In this work we focus on a rate model that accounts for the spontaneous activity in the developing spinal cord of the chicken embryo [16]. The dynamics is that of a classical square-wave burster, with alternation of silent and active phases. Tabak *et al.* [16] have proposed two different three-dimensional (3D) models with variables representing average population activity, fast activity-dependent synaptic depression and slow activity-dependent depression of two forms. In [17, 18, 19] various 3D combinations of these four variables have been studied further to reproduce rough experimental observations of spontaneous rhythmic activity. In this talk, we first show the spike-adding mechanism via canards in one of these 3D models from [16] where the fourth variable is treated as a control parameter. Then we discuss how a canard-mediated slow passage in the 4D model explains the sub-threshold oscillatory behavior which cannot be reproduced by any of the 3D models. Finally, we relate the canard-mediated slow passage to the intervals of burst and silent phase which have been linked to the blockade of glutamatergic or GABAergic/glycinergic synapses over a wide range of developmental stages [17].

Minisymposium: Mathematical Neuroscience

TMS-INDUCED SYNCHRONISATION IN HUMAN BRAIN NETWORKS

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Keywords: Transcranial Magnetic Stimulation, Neural-Mass Models, Functional Connectivity.

Transcranial Magnetic Stimulation (TMS) is a non-invasive method of provoking significant changes in mental states. While TMS has proven itself as a treatment for depression, schizophrenia and chronic pain, the neurological mechanisms behind the alleviation of these symptoms is poorly understood. TMS perturbs neurons by inducing a current along axons, facilitating excitatory activity and entraining neurons to synchrony. It is thought that this can fix disrupted functional connectivity that causes major depression, by activating the neural ‘switch’ that allows the brain to shift between two major brain subnetworks: the default mode and central executive networks [20].

Using a neural-mass model [21], we study the influence of TMS on networks of connected brain regions comprising millions of neurons. The model is particularly suited to studying TMS since simulated dynamics accommodate underlying neural population synchrony, yet within a course-grained framework appropriate for the modelling of macroscopic neural systems. Furthermore, connectivity is defined using human DTI data so that networks are neurologically relevant. In this way, the model comprises dynamics on a neuronal level as well as the much greater scale of whole-brain connectivity. This allows us to understand how stimulation of one brain region can affect how neurons interact in other parts of the brain, which may elucidate how TMS can work as a treatment for major depression. In particular, we use the metric of phase coherence to investigate how TMS can evoke new patterns of synchrony in the network model that relate to the switching between resting (default mode) and stimulated (central executive) network states, a proxy for the functional behaviour that would be expected in the brain of a healthy person. Graph theoretic methods of node centrality and clustering are employed to give a qualitative analysis of how the functional network has changed due to TMS.

Changing the parameters of TMS delivery (frequency, amplitude, target region etc.), we explore how different methods of stimulation affect resultant functional networks and speculate which of these may relate to TMS ‘fixing’ an irregular connectivity.

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