TYPE - ORAL • JULY 19 • SUNDAY

O Oral

JULY 19 • SUNDAY

1:40pm – 2:00pm

O **O1: Dopamine role in learning and action inference**

Crowdcast (link TBA)

Speakers: Rafal Bogacz

Rafal Bogacz

Much evidence suggests that some dopaminergic neurons respond to unexpected rewards, and computational models have suggested that these neurons encode reward prediction error, which drives learning about rewards. However, these models do not explain recently observed diversity of dopaminergic responses, and dopamine function in action planning, evident from movement difficulties in Parkinson's disease. The presented work aims at extending existing models to account for these data. It proposes that a more complete description of dopaminergic activity can be achieved by combining reinforcement learning with elements of other recently proposed theories including active inference.

The presented model describes how the basal ganglia network infers actions required to obtained reward using Bayesian inference. The model assumes that a likelihood of reward given action in encoded by the goal-directed system, while the prior probability of making a particular action in a given context is provided by the habit system. It is shown how the inference of the optimal action can be achieved through minimization of free-energy, and how this inference can be implemented in a network with an architecture bearing a striking resemblance to the known anatomy of the striato-dopaminergic circuit. In particular, this network includes nodes encoding prediction errors, which are connected with other nodes in the network in a way resembling the "ascending spiral" structure of dopaminergic connections.

In the proposed model, dopaminergic neurons projecting to different parts of the striatum encode errors in predictions made by the corresponding systems within the basal ganglia. These prediction errors are equal to differences between rewards and expectations in the goal-directed system, and to differences between the chosen and habitual actions in the habit system. The prediction errors enable learning about rewards resulting from actions and habit formation. During action planning, the expectation of reward in the goal-directed system arises from formulating a plan to obtain that reward. Thus dopaminergic neurons in this system provide feedback on whether the current motor plan is sufficient to obtain the available reward, and they facilitate action planning until a suitable plan is found. Presented models account for dopaminergic responses during movements, effects of dopamine depletion on behaviour, and make several experimental predictions.

2:00pm – 2:20pm

O **O2: Neural Manifold Models for Characterising Brain Circuit Dynamics in Neurodegenerative Disease**

Speakers: Seigfred Prado

Crowdcast (link TBA)

Seigfred Prado, **Simon R Schultz**, **Mary Ann Go**

Although much is known about neural circuits and molecular pathways required for normal hippocampal functions, the processes by which neurodegenerative diseases, such as Alzheimer's Disease (AD), disable the functioning of the hippocampus and connected structures remain to be determined. In order to make substantial advances in the treatment of such diseases, we must improve our understanding of how neural circuits process information and how they are disrupted during the progression of these diseases. Recent advances in optical imaging technologies that allow simultaneous recording of large populations of neurons in deeper structures [1] have shown great promise for revealing circuit dynamics during memory tasks [2]. However, to date, no study has revealed how large numbers of neurons in hippocampal-cortical circuits act together to encode, store and retrieve memories in animal models of AD. In this work, we explored the use of neural manifold analysis techniques to characterising brain circuit dynamics in neurodegenerative disease. To understand more precisely the basis of memory and cognitive impairments in AD, we extracted the underlying neural manifolds in large-scale neural responses of hippocampal circuits involved in spatial cognition of behaving mice. For validation, we simulated a model that generates a set of data that mimics the neural activity of hippocampal cells of mouse models running on a linear circular track, while taking into account the effects of amyloid-beta plaques on circuit dynamics [3]. We compare our model with real data obtained by multiphoton imaging of hippocampal CA1 cells in mice engaged in a spatial memory task. We used recurrence analysis to show how neural manifolds evolve over time during memory encoding, storage and recall processes in a repetitive memory task. This work will help with understanding how amyloid-beta proteins affect the neural manifolds for spatial memory, which is particularly disturbed during AD.

