## SCINDU: Systems & Computational Neuroscience Down Under

## Wednesday 13th-Friday 15th December, 2017

Queensland Brain Institute, The University of Queensland, Brisbane, Australia

A joint meeting with the 10th Australasian Workshop on Neuro-Engineering and Computational Neuroscience, and the 2017 QBI Plasticity Workshop





Australian Research Council Centre of Excellence for Integrative Brain Function

#### **Conference Program**

Time	Wednesday 13th	Thursday 14th	Friday 15th
0.00			
9.00 9.30 10.00	Tutorials Kwabena Boahen (3hr).	Cortex Chair: Rodrigo Suárez 9:00 Rafael Yuste 9:45 John Bekkers 10:15 Yifan Gu	Plasticity and learning Chair: Patricio Opazo Olavarria 9:00 Tobias Bonhoeffer 9:45 Adrienne Fairhall
10.30	Level 7 seminar room Alex Pouget (3hr),	Morning tea	Morning tea
11.30 12.00	Building 76, Room 228 Rafael Yuste (3hr), QBI Auditorium	Neuromorphic computing Chair: Martyna Grabowska 11:00 Kwabena Boahen 11:45 Andre Van Schaik 12:15 Mostafa Rahimiazghadi	Cognition Chair: Ilvana Dzafic 11:00 Daphne Bavelier 11:45 Marta Garrido 12:15 James Pang
1.00	Lunch for tutorial	Lunch	Lunch
1.30	registrants	Neural interfaces and more Chair: Pranesh Padmanabhan	Decision making, & neural coding
2.30	Hippocampus & amygdala	<ul><li>1:30 Polina Anikeeva</li><li>2:15 Elizabeth Zavitz</li><li>2:30 James McFadyen</li><li>2:45 Leonie Kirszenblat</li></ul>	Chair: Matt Tang 1:30 Alex Pouget 2:15 Geoff Goodhill 2:45 Gilles Vanwalleghem
3.30	2:30 Rosa Cossart	Afternoon tea	Afternoon tea
4.00	3:15 Pankaj San 3:45 Peter Stratton	Reinforcement & the Basal Ganglia Chair: Helen Gooch	Conference ends
4.30	<b>Poster session I</b>	3:30 Kenji Doya 4:15 Bernard Balleine 4:45 Miriam Matamales	
5.00	Odd humbered posters		
5.30 6.00		<b>Poster session 2</b> Even numbered posters*	*Additional information for poster presenters
6.30	weicome reception		Odd numbered posters may be put up from 1:30pm on Wednesday, and should be removed by Jpm on Thursday
7.00	• • • • • • • • • • • • • • • • • • • •	Conference dinner	Even numbered posters may be put up from 1pm on Thursday.
8.30			

## **Tutorial: Neuromorphic computing**

Kwabena Boahen (QBI Level 7 Seminar Room)

As transistors shrink to nanoscale dimensions, trapped electrons—blocking "lanes" of electron traffic—are making it difficult for digital computers to work. In stark contrast, the brain works fine with single-lane nanoscale devices that are intermittently blocked (ion channels). Conjecturing that it achieves error-tolerance by combining analog dendritic computation with digital axonal communication, neuromorphic engineers (neuromorphs) began emulating dendrites with subthreshold analog circuits and axons with asynchronous digital circuits in the mid-1980s. Three decades in, they achieved a consequential scale with Neurogrid, the first neuromorphic system with billions of synaptic connections. Neuromorphs then tackled the challenge of mapping arbitrary computations onto neuromorphic chips in a manner robust to lanes intermittently—or even permanently—blocked by trapped electrons. Having demonstrated scalability and programmability, they now seek to encode continuous signals with spike trains in a manner that promises more energy-efficient computing than all-analog or all-digital approaches across a five-decade precision range.

## **Tutorial: The probabilistic brain**

Alexandre Pouget (Building 76, Room 228)

Multiple psychophysical experiments have established that humans and animals are capable of performing probabilistic inference, sometimes near optimally. These results indicate that neural circuits can represent variables with probability distributions and can perform probabilistic inference over these distributions. I will review computational models that have explored how neurons might represent theses distributions and how neural computation and dynamics could implement these inference. I will also present some of the experimental evidence in support of these recent theories. One of the most appealing properties of this approach is its generality. While I will focus on multisensory integration and decision making, the very same framework can be used for virtually any of the computation performed by the brain suggesting that probabilistic inference might be a form of canonical computation performed by all neural circuits across all species.

# Tutorial: Imaging and optically manipulating neuronal circuits

#### Rafael Yuste (QBI Level 7 Auditorium)

The neural code that relates the firing of neurons to the generation of behavior and mental states must be implemented by spatiotemporal patterns of activity across neuronal populations. These patterns engage selective groups of neurons, called neuronal ensembles, which are emergent building blocks of neural circuits. I will discuss optical and computational methods, based on two-photon calcium imaging and two-photon optogenetics, to detect, characterize, and manipulate neuronal ensembles in three dimensions. I will review data using these methods in the mammalian cortex that demonstrate the existence of neuronal ensembles in the spontaneous and evoked cortical activity *in vitro* and *in vivo*. Moreover, two-photon optogenetics enable the possibility of artificially imprinting neuronal ensembles into awake, behaving animals and of later recalling those ensembles selectively by stimulating individual cells. These methods could enable deciphering the neural code and also be used to understand the pathophysiology of neurological and mental diseases and design novel therapies.

## Vitamin D deficiency disrupts right-hippocampal structural connectivity: evidence from mouse and human data

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Adult vitamin D (AVD) deficiency reduces hippocampal volume in elderly individuals with memory impairments. AVD deficiency results in white matter abnormalities and impaired neuronal integrity. Moreover, AVD deficiency lowers hippocampal grey matter (GM) volume in schizophrenia. The aim of this study was to compare the structural connectivity in between control and AVD deficiency. We hypothesized that AVD deficiency would reduce hippocampal structural connectivity. We analysed a diffusion MRI dataset of elderly human, previously collected. The human samples were categorised into low serum 25-OHD (n= 25) and high serum 25-OHD (n=29) groups. We also acquired control and AVD-deficient diffusion MRI data of BALB/c mice (n=8/group). Whole-brain human and mouse structural connectomes were generated using probabilistic tractography and differences in the networks were analysed using network-based statistics. In human, connection deficits were observed in 13 regions and the right-hippocampus was found to be central in the disrupted network in AVD deficiency. In mice, connection deficits were detected in 29 regions and the right hippocampus was also disrupted, similar to that observed in human with AVD. Our results indicate a vulnerability in hippocampal connectivity associated with AVD deficiency in mice and humans and that the right-hippocampus was at the central hub of the disrupted network. Our result is consistent with a previous study that reported right hippocampal GM volume reduction in AVD-deficient individuals with schizophrenia. The reduction of hippocampal GM volume could be part of the pathology of schizophrenia and could be associated with the observed disrupted hippocampal structural connectivity.

# On classification of simple and complex cells in primary visual cortex

#### Almasi A<sup>1,2,3</sup>, Cloherty SL<sup>5</sup>, Wong YT<sup>3,6</sup>, Grayden DB<sup>3</sup>, Ibbotson MR<sup>1,2,4</sup>, Meffin H<sup>1,2</sup>

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Cortical cells have traditionally been divided into simple and complex types based on their linear and nonlinear summation properties, respectively. Studies have mainly used oriented slit, spot and grating stimuli to investigate the spatial receptive field properties of such cells. Here, we have studied the spatial receptive fields of cells in the cat primary visual cortex using white Gaussian noise stimuli, which enables an unbiased and artefact-free estimation of the linear and nonlinear visual receptive field filters of the cells. We measured the set of visual spatial features to which a cell exhibits the most sensitivity. We also examined the response profile of the cells as a function of the degree of similarity between the input stimuli and the estimated receptive field filters.

Classically, simple cells have been modelled using a linear filter followed by a one-sided (e.g. rectifying) nonlinearity. Classic complex cells have been best described using quadrature pair filters followed by an even-symmetric (e.g. squaring) nonlinearity, similar to the "energy model". In our experiments, in addition to classical simple (43%) and classical complex cells (6%), we found a large population of cells (51%) that showed mixed properties of the classical simple and complex cells such as partial spatial phase sensitivity. These findings challenge the dogmatic view of a strict division between simple and complex cells.

### TALK THURSDAY I.30PM

# Probing neural function with electronic, optical and magnetic materials

#### Polina Anikeeva

Materials Science and Engineering, Massachusetts Institute of Technology

Mammalian nervous system contains billions of neurons that exchange electrical, chemical and mechanical signals. Our ability to study this complexity is limited by the lack of technologies available for interrogating neural circuits across their diverse signaling modalities without inducing a foreign-body reaction. My talk will describe neural interface strategies pursued in my group aimed at mimicking the materials properties and transduction mechanisms of the nervous system. Specifically, I will discuss (1) Fiber-based probes for multifunctional interfaces with the brain and spinal cord circuits; (2) Magnetic nanotransducers for minimally invasive neural stimulation; and (3) Active scaffolds for neural tissue engineering and interrogation.

Fiber-drawing methods can be applied to create multifunctional polymer-based probes capable of simultaneous electrical, optical, and chemical probing of neural tissues in freely moving subjects. Similar engineering principles enable ultra-flexible miniature fiber-probes with geometries inspired by nerves, which permit simultaneous optical excitation and recording of neural activity in the spinal cord allowing for optical control of lower limb movement. Furthermore, fiber-based fabrication can be extended to design of scaffolds that direct neural growth and activity facilitating repair of damaged nerves.

Molecular mechanisms of action potential firing inspire the development of materials-based strategies for direct manipulation of ion transport across neuronal membranes. For example, hysteretic heat dissipation by magnetic nanomaterials can be used to remotely trigger activity of neurons expressing heat-sensitive ion channels. Since the alternating magnetic fields in the low radiofrequency range interact minimally with the biological tissues, the magnetic nanoparticles injected into the brain can act as transducers of wireless magnetothermal deep brain stimulation. Similarly, local hysteretic heating allows magnetic nanoparticles to disrupt protein aggregates associated with neurodegenerative disorders.

## A curious robot that learns spatio-temporal features

#### Joshua Arnold and Janet Wiles

University of Queensland

An artificial agent acting or sensing in the real world must have a system capable of encoding time and its actions together either implicitly or explicitly. Often, time is implicit within a model and overlooked for the complications it adds to a task. This is the case in many neural models which discretise time into uniform steps at which to sample the world. Recently, there has been a surge of interest in neuromorphic sensors which asynchronously sample the world like the biological sensors of mammals. This has facilitated a paradigm shift where time directly influences computation. This work will analyse the prediction performance of neural networks with different data representations that make temporal information explicit. The representations and models will then be validated in a real world task of a 'curious' robot that actively explores phenomena that it can only partially predict in an attempt to improve its model. Results will demonstrate the performance possible with explicit temporal representations and show they can be functional in real world tasks.

### POSTER NUMBER 4

## Spontaneous activity in the developing zebrafish tectum

## Lilach Avitan<sup>1</sup>, Zac Pujic<sup>1</sup>, Jan Mölter<sup>1,2</sup>, Biao Sun<sup>1</sup>, Matthew Van De Poll<sup>1</sup>, Haotian Teng<sup>1</sup>, Rumelo Amor<sup>1</sup>, Ethan K Scott<sup>1,3</sup> and Geoffrey J Goodhill<sup>1,2</sup>

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Spontaneous patterns of activity in the developing visual system may play an important role in shaping the brain for function. During the period 4–9 dpf (days post-fertilization), larval zebrafish learn to hunt prey, a behavior that is critically dependent on the optic tectum. The transparency of the larval zebrafish gives us the opportunity to examine how spontaneous activity is evolving during this time. We therefore performed two-photon calcium imaging of GCaMP6s zebrafish larvae at all days from 4 to 9 dpf. Similarly to the analysis of resting state fMRI data, we applied graph theoretic techniques to investigate how functional connectivity and neural assembly statistics change over this period. This allowed us to identify days 5–6 as a critical moment in the reorganization of the underlying functional network. We then asked whether the development of this network was purely intrinsically driven, or could be altered by visual experience. Enucleation, dark rearing and featureless rearing all changed the structure of the functional network in the tectum. Furthermore, dark rearing caused a profound and long-lasting behavioural change in the ability of larvae to capture Paramecia. Thus, tectal development is shaped by both intrinsic factors and visual experience.

## In vivo single molecule imaging of SyntaxinIA in motor nerve terminals

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Syntaxin IA is a key protein involved in mediating synaptic transmission through its ability to form the SNARE complex with cognate partners – SNAP-25 and VAMP2. Syntaxin I A molecules on the plasma membrane of neuro-secretory cells are organized in nano-clusters, which have been shown to play an important role in docking and priming of secretory vesicles. How individual molecules of Syntaxin I A enter and exit these nano-clusters by lateral diffusion and how stimulation affects their dynamic equilibrium at the pre-synapse in vivo in unknown. To image single molecules of Syntaxin I A in live synapses, we generated a Drosophila line constitutively expressing photo-convertible fluorescently tagged Syntaxin I A (SxIA-mEos2) to carry out single particle tracking Photoactivated Localization Microscopy on live Drosophila larva neuromuscular junction. We investigated the change in Syntaxin I A mobility and nano-domain organisation elicited by increased pre-synaptic activity using both opto-genetic and thermo-genetic tools. Here, we show that in Drosophila larva motor nerve terminals, the overall mobility of Syntaxin I A molecules was low and raising synaptic activity led to an increase in Syntaxin I A mobility. This suggested that a significant proportion of Syntaxin I A molecules are pre-engaged in the SNARE complex, which confer such relatively low mobility. Indeed, concomitant expression of tetanus toxin light chain, which prevents SNARE complex assembly, significantly increased Syntaxin I A mobility. Preventing SNARE complex dissociation using the temperature sensitive NSF mutation decreased Syntaxin IA mobility. Further interfering with Syntaxin IA interaction with polyphosphoinositides increased Syntaxin I A and blocked the activity-dependent change in mobility. Our results suggest that the relative immobility of Syntaxin IA molecules within synapses is indicative of a high level of primed vesicles in live motor nerve terminals.

## A model of cortical learning inspired by machine learning for functionality, but constrained by neurobiological plausibility

#### Samya Bagchi and Mark D. McDonnell

Computational Learning Systems Laboratory, School of Information Technology and Mathematical Sciences, University of South Australia

An open challenge for computational neuroscience is to identify whether the spectacular success of deep-learning can offer insights for realistic models of neurobiological learning that are constrained by known anatomy and physiology. A big step towards achieving this will follow by validating proposed neurobiological learning rules using challenging real data sets like those used in deep-learning and ensuring their learning capability is comparable to that of deep ANNs.

Motivated by this goal, we show mathematically how a standard loss-function used for supervised training of artificial neural networks can be decomposed into an unsupervised stage that learns to decorrelate and a supervised Hebbian-like stage that learns to associate decorrelated activations with categories. We demonstrate results comparable with the state of the art deep-learning algorithms applied to well-known benchmark datasets. Based on this method, we propose a conceptual model of recurrently-connected layer 2/3 and layer 4 cortical neurons that can instantiate these two stages. The online learning model includes, as essential components: nonlinear dendritic activation; anti-Hebbian plasticity at synapses on distal dendrites receiving lateral input from other principal cells; top-down modulation during learning; lateral inhibition enforcing winner-take-all effects to determine inference; and particular subsets of synapses with random weights.

## TALK THURSDAY 4.15PM

## **Cortico-striatal circuits controlling goal-directed** action

#### **Bernard Balleine**

Decision Neuroscience Lab School of Psychology UNSW

Decision-making reflects our ability to extract and encode specific action-outcome relationships from the environment and to integrate those relationships with outcome values to choose between alternative courses of action. The fronto-striatal pathway has long been known to play an important role in this process, and changes in this pathway have been linked to the cognitive symptoms associated with various forms of psychiatric disorder, neurodegenerative conditions and addiction. Recent research in animal models has established this pathway's essential role in striatal plasticity induced by the acquisition of new actions; damage to this pathway renders actions less deliberated and more impulsive or habitual. By examining pathway specific activity, we have found direct evidence that this pathway mediates the acquisition and consolidation of goal-directed actions. Furthermore, using a variety of procedures to disconnect aspects of this pathway, we have found that the contralateral projection is essential to normal goal-directed learning, the consolidation of which in the striatum is driven by the prelimbic cortex. We hypothesize as to the nature of this corticostriatal integration, the learning rules governing striatal plasticity and the feedback processes that modulate this form of learning.

## Evidence against the detectability of a hippocampal place code using functional magnetic resonance imaging

#### Oliver Baumann, Christopher Nolan, Joyce Vromen & Allen Cheung

Queensland Brain Institute, The University of Queensland

Electrophysiological recordings in humans and rodents have shown that neurons in the hippocampus selectively increase their firing rates when the animal traverses specific regions of the environment, thereby establishing a neural code of that environment. This neural code is demonstrably sparse and distributed, theoretically rendering such a code as undetectable with population recording methods such as functional magnetic resonance imaging. Despite these theoretical considerations, several recent studies have reported decoding of place related signals from the human hippocampus using fMRI. We identified several task-related confounds and statistical shortcomings in these existing fMRI studies, calling into question the validity of their findings. To resolve these concerns, the present study reinvestigated the detectability of purely spatial hippocampal place codes via fMRI. We tested 18 participants and employed a virtual environment that eliminated visual and path related confounds to ensure that any positive findings of the signal decoding analysis would be indicative of a pure spatial code rather than a view code or a conjunctive view-trajectory code. We also employed a wide-range of signal processing and classification approaches, as well as a positive control condition to evaluate carefully the possibility of the nonexistence of a purely spatial voxel- place code. Our experiment showed that, while participants were fully orientated during the navigation task, there was no statistical evidence for a place code. Taken together with electrophysiological data on the nature of place cells, our results suggest that the claim of place codes at the level of large neuronal populations from fMRI studies is incorrect.

## TALK FRIDAY IIAM

## Learning to learn: lessons from action video games

#### Daphne Bavelier

A vexing issue in the field of learning is that, while we understand how to promote superior performance through practice, the resulting behavioral enhancement rarely extends beyond the practiced task. Such learning specificity is a major limitation for effective interventions, whether educational or clinical ones. Here we will consider first what may be the inter-inidvidual determinants of learning to learn, or the ability to gracefully adapt to new tasks; we will then consider lessons from action video game play as to how one can train learning to learn for the better.

### TALK THURSDAY 9.45AM

## Spontaneous spiking in the olfactory cortex

#### John M. Bekkers & Malinda L. S. Tantirigama

Eccles Institute of Neuroscience, John Curtin School of Medical Research, The Australian National University, Canberra, ACT 2601

Olfactory circuits are spontaneously active in the absence of odours, raising the question: is this stimulus-decoupled activity merely inconvenient "noise", or does it serve a useful computational function? Here we show that spontaneous electrical activity in the primary olfactory (piriform) cortex plays two important roles, thereby enriching the cortical coding of olfactory information. In a first series of experiments using *in vivo* 2-photon calcium imaging, we found that principal cells in the piriform cortex (PC) of mice exhibited spontaneous spiking that was entirely driven by bottom-up spontaneous input from the olfactory bulb. Odour stimulation produced two types of odour-distinctive patterns of responses in PC cells: some cells were further excited by the odour, whereas others had their spontaneous activity suppressed. Thus, by allowing for bidirectional changes in activity around an elevated baseline, spontaneous "noise" extends the dynamic range for odour coding in the PC. In a second series of experiments, we found that the dendrites of PC principal cells in vivo support backpropagating action potentials (bAPs), whereas such bAPs are absent in vitro. The occurrence of bAPs in vivo required spontaneous drive from the olfactory bulb as well as functional NMDA receptors. Our results suggest that the ongoing depolarization provided by spontaneous activity (which is absent in vitro) enables bAPs to occur in vivo. We speculate that bAPs are required for olfactory learning. In summary, spontaneous spiking in the PC appears to be critical for the encoding and learning of odour information.

# Organization of a reverberating cell assembly in the basolateral amygdala

#### Madhusoothanan Bhagavathi Perumal, Pankaj Sah

Queensland Brain Institute, Brisbane

Synchronized activity of neurons in specific time-windows generate network oscillations, and hypothesised to perform many functions such as memory consolidation. Hebb's cell assembly hypothesis is one of the important conceptual framework to correlate network oscillations and memory. Hebb postulated recurrently connected neurons generate synchronized activity within specific time-windows by 'reverberation' to form functional networks called a cell assembly. However, what types of neurons, circuits, and synapses are present in a cell assembly are not known. We investigated cell assembly like networks in the basolateral amygdala (BLA), a key structure for emotional learning and memory. In our preparation, BLA circuits spontaneously generated SW oscillations (SWs), a distinct network activity associated with memory consolidation processes. A single action potential in a single Chandelier neuron (Chn) - a unique subset of interneurons, initiated BLA SWs. The Chn evoked SWs occurred as reverberating multi-synaptic episodes with consistent temporal dynamics activating feedforward and feedback glutamatergic and GABAergic circuits. We suggest a novel circuit model for a Hebb's reverberating cell assembly to generate SWs in the BLA.

### POSTER NUMBER 9

## Control of neurite growth and guidance by an inhibitory cell-body signal

#### B.A. Bicknell<sup>1,2</sup>, Z. Pujic<sup>1</sup>, P. Dayan<sup>3</sup>, G. J. Goodhill<sup>1,2</sup>

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Building the brain during development requires the orderly wiring of billions of cells. An important mechanism that mediates this is the regulation of neurite growth and guidance by secreted chemical cues. A canonical example is the finely tuned developmental control of sensory and sympathetic neurons by nerve growth factor (NGF). Although well studied, critical biophysical details of the effects of NGF remain elusive, and a systems-level understanding of neurite growth and guidance is lacking. Here, through computational modelling of neurite extension, we show how integration of an inhibitory cell-body signal with an activating signal at the neurite tip can account for multiple unexplained features of NGF regulation. The model consists of two general signalling motifs, which are constrained by experimental data on the response of dorsal root ganglia explants to a wide range of NGF concentration conditions. The first motif accounts for the commonly observed suppression of growth by high NGF concentrations, and the second provides a mechanism that explains the remarkable sensitivity of neurite outgrowth to very shallow NGF gradients. Coupling these motifs together by production and transport of signalling components gives a unified and quantitative description of experimentally observed behaviour. The model makes testable predictions about unknown details of signalling by NGF and other growth and guidance cues, with implications for understanding brain development and repair after injury.

## A novel marsupial model to investigate patterned neuronal activity in the developing neocortex *in vivo*

Tobias Bluett<sup>1</sup>, Lilach Avitan<sup>1</sup>, Annalisa Paolino<sup>1</sup>, Laura R. Fenlon<sup>1</sup>, Geoffrey J. Goodhill<sup>1,2</sup>, Rodrigo Suárez<sup>1</sup>,\* & Linda J. Richards<sup>1,3</sup>,\*

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In the embryonic and early postnatal brain of rodents, spontaneously generated neuronal activity plays key neurodevelopmental roles in the formation and refinement of cortical circuits. Interestingly, the precise patterns of such early neuronal activity are critical for appropriate neurodevelopment to occur, and subtle changes in such patterns can result in significant neuroanatomical changes later in development. In the early postnatal neocortex, neuronal activity is characterised by transient patterns of depolarisation that engage spatially distinct regions, resembling stereotyped cortical architectures, in age- and area- dependent fashions. However, as spontaneous activity begins prenatally, inside the uterus, efforts to fully characterise its development in vivo have been hindered by a lack of experimental paradigms to measure neuronal activity in the embryonic brain. To overcome this, we performed 2-photon microscopy in developing joeys of the Australian marsupial fat-tailed dunnart (Sminthopsis crassicaudata). We overexpressed the genetically encoded calcium indicator, GCaMP6s, via in-pouch electoporation and imaged the dunnart neocortex in vivo at developmental stages equivalent to intra-uterine rodents and humans. Whereas similar approaches are unfeasible in mice, our method was comparatively non-invasive, owing to the extra-uterine cortical development and highly transparent skull of dunnart joeys. Here, we describe at least four distinct classes of large-scale neuronal activity in the developing neocortex, including: a) asynchronous bursts, b) synchronous bursts, c) travelling waves and d) long-lasting events. To our knowledge, this presents the first in vivo characterisation of patterns of neuronal activity in the mammalian neocortex at developmental stages equivalent to embryonic placental mammals. We anticipate this will open the way for future investigations into the developmental role of spontaneous neuronal activity, the molecular mechanisms of its onset and propagation, and allow for in vivo assays of calcium activity under genetic manipulations, which will deepen our overall understanding of brain development and function.

## TALK THURSDAY IIAM

## **The Neuromorphics Project**

#### Kwabena Boahen

The Neuromorphics Project, a collaboration between Yale, Waterloo and Stanford that started in April 2013, has two major aims: (i) Build the first neuromorphic chip (Brainstorm) designed to perform arbitrary computations with networks of spiking neurons. (ii) Given a functional specification of the desired computation, write a synthesis tool (Neuromorph) that configures the chip automatically. In brief, the neurons' measured heterogeneous input-output functions serve as physical computational primitives. Computations are mapped onto this substrate by using Eliasmith & Anderson's Neural Engineering Framework to assign encoding and decoding vectors to the neurons, grouped into functional units called ensembles. Encoding vectors define how a vector of continuous signals is encoded in an ensemble's spiking activity. Decoding vectors define how a static or dynamic mathematical transformation of this vector is decoded from an ensemble's spiking activity. This transformation may be performed in a single step by combining decoding and encoding vectors to obtain synaptic weights that connect one ensemble directly to another (two-layer core) or back to itself (for a dynamic transformation). We eschew this two-layer core design, which consumes resources quadratic in the number of neurons per ensemble. Instead, we designed a three-layer core, with first-to-second and second-to-third layer weights defined by decoding and encoding vectors, respectively. This novel architecture cuts memory, computation, and communication resources by an order-of-magnitude. Preliminary measurements from a test-chip with a 4,096-neuron core (Braindrop) fabricated in a 28 nm mixed-signal FDSOI process will be presented.

### TALK FRIDAY 9.00AM

## How experience changes synapses in the mammalian brain

#### **Tobias Bonhoeffer**

Max-Planck-Institute of Neurobiology, 82152 Munich-Martinsried, GERMANY

One of the most fundamental properties of the brain is its ability to adapt rapidly to environmental changes. This is achieved mainly by changes in the connectivity between individual nerve cells. We have, over the years, investigated many different aspects of the underlying mechanisms, in particular morphological changes that occur alongside with the process of strengthening and weakening of individual synapses. The discovery – obtained *in vitro* – that such changes occur on the level of dendritic spines has been an important one but it is equally important to investigate whether such changes also occur in the intact brain during synaptic plasticity and learning. We have therefore used new imaging methods to investigate the effects of sensory experience on synaptic changes in cortical circuits. In particular, *in vivo* two-photon microscopy has enabled us to study morphological as well as functional plasticity at the level of individual neurons in the neocortex of anesthetized and lately also behaving animals. These experiments are now closing the gap between traditional cellular and systems studies, and they will enable us to obtain a much more comprehensive understanding of the phenomenon of synaptic plasticity and its role in cortical function and ultimately behaviour.

### Extra-synaptic GABAa-mediated tonic inhibition modulates response properties of detailed cortical interneuron models

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Extrasynaptic GABAa-mediated 'tonic' inhibition (TI) has an important influence on cortical activity and is implicated in disease states such as epilepsy [1]. We investigated the impact of TI on response properties of cortical interneurons. To do this we optimised biophysically-detailed neuron models to reproduce electrophysiological features obtained from patch clamp data using the Blue Brain Project model fitting pipeline [2,3]. Each model was optimised to fit spiking behaviour of one of four electrophysiologic classes: continuous non-accommodating (cNAC or 'fast spiking'), continuous accommodating, burst non-accommodating or burst accommodating [4]. TI was modelled as an outward rectifying current with conductance bounds based on previous experimental results [5].

In response to somatic constant-current input TI had minimal effect on the slope (gain) of the current-frequency relationship in cNAC models. Surprisingly, large increases in gain were observed within a subset of bursting and accommodating models. Increased gain was dependent upon the presence of TI within the dendritic compartment but independent of GABA reversal potential. Similar changes in gain were observed when models were stimulated with random Poisson-distributed synaptic input.

Analysis of component currents revealed that dendritic TI enhanced depolarisation during the early interspike interval in all models due to reductions of (outward) axonal and somatic potassium current. During spiking, TI hyperpolarised the dendrites and increased outward axial current from the soma, thereby reducing action potential height/width and potassium channel activation.

These results suggest that TI may influence the activity of cortical interneurons differently, depending on their intrinsic electrophysiologic properties, and warrant experimental verification. They also suggest a novel mechanism by which reductions in dendritic excitability may modulate neuron response properties.

#### References

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### POSTER NUMBER 12

## The role of nuclear factor one (NFI) genes in cortical radial glia, developmental disorders and brain cancer

#### J. Bunt<sup>1</sup>, J.W.C. Lim<sup>1</sup>, K-S. Chen<sup>1</sup>, S. Boogert<sup>1</sup>, Z. Liu<sup>1</sup>, L.J. Richards<sup>1,2</sup>

The University of Queensland, QLD 4072, Australia. I Queensland Brain Institute 2 School of Biomedical Sciences

During normal development, radial glial cells are the progenitors producing both neurons and glia that will form the complex structure of mammalian cortex. Transcription factors, such as the Nuclear Factor I (NFI) family, ensure that this highly complex process is tightly controlled. Loss of NFI protein have been associated with human congenital disorders characterized by intellectual disability and structural cortical abnormalities, as well as paediatric brain tumours.

We are investigating how NFI proteins are regulating the development of the cortex using mouse models with cortical-specific knockout of *Nfi*. We found that disruption of NFI proteins in the cortex only resulted in megalencephaly, but not agenesis of the corpus callosum in these mice. This enlargement of the cortex was caused by a defect in radial glial differentiation during early development. In knockout mice, the switch from proliferative to differentiative cell divisions was delayed. Hence, the radial glial populations expanded and subsequently produced more neurons and adult glia. When multiple *Nfi* family members were deleted, more radial glial progenitors were retained, which resulted in the formations of neoplastic tissue. Together, our study shows that NFI protein levels are essential for the regulating balance between radial glial differentiation. Disruption of this balance cortical overgrowth.