2:20pm – 2:40pm

O **O3: Coupled experimental and modeling representation of the mechanisms of epileptic discharges in rat brain slices**

Crowdcast (link TBA)

Speakers: Anton Chizhov

Anton Chizhov, **Dmytry Amakhin**, **Elena Smirnova**, **Aleksey Zaitsev**

Epileptic seizures and interictal discharges (IIDs) are determined by neuronal interactions and ionic dynamics and thus help to reveal valuable knowledge about the mechanisms of brain functioning in not only pathological but also normal state. As synchronized pathological discharges are much simpler to study than normal functioning, we were able to accomplish their description with a set of electrophysiological evidences constrained by a biophysical mathematical model. In the combined hippocampal-entorhynal cortex slices of rat in high potassium, low magnesium and 4-AP containing solution we evaluated separate AMPA, NMDA and GABA-A conductances for different types of IIDs, using an original experimental technique [1]. The conductances have shown that the first type of the discharges (IID1) is determined by activity of only GABA-A channels due to their pathologically depolarized reversal potential. The second type (IID2) is determined by an early GABA-A followed by AMPA and NMDA components. The third type is pure glutamatergic discharges observed in case of disinhibition. Our mathematical model of interacting neuronal populations reproduces the recorded synaptic currents and conductances for IIDs of the three types [2,3], confirming the major role of interneuron synchronization for IID1 and IID2, and revealing that the duration of IIDs is determined mainly by synaptic depression. IIDs occur spontaneously and propagate as waves with a speed of about a few tens of mm/s [4]. IDs are clusters of IID-like discharges and are determined by the ionic dynamics [5]. To reveal only major processes, main ions and variables, we have formulated a reduced mathematical model “Epileptor-2”, which is a minimal model that reproduces both IDs and IIDs [6] (Fig. 1). It shows that IIDs are spontaneous bursts that are governed by the membrane depolarization and synaptic resource, whereas IDs represent bursts of bursts. Important is the role of the Na/K-ATPhase. Potassium accumulation governs the onset of each ID. The sodium accumulates during the ID and activates the sodium-potassium pump, which terminates the ID by restoring the potassium gradient and thus repolarizing the neurons. A spatially-distributed version of the Epileptor-2 model reveals that it is not extracellular potassium diffusion but synaptic connectivity determines the speed of the ictal wavefront [7], which is consistent with our optogenetic experiments. The revealed factors are to be potential targets for antiepileptic medical treatment.

This work was supported by the Russian Science Foundation (project 16-15-10201).

4:20pm – 4:40pm

O **O4: Towards multipurpose bio-realistic models of cortical circuits**

Crowdcast (link TBA)

Speakers: antona@alleninstitute.org
Anton Arkhipov

One of the central questions in neuroscience is how structure of brain circuits determines their activity and function. To explore such structure- function relations systematically, we integrate information from large-scale experimental surveys into data-driven, bio-realistic models of brain circuits, with the current focus on the mouse cortex. Here, we will discuss our recent progress in developing and sharing with the community highly realistic, data- driven models1 of mouse primary visual cortex (area V1) and software tools for modeling.

Our models are shared freely with the community (**Figure 1A**): [https://portal.brain-map.org/explore/models/mv1-all- layers](https://portal.brain-map.org/explore/models/mv1-all-layers). In addition to models, we also freely share the software tools that we developed to facilitate construction, simulation, and dissemination of the bio- realistic, large-scale models of brain circuits. These tools include the Brain Modeling ToolKit (BMTK; [alleninstitute.github.io/bmtk/] (https://alleninstitute.github.io/bmtk/); **Figure 1B**), which is a software suite for model building/simulation2, and the SONATA3 file format (github.com/allenInstitute/sonata; **Figure 1C**) for efficient storage of model and simulation data. Notably, these tools are developed in close coordination with related initiatives, such as NEURON4, NEST5, NWB6, NeuroML7, PyNN8, NetPyNE9, and the European Human Brain Project10.

Our recent 230,000-neuron models of the mouse cortical area V11 were constructed at two levels of granularity – using either biophysically-detailed or point-neurons (**Figure 2A, B, C**). These models systematically integrated a broad array of experimental data: the information about distribution and morpho-electric properties of different neuron types in V111,12; connection probabilities, synaptic weights, axonal delays, and dendritic targeting rules inferred from a thorough survey of the literature; and a sophisticated representation of visual inputs into V1 from the Lateral Geniculate Nucleus, fit to _in vivo_ recordings (e.g.,13,14) and capable of stimulating the V1 network with arbitrary visual stimuli. The model activity has been tested against large-scale _in vivo_ recordings of neural activity15,16 (**Figure 2D, E**). We found a good agreement between these experimental data and the V1 models for a variety of metrics, such as direction selectivity, as well as less good agreement for other metrics, suggesting avenues for future improvements. In the process of building and testing models, we also made predictions about the logic of recurrent connectivity with respect to functional properties of the neurons, some of which have been verified experimentally1,17.