## Computing by modulating spontaneous activity patterns: A mechanism of active cortical processing

#### Guozhang Chen and Pulin Gong

School of Physics, University of Sydney, NSW 2006, Australia

It has been widely observed that cortical populations produce complex spatiotemporal activity patterns spontaneously without sensory input. The functional roles of such spontaneous activity patterns in cortical computation, however, remain unclear. In this study, we first demonstrate that spatiotemporal patterns with criticality emerging from a spatially-extended neural circuit model can capture salient features of spontaneous cortical dynamics, and that these patterns can be modulated by natural stimuli such as faces. We then illustrate that the modulating process provides a mechanistic explanation for a range of experimental observations, including the similarity between spontaneous and evoked patterns, and the variability of response latency and firing rates. In addition, we show that the modulating process can be formulated as a process of Bayesian inference, in which the dynamical spontaneous patterns sample target probability distributions to speed up network responses. Our results thus suggest that spontaneous activity is essential for understanding the mechanism of active cortical processing.

## The role of transcription factor NFIB in glioblastoma

#### K.S. Chen<sup>1</sup>, L.J. Richards<sup>1,2</sup>, J. Bunt<sup>1</sup>

The University of Queensland, QLD 4072, Australia I Queensland Brain Institute 2 School of Biomedical Sciences

Glioblastoma (GBM) is the most aggressive brain tumor with poor survival. GBM tumors could originate from cells of the glial lineage that have escaped the normal glial differentiation mechanisms. Therefore, we propose that by reactivating the normal glial differentiation program in proliferative tumor cells, we could stop the tumour growth. We have identified the Nuclear factor I B (NFIB) transcription factor as an important regulator of glial differentiation. During normal prenatal development, Nfib is expressed within neural progenitor cells that give rise to glial and neuronal cell populations throughout the brain. However, disruption of NFIB in knockout mouse model results in reduced and delayed differentiation of glial cells, causing a retention of proliferative progenitor cells. NFIB has also been implicated as tumor suppressor in insertional mutagenesis mouse models aimed at identifying genes involved in brain tumor initiation. Furthermore, loss of NFIB is common in human astrocytoma. To determine whether loss of *Nfib* contributes to tumor initiation and progression, we have crossed inducible glioma mice with conditional Nfib deletion mice to follow tumor initiation and progression using fluorescence imaging and immunohistochemistry. Using immunofluorescence, we determined that NFIB is mainly expressed within the non-proliferative and differentiated cells in primary GBM tissues. To establish whether NFIB expression can inhibit tumor proliferation and induce differentiation, we induced NFIB expression via in vivo electroporation in patient-derived GBM xenografts in mice. Our data suggests that NFIB-mediated glial differentiation can be induced in GBM to inhibit tumor growth and may prevent recurrence.

## TALK WEDNESDAY 2.30PM

## Shaping the functional structure of the hippocampus

#### Rosa Cossart

The hippocampus forms discrete and ordered representations of locations and events in the context in which they occur. We study the functional structure of the hippocampus. Hippocampal dynamics result from the interaction between self-organized internal dynamics (internal mode) and various external inputs from the environment and context. To describe structure-function relationships in hippocampal networks, we have developed an approach that combines *in vivo* calcium imaging, electrophysiology, neuroanatomy, mathematics, modeling and behaviour. We have recently uncovered the spatial organization and lifetime of the basic hippocampal functional units (assemblies) in CA1 in the internal mode (Malvache *et al; Science* 2016). Such assemblies represent default building blocks that can be reused and combined into sequences of neuronal activation to encode or retrieve information about traveled distance or elapsed time (Villette *et al. Neuron* 2015). Here, combining data analysis of long-term hippocampal dynamics across days and network modeling, I will show how the same circuit can integrate and/or alternate information about traveled distance and elapsed time and provide a candidate mechanism by which such switch could occur. Such stability of internal dynamics suggests a possible scaffolding during development, an hypothesis we are currently testing. Last, I will present data indicating how external cues influence this stable internal organization to support spatial cognition.

## Correlated tuning within superficial amygdaloid nuclei and olfactory tubercle

#### Cousens<sup>1</sup>, GA, Savage<sup>2</sup>, V, & Moutenot<sup>1</sup>, K

I Drew University, Department of Psychology and Neuroscience Program 2 Department of Neuroscience, Tufts University

Diffuse patterns of divergent and convergent projections from main olfactory bulb mitral and tufted cells contribute to an apparent lack of spatial topography in piriform cortex (PC), and evidence suggests that odor-selective responses of PC neurons are sparsely distributed and randomly organized. However, differences in the topography and cellular composition of bulbar projections to other primary olfactory structures, as well as differences in the local circuit organization of these regions, suggests that features of odor representation across the ventral telencephalon may be quite diverse. In particular, the finding that glomerular projections to cortical amygdaloid nuclei are patchy suggests some extent of spatial segregation. Here we examine correlated tuning within superficial amygdaloid nuclei and the olfactory tubercle (OT) using single- and multi-electrode recording techniques in urethane-anesthetized rats. Consistent with published reports, a large proportion of neurons in both areas exhibited odor-selective alterations in firing rate often in phase with ongoing respiration and MOB local field potential oscillations. Cells exhibited a range of tuning breadths to molecularly distinct odorants, including monomolecular odorants and biologically significant pheromones. However, surprisingly, adjacent cells were often similarly tuned. Preliminary evidence shows that interneuronal distance predicts the likelihood of correlated tuning between simultaneously recorded cells, suggesting a functional organization that differs from that of PC. Ongoing work using configurable high-density silicon probes within these areas and PC is examining the extent to which spatial and temporal features of odor-elicited neuronal activity compare directly across regions.

### POSTER NUMBER 16

## Impact of delay on the receptive field size of simple cells resulting from Hebbian learning

#### Catherine E. Davey<sup>1</sup>, David B. Grayden<sup>1</sup>, Anthony Burkitt<sup>1,2</sup>

I Department of Electrical and Electronic Engineering, University of Melbourne, Vic, Australia. 2 Bionic Vision Australia, Vic, Australia.

Synaptic plasticity is one of the neurological processes that supports learning, in which synaptic strength is modified in response to received inputs [1]. Learning begins prior to birth, with most mammals being born with some functionality in the hearing, movement and visual domains. This implies that neural structure is created in the absence of structured input. Linsker [2] proposed a mechanism by which this process may occur. Linsker demonstrated how spatial structure in synaptic connections across multiple layers produces a system in which input noise drives the development of simple cells, such as spatial opponent cells and spatial orientation cells [2,3,4].

Linsker showed that it was the spatial structure of the synaptic connections that triggered evolution of structure in simple cells.

The system described in the Linsker papers employed rate-based neurons with an assumption of no axonal or dendritic delays. While hugely important to our current understanding of neural learning, such models lack biological realism. An action potential emitted by a neuron experiences a propagation delay, primarily determined as a linear function of axonal diameter and distance for myelinated axons. Given the importance of moving images in everyday life, it is essential to develop an understanding of how temporal delays in visual input impact plasticity.

In this work we consider the impact of spatially dependent axonal delay on the evolution of simple cells. Analogous to the spatial distribution of synaptic connections driving network structure, we show that a temporal distribution to propagation delays is an important factor in the evolution of simple cells. More specifically, we analytically determine the impact of temporal delay, determined by velocity, and both inter- and intra-laminar neural connection distance, on the receptive field size of a simple cell. Preliminary results suggest that increasing distance, and hence delay, between neurons reduces covariance between presynaptic neurons, which increases the receptive field size of the resulting simple cell. This result potentially describes one of the mechanisms by which receptive field sizes of cells processing peripheral visual input become comparatively large, thereby reducing visual acuity in the periphery.

#### Acknowledgements

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## Brain white matter structure in individuals with autism spectrum disorder

#### Dean RJ<sup>1</sup>, FenIon LR<sup>1</sup>, Edwards TJ<sup>1</sup>, Richards LJ<sup>1,2</sup>

The University of Queensland, Brisbane, Australia, 4072 I Queensland Brain Institute 2 School of Biomedical Sciences

There is mounting evidence that the symptoms of Autism spectrum disorder (ASD) are related to changes in communication between brain regions, as reflected in alterations to the structure of brain white matter. These changes in white matter integrity are commonly characterised using diffusion-weighted magnetic resonance imaging (dMRI). While significant differences in diffusivity (relative to neurotypical controls) have been reported in ASD, there has been much conjecture about the implication of these results, as they signify non-specific structural changes. Possible explanations for these differences include changes in neural fibre density or diameter, voxel averaging of multiple neural fibre populations, changes in myelination, and motion artefacts.

We hypothesise that dMRI properties can be combined to better discriminate specific structural changes and hence improve our understanding of the structural brain changes underlying ASD. Similar to previous studies, our cohort of twelve, high-functioning individuals with ASD exhibited differences in white matter fractional anisotropy and radial diffusivity relative to a cohort of ten, age and gender matched, neurotypical controls. Motion artefacts were minimal, and were corrected for before deriving the diffusion metrics. Apparent fibre density and white matter tract cross-sectional area remained consistent between the two groups. Consequently, it is probable that a combination of myelination events and meso-level changes in fibre orientation are responsible for the reported differences in white matter tract integrity. To distinguish between these two remaining structural features, fibre tractography will be used to examine differences in whole brain connectivity as well as neural fibre distributions at the voxel level.

#### Funding Acknowledgement

This work was funded by the Brain Injured Children Aftercare Recovery Endeavours (BICARE), Australia.

### TALK THURSDAY 3.30PM

# Neural circuits for reinforcement learning and mental simulation

#### Kenji Doya

Okinawa Institute of Science and Technology Graduate University

In the standard "model-free" reinforcement learning, an agent learns a policy simply through the experiences of state-action-reward sequence. In the "model-based" framework, an agent first learns an internal model of the state transition, state-action-next state, and use that for planning of action sequences to reach a goal or for estimation of the present sate from past state and action despite sensory uncertainty. A large body of study suggests that the basal ganglia play an essential role in model-free reinforcement learning. The neural mechanism of model-based reinforcement learning through mental simulation of imaginary states is less clear and a hot topic of research. We will present recent studies regarding how the brain implements mental simulation and how model-free and model-based mechanisms are selected or combined.

### POSTER NUMBER **18**

## Impaired regularity learning in healthy individuals with psychotic experiences is mediated by reduced top-down frontotemporal effective connectivity

#### Ilvana Dzafic<sup>1</sup>, Roshini Randeniya<sup>1</sup>, Marta I. Garrido<sup>1,2,3,4</sup>

I Queensland Brain Institute, University of Queensland, Brisbane, Australia

2 School of Mathematics and Physics, University of Queensland, Brisbane, Australia

3 Australian Research Council Centre of Excellence for Integrative Brain Function, Australia

4 Centre for Advanced Imaging, University of Queensland, Brisbane, Australia

Sensory perception is facilitated by prior beliefs about forthcoming experiences, which are based on our brain's predictive model about the world and its regularities. However, in our dynamic environment these regularities may suddenly change, leading to environmental 'volatility', which requires us to have a flexible predictive model that is able to update prior beliefs accordingly. Recently, it has been proposed that psychotic traits may result from aberration in the precision of prior beliefs and a resistance to updating prior beliefs. Here, we examine how brain dynamics underlying regularity learning are altered in volatile environments, in a population of healthy individuals with a range of psychotic experiences. We designed a novel paradigm, which incorporated both stable and volatile environments by playing auditory oddball sequences with either fixed or alternating sound probabilities for short and long sounds. We measured the elicited prediction error with electroencephalography; moreover, we gauged regularity learning explicitly, by recording the participants' ability to estimate the probability of sounds. The findings show that during stable conditions there is greater prediction error response and this relates to improved regularity learning (i.e. a stronger predictive model). Critically, with Dynamic Causal Modelling we were able to delineate the mediating role of frontotemporal connectivity in the relationship between regularity learning and psychotic experiences. The findings provide evidence for a continuum of psychosis and have implications for understanding the neurobiological underpinnings of impaired regularity learning, with the potential to inform the application of neuromodulation therapies for psychotic disorders.

### TALK FRIDAY 9.45AM

## Variability and learning in birdsong

#### Adrienne Fairhall

Variation is necessary for ongoing maintenance of motor skills. The zebrafinch song system is an excellent model for motor learning as there is one well-defined behaviour, subserved by a well-delineated neuroanatomical architecture whose components have been approximately mapped to the elements of reinforcement learning. We will discuss potential circuit dynamics by which song variability can be contextually modulated and the implications for learning algorithms.

### POSTER NUMBER 19

### The anatomy, organisation and activitydependent development of contralateral targeting of the mouse somatosensory corpus callosum

#### Laura R. Fenlon<sup>1</sup>, Rodrigo Suárez<sup>1</sup>, Linda J. Richards<sup>1,2</sup>

The University of Queensland, Brisbane, QLD, 4072, Australia

I Queensland Brain Institute

2 The School of Biomedical Sciences

The two cortical hemispheres communicate via the corpus callosum, the largest fibre tract in the brain. However, despite the importance of this structure in mediating communication between the two cortical hemispheres, many aspects of its anatomy, organisation and development remain unclear. A particular aspect of callosal development that is poorly understood is how callosal axons locate and innervate their targets in the contralateral cortex, after crossing the midline. Recently we demonstrated that two major contralateral callosal projections that arise from mouse L2/3 primary somatosensory cortical neurons are differentially affected by manipulations of neuronal activity (Neuron, 2014, 82(6): 1289-1298). However, the precise organisation, sequence of development and temporal dependence upon sensory input that these projections undergo remain unclear. Here, using in utero electroporation in mice, we investigated these questions and found that projections to the contralateral S1/S2 border and insular cortex have distinctive anatomical organisations and arise from separate neuronal populations. By analysing the mean axonal innervation over different developmental stages, we found that these projections enter the cortex in a dorsal-to-ventral and region-specific order. Furthermore, we identify two periods of region- and layer-specific developmental exuberance that correspond to initial callosal axon innervation and subsequent arborisation. Early sensory deprivation affects only the latter of these events. Taken together, this work constitutes the first systematic, quantitative characterisation of the organisation and development of callosal projections from a single cortical area in mouse. These results also provide an experimental model for the investigation of neurodevelopmental disorders of interhemispheric connectivity in the future.

## Rostro-caudal gradient of the dendritic integrative properties of layer 5 pyramidal neurons across the primary visual cortex

#### Lee N. Fletcher and Stephen R. Williams

Queensland Brain Institute, University of Queensland, Australia

The thickness of the neocortex varies over the neocortical mantle, a property that governs the size of the dendritic arbor of cortical neurons. In order to preserve canonical cell-class properties across the neocortex, the electrical architecture of the dendritic arbor must parallel such morphological changes. The conservation of the integrative properties of a defined class of neuron with dendritic size has, however, not been directly explored. Here we use structural magnetic resonance imaging, high-resolution neuronal reconstruction, multi-site somato-dendritic electrophysiological recordings, and computational modelling approaches to demonstrate that the physical size, electrotonic architecture, and mode of dendritic integration of thick-tufted layer 5B pyramidal neurons vary as a gradient across the rostro-caudal axis of the rat primary visual cortex. Our findings reveal that the integrative capacity of layer 5B pyramidal neurons, the major output neuron of the cortex, transforms from multi-compartment, layered computations, to compact axo-somatic integration across the primary visual cortex (V1). The axis of this gradient has important parallels to the retinotopic gradient in V1. These data challenge the view that neocortical neuronal populations carry out canonical computations, instead suggesting the computations performed may be functionally dependent.