In this presentation, we will focus on the model's successes in quantitative matching of multiple experimental measures, as well as failures in matching other metrics. Both successes and failures shed light on the potential structure-function relations in cortical circuits, leading to experimentally testable hypotheses. We will also discuss a set of more recent unpublished studies using these models that involve investigations of the effects of optogenetic perturbations and cell-type-specific activations in the V1 circuit in response to specific visual stimuli.

4:40pm – 5:00pm

O **O5: How Stimulus Statistics Affect the Receptive Fields of Cells in Primary Visual Cortex** Crowdcast (link TBA)

Speakers: Ali Almasi

Ali Almasi, **Hamish Meffin**, **Shi Sun**, **Michael R Ibbotson**

Our understanding of sensory coding in the visual system is largely derived from parametrizing neuronal responses to basic stimuli. Recently, mathematical tools have developed that allow estimating the parameters of a receptive field (RF) model, which are typically a cascade of linear filters on the stimulus, followed by static nonlinearities that map the output of the filters to the neuronal spike rates. However, how much do these characterizations depend on the choice of the stimulus type?

We studied the changes that neuronal RF models undergo due to the change in the statistics of the visual stimulus. We applied the nonlinear input model (NIM) [1] to the recordings of single units in cat primary visual cortex (V1) in response to white Gaussian noise (WGN) and natural scenes (NS). These two stimulus types were matched in their global RMS contrast; however, they are fundamentally different in terms of second- and higher-order statistics, which are abundant in natural scenes but do not exist in white noise. We estimated for each cell the spatial filters constituting the neuronal RF and their corresponding nonlinear pooling mechanism, while making minimal assumptions about the underlying neuronal processing.

We found that cells respond differently to these two stimulus types, with mostly higher spike rates and shorter response latencies to NS than to WGN. The most striking finding was that NS stimuli resulted in around twice as many uncovered RF filters compared to using WGN stimuli. Via careful analysis of the data, we discovered that this difference between the number of identified RF filters is not related to the higher spike rates of cells to NS stimuli. Instead, we found it to be attributed to the difference in the contrast levels of specific features that exhibit different prevalence in NS versus WGN. These features correspond to the V1 RF filters recovered in the model. This specific feature-contrast attains much higher values in NS compared to WGN stimuli. When the feature-contrast is controlled for, it explains the differences in the number of RF filters obtained. Our findings imply that a greater extent of nonlinear processing in V1 neurons can be uncovered using natural scene stimulation.

We also compared the identified RF filters under the two stimulation regimes in terms of their spatial characteristics. Population analysis of the RF filters revealed a statistically significant bias towards higher spatial frequency filters with narrower spatial frequency bandwidth under the NS stimulation regime (p-value < 0.0025).

Acknowledgements The authors acknowledge the support the Australian Research Council Centre of Excellence for Integrative Brain function (CE140100007), the National Health and Medical Research Council (GNT1106390), and Lions Club of Victoria.

References

[1] McFarland JM, Cui Y, Butts DA. Inferring nonlinear neuronal computation based on physiologically plausible inputs. PLoS Comput Biol. 2013, 9(7).

5:00pm – 5:20pm

O **O6: Analysis and Modelling of Response Features of Accessory Olfactory Bulb Neurons** Crowdcast (link TBA)

Speakers: Yoram Ben-Shaul

Yoram Ben-Shaul, **Rohini Bansal**, **Romana Stopkova**, **Maximilian Nagel**, **Pavel Stopka**, **Marc Spehr**

The broad goal of this work is to understand how consistency on a macroscopic scale can be achieved despite random connectivity at the level of individual neurons.

A central aspect of any sensory system is the manner by which features of the external world are represented by neurons at various processing stages. Yet, it is not always clear what these features are, how they are represented, and how they emerge mechanistically. Here, we investigate this issue in the context of the vomeronasal system (VNS), a vertebrate chemosensory system specialized for processing of cues from other organisms. We focus on the accessory olfactory bulb AOB, which receives all vomeronasal sensory neuron inputs. Unlike the main olfactory system, where MTCs sample information from a single receptor type, AOB MTCs sample information from a variable number of glomeruli, in a manner that seems largely random. This apparently random connectivity is puzzling given the presumed role of this system in processing cues with innately relevant significance.