## Non-neuronal component removal in fMRI signal using neural field theory and eigenmode analysis

#### Xiao Gao<sup>1,2</sup> and P.A. Robinson<sup>1,2</sup>

I School of Physics, The University of Sydney, Sydney, New South Wales 2006, Australia 2 Center of Excellence for Integrative Brain Function, The University of Sydney, New South Wales 2006, Australia

A method for removal of non-neuronal signal component of functional magnetic resonance imaging (fMRI) BOLD signal is proposed based on neural field theory (NFT) and eigenmode analysis. The global part of the BOLD signal contains artifacts due to motion, heartbeat, and other effects, as well as neural contributions. However, how best to remove artifacts remains an open question and the alternatives of total removal, or no removal, of the global part of BOLD have been debated. Here, the global signal is interpreted as the lowest eigenmode of BOLD. The brain activity that drives BOLD has well understood relationships between the power in the global mode and other modes, quantified by NFT. By fitting NFT results to the power in other modes, the present work extrapolates to estimate how much of the global mode is neural, and the remainder is removed. The proposed method is then tested on NKI-Rockland experimental fMRI data.

### TALK FRIDAY II.45AM

# Connectivity underpinnings of statistical learning in healthy people with psychotic experiences

#### M.I. Garrido

Queensland Brain Institute, University of Queensland, Brisbane, Australia School of Mathematics and Physics, University of Queensland, Brisbane, Australia Australian Research Council Centre of Excellence for Integrative Brain Function, Australia Centre for Advanced Imaging, University of Queensland, Brisbane, Australia

Psychotic experiences such as hallucinations and delusions are exacerbated in people with psychotic disorders but they can also occur, to some extent, in the healthy population. Aberrant brain connectivity and prediction error signaling has been put forward as a possible cause for behavioural dysfunction and poor cognition in schizophrenia. However, it is unknown whether the same processes go awry in healthy people with psychotic experiences, albeit to a lesser extent. In this talk, I will show that increases in psychotic experiences in healthy individuals are associated with: I) anatomical brain connectivity decreases (as measured with Diffusion Weighted Imaging in 89 individuals), 2) compromised statistical learning, 3) reduced prediction error responses (indexed by Electroencephalography in 133 people), and 4) disrupted top-down fronto-temporal connectivity (inferred with Bayesian model selection of Dynamic Causal Models). Finally, I will show that 5) such top-down disruptions are also present in non-psychotic people with a genetic predisposition to schizophrenia (22q11.2 Deletion Syndrome). I will discuss these findings in the light of the continuum of psychosis hypothesis.

### POSTER NUMBER 22

## Adaptive gain modulation maintains the feature selectivity of neurons in primary visual cortex

#### Masoud Ghodrati, Elizabeth Zavitz, Marcello GP Rosa, Nicholas S.C. Price

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Reliably perceiving a dynamic environment requires sensory neurons to accurately code current stimuli, but to also adapt to accommodate changes in the statistics of the input signals. Variations in the statistics of a specific stimulus dimension (such as intensity or speed) affect a neuron's coding efficiency of that same stimulus dimension, but it remains largely unclear how adaptation to one dimension in a multidimensional stimulus space affects the coding of other orthogonal dimensions.

We recorded extracellular neuronal activity in V1 of anaesthetised marmoset monkeys, using a switching stimulus paradigm to systematically study how adaptation to variations in low-order stimulus dimensions affects coding of higher-order properties. Specifically, rapid variations in a high-order stimulus property (orientation) occurred every 16.7 ms, while changes in low-order properties (luminance and contrast) occurred every 5 seconds. We examined how neural information about orientation depended on steady-state luminance and contrast, and the time since luminance or contrast switches.

We found that: (1) the information conveyed by individual neurons about stimulus orientation is significantly luminance and contrast dependent; (2) this information, and the ability to decode orientation using population activity, change during adaptation to a single luminance-contrast condition; (3) these changes in information and discriminability are correlated with changes in firing rate, meaning that information rates are relatively constant; and (4) a model incorporating gain control in which luminance and contrast separately affect feed-forward drive can explain our results.

Our study demonstrates that neural populations in visual cortex adapt their coding strategies under different complex stimulation paradigms.

## Rapid modulation of neuronal L-type voltagegated calcium channels during development by vitamin D

#### Gooch HM, Cui X, Burne T, Eyles D, Anggono V, Sah P, McGrath J

The Queensland Brain Institute, The University of Queensland, St Lucia, QLD 4072

The secosteroid vitamin D [1,25(OH)<sub>2</sub>D<sub>3</sub>] drives genomic changes in the body via classical steroid hormone pathways. While 1,25(OH)<sub>2</sub>D<sub>3</sub> is also known to drive *non-genomic* effects in some peripheral tissues, principally the rapid modulation of L-type voltage-gated calcium channels (L-VGCC), its non-genomic effects within the brain remain unexplored. Since developmental vitamin D deficiency is a risk factor for schizophrenia, and accumulating evidence links common L-VGCC genetic variants with neuropsychiatric disorders, we are investigating the non-genomic effects of  $1,25(OH)_2D_3$  on VGCCs in the developing brain. Using calcium imaging and electrophysiology in acute mouse brain slices, we demonstrate that physiological concentrations of 1,25(OH)<sub>2</sub>D<sub>3</sub> rapidly increased VGCC current amplitudes in a subset of neurons in the PFC, termed vitamin D responsive neurons (VDRNs). Using wide-field calcium fluorescent imaging,  $1,25(OH)_2D_3$  increased cytosolic calcium levels by as much as 250% in VDRN (average  $\Delta F/F$ increase  $49 \pm 4\%$ ; n=11/1245 cells, 8.9%), an effect that was almost entirely blocked by pre-incubation in the L-VGCC antagonist nifedipine (average  $\Delta$ F/F increase 11 ± 1%; n=8/675 cells, 1.2%). Consistent with this, nucleated patch recordings revealed a 1,25(OH)<sub>2</sub>D<sub>3</sub>-induced enhancement of high voltage-activated (HVA) calcium channel currents (33 ± 5%, n=5) in a subset of layer 2/3 PFC cells (n=5/21, 24%). These findings demonstrate that physiologically relevant levels of 1,25(OH)<sub>2</sub>D<sub>3</sub> rapidly modulate L-VGCCs in a subset of PFC neurons during development. Since developmental L-VGCC activity is required for critical processes such as neuronal maturation and gene transcription, these findings suggest significant consequences of vitamin D deficiency for healthy brain development.
### TALK FRIDAY 2.15PM

### Spontaneous activity in the developing brain

#### Geoffrey J Goodhill

Queensland Brain Institute and School of Mathematics & Physics, University of Queensland, St Lucia, QLD 4072, Australia

The developing brain often displays exuberant patterns of spontaneous activity. These patterns frequently take the form of neural assemblies, i.e. groups of neurons which tend to be coactive. However, little is known about how the structure of these assemblies changes over development, or how they are related to neural coding. Using GCaMP6s imaging of the developing zebrafish optic tectum as a model I will discuss how spontaneous activity changes over time, and how this is related to visual experience. This includes identifying algorithms which are able to reliably extract neural assemblies from noisy data. Furthermore I will present a computational model which explains how spontaneous neural assemblies could arise even in the absence of structured input.

### Fluorescent intra-body Localization Microscopy (FiLM): a novel method for tracking single intracellular endogenous and GFP-tagged proteins in vitro and in vivo

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By breaking the Abbe law of diffraction, super-resolution microscopy techniques provide unprecedented detail of biological structures and processes. However, the requirement for fluorescent photoconvertible tags has hampered progress and exposed PALM and sptPALM techniques to over-expression artifacts, raising the need for developing novel tools to bypass these limitations. Herein, we describe the development of single chain expressed in cells as intra-nanobodies to perform single molecule imaging of any GFP-tagged or endogenous intracellular proteins. Configuration 1: Co-expression of a GFP binding nanobody tagged with a photoconvertible mEOS2 to image any GFP-tagged protein in cells. We co-expressed anti GFP-intra-nanobody-mEos with PH-PLC∂-GFP allowed super-resolution imaging of phosphatidylinositol(4,5)bisphosphate nanodomains in fixed and live neurosecretory PC12 cells. We found identical domain size and mobility when using PH-PLC∂-mEos2. We also visualized cell-cell junctions at nanoscale in genetically modified CACO2 cell line expressing GFP tagged E-cadherin at endogenous levels. Expressing the GFP intra-nanobody, within the nematode C. elegans PLM mechanosensory neurons, allowed us to visualize the fusogen protein EFF-1 at nanoscale in vivo. In addition, using zebrafish D. rerio expressing the GFP intra-nanobody, we were able to visualize Caveolin 3 within its muscle fibers. Configuration 2: Purpose-designed intra-nanobodies to probe the nanoscale organization of endogenous proteins. Two specific nanobodies developed against the B2 adrenoreceptor were used to track endogenous receptors. Fluorescent intra-body Localization Microscopy (FiLM), therefore enables GFP-tagged constructs to be localized by super-resolution microscopy for existing in vitro or in vivo models. This technique can also be extended to identify the diffusional signature and nanoscale organization of endogenous proteins by expressing selective purpose-designed intra-nanobodies.

### TALK THURSDAY 10.15AM

# Interrelating the structural connectivity and spatiotemporal dynamics of cortical microcircuits

#### Yifan Gu, Yang Qi and Pulin Gong

School of Physics and the ARC Center of Excellence for Integrative Brain Function, University of Sydney, NSW 2006, Australia

Experimental studies have begun revealing essential properties of the structural connectivity and the spatiotemporal activity patterns of cortical microcircuits. To integrate these properties from connectivity and physiology, and to elucidate the mechanistic links between them, we develop and investigate a cortical microcircuit model that captures a range of realistic features of synaptic connectivity. We show that the model accounts for the emergence of higher-order connectivity structures, including overrepresented three-neuron motifs and highly connected hub neurons that form an interconnected rich club. The microcircuit model exhibits a rich repertoire of activity states, ranging from asynchronous to propagating wave states. We find that around the transition between asynchronous and propagating states, our model quantitatively reproduces a variety of major empirical findings regarding neural spatiotemporal dynamics which otherwise remain disjointed in existing studies. These include diverse correlations between spiking activity of individual neurons and the population, propagating wave patterns with variable speed and precise temporal structures of neural spikes. We further illustrate how these neural dynamics are linked to the connectivity properties by analyzing the contributions of connectivity to neural spiking dynamics and by showing that the rich club connection is fundamentally related to the emergence of the diverse population correlations. Our study thus provides an integrated view of the structural connectivity and neural dynamics for understanding cortical microcircuits.

### Neurons in the binocular zone of mouse visual cortex that receive callosal input are intrinsically less excitable

### Suraj Honnuraiah, Helena Huang, Guilherme Testa-Silva, William Connelly and Greg Stuart

Eccles Institute of Neuroscience, The John Curtin School of Medical Research, The Australian National University, Canberra, Australia.

The binocular region in primary visual cortex (V1) plays a critical role in processing visual inputs from the eyes. Recent work from our lab and by others has demonstrated that binocular inputs in the layer 2/3 of visual cortex are integrated sublinearly. The degree of sublinear integration cannot be explained solely by spatio-temporal organization of excitatory synapse but requires the balanced recruitment of inhibition. Understanding the principles of synaptic integration in binocular visual cortex could provide insight into the generic rules used by cortical circuits during bilateral sensory processing.

In this study, we have combined optogenetics and electrophysiology methods to identify putative binocular and monocular neurons *in vitro* and have characterized their active and passive properties. We have identified two distinct populations of neurons in the binocular visual cortex, one that receives long-range excitatory callosal input from the contralateral visual cortex (putative binocular neurons) and one that does not (putative monocular neurons). While we found no differences in passive properties, the active properties of putative binocular neurons were significantly different from putative monocular neurons. Specifically, the slope of the input/output (f/l) curve generated during somatic current injection was lower in putative binocular neurons, leading to reduced action potential firing. These data suggest that binocular neurons are intrinsically less excitable than monocular neurons. Differences in biophysical properties suggest that binocular neurons might have different cellular integration rules during synaptic integration. In addition, callosal input from the contralateral visual cortex excited a subset of fast-spiking, putative parvalbumin positive (PV) interneurons in binocular visual cortex, activating feed-forward inhibition that could drive excitatory neurons in a sublinear regime.

In conclusion, we provide evidence that distinct populations of both excitatory and inhibitory neurons are involved in processing binocular visual input in binocular visual cortex. Furthermore, we show that these different neuronal populations have different active properties. We propose that these findings could provide insight into the generic cellular and circuit integration principles used by the cortex to process input from bilateral sensory organs such as the eyes.

# Rationale and methods for a novel operant task to test executive function in the rat

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Cognitive deficits, particularly executive deficits, are key drivers of adverse functional outcomes in neuropsychiatric disorders. However, they remain currently unresolved by pharmacological and behavioural intervention. While several models have been developed to assess executive functioning, most are non-automated and labour intensive. Thus, this study aims to develop an automated operant task in rodents that mimics the human intra-/extra-dimensional (ID/ED) task to look at the neurobiological components of executive function. Two dissociable components of executive function will be measured in this task: reversal learning and set-shifting within the same dimension or between different dimensions. During this task, rats will be trained during  $\sim$ 5 daily sessions and then tested over  $\sim$ 10 daily sessions. The main outcome variables are intra-dimensional and extra-dimensional set-shifting and reversal learning ability. This task aims to provide the possibility to test the effects of various neural, pharmacological and behavioural manipulations on discrete measures of executive function, including accuracy, perseverative responses and response latencies. The neural circuits underlying behaviour during reversal learning and set-shifting are highly conserved across humans, nonhuman primates and rodents. Thus, this operant task aims to provide face, construct and predictive validity for executive deficits present in neuropsychiatric disorders. It aims to address limitations of existing tasks by reducing extensive training periods and omission rates, and controlling body position by using central nose poke to self-initiate a trial. This task has the potential to be used by a variety of fields to assess cognitive phenotypes and specific differences in animal models relevant to neuropsychiatric disorders.

### **Duffing Neural Mass Model**

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A mesoscopic model of a cortical column, known as a Duffing Neural Mass Model (DNMM), is developed to emulate stochastic mechanisms of initiation and termination of seizures in intracranial electroencephalogram (iEEG) recordings. The DNMM is constructed by applying perturbations to linear models of synaptic transmission in the Jansen and Rit neural mass model. Random input (noise) can cause switches between normal activity and pathological activity similar to seizures in the DNMM. A bifurcation analysis and simulations are performed to provide insights into the behaviour of the model. To replicate the pathological dynamics of ion currents, the model is extended to a slow-fast DNMM by considering a slow dynamics model (relative to the membrane potentials and firing rates) for some internal model parameters. The slow-fast DNMM can replicate initiation and termination of seizures that are caused by both random input fluctuations and pathological dynamics. The patient-specific model most likely to capture the underlying dynamics of recorded iEEG is sought through estimation of a likelihood function using a continuous-discrete unscented Kalman filter.

This research was supported by the Australian Research Council (Linkage Project LP100200571)

### The role of non-linear adaptation in an insectinspired target detection model

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Previous research has demonstrated the effectiveness of a target detection and tracking model inspired by small target motion detecting neurons in the insect visual system. The model incorporates a fast, non-linear adaptation mechanism which separately adapts to increments or decrements in luminance, reflecting observations of neuronal responses in the insect brain. Despite its inclusion in the model, the role that this mechanism plays in target detection was not understood. It had been hypothesised that the mechanism may assist in removing noise caused by cluttered backgrounds. We investigated this by assessing the effectiveness of our model in detecting targets moving against simulated natural scenery. We used a gradient ascent optimisation algorithm to find values for the mechanism's parameters which result in the best performance. Using those parameters, the effect of the presence or absence of the adaptation mechanism was evaluated. We identified components of the adaptation mechanism that enhanced detection performance in the presence of background clutter. This provides greater understanding of how non-linear interactions are used in biological processing to enhance signals and suppress noise.

# Evidence for newly generated interneurons in the basolateral amygdala of adult mice

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New neurons are continually generated from the resident populations of precursor cells in selective niches of the adult mammalian brain, but whether such cells are present in the adult amygdala is not known. Using the neurosphere assay, we demonstrate that a small number of precursor cells, the majority of which express Achaete-scute complex homolog I (AscII), are present in the basolateral amygdala (BLA) of the adult mouse. Using neuron-specific Thy I-YFP transgenic mice, we show that YFP+ cells in BLA-derived neurospheres have a neuronal morphology, co-express the neuronal marker ßIII-tubulin, and generate action potentials, confirming their neuronal phenotype. In vivo, we demonstrate the presence of newly generated BrdU-labeled cells in the adult BLA, and show that a proportion of these cells co-express the immature neuronal marker doublecortin (DCX). Furthermore, we reveal that a significant proportion of GFP+ neurons (~23%) in the BLA are newly generated (BrdU+) in DCX-GFP mice, and using whole-cell recordings in acute slices we demonstrate that the GFP+ cells display electrophysiological properties that are characteristic of interneurons. Using retrovirus-GFP labelling as well as the AscII CreERT2 mouse line, we further confirm that the precursor cells within the BLA give rise to mature and functional interneurons that persist in the BLA for at least 8 weeks after their birth. These results demonstrate that neurogenic precursor cells are present in the adult BLA, and generate functional interneurons.

### VAMP2 controls the exit of Munc18-1 from nanocluster confinement of following SNARE complex assembly

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Munc 18-1 is a key regulatory protein essential for docking and priming of secretory vesicles at the plasma membrane through its involvement in SNARE complex assembly. Using super resolution techniques our lab has previously demonstrated that Munc18-1 domain 3a hinge-loop controls (1) syntaxin-1A opening, (2) its ensued engagement into SNARE complex and Munc18-1 release from the confinement of plasma membrane nanoclusters (Kasula et al., 2016). The release of Munc18-1 from syntaxin-1A could define a specific set of "ready for fusion" nanoclusters of open syntaxin-IA as previously envisaged (Sieber et al., 2007). Alternatively, Munc I 8-1 could directly trigger SNARE complex formation via opening of syntaxin-IA within the context of vesicular SNARE, VAMP2. To assess the potential role of VAMP2-Munc18-1 interaction in triggering SNARE complex formation we examined the nanoscale organisation and dynamics of Munc18-1<sup>WT</sup> and two mutants with highly reduced binding to VAMP2 (A297H and T304H) tagged with photoconvertible mEos2 and expressed in Munc18-1/2 double knockout (DKO)-PC12 cells. We demonstrated that Munc18-1 secretagogue stimulation increased the mobility of Munc18-1 due to its release from syntaxin-IA. However, expression of the two mutants blocked this increase in mobility suggesting that VAMP2 binding to Munc18-1 is necessary for triggering the release of Munc18-1 in an activity-dependent manner. We also showed that both mutants reduced Ba<sup>2+</sup>-induced stimulated secretion. Our results demonstrate that syntaxin-IA opening also depends on Munc18-I's binding to VAMP2 casting a doubt on the existence of opened syntaxin-IA nanoclusters and suggest that such opening only occur within the confinement of primed vesicles upon VAMP2 binding to Munc18-1.

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### TALK THURSDAY 2.45PM

# **Optogenetic stimulation of visual object and motion detection circuits promotes sleep**

#### Leonie Kirszenblat, Aoife Larkin, Yanqiong Zhou, Bruno van Swinderen

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Sleep is a fundamental process observed in most animal species, yet we still know little about what drives the need to sleep and the neural mechanisms involved. In this study, we used the fruit fly, *Drosophila melanogaster*, as a model to understand how visual processing affects sleep. We found that visual responses and sleep architecture in wild-type individuals were correlated; individuals with fragmented sleep had a lowered ability to fixate on objects, and an increased response to motion stimuli. We further investigated how different types of visual processing influences sleep need by optogenetically activating several types of motion and object processing neurons throughout the day and simultaneously monitoring sleep during the day and the night. We identified two different types of visual circuits, one that processes motion, and another that detects objects, that consolidate night time sleep following extended periods of neural activity. Consistent with this, we found that a classical visual mutant called optomotor blind – which has defective visual responses to motion and objects – had less consolidated sleep. Together, our results suggest that specific forms of visual processing drive sleep need in *Drosophila*.

# A transcriptomic investigation of mammalian telencephalic development and evolution

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Commissures that form between the two hemispheres of the mammalian neocortex are crucial for integrating a range of important neural processes. In eutherian mammals, most interhemispheric connections are formed via the corpus callosum, an evolutionarily new commissure and the largest tract in the human brain. The corpus callosum is absent, however, in non-eutherian mammals such as marsupials and monotremes, and projections between the two cortical hemispheres form via the anterior commissure. To study the molecular mechanisms involved in cortical commissure development and evolution, we established a high-depth de novo transcriptomic database of whole neocortex in the marsupial fat-tailed dunnart, before and during formation of the anterior commissure (P12 and P20), and compared with developmental mouse brain transcriptomes of equivalent stage of commissure formation (E12.5 and E16). Interspecies gene ontology analyses at the younger age-point showed a significantly high expression of genes in dunnart associated with epigenetic control and early-onset neuronal development. In contrast, at the older age-point there was significantly high expression of genes in mouse associated with more advanced neuronal cell maturation, including mitochondrial development. Genes differentially expressed between species and developmental stages included transcription factors, RNA regulatory elements, axon guidance genes and intracellular signalling pathways. The assembly of the dunnart transcriptome also provided species-specific sequences for additional experiments including in situ hybridisation, quantitative PCR, and overexpression and downregulation assays in vivo. These findings will help elucidate the developmental mechanisms involved in the origin of the corpus callosum, and the basic processes guiding brain wiring in health and disease.

### TALK THURSDAY 12.15PM

# Digital, analog, and memristive implementation of spike-based synaptic plasticity

#### Corey Lammie, and Mostafa Rahimi Azghadi

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Synaptic plasticity is believed to play an essential role in learning and memory in the brain. To date, many plasticity algorithms have been devised, some of which confirmed in electrophysiological experiments. Perhaps the most popular synaptic plasticity rule, or learning algorithm, among neuromorphic engineers is the Spike Timing Dependent Plasticity (STDP). The conventional form of STDP has been implemented in various forms by many groups and using different hardware approaches. It has also been used for applications such as pattern classification. However, a newer form of STDP, which elicits synaptic efficacy modification based on the timing among a triplet of pre- and post-synaptic spikes, has not been well explored in hardware.

We have investigated and designed a number of STDP and TSTDP electronic circuits using different hardware approaches, including analog, digital, and memristors. All these implementations are able to completely and with a minimal error replicate the outcome of a wide range of biological experiments. They have also been verified to reproduce a spike rate-based synaptic plasticity behavior similar to the Bienenstock Cooper Munro (BCM) rule. We have used a number of these implementations in a spiking neural architecture comprising of different types of neurons to perform cognitive tasks such as pattern classification and unsupervised character recognition.

Our electronic implementations of the TSTDP rule can be used in large-scale analog, digital, or memristive neural architectures, to improve their synaptic plasticity capabilities. This will result in more biophysically faithful neuromorphic systems providing a better medium for neuroscience research.

# Altered auditory processing and top-down connectivity in 22q11.2 Deletion Syndrome

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22q11.2 deletion syndrome (22q11.2DS) is one of the most common copy number variants and confers a markedly increased risk for schizophrenia. As such, 22q11.2DS is a homogeneous genetic liability model which enables studies to delineate functional abnormalities that may precede disease onset. Mismatch negativity (MMN), a brain marker of change detection, is reduced in people with schizophrenia compared to healthy controls. Using dynamic causal modelling (DCM), previous studies showed that top-down effective connectivity linking the frontal and temporal cortex is reduced in schizophrenia relative to healthy controls in MMN tasks. In the search for early risk-markers for schizophrenia we investigated the neural basis of change detection in a group with 22q11.2DS. We recorded high-density EEG from 19 young non-psychotic 22q11.2 deletion carriers, as well as from 27 healthy non-carriers with comparable age distribution and sex ratio, while they listened to a sequence of sounds arranged in a roving oddball paradigm. Despite finding no significant reduction in the MMN responses, whole-scalp spatiotemporal analysis of responses to the tones revealed a greater fronto-temporal NI component in the 22g11.2 deletion carriers. DCM pointed to group differences in the intrinsic connection within right primary auditory cortex as well as in the top-down, connection from the right inferior frontal gyrus to right superior temporal gyrus. We discuss these findings in terms of reduced adaptation and a general increased sensitivity to tones in 22g11.2DS.

# A biologically plausible neural model of visual pathways based on efficient coding

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Various models of efficient coding have been proposed to explain physiological responses observed in the primary visual cortex (VI), such as orientation tuning and end-stopping effects. However, there is not a biologically plausible model that can explain the diverse shapes of receptive fields of VI simple cells and account for phase-reversed cortico-thalamic feedback, which has been observed in cat cortex. Here, we build a two-layer biologically plausible neural model of visual pathways from the lateral geniculate nucleus to VI that is based on efficient coding. The model is biologically plausible in many aspects: local learning rule, local computation, non-negative neural responses, rate-based neuron dynamics, and consistency with Dale's law. Simulations show that our model can account for the emergence of Gaborlike receptive fields and a large percentage of blob-like receptive fields observed in VI. Phase-reversed cortico-thalamic feedback naturally emerges as a result of the structure of learned connections when the model is trained on natural images. Our results suggest that efficient coding can be implemented by simple neural circuits and account for important properties of VI.

### The regulation of developmental enhancers during brain development: insights from motif discovery

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The generation of specific cell types in a timely and orderly manner is a prerequisite for the formation of neural circuits during development. This process is largely governed by sequence-specific transcription factors, which bind to their cognate motifs on DNA to modulate gene expression. One such family of transcription factors known to regulate important developmental processes is the Nuclear factor one (NFI) family of transcription factors. Our analyses of cis-regulatory elements that were previously identified by the Mouse ENCODE project suggest that these transcription factors play a critical role in neuronal differentiation during cortical development. Specifically, we observed that the NFI motif, characterized by the palindromic sequence TTGGC(N)<sub>5</sub>GCCAA, is highly enriched at developmental enhancers derived from the embryonic forebrain. Our analyses demonstrate that the NFI motif is also the most abundant and most highly enriched transcription factor motif during early neurogenesis – between E11.5 and E13.5 in the developing cortex. These findings, coupled to the analyses of knockout mouse models, demonstrate the significance of developmental enhancers in driving neurogenesis during brain development.

### Gamma-band correlations in primary visual cortex

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Neural field theory (NFT) is used to calculate two-point gamma-band correlations in primary visual cortex (VI), including their dependence on the ocular dominance (OD) and orientation preference (OP) properties of the regions involved, and the results are compared with published experimental data.

It has long been known that visual stimuli can produce oscillatory responses in the gamma band (30-70 Hz) in the mammalian primary visual cortex, and that the local field potentials and firing rates of groups of neurons with similar feature preference are highly correlated. NFT has been used to show that gamma oscillations with spatiotemporally structured correlations can be supported by VI neural populations and connectivity. Here, we quantitatively examine the correlation properties of the gamma oscillation modulated with the periodic spatial structure of VI and including the underlying spatial layout of OP and OD properties. A unit cell with mm-scale spatial structure is used to represent a small piece of visual cortex and a wave propagator is derived to incorporate the spatial variation introduced by OP and OD structure. The corresponding gamma correlations are then derived analytically under different stimulus and measurement conditions. The theoretical predictions are shown to reproduce published experiment observations, including the existence of two-point oscillatory temporal cross-correlations with zero time-lag between two group of neurons with similar feature preference, the influence of the spatial distance between the neurons on the strength of the responses, and also other influences on the oscillatory responses introduced by stimulus properties and measurement locations.

# Gamma oscillations as dynamical patterns for optimally implementing distributed information communication

#### Yuxi Liu and Pulin Gong

School of Physics, University of Sydney

Gamma oscillations (30–90 Hz) have been widely observed in many brain areas, but their dynamical nature and functions remain a matter of debate. In this study, we investigate a spatially extended, spiking neural network model with realistic connectivity features, and find that gamma oscillations can emerge when the network is near the transition from asynchronous to propagating wave states. In this critical regime, gamma oscillations are organized as propagating patterns with metastable dynamics. We further show that such metastable gamma patterns generate intermittent gamma bursts, with their statistical properties consistent with empirical results. The dynamics of these intermittent gamma patterns can also account for why there are great fluctuations in the amplitude and frequency of gamma oscillations, as found in experimental studies. By using information-theoretical analyses, we then demonstrate that the metastable gamma patterns are optimal for communicating information to multiple sites of the network within a given time interval.

# Simple cells in the primary visual cortex predicted to match key properties of natural images

#### Peter N Loxley

The University of New England

Natural images represent the natural environment and objects we see every day, such as shadows, flowers, foliage, landscapes, and textures. The primary visual cortex is one of the first areas in our visual system that is sensitive to complex visual stimulus features, such as the orientation of a bar or an edge in the visual field. Evidence also suggests simple cells carry out efficient coding of natural sensory data: re-coding sensory data in a way that reduces redundancy. This step may facilitate visual information processing at later stages of the visual system. This work takes a well-established model of simple-cell receptive field profiles and adapts it to perform efficient coding. Two key properties of natural images are reproduced; namely, a set of "statistically independent" basis functions that have a power-law distribution of sizes. Discrepancies with macaque data suggest efficient coding alone is not sufficient to explain the observed structure of simple-cell receptive field profiles.

### Malformations of the human corpus callosum compromise low-level visual perception

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People with agenesis of the corpus callosum (ACC) do not normally display the cognitive deficits typically observed in "split-brain" patients, in whom the corpus callosum has been surgically cut. Therefore, ACC is an interesting model for how the brain compensates for altered brain development and wiring. Some individuals with ACC have been shown to perform within the normal range even for tasks requiring interhemispheric communication, such as bilateral matching of letters, colours, or shapes. Other work, however, has identified conditions under which ACC individuals perform poorly, such as bilateral pattern matching. Here we compared visual perception of stimuli presented bilaterally across the two visual fields, or unilaterally within the left or right visual field alone, in a small group of ACC participants and in controls. MRI results showed no direct connection between the left and right visual cortices in the ACC cohort. During the behavioural tasks, we measured response accuracy and latencies. We also tested performance in spatial matching across hemifields. In controls, there were no significant differences in reaction to unilateral and bilateral stimuli. They also had guick and accurate responses to bilateral spatial matching. In the ACC individuals, we observed three patterns of performance, in which an individual showed either: (i) significantly decreased accuracy and/or longer response times in tasks requiring interhemispheric communication, (ii) significantly decreased accuracy when responding to low-level stimuli for both unilateral and bilateral presentations; or (iii) performance similar to controls. Our results suggest heterogeneity in visual processing deficits in the congenitally acallosal brain.