We use multisite extracellular recordings to measure the responses of mouse AOB MTCs to controlled presentation of natural urine stimuli from male and female mice from various strains, including from wild mice. Crucially, we also measured the levels of both volatile and peptide chemical components in the very same stimulus samples that were presented to the mice. As subjects, we used two genetically distinct mouse strains, allowing us to test if macroscopic similarity can emerge despite variability at the level of receptor expression.

First, we then explored neuronal receptive fields, and found that neurons selective for specific strains (regardless of sex), or a specific sex (regardless of strain), are less common than expected by chance. This is consistent with our previous findings indicating that high level stimulus features are represented in a distributed manner in the AOB. We then compared various aspects of neuronal responses across the two strains, and found a high degree of correlation among them, suggesting that despite apparent randomness and strain specific genetic aspects, consistent features emerge at the level of the AOB.

Next, we set out to model the responses of AOB neurons. Briefly, AOB responses to a given stimulus are modelled as dot products of random tuning profiles to specific chemicals and the actual level of those chemicals in the stimulus. In this manner we derive a population of AOB responses, which we can then compare to the measured responses. Our analysis thus far reveals several important insights. First, neuronal response properties are best accounted for by sampling of protein/peptide components, but not by volatile urinary components. This is consistent with the known physiology of the VNS. Second, several response features (population level neuronal distances, sparseness, distribution of receptive field types) are best reproduced in the model with random sampling of multiple, rather than single molecules per neuron. This suggests that the sampling mode of AOB neurons may mitigate some of the consequences of random sampling. Finally, we note that random sampling of molecules provides a reasonable fit for some, but not all metrics of the observed responses. Our ongoing work aims to identify which changes must be made to our initial simplistic model in order to account for these features.

This work is funded by GIF and DFG grants to Marc Spehr and Yoram Ben-Shaul

6:20pm – 6:40pm

O **O7: 'Awake Delta' and Theta-Rhythmic Modes of Hippocampal Network Activity Track Intermittent Locomotor Behaviors in Rat**

Crowdcast (link TBA)

Speakers: Nathan Schultheiss

Nathan Schultheiss, **Tomas Guilarte**, **Tim Allen**

Delta-frequency activity in the local field potential (LFP) is widely believed to correspond to so-called 'cortical silence' during phases of non-REM sleep, but delta in awake behaving animals is not well understood and is rarely studied in detail. By integrating novel analyses of the hippocampal (HC) LFP with simultaneous behavioral tracking, we show for the first time that HC synchronization in the delta frequency band (1-4 Hz) is related to animals' locomotor behaviors during free exploration and foraging in an open field environment. In contrast to well-established relationships between animals' running speeds and the theta rhythm (6-10 Hz), we found that delta was most prominent when animals were stationary or moving slowly (i.e. when theta and fast gamma (65-120 Hz) were weak). Furthermore, delta synchronization often developed rapidly when animals paused briefly between intermittent running bouts.

Next, we developed an innovative strategy for identifying putative _modes_ of network function based on the spectral content of the LFP. By applying hierarchical clustering algorithms to time-windowed power spectra throughout behavioral sessions (i.e. the spectrogram), we categorized moment-by-moment estimations of the power spectral density (PSD) into spectral modes of HC activity. That is, we operationalized putative _functional modes_ of network computation as _spectral modes_ of LFP activity. Delta and theta power were strikingly orthogonal across the resultant spectral modes, suggesting the possibility that delta- and theta-dominated hippocampal activity patterns represent distinct modes of HC function during navigation. Delta and theta were also remarkably orthogonal across precisely-defined bouts of running and stationary behavior, indicating that the stops-and-starts that compose rats' locomotor trajectories are accompanied by alternating delta- and theta-dominated HC states.