# Turning flight characteristics of freely flying honeybees

#### M.Mahadeeswara Yadav & M.V.Srinivasan

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Turning during flight is a complex behaviour that requires co-ordination to ensure that the resulting centrifugal force is never large enough to disrupt the intended turning trajectory. The centrifugal force increases with the curvature (sharpness) of the turn, as well as the speed of flight. Consequently, sharp turns would require lower flight speeds, in order to limit the centrifugal force to a manageable level and prevent unwanted sideslips. We have video-filmed freely flying honeybees near a hive entrance when the entrance is temporarily blocked. A 3D reconstruction and analysis of the flight trajectories reveals that sharper turns are indeed executed at lower speeds. In fact, flight speed during turns is matched to the curvature in such a way as to maintain the centrifugal force at an approximately constant, low level of about 20% of the body weight, irrespective of the speed or the curvature of the turn. This ensures that turns are well coordinated, with few or no sideslips - as is evident from analysis of the flight trajectories.

### TALK THURSDAY 4.45PM

#### POSTER NUMBER 40

### **Corticostriatal deficit introduces temporal limits** to automatic action in ageing

### Miriam Matamales<sup>1,2</sup> Zala Skrbis<sup>1</sup> Matthew R. Bailey<sup>3</sup> Peter D. Balsam<sup>4</sup>, Bernard W. Balleine<sup>2</sup> Jürgen Götz<sup>1</sup> and Jesus Bertran-Gonzalez<sup>1,2\*</sup>

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The acquisition of motor skills involves implementing action sequences that increase task efficiency while reducing cognitive loads. This learning capacity depends on specific cortico-basal ganglia circuits that are affected by normal ageing. Here, combining a series of novel behavioural tasks with extensive neuronal mapping and targeted cell manipulations in mice, we explored how ageing of cortico-basal ganglia networks alters the microstructure of action throughout sequence learning. We found that, after extended training, aged mice produced shorter actions and displayed squeezed automatic behaviours characterised by ultrafast oligomeric action chunks that correlated with deficient reorganization of corticostriatal activity. Chemogenetic disruption of a striatal subcircuit in young mice reproduced age-related within-sequence features, and the introduction of an action-related feedback cue temporarily restored normal sequence structure in aged mice. Our results reveal static properties of aged cortico-basal ganglia networks that introduce temporal limits to action automaticity, something that can compromise procedural learning in ageing.

### Greater fibre density of the subcortical route to the amygdala enhances fearful face perception: a tractography and DCM Analysis of the HCP dataset

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Our survival depends on our ability to rapidly detect threats. To do this, there is allegedly an old subcortical neural pathway that quickly conveys visual information to the amygdala for fear processing. This neural shortcut has been demonstrated in animals but the limitations of non-invasive neuroimaging have posed a unique methodological challenge to demonstrate it in the human brain. To settle the conflict, we conducted a state-of-the-art neuroimaging analysis of 622 participants from the Human Connectome Project. We applied global and local probabilistic tractography methods to diffusion images to reconstruct a subcortical pathway to the amygdala from the superior colliculus and the pulvinar. In a subsample of 237 participants, we then computationally modelled the flow of neural activity during a face viewing task and found strong evidence for a functional subcortical pathway. Critically, greater fibre density of the pathway enhanced accuracy of fearful face perception and the strength of effective connectivity. This convergent evidence from structural and effectivity connectivity strongly supports a functional subcortical route to the amygdala in the human brain.

### TALK THURSDAY 2.30PM

# Population coding of gaze direction in parietal cortex during reaching and changing visual scenes

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Humans rely on visual information and eye movements to locate objects in the environment. While the neural and computational basis of visual processing has been well studied, it is less clear how the brain takes into account the ever-changing direction of gaze. Work from our lab and others has shown that neurons in the posterior parietal cortex (PPC) carry a reliable population-code for eye-position. In these studies, however, there was little change in the behavioural state of the animal or the content of the visual scene, both of which can modulate the activity of these neurons. Here we tested whether PPC neurons form a code for eye-position that is invariant to these extraneous sources of modulation. We decoded the spiking activity of neurons recorded in area 7a and dorsal prelunate cortex (DP) in awake behaving macaques while they performed visually-guided reaches in response to a change in the scene. We assessed the generality of a code for eye-position by training the decoder on data from one epoch (e.g. fixation) and testing it on another (e.g. pre-reach). The predicted eye-position was close to the true position when trained and tested using data from the same epoch, but was inaccurate when trained and tested across different epochs. Performance was rescued, however, when the decoder accounted for global changes in gain that were unrelated to eye-position. Our results suggest that neurons in PPC can support a read-out of eye-position that is invariant to the influence of visual stimulation, reach planning, and reach execution.

# Neural connectivity analysis of an EEG data set with a motor imagery task

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The brain computer interface (BCI) which decode the user's thoughts of their body movement is called motion imagery type, and it is expected to play a crucial part in the rehabilitation field. Currently, the development of BCI which identifies four types of imaginary task has been carried out. Network connectivity analysis of the brain based on graph theory is performed to understand relationship between the role of the brain region and its function. However, there are few studies attempting to distinguish imaginary tasks using a parameter of the network connectivity. Therefore, we aim at developing an analytical method based on the connectivity in the brain. A data set of a motor imagery task with electroencephalography (EEG) on the website of BNCI Horizon 2020 was used. Cross correlation coefficients were calculated for 22 × 22 combinations on participants' scalp and adopted as the strength of the connection between the two electrodes. Each element of the correlation matrix showed z scores from each node combination, and performed t-test using the period of pre-cue and post-cue. The node correlations of EEG data recording in pre-cue and post-cue conditions for all 4 types of the imagery movement, hands, feet and tongue, were calculated. The correlation of the neural connectivity was reduced with 9 combinations of the EEG nodes after cue's presentation in the only tongue imagery task. Any other neural connectivity correlation in the remained imaginary tasks (left hand, right hand and foot) were not changed significantly in this analysis.

# Functional modularity as a biomarker of neuroplastic response to anodal tDCS

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Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that can modulate cortical excitability. However, the tDCS response shows high inter- and intra-individual variability. This study is a step towards predicting the tDCS response using brain functional connectivity profiles. We previously showed that connectivity in high beta frequency band is associated with anodal tDCS response in healthy subjects. A balance between local specialization and large-scale integration of brain functional networks is required for normal brain function and can be quantified using maximized modularity. We applied anodal and sham tDCS to left primary motor cortex (MI) in 15 healthy subjects (mean age 26.4 years) and lesioned M1 in 10 stroke patients (mean age 63.8 years). We applied tDCS immediately after recording resting EEG in stroke patients. EEG data and the response to tDCS were recorded in separate sessions for healthy subjects. We reconstructed source activity, calculated functional connectivity matrices, thresholded to construct undirected graphs and computed maximized modularity. Change in the amplitude of motor evoked potential (MEP) was used as a marker of the tDCS response. In healthy subjects, lower maximised modularity in high beta band was associated with greater MEP facilitation following anodal but not sham tDCS. In stroke patients, maximized modularity was not significantly correlated with MEP facilitation following anodal tDCS. These results suggest that after-effects of tDCS depend upon brain network modularity in healthy adults, but not stroke patients. This may reflect disruption to brain networks as a result of the lesion.

# Detection of neuronal assemblies from calcium fluorescence activity

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The University of Queensland I Queensland Brain Institute 2 School of Mathematics and Physics

Patterns of neuronal activity form the key substrate for information processing in the brain. An important property of these patterns is that the activity of single neurons is generally not statistically independent from other neurons, and assemblies of neurons that tend to coactivate are observed. In order to study the properties of these assemblies it is crucial to first reliably identify them, even in the presence of considerable levels of noise. Recently, very large scale neuronal recordings have become possible by optical recording of calcium fluorescence activity; since neuronal activity is accompanied by the release of calcium ions, these calcium transients can be used as a proxy to track neuronal activity. Although several algorithms to extract neuronal assemblies from such recording have been proposed, their performance has not been systematically evaluated.

Here we show that a new algorithm we recently proposed for this problem, in which we formulate the problem as one of graph clustering, outperforms other algorithms. These algorithms are either based on principal- and independent-component-analysis on pairwise correlations between the neuronal units, or frequent item set mining on sets of coactive neuronal units. Besides identifying the weaknesses of these algorithms, we also show how the one based on independent-component-analysis can be improved to achieve performance comparable with the one on graph clustering.

### DCC signalling initiates glial-mediated interhemispheric midline remodelling during formation of the corpus callosum by regulating glial cell morphology

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The corpus callosum is the largest fibre tract mediating interhemispheric communication in placental mammals. Remodelling of the interhemispheric fissure (IHF) that initially separates the two brain hemispheres is required for formation of the corpus callosum at the midline. Defects in this process are common in individuals with congenital absence of the corpus callosum (Gobius et al., 2016) and are associated with mutations in the axon guidance receptor, DCC (Marsh, Heron, Edwards et al., 2017). Given these results, we investigated the role of Dcc signalling in IHF remodelling. During midline remodelling, glial cells known as the midline zipper glia (MZG), align on either side of the IHF and intercalate their processes with one another and degrade components of the IHF (Gobius et al., 2016). Dcc and Dcc ligands, Ntn I and Draxin are expressed in MZG throughout midline remodelling. In glial cell culture, Dcc signalling promotes cell process extension and elongation by modulating the actin cytoskeleton. In Dcc and Ntn1 mouse mutants, MZG show aberrant process extension during somal translocation to the IHF and are unable to distribute evenly along the IHF. Following this, IHF remodelling is not initiated as MZG are unable to extend processes into the IHF or intercalate with contralateral MZG. Together our results reveal a novel role for axon guidance genes in regulating glial cell morphology. Our results also strongly suggest that defects in astroglial-mediated IHF remodelling are likely to underlie congenital absence of the corpus callosum associated with DCC mutations in human individuals.

# Age and disease-specific MRI templates in the optimization of DBS electrode targeting

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The success of DBS is critically dependent on the precise targeting of stimulating electrodes to small deep brain nuclei such as the sub-thalamic nucleus (STN) and the ventro-intermediate nucleus of the thalamus (VIM). The difficulty with accurately identifying these small nuclei with standard MRI sequences means that indirect atlas-based approaches, often combined with electrophysiological data, are frequently used to provide target coordinates for surgery (1). Most atlases however, are based on healthy populations or even single healthy individuals, and may not represent the neuroanatomy of a particular disease population, e.g. Parkinson's Disease (2). In addition to disease-specific changes in neuroanatomy, the prevalence of age-related changes in brain structure further limit the potential accuracy of single template based atlases (3).

Recently, several studies have addressed the limitations inherent in atlases based on a restricted population or a single individual. Xiao et al. (4) describe the construction of a multi-contrast MRI brain atlas based on 25 Parkinson's Disease patients, which provided significantly improved registration performance compared to a template derived from a healthy population. At QBI, in collaboration with St Andrew's Memorial Hospital in Brisbane, we aim to extend this approach by constructing a range of MRI templates for specific diseases, e.g. Parkinson's Disease, essential tremor, obsessive compulsive disorder, and for specific age ranges. The project is made possible by access to a large archive of c.500 MRI scans of DBS patients treated by the Hospital. The performance of the templates will be evaluated using the methods of Xiao et al (4).

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# Neogenin regulates radial progenitor function in the developing cortex

#### Conor O'Leary, Cathrin Nourse, Natalie Lee, Helen Cooper

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Within the developing cortex radial glial cells (RGCs) maintain the progenitor stem cell pool through symmetric cell division. Alternatively, they undergo asymmetric division, generating intermediate progenitor cells or neurons. Maintenance of apicobasal polarity is crucial for RGC function. RGCs exhibit a bipolar morphology, expanding across the entire thickness of the developing cortex, where their basal process attaches to the pial surface and their apical membrane contributes to the ventricular surface. Adherens junctions, the sites of cadherin-mediated cell adhesion, are localised to the border between the apical and lateral membranes and are essential for the maintenance of RGC morphology and function. We have found that the axon guidance receptor, Neogenin, is concentrated at the adherens junctions of RGCs throughout cortical development. In order to investigate the role of Neogenin in adherens junction formation, Neogenin short hairpin RNA plasmids were electroporated into the embryonic mouse cortex in utero. Depletion of Neogenin resulted in the disruption of adherens junctions and loss of RGC polarised morphology. As a result, the total number of proliferating RGCs was greatly increased, indicating enhanced production of neuronal progenitors. Furthermore, actively dividing ectopic RGCs were distributed throughout the cortical plate. These data indicate that Neogenin is essential for the maintenance of RGC structure and asymmetric division in the developing cortex, and suggest its loss may contribute to cortical malformations.

# White matter connectivity disruptions associated with psychotic experiences in healthy individuals

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Widespread fronto-temporal white matter abnormalities in schizophrenia have been reported across several studies. However, it is questionable whether these abnormalities are associated with psychotic symptoms specifically or with schizophrenia in general. The present study compared the structural connectome between healthy individuals with high and low quantities of psychotic experiences. By investigating the extent to which white matter connectivity disruptions are specific to psychotic experiences in healthy individuals we avoid common confounding variables, which are almost always present in schizophrenia studies, such as medication, deterioration of cognitive functioning, and institutionalization. High resolution, multi-shell diffusion-weighted magnetic resonance images were acquired from 44 healthy individuals with a low quantity of psychotic experiences (PE-) and 45 healthy individuals with a high quantity of psychotic experiences (PE+). Whole-brain white matter fiber tracking was performed to quantify the strength of white matter connections. Network-based statistics were applied to white matter connections in order to test for significant streamline count differences between the PE+ group and the PE- group. Compared with the PE- group, the PE+ group displayed significant streamline count reductions across fronto-temporal networks, mainly lateralized to the right hemisphere. The observed white matter disruptions in healthy individuals with psychotic experiences across fronto-temporal networks overlap with those commonly reported in schizophrenia, albeit to a lesser degree. This reveals that white matter abnormalities connecting frontal and temporal brain regions might be associated with psychotic experiences specifically as opposed to schizophrenia in general.

# Axon growth regulation by a bistable molecular switch

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For the brain to function properly, billions of neurons must grow in a controlled manner to establish a functional neural circuit. A key aspect of this process is the tight regulation of axon growth during brain development. Although a large number of intracellular and extracellular molecules involved in axon growth and guidance have been identified, a systems-level understanding of how these molecules interact to regulate axon growth rate is still lacking. Here, we used mathematical modelling to show that the molecular interaction network involved in axon growth exhibits bistability, with one stable steady state representing a growth state and the other a paused state. Due to stochastic effects, even in an unchanging external environment, axons in the model reversibly switch between the growth and paused states. The model predicts that environmental signals regulate axon growth rate by altering the basin of attraction of the steady states and by controlling the switching rates between the two states. These results suggest that axon guidance depends critically on a balance between cell intrinsic bistability and environmental signals.

### TALK FRIDAY 12.15PM

#### POSTER NUMBER 50

# Deconvolving a palimpsest of brain activity and hemodynamics from fMRI

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Functional magnetic resonance imaging (fMRI) is commonly used to infer hemodynamic changes in the brain due to neural activity, by measuring the blood oxygen level-dependent (BOLD) signal. An important challenge in the analyses of fMRI data is to develop methods that can accurately deconvolve the BOLD signal to extract the driving neural activity and the under-lying cerebrovascular effects. Here, we use a physiologically based hemodynamic model to do this and extract and image the spatiotemporal patterns of multiple aspects of neural activity and hemodynamics that underlie fMRI, including cerebral blood flow, cerebral blood volume, and deoxygenated hemoglobin concentration. This opens new noninvasive windows to analyze dynamics of stimulus-evoked physiological signals directly from fMRI measurements, thereby allowing new information to be obtained from BOLD-fMRI data. This also provides a unified simultaneous imaging alternative to current approaches that measure each quantity separately via multiple neuroimaging modalities that rely on complex and expensive equipment and protocols, and which cannot always be used simultaneously. The deconvolution method is tested on simulated data to establish its accuracy, then it is applied to experimental data to show that the resulting profiles of the deconvolved responses are consistent with measurements reported in the literature. This demonstrates the ability of the technique to noninvasively image the multi-layered palimpsest of brain activity and hemodynamics underlying BOLD-fMRI data, thereby significantly advancing the analysis, interpretation, and utility of fMRI.