We then asked whether the incidence of delta and theta modes was related to the coherence between recording sites in hippocampus or between hippocampus and medial prefrontal cortex (mPFC). We found that intrahippocampal coherences in both the delta-band and the theta-band were monotonically related to theta-delta ratios across modes. Furthermore, in two rats implanted with dual-site recording arrays, we found that theta coherence between HC and mPFC increased during running, and delta-band coherence between mPFC and HC increased during stationary bouts. Taken together, our findings suggest that delta-dominated network modes (and corresponding mPFC-HC couplings) represent functionally-distinct circuit dynamics that are temporally and behaviorally interspersed among theta-dominated modes during spatial navigation. As such, delta modes could play a fundamental role in coordinating mnemonic functions including encoding and retrieval mechanisms, or decision-making processes incorporating prospective or retrospective representations of experience, at a timescale that segments event sequences within behavioral episodes.

1:40pm – 2:00pm

O **O8: Finite element simulation of ionic electrodiffusion in cellular geometries**

Crowdcast (link TBA)

Speakers: Ada Johanne Ellingsrud

Ada Johanne Ellingsrud

Electrical conduction in brain tissue is commonly modeled using classical bidomain models. These models fundamentally assume that the discrete nature of brain tissue can be represented by homogenized equations where the extracellular space, the cell membrane, and the intracellular spare are continuous and exist everywhere. Consequently, they do not allow simulations highlighting the effect of a nonuniform distribution of ion channels along the cell membrane or the complex morphology of the cells. In this talk, we present a more accurate framework for cerebral electrodiffusion with an explicit representation of the geometry of the cell, the cell membrane and the extracellular space. To take full advantage of this framework, a numerical solution scheme capable of efficiently handling three-dimensional, complicated geometries is required. We propose a novel numerical solution scheme using a mortar finite element method, allowing for the coupling of variational problems posed over the non-overlapping intra and extracellular domains by weakly enforcing interface conditions on the cell membrane. This solution algorithm flexibly allows for arbitrary geometries and efficient solution of the separate subproblems. Finally, we study ephaptic coupling induced in an unmyelinated axon bundle and demonstrate how the presented framework can give new insights in this setting. Simulations of 9 idealized, tightly packed axons show that inducing action potentials in one or more axons yields ephaptic currents that have a pronounced excitatory effect on neighboring axons, but fail to induce action potentials there [1].

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme under grant agreement 714892 (Waterscales), and from the Research Council of Norway (BIOTEK2021 Digital Life project 'DigiBrain', project 248828).

[1] Ellingsrud A J, Solbrå A, Einevoll G T, et al. Finite element simulation of ionic electrodiffusion in cellular geometries. arXiv.org. 2019.

2:00pm – 2:20pm

O9: Discovering synaptic mechanisms underlying the propagation of cortical activity: A model-driven experimental and data analysis approach

Crowdcast (link TBA)

Speakers: Heidi Teppola

Heidi Teppola, **Jugoslava Acimovic**, **Marja-Leena Linne**

Spontaneous, synchronized activity is a well-established feature of cortical networks _in vitro_ and _in vivo_. The landmark of this activity is the repetitive emergence of bursts propagating across networks as spatio-temporal patterns. Cortical bursts are governed by excitatory and inhibitory synapses via AMPA, NMDA and GABA A receptors. Although spontaneous activity is a well known phenomenon in developing networks, its specific underlying mechanisms in health and disease are not fully understood. In order to study the synaptic mechanisms regulating the propagation of cortical activity it is important to combine the experimental wet-lab studies with _in silico_ modeling and build detailed, realistic, computational models of cortical network activity. Moreover, experimental studies and analysis of microelectrode array (MEA) data are not typically designed to support computational modeling. We show here how the synaptic AMPA, NMDA and GABA A receptors shape the initiation, propagation and termination of the cortical burst activity in rodent networks _in vitro_ and _in silico_ and develop model-driven data analysis workflow to support the development of spiking and biophysical network models _in silico_ **[1].**

We created a model-driven data analysis workflow with multiple steps to examine the contributions of synaptic receptors to burst dynamics both _in vitro_ _and in silico_ neuronal networks **(Fig.** **1)**. First, the cortical networks were prepared from the forebrains of the postnatal rats and maintained on MEA plates. Second, network-wide activity was recorded by MEA technique under several pharmacological conditions of receptor antagonists. Third, multivariate data analysis was conducted in a way that supports both neurobiological questions as well as the fitting and validation of computational models to quantitatively produce the experimental results. Fourth, the computational models were simulated with different parameters to test putative mechanisms responsible for network activity.

The experimental results obtained in this study show that AMPA receptors initiate bursts by rapidly recruiting cells whereas NMDA receptors maintain them. GABAA receptors inhibit the spiking frequency of AMPA receptor-mediated spikes at the onset of bursts and attenuate the NMDA receptor-mediated late phase. These findings highlight the importance of both excitatory and inhibitory synapses in activity propagation and demonstrate a specific interaction between AMPA and GABAA receptors for fast excitation and inhibition. In the presence of this interaction, the spatio-temporal propagation patterns of activity are richer and more diverse than in its absence. Moreover, we emphasize the systematic data analysis approach with model-driven workflow throughout the study for comparison of results obtained from multiple _in vitro_ networks and for validation of data-driven model development _in silico_. A well-defined workflow can reduce the amount of biological experiments, promote more reliable and efficient use of the MEA technique, and improve the reproducibility of research. It helps reveal in detail how excitatory and inhibitory synapses shape cortical activity propagation and dynamics in rodent networks _in vitro_ and _in silico_.

Reference

** **

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2:20pm – 2:40pm

O10: Neural flows: estimation of wave velocities and identification of singularities in 3D+t brain data

Speakers: paula.sanz-leon@qimrberghofer.edu.au

Paula Sanz-Leon, **Leonardo L Gollo**, **James A Roberts**

Crowdcast (link TBA)

Background. Neural activity organizes in constantly evolving spatiotemporal patterns of activity, also known as brain waves (Roberts et al., 2019). Indeed, wave-like patterns have been observed across multiple neuroimaging modalities and across multiple spatiotemporal scales (Muller et al., 2016; Contreras et al. 1997; Destexhe et al. 1999). However, due to experimental constraints most attention has thus far been given to localised wave dynamics in the range of micrometers to a few centimeters, rather than at the global or large-scale that would encompass the whole brain. Existing toolboxes (Muller et al., 2016; Townsend et al., 2018) are geared particularly for 2D spatial domains (e.g., LFPs or VSDs on structured rectangular grids). No tool exists to study spatiotemporal waves naturally unfolding in 3D+t as recorded with different non-invasive neuroimaging techniques (e.g, EEG, MEG, and fMRI). In this work, we present results of using our toolbox neural flows (shown in Fig. 1).

Methods and Results. Our toolbox handles irregularly sampled data such as those produced via brain network modelling (Sanz-Leon et al., 2015; Breakspear, 2017) or source-reconstructed M/EEG, and regularly sampled data such as voxel-based fMRI. The toolbox performs the following steps: 1) Estimation of neural flows (Destexhe et al. 1999; Townsend et al., 2018; Sanz- Leon et al. 2020). 2) Detection of 3D singularities (i.e., points of vanishing flow). 3) Classification of 3D singularities. In that regard, the key flow singularities detected so far had been sources and sinks (from where activity emerges and vanishes, respectively), but no methods or tools existed to detect 3D saddles (around which activity is redirected to other parts of the brain). 4) Quantification of singularity statistics. 5) Finally, modal decomposition of neural flow dynamics. This decomposition allows for the detection and prediction of the most common spatiotemporal patterns of activity found in empirical data.

Conclusions. Representation of neural activity based on singularities (commonly known as critical points) is essentially a dimensionality reduction framework to understand large-scale brain dynamics. The distribution of singularities in physical space allows us to simplify the complex structure of flows into areas with similar dynamical behavior (e.g., fast versus slow, stagnant, laminar, or rotating). For modelling work, this compact representation allows for an intuitive and systematic understanding of the effects of various parameters in brain network dynamics such as spatial heterogeneity, lesions and noise. For experimental work, neural flows enable a rational understanding of large-scale brain dynamics directly in anatomical space which facilitates the interpretation and comparison of results across multiple modalities. Toolbox capabilities are presented in the accompanying figure. Watch this space for the open-source code: [https://github.com/brain- modelling-group](https://github.com/brain-modelling-group)

References

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5:00pm – 5:20pm

O11: Experimental and computational characterization of interval variability in the sequential activity of the Lymnaea feeding CPG

Crowdcast (link TBA)

Speakers: Alicia Garrido-Peña

Alicia Garrido-Peña, **Irene Elices**, **Rafael Levi**, **Francisco B Rodriguez**, **Pablo Varona**