### Investigating cortical connectivity in the developing Australian marsupial fat-tailed dunnart (Sminthopsis crassicaudata, Dasyuridae)

Annalisa Paolino<sup>1,\*</sup>, Rodrigo Suárez<sup>1,\*</sup>, Peter Kozulin<sup>1</sup>, Laura R. Fenlon<sup>1</sup>, Linda J. Richards<sup>1,2</sup>

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The correct formation of circuits within and between neocortical regions is crucial for higher brain functions. In the mammalian neocortex, neurons projecting intracortically occupy layers 2/3 and 5, and send axons to the same and/or the contralateral hemisphere. Despite increasing knowledge regarding the mechanisms regulating brain wiring, research in eutherians has been limited due to technical challenges of genetically manipulating independent neuronal populations in utero. To overcome this, we established a new experimental paradigm, the Australian marsupial fat-tailed dunnart. Marsupials are born at an early stage of brain development, comparable to mid-embryogenesis in eutherians, and most forebrain development occurs postnatally, allowing multiple experimental procedures to be performed on the same animal in a minimally invasive manner. We performed serial experiments to reconstruct neuronal birthdate and circuit formation in dunnarts and found a broadly conserved mammalian pattern of neurogenesis, migration and distribution of projecting neurons, similar to eutherians, with the main exception of the absence of a corpus callosum. Interestingly, however, ipsilateral axons from layers 2/3 and 5 extend medially towards the cingulate cortex after commissural axons have extended laterally towards the anterior commissure. Moreover, commissural axons from layer 5 neurons reach the contralateral hemisphere first, and then 'wait' for a few days in the contralateral deeper layers until the arrival of layer 2/3-derived axons to then innervate the cortical plate together. This suggests that contralateral targeting might occur in sequential steps, and that axons from upper and deeper layer neurons may interact in the formation of long-range neural circuits. Altogether, we show the potential of marsupial neurobiology to gain insights into the mechanisms of cortical development and evolution.

### TALK FRIDAY I.30PM

### The agony of choice: optimal policies for valuebased decision making

#### Alexandre Pouget

Department of Basic Neuroscience. University of Geneva. Switzerland.

When faced with two equally high valued choices (e.g., a weekend in London or in Paris, all expenses covered), most people agonize and take an unusually long time to decide. This is quite counterintuitive: given that subjects are guaranteed a high reward regardless of their choice, they should decide quickly since there is little to lose. In addition, people take even longer if a third low reward choice (e.g. a weekend in Pyongyang) is added to the list of options. Why would a choice that is very unlikely to be picked, interfere with the other high valued choices? These puzzling behaviours have led to the notion that value-based decision making is highly suboptimal in humans. We revisited this issue and derived the optimal policy for value-based decision making. Surprisingly, the optimal strategy predicts long reaction times when confronted with two equally high valued choices as well as interferences from irrelevant choices. Moreover, this policy can be easily implemented in neural circuits using a form of nonlinearity known as normalization, which is known to exist in cortical areas implicated in decision making. While this work lays the foundations of a neural theory of optimal value-based decision making. I will argue that these models are nonetheless too limited to deal with complex decision making. I will end with speculations about what it will take to develop models of complex decision making.

# Spatiotemporal probabilistic inference emerging from balanced cortical circuits

#### Yang Qi and Puling Gong

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Probabilistic inference is a principled framework for understanding cortical computation, but its neural circuit implementations remain largely unclear. Here we first show that dynamical, spatiotemporal activity patterns emerging from a biologically plausible, balanced cortical circuit can capture the complexity of neural dynamics found in experiments. We then demonstrate that the collective dynamics of such patterns implement a novel type of spatiotemporal probabilistic representation. In particular, the non-Gaussian dynamics of these patterns, as characterised by a Levy process with increments following heavy-tailed distributions, allows the network to perform probabilistic sampling from multimodal distributions, even when the modes are separated by long distances. This dynamical sampling thus overcomes a long-standing challenge in Markov Chain Monte Carlo algorithms such as Langevin and Hamiltonian Monte Carlo for probabilistic inference, whose sampling processes can often be trapped around the local peaks of probability distributions. In addition, we demonstrate that the quasi-instantaneous activity of the patterns can implement probabilistic population coding when the stimulus contrast is high. Our results thus indicate that spatiotemporal dynamics with the experimentally reported complexity in cortical circuits can reconcile different probabilistic inference schemes over population and over time, thus providing a unified dynamical mechanism for implementing cortical computation.

# Translating thoughts into text: rapid communication with a brain computer interface virtual keyboard

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Text-based communication is one of the cornerstones of modern civilisation. While keyboards currently allow us to interface with computers and physically manifest our thoughts, the next frontier in communication is text generation without motor control. Brain computer interface (BCI) spellers attempt to achieve this by decoding patterns of neural activity as participants attend to keys on a virtual keyboard. The highest performing BCI spellers to date allow communication at about 6 words/min. While impressive, these rates are usually derived for highly trained participants typing single phrases. We set out to determine whether high typing speeds could be maintained by novice BCI users during naturalistic free typing. To this end, we developed and evaluated a high performance BCI speller using seventeen BCI naïve participants. Eight participants were classified with sufficient accuracy to free type self- generated text. It was evident from this test that the short, cued typing tests which are usually used to assess BCI spellers are not a reliable index of free typing performance. Participants were able to type freely at an average of 4.5 words/min. We performed offline analyses to assess how different EEG features accounted for individual differences in performance. These analyses revealed that previously proposed methods are not necessarily optimal. Modifications could allow free typing rates of up to 11.8 words/min, suggesting that current BCI typing methods have further potential for improvement. However, performance appraisals of future BCI spellers should be restructured to reflect the naturalistic text-based communication for which BCI spellers are intended.
#### POSTER NUMBER 54

# Bayesian model selection maps for group studies using EEG data

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Predictive coding postulates that we make (top-down) predictions about the world and that we continuously compare incoming (bottom-up) sensory information to these predictions, in order to update our models and perception so as to better reflect reality. That is, our so-called "Bayesian brains" continuously create and update generative models of the world, mapping out (hidden) causes to (sensory) consequences. Such modelling and updating processes can be studied with high temporal resolution using electroencephalography (EEG) data. Importantly, by using Bayesian approaches to analyse EEG data itself, any number of models can be compared, the models need not be nested, and the 'null model' is able to be accepted (rather than only failing to be rejected). This methods poster explains how to construct posterior probability maps (PPMs) for Bayesian Model Selection (BMS) at the group level using EEG data. The method has been used for EEG data only recently (Garrido et al. 2017) after first being introduced and applied by Rosa and colleagues (2010) in the context of functional magnetic resonance imaging (fMRI) analysis. Here, we describe how this method can be adapted for EEG data analysis using the Statistical Parametric Mapping (SPM) software package for MATLAB. The method enables the comparison of an arbitrary number of computational models at each and every voxel in the brain, both within participants and at the group level. The adapted method is illustrated here using new mismatch negativity (MMN) data from a group of participants performing an audio-spatial attention task involving an Oddball prediction paradigm.

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#### POSTER NUMBER 55

### Independent effects of attention and expectation on stimulus representation in the visual cortex

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I Queensland Brain Institute, The University of Queensland 2. School of Psychology, The University of Queensland

Despite growing interest in the brain mechanisms associated with attention and expectation, it remains unclear how these processes interact to influence neural representations of visual stimuli. Selectively attending to a stimulus is typically assumed to increase the gain of its neural representation, whereas generating an expectation about a stimulus has been suggested to either sharpen or suppress its representation. To date, however, no study has orthogonally manipulated attention and expectation to investigate their independent and interactive effects on stimulus representations. Here we recorded EEG while participants attended or ignored a stream of expected and unexpected gratings, and used a multivariate forward encoding model to characterise orientation tuning. Participants fixated centrally and were presented with a periodic stream of gratings (500ms ISI). Grating orientation was repeated over successive stimuli (range: 4-11), before changing to a new (random) orientation. Grating orientation was thus either expected (toward the end of a repeated sequence) or unexpected (when it deviated from the preceding sequence). Attention was manipulated by having participants look for rare targets in which one grating within the stream changed to a different spatial frequency (attended condition), or for rare luminance changes at fixation (unattended condition). Results of the encoding analysis revealed main effects of attention and expectation on stimulus representations, but no interaction. Attention enhanced stimulus representations throughout the epoch (70-500 ms), whereas prediction suppressed (rather than sharpened) neural representations only late in the epoch (300-500 ms). These results further our understanding of the complex relationship between the neural mechanisms underlying attention and expectation, and support predictive coding theories that claim neural representations of expected stimuli are suppressed in order to optimise visual processing.

### TALK WEDNESDAY 3.45PM

POSTER NUMBER 56

## Neural oscillations and spiking assemblies drive each other in the amygdala during fear conditioning

#### Peter Stratton\*, Francois Windels, Allen Cheung, Shanzhi Yan, Pankaj Sah\*

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Oscillations in activity are hallmarks of all neural systems. These oscillations are implicated in almost every sensory, motor and cognitive function, and are perturbed in characteristic ways in brain diseases. Despite their significance, little is known about how these oscillations are controlled through time across the brain, or how they are causally connected with the underlying activities of individual neurons. We recorded local field potential (LFP) oscillations and neural spiking activity using tetrodes in the rat basolateral amygdala during fear conditioning. We show that brief spike correlations between neurons continuously form short-lived networks (transient spike time assemblies – TSTA), that different information is multiplexed in these assemblies across a range of distinct coupling intervals, and that assembly couplings are transformed during conditioning and revert during fear extinction. Significantly, the couplings drive oscillations across frequencies which, in turn, reconfigure the assemblies. This interplay of meso-scale population oscillations with micro-scale neuronal coupling promotes a rich neurodynamical repertoire and establishes reciprocal control across scales.

# Function follows form: estimating the dependency structure of the brain resource international database

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Age has a multitude of effects on both the physiology and the functionality of the brain. In this work, we analyse data from the Brain Resource International Database, the world's largest brain structure and activity database, to assess the dependency structure of the dataset and thus the extent to which variation in brain functionality can be explained by either age, or brain anatomy and physiology. Up to 250 separate measures are available for each subject, including demography (age, sex, etc.), mood (anxiety, depression, etc.), personality (extroversion, openness, etc.), cognition (verbal memory, reaction time, maze completion, etc.), electroencephalography (EEG; eyes-open and closed power spectra), and structural magnetic resonance imaging (MRI; gray and white matter volumes). We determine the dependency structure of the dataset by estimating a probabilistic graphical model. Such models offer powerful methods for decoding the underlying conditional dependency structure in high-dimensional data. We use a trans-dimensional Markov chain Monte Carlo approach based on a continuous-time birth-death process to estimate the graphical model. We find that gray matter volumes have the most explanatory power in models for maze completion time, choice reaction time and emotional resilience; white matter volumes matter most for working memory capacity, negativity bias and motor tapping; EEG matters most for memory recall and social skills. Whilst age is the single most significant variable in terms of explaining performance in cognition tests, a combination of brain structure and activity variables is able to capture significant proportions of the variability in different measures.

# Ancient origin of an interhemispheric connectome in the mammalian cortex

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The brain of mammals differs from that of all other vertebrates by having a six-layered neocortex extensively interconnected within and between hemispheres. In monotremes and marsupials, the left and right cortices are connected through the anterior commissure, whereas eutherians evolved the corpus callosum, the largest axon tract in the human brain, as the main interhemispheric connection. While the corpus callosum conveys a pattern of interhemispheric connectivity broadly shared throughout species, it is not known whether this pattern arose as a consequence of callosal evolution, or instead corresponds to a more ancient feature of mammalian cortical organisation. Here we show that monotremes and marsupials share features of interhemispheric connectivity with eutherians that likely pre-date callosal origin. By performing ex-vivo diffusion tensor tractography, we found that interhemispheric connections through the anterior commissure in both fat-tailed dunnarts (Marsupialia) and platypus (Monotremata) are spatially segregated according to the topography of cortical areas. Moreover, interhemispheric circuit mapping in dunnarts revealed not only connections between equivalent regions of each hemisphere (homotopic circuits), but also the presence of bilaterally hyper-connected hubs along the medial and temporal borders of the cortex, similar to the callosal connectome of eutherians. We propose that an interhemispheric connectome originated in early mammalian ancestors as a key feature of neocortical organisation, and that such a connectome has been conserved during the evolution of mammalian lineages with or without a corpus callosum.

# Excitatory and inhibitory circuits are modified to produce odour habituation in the mouse piriform cortex *in vivo*

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Olfaction employs habituation to de-emphasize static or repetitive odour inputs in order to process novel, potentially more important odours. Piriform cortex (PC) is the first cortical destination of odour information but little is known about how habituation to an odour manifests in the PC circuitry. We applied repetitive odour stimuli and simultaneously measured the responses of up to 250 neurons in the PC of anaesthetized mice using 2-photon calcium imaging. A given odour excited a unique ensemble pattern of principal neurons in layer 2. With each reapplication of the odour, neurons participating in the ensemble were dropped or replaced, but the total number of excited cells declined, indicative of habituation. Reinstatement of the responses occurred over a recovery period of >60 min. The habituated state was absent when a novel odour was presented and a different ensemble of neurons was excited; thus, habituation is odour-specific. Habituation is not inherited from the upstream mitral/tufted (M/T) cells in the olfactory bulb because M/T cells did not change their odour responses upon repeated exposure. However, imaging activity in somatostatin-expressing (SOM+) interneurons in the PC revealed an upregulation of their activity. Local superfusion of the NMDA channel blocker MK801 into PC blocked both the upregulation of SOM+ interneuron activity and the habituation of layer 2 principal cells. In summary, we find long-lasting odour-specific NMDA receptor-dependent changes to odour representation in the PC that are accompanied by upregulated inhibitory activity, suggesting a novel mechanism for the habituation of odour responses in the PC.

# Auditory prediction errors as individual biomarkers of schizophrenia

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Schizophrenia is typically diagnosed through symptomatic evidence collected through patient interview. We aim to develop an objective biologically-based computational tool which aids diagnosis and relies on accessible imaging technologies such as electroencephalography (EEG). To achieve this, we used machine learning techniques and a combination of oddball paradigms designed to Mismatch Negativity (MMN) responses.

MMN, an EEG component elicited by unpredictable changes in sequences of auditory stimuli, is reduced in people with schizophrenia and is arguably one of its most reproducible neurophysiological markers.

We acquired EEG data from 21 patients with schizophrenia and 22 healthy controls whilst they listened to sequences of tones which changed occasionally (10% of trials were deviant tones). Three specific deviant tone types shared the same properties as standard tones, except for one physical aspect: 1) duration - the deviant stimulus was twice the duration of the standard; 2) monaural gap - deviants had a silent interval omitted from the standard, or 3) inter-aural timing difference - deviants perceived as 90° away from the standards.

We used machine learning techniques to classify images generated through statistical parametric mapping of spatiotemporal EEG data, i.e. event-related potentials measured on the two-dimensional surface of the scalp over time. Using support vector machine and Gaussian process (GP) classifiers, we were able classify individual patients and controls with balanced accuracies of up to 80.48% (p = 0.0326, FDR corrected). Crucially, GP regression also revealed that MMN predicted global assessment of functioning (GAF) scores (correlation = 0.73,  $R^2 = 0.53$ , p = 0.0006).