Central Pattern Generators (CPG) generate and coordinate motor movements by producing rhythms composed of patterned sequences of activations in their constituent neurons. These robust rhythms are yet flexible and the time intervals that build the neural sequences can adapt as a function of the behavioral context. We have recently revealed the presence of robust dynamical invariants in the form of cycle-by-cycle linear relationships between two specific intervals of the crustacean pyloric CPG sequence and the period [1]. Following the same strategy, the present work characterizes the intervals that build the rhythm and the associated sequence of the feeding CPG of the mollusk _Lymnaea Stagnalis_. The study entails both the activity obtained in electrophysiological recordings of living neurons and the rhythm produced by a realistic conductance-based model. The analysis reported here first assesses the quantification of the variability of the intervals and the characterization of relationships between the intervals that build the sequence and the period, which allows the identification of dynamical invariants. To induce variability in the CPG model, we use current injection ramps in individual CPG neurons following the stimulation used in experimental recordings in [2]. Our work extends previous analyses characterizing the _Lymnaea_ feeding CPG rhythm from experimental recordings and from modeling studies by considering all intervals that build the sequence [3]. We report the presence of distinct variability in the sequence time intervals and the existence of dynamical invariants, which depend on the neuron being stimulated. The presence of dynamical invariants in CPG sequences, not only in the model but also in two animal species, points out the universality of this phenomena.

Acknowledgements

We acknowledge support from AEI/FEDER PGC2018-095895-B-I00 and TIN2017-84452-R.

References

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5:40pm – 6:00pm

O **O12: A Spatial Developmental Generative Model of Human Brain Structural Connectivity** Crowdcast (link TBA)

Speakers: Stuart Oldham

Stuart Oldham, **Ben Fulcher**, **Kevin Aquino**, **Aurina Arnatkevičiūtė**, **Rosita Shishegar**, **Alex Fornito**

The human connectome has a complex topology that is thought to enable adaptive function and behaviour. Yet the mechanisms leading to the emergence of this topology are unknown. Generative models can shed light on this question, by growing networks in silico according to specific wiring rules and comparing properties of model-generated networks to those observed in empirical data [1]. Models involving trade-offs between the metabolic cost and functional value of a connection can reproduce topological features of human brain networks at a statistical level, but are less successful in replicating how certain properties, most notably hubs, are spatially embedded [2,3]. A potential reason for this limited predictive ability is that current models assume a fixed geometry based on the adult brain, ignoring the major changes in shape and size that occur early in development, when connections form.

To address this limitation, we developed a generative model that accounts for developmental changes in brain geometry, informed by structural MRIs obtained from a public database of foetal scans acquired from 21–38 weeks gestational age [4]. We manually segmented the cortical surface of each brain and registered each surface to an adult template surface using Multimodal Surface Matching [5,6]. This procedure allowed us to map nodes to consistent spatial locations through development and measure how distances between nodes (a proxy for connectome wiring cost) change through development. We evaluated the performance of classic trade-off models [2] that either assume a fixed, adult brain geometry (static), or those where cost-value trade-offs dynamically change in accordance with developmental variations in brain shape and size (growth). We used connectomes generated from 100 healthy adults with diffusion MRI to benchmark model performance. Model fit was calculated by comparing model and empirical distributions of topological properties. An optimisation procedure was used to find the optimal parameters and best-fitting models for each individual adult brain network [2]. For fair comparison of model fit across models of varying parametric complexity, we used a leave-one out cross- validation procedure.

Spatial models (sptl; which include only distance information) produced poorer fits than those involving distance–topology trade-offs. Homophily models (matching , neighbors; where connections form between nodes with common neighbours) were among the best fitting. Growth models produced slightly better fits than static models overall. These results still generally held when the cross-validation procedure was employed (Fig. 1A). Neither growth nor static models reproduced the spatial topography of network hubs, but growth models are associated with a less centralized anatomical distribution of hubs across the brain, which is more consistent with the empirical data (Fig. 1B).

In summary, we introduce a new framework for examining how developmental changes in brain geometry influence brain connectivity. Our results suggest that while such changes influence network topology, they are insufficient to explain how complex connectivity patterns emerge in brain networks.

References: **[1]** Betzel R, Bassett D. _J. R. Soc. Interface_ 2017; 14. **[2]** Betzel R et al. _NeuroImage_ 2016; __ 124: 1054-64. **[3]** Zhang X et al. _BioRxiv_ 2019. **[4]** Gholipour A et al. _Sci Rep_ 2017; 7. **[5]** Robinson E et al (2014). _NeuroImage_ 100: 414-26. **[6]** Robinson E et al. _NeuroImage_ 2018; 167: 453-65.

6:00pm – 6:20pm

O13: Cortical integration and segregation explained by harmonic modes of functional connectivity

Speakers: Katharina Glomb

Crowdcast (link TBA)

Katharina Glomb, **Gustavo Deco**, **Morten L. Kringelbach**, **Patric Hagmann**, **Joel Pearson**, **Selen Atasoy**

The idea that harmonic modes - basis functions of the Laplace operator - are meaningful buildingblocks of brain function are gaining attention [1–3]. We extracted harmonic modes from the HumanConnectome Project's (HCP) dense functional connectivity (dFC), an average over 812 participants'resting state fMRI dFC matrices. In this case, harmonic modes give rise tofunctional harmonics.Each functional harmonic is a connectivity gradient [4] that is associated with a different spatialfrequency, and thus, functional harmonics provide a frequency-ordered, multi-scale, multi-dimensionaldescription of cortical functional organization.

We propose functional harmonics as an underlying principle of integration and segregation. Figure 1a shows 2 functional harmonics on the cortical surface. In harmonic 11 (ψ11), the two functional regions that correspond to the two hands are on opposite ends of the gradient (different colors on thesurface) and are thus functionally segregated. In contrast, in harmonic 7 (ψ7), the two areas are onthe same end of the gradient, and are thus integrated. This way, functional harmonics explain howtwo brain regions can be both functionally integrated and segregated, depending on the context.

Figure 1a illustrates how specialized areas emerge from the smooth gradients of functional harmonics: the two hand areas occupy well-separated regions of the space spanned by ψ7and ψ11. Thus, functional harmonics unify two perspectives, a view where the brain is organized in discrete modules,and one in which function varies gradually [4].

The borders drawn on the cortex correspond to functional areas in the HCP's multimodal parcellation [5]. In this example, the isolines of the gradients of the functional harmonics follow the borders. We quantified how well, in general, the first 11 functional harmonics follow the borders of corticalareas by comparing the variability of the functional harmonics within and between the areas given by the HCP parcellation; i.e. we computed the silhouette value (SH), averaged over all 360 cortical areas. The SH lies between 0 and 1, where 1 means perfect correspondence between isolines and parcels. We found average SHs between 0.65 (ψ10) and 0.85 (ψ1), indicating a very good correspondence. Thus, functional harmonics capture the "modular perspective" of brain function.

On the other hand, several functional harmonics are found to capture topographic maps and thus, gradually varying function. One important example is retinotopic organization of the visual cortex. Figure 1b shows functional harmonic 8 (ψ8) as an example in which both angular and eccentricity gradients are present [6]. Topographic organization is also found in the somatosensory/motor cor-tex, known as somatotopy. This is shown in Figure 1a, where several somatotopic body areas are reproduced.

Taken together, our results show that functional specialization, topographic maps, and the multi-scale, multi-dimensional nature of functional networks are captured by functional harmonics, thereby connecting these empirical observations to the general mathematical framework of harmonic eigenmodes.

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6:20pm – 6:40pm

O **O14: Reconciling emergences: An information-theoretic approach to identify causal emergence in multivariate data**

Crowdcast (link TBA)

Speakers: Pedro Mediano

Pedro Mediano, **Fernando Rosas**, **Henrik Jensen**, **Anil Seth**, **Adam Barrett**, **Robin Carhart-Harris**, **Daniel Bor**

The broad concept of emergence is instrumental in various key open scientific questions – yet, few quantitative theories of what constitutes emergent phenomena have been proposed. We introduce a formal theory of causal emergence in multivariate systems, which studies the relationship between the dynamics of parts of a system and macroscopic features of interest. Our theory provides a quantitative definition of downward causation, and introduces a complementary modality of emergent behaviour, which we refer to as causal decoupling. Moreover, we provide criteria that can be efficiently calculated in large systems, making the theory applicable in a range of practical scenarios. We illustrate our framework in a number of case studies, including Conway's Game of Life and ECoG data from macaques during a reaching task, which suggest that the neural representation of motor behaviour may be causally decoupled from cortical activity.