# Emergence of spontaneous assembly activity in developing neural networks without afferent input

Marcus A. Triplett<sup>1,2</sup>, Lilach Avitan<sup>1</sup>, and Geoffrey J. Goodhill<sup>1,2</sup>

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Developing nervous systems exhibit ongoing neural activity, even in the absence of sensory stimulation. With recent advances in imaging technology, this spontaneous activity has been shown to be highly organized at the population level, and often consists of a number of structured neural assemblies; i.e., groups of neurons that tend to fire together. Previous studies have modelled the formation of neural assemblies with spiking recurrent neural networks that modify their structure through STDP rules according to patterns of correlated afferent input. Surprisingly, even when animals are deprived of sensory stimuli during development, spontaneous activity still exhibits a highly structured form. While computational analyses have been given for assembly formation under sensory stimulation, the mechanisms underlying the development of neural assemblies in systems with no structured afferent input remain unknown. Here we show that a recurrent neural network undergoing unsupervised Hebbian learning can reorganize its network structure into a modular state where assemblies activate spontaneously. We show that the spatiotemporal patterns of activity produced by our model match well with recent *in vivo* recordings from the zebrafish tectum. Our results thus show that Hebbian learning is sufficient to explain the emergence of highly structured patterns of neural activity in the absence of structured input.

### TALK THURSDAY II.45AM

# **DeepSouth: A neuromorphic ecosystem**

#### André van Schaik

The MARCS Institute, Western Sydney University, Penrith, NSW 2747, Australia

We present a low-power, scalable, massively-parallelised neuromorphic ecosystem, called DeepSouth, which can provide turnkey solutions from front-end sensors to back-end processors. It is designed to be flexible so that its subsystems can work either independently, or together, using data represented as continuous values, as events (spikes), or a mixture of both. DeepSouth consists of several subsystems: a silicon cochlea, a deep learning accelerator, and two general purpose neuromorphic processors - one with 1.5M reconfigurable components, and a larger one with 8M components. Each component can be configured as a leaky-integrate-fire (LIF) neuron, a learning synapse, or axon with adaptive delay. Deep-South uses high-speed digital circuits while embodying some of the biologically-inspired principles of neuromorphic computing. The components were developed as fully digital Application Specified Integrated Circuits (ASICs) using a process independent design flow, so that they can be manufactured in various state-of-the-art manufacturing technologies. We have implemented them using standard digital libraries in a 130 nm technology. Along with the ASICs, we also provide FPGA versions of the components for evaluation and easy distribution. The neuromorphic architectures used in DeepSouth are useful for realtime sensory applications, and can be integrated in embedded systems for many applications, including: robotics, control (industrial; automotive), surveillance and distributed monitoring, and computational neuroscience. Along with the hardware platform, we are developing an interface that will allow users to specify the parameters of neurons and connections, as well as the network structure using Python and the PyNN and NEST APIs.

### TALK FRIDAY 2.45PM

## A whole-brain analysis of water-flow responses in larval zebrafish

#### Vanwalleghem G, Schuster K, Scott EK

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As a transparent animal and with powerful light-based tools to monitor and manipulate the brain, the larval zebrafish offers a perfect window into functioning neural circuits. We focus on the lateral line that allows fish to detect the movement of water. How the brain processes water flow to drive behaviours such as hunting or rheotaxis is unknown.

We have used genetically encoded calcium sensors and SPIM to map the brain-wide processing of lateral line information. To apply water flow stimuli, we developed a custom microfluidics device capable of delivering a range of flow rates in both forward and reverse directions. Using this device, we have delivered a stimulus train that allows us to distinguish neural responses based on the direction, velocity, and duration of water flow.

We observed eight functional response profiles, which can be divided between neurons that responded at the onset of the stimulus, for the duration of the stimulus, or in a steadily increasing fashion throughout the stimulus ("integrators"). Each functional profile could be subdivided per their direction selectivity, but some onset and on neurons responded to both directions. Surprisingly, we did not find evidence for encoding of the flow speed, which leads us to suspect it may be temporally encoded using the topographic map.

These results will form the basis for a neural model of flow processing, and set the stage for studies of how water flow is integrated with visual and vestibular processing to give the larva a comprehensive representation of space.

#### POSTER NUMBER 62

# State-specific neural activity in the medial prefrontal cortex and hippocampus that encodes fear learning and extinction behaviour

#### Cong Wang, Roger Marek, Peter Stratton, Pankaj Sah

Queensland Brain Institute, The University of Queensland, Brisbane, Queensland, Australia

The medial prefrontal cortex (mPFC) and the hippocampus (HPC) have been shown to play an important role in the modulation of fear learning and extinction, respectively. However, the mechanism of how neuronal activity and synchrony in subregions of the mPFC and the HPC encode fear learning and extinction are not widely studied.

Using male Sprague Dawley rats (n=6), we implanted two microdrives with 2 tetrodes each in the prelimbic (PL), infralimbic (IL) cortex of the mPFC and the ventral and dorsal CA1 of the HPC, respectively. Following recovery for 7 days and tetrode-adjustment until spike detection was sufficient, animals were taken for recordings of single-unit activity and local field potentials during contextual fear learning and extinction.

The conditioned rats showed a significant increasing freezing behaviour (from  $22.0\pm5.1\%$  to  $65.6\pm8.9\%$ ) with a rise in theta activity power in both the PL and IL. After extinction, the rats showed a descending freezing rate (down into  $36.1\pm8.3\%$ ) with an increasing HPC power and a higher level of synchronized oscillation between the IL and HPC, suggesting novel activity patterns in the investigated brain regions to encrypt different behavioral states. Our results also showed an increase in synchronized theta oscillation between IL and HPC during extinction learning, indicating that this rise in functional connectivity between IL and HPC might be one of the crucial keys to inhibit freezing behaviour.

# A fractional diffusion theory of balanced, heterogeneous cortical circuits

#### Asem Wardak and Pulin Gong

School of Physics, University of Sydney, NSW 2006, Australia

Cortical neurons *in vivo* fire highly irregularly. Understanding the origin of this irregularity has been a long-standing topic of interest in theoretical neuroscience. Conventionally, irregular neural dynamics are formulated as balanced, uncorrelated excitatory and inhibitory inputs with Gaussian dynamics. This theory, however, is at odds with recent experimental observations, which instead have shown the existence of transient synchronized inputs with heterogeneous magnitudes to cortical neurons. In addition, it has been observed that these heterogeneous inputs result in heavy-tailed distributions of both membrane potential and neural firing rates. In this study, we develop a new, fractional diffusion theory of balanced networks to account for these key experimental results. In this theory, the heterogeneous, correlated synaptic inputs are modelled as a Lévy process. This formulation results in a fractional Fokker-Planck formalism, which is then used to account for the non-Gaussian dynamics of the membrane potential, firing rates and linear response of cortical networks. These theoretical results are then compared with simulated results of biologically plausible networks along with experimental observations. The fractional diffusion theory thus allows for a significant extension of the analysis of homogeneous cortical networks into the biologically realistic heterogeneous domain, providing a theoretical framework for understanding balanced cortical circuits.

### TALK WEDNESDAY 3.15PM

# Coding of cued fear by neural ensembles in the lateral amygdala

#### Francois Windels, Shanzi Yan, Peter Stratton and Pankaj Sah\*

Queensland Brain Institute, The University of Queensland, Australia

In fear conditioning, a neutral sensory stimulus such as a tone (the conditioned stimulus, CS) is contingently paired with an aversive stimulus, typically a footshock (the unconditioned stimulus, US). Following a small number of pairings, animals learn to respond to the CS with an avoidance response that is measured as freezing or fleeing A large and growing body of literature has led to a model in which paring of the CS with the US results in NMDA receptor dependent plasticity at inputs mediating CS information to the lateral amygdala (LA), and thus enhanced activation of neurons in the LA. In this talk I will discuss the biophysical constraints that underpin this idea and test the role of NMDA-receptor inhibition on fear learning. Using single, unit recordings in awake behaving animals we examine the impact of fear learning on CS driven activity in the LA. Our results suggest that while NMDA receptors do play a key role in fear learning, they may not be activated by CS-US pairing. We further show that the CS coding in the LA is sparse, and learning likely results from encoding of CS-driven ensembles of neurons in the LA.

## IDTxl - The Information Dynamics Toolkit xl: a Python package for the efficient analysis of multivariate information dynamics in networks

Patricia Wollstadt<sup>1</sup>, Joseph T. Lizier<sup>2</sup>, Raul Vicente<sup>3</sup>, Conor Finn<sup>2,4</sup>, Mario Martinez Zarzeula<sup>5</sup>, Michael Lindner<sup>6</sup>, Pedro Martinez Mediano<sup>7</sup>, Leonardo Novelli<sup>2</sup>, Michael Wibral<sup>1</sup>

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We present IDTxl, a new open source toolbox for effective network inference from multivariate time series using information theory, available from Github. IDTxI utilises a greedy or iterative approach with multivariate transfer entropy for building sets of parent sources for each target node in the network. This iterative conditioning is designed to both remove redundancies and capture synergistic interactions in building each parent set. Rigorous statistical controls (based on comparison to null distributions from time series surrogates) are used to gate parent selection and to provide automatic stopping conditions for the inference. The toolkit is a next generation combination of the existing TRENTOOL and JIDT toolkits, extending TRENTOOL's pairwise transfer entropy analysis to a multivariate one, and adding a wider variety of estimator types. Further, IDTxI is Python3 based, requiring no proprietary libraries, with parallel computing engines for both GPU and CPU platforms. The toolkit is highly flexible, providing various information theoretic estimators for the user to select from; these handle both discrete and continuous time-series data, and allow choices, e.g. using linear Gaussian estimators (i.e. Granger causality) for speed versus nonlinear estimators (e.g. Kraskov-Stoegbauer-Grassberger) for accuracy. IDTxI also automates parameter selection for the user, including selecting source-target delays and constructing non-uniform embeddings of the sources via conditional mutual information. Tools are included for group-level analysis of the inferred networks, e.g. comparing between subjects or conditions. Finally, IDTxl includes additional tools for studying the dynamics of various information flows on the inferred networks. The primary application area for IDTxI lies in analysing brain imaging data (import tools for common neuroscience formats, e.g. FieldTrip, are included). However, the toolkit is generic to analysing multivariate time-series data from any discipline. We will demonstrate the efficacy of IDTxl in inferring networks from various synthetic data sets.

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# **Top-down modulation of alpha-band oscillations** by arbitrary self-association

#### Mateusz Woźniak

Monash University, Cognition & Philosophy Lab, Melbourne, Australia

Self-associated information is typically prioritized in cognitive processing, as evidenced by faster reaction times and lower error rate. It also affects the amplitude of event-related components such as P3 and N2 which are frequently associated with attentional processing. In the current study we found evidence that self-association also influences preparatory alpha-band activity. We present data showing that activation of self-related information leads to subsequent modulation of posterior alpha-band oscillatory activity immediately preceding the target stimulus in the matching task. In the beginning of our task participants were told to associate each of three arbitrary faces with themselves, a friend, and a stranger. Then they participated in a perceptual matching task in which they were first presented with a label corresponding to one of the three identities and then, after a 1.5s delay, with one of the three faces. Their task was to judge whether the face matches with the label. We found that when the first stimulus was self-associated, the participants exhibited decreased alpha power in the posterior areas several hundred milliseconds before the second stimulus. We suggest that it provides evidence that self-association modulates top-down influence on predictive processing via alpha-band activity.

# High-frequency transient wave at the onset of focal seizure generalization

#### Dongping Yang and P.A. Robinson

School of Physics, and Center for Integrative Brain Function, University of Sydney, New South Wales 2006, Australia

A physiologically based corticothalamic neural field model of large-scale brain activity is investigated to understand how the focal seizure activity (3 Hz) can be generalized, which is found to be determined by the ratio of lesion size to axon range. We found there are two different routes to generalize the focal absence seizure with different features of the transient dynamics at the onset in the transition from suppression to generalization. Especially, high-frequency transients (10 Hz) can be induced at the onset, which can possibly serve as precursors for focus seizure generalization. Such emergent transient waves due to spatiotemporal instability initiate from a lesion-shadowed region and then propagate to the focal center. Linear stability analysis is conducted to give more insight in the underlying dynamical mechanism for the emerged spatiotemporal patterns.

## Nfib regulates radial glial cell proliferation and differentiation by repressing Hmga2 during cortical development

#### Y.Yunan<sup>1</sup>, J.W.C. Lim<sup>1</sup>, J.Bunt<sup>1</sup>, J. Richards<sup>1,2</sup>

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The Nuclear Factor One B (*Nfib*) is a transcription factor important for maintaining balanced radial glial cell proliferation and differentiation during corticogenesis. *Nfib* knockout embryos exhibit an enlarged and immature ventricular zone, accompanied by a delay in the production of intermediate progenitors and neurons. We investigated the downstream effectors of NFIB during radial glial proliferation and differentiation. Gene expression analyses using both RNA sequencing and real-time qPCR revealed robust upregulation of another transcriptional regulator, *Hmga2*, in *Nfib* knockout cortices. *In vivo*, NFIB and HMGA2 are expressed in reciprocal gradients throughout the developing cortex, and are co-expressed in the ventricular zone. Quantification of HMGA2 protein expression using immunofluorescence also revealed a concomitant increase in HMGA2 protein in *Nfib* knockout ventricular zones compared to their wildtype littermates. These results suggested that NFIB may repress *Hmga2* during normal embryonic development. ChIP-qPCR further validated HMGA2 as a direct *bona fide* downstream target for NFIB. Our results expand on the regulatory network underlying cortical development by demonstrating a direct inhibitory effect of the transcription factor NFIB on *Hmga2*. During normal development, NFIB drives self-renewing radial glial cells down the neurogenic and gliogenic pathways. When this inhibitory regulation is removed by *Nfib* deletion, HMGA2 level increases and favours self-renewal of radial glial cells.

### TALK THURSDAY 9.00AM

# Neuronal ensembles: emergent units of cortical function?

#### **Rafael Yuste**

Columbia University

Since the time of Cajal and Sherrington, it has been traditional assumed that the individual neurons are the basic units of cortical function. At the same time, it is possible that coactive groups of neurons, i.e. neuronal ensembles, could represent emergent building blocks of cortical circuits. I will review our efforts to test this hypothesis, by characterizing the phenomenology, mechanisms and potential functional and pathological roles of neuronal ensembles in the primary visual cortex of mice, using optical methods to record and functionally manipulate ensembles in both *in vitro* and *in vivo* preparations.

### TALK THURSDAY 2.15PM

#### POSTER NUMBER 68

## Population codes in VI and MT are optimised for the structure of natural images

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The middle temporal area (MT) computes motion direction based on the inputs it receives from direction-selective neurons in primary visual cortex (V1). Existing models of the hierarchical computations between these areas are among the best defined of any model of cortical processing, yet the stimulus space of visual inputs on which they have been tested remain poorly explored. While most studies explore neural responses using only gratings or dots, the natural visual world contains information at a range of spatial scales, and this information is often phase aligned. There is evidence that this structure shapes the nervous system so that natural images are encoded efficiently by single neurons. Here, we examine how the structure of visual information impacts the way it is encoded by both single-neurons and populations, across two levels of the visual hierarchy.

To examine how visual information is successively represented by VI and MT, we used separate multi-electrode arrays in each area to measure neural responses simultaneously from dozens of neurons in VI and MT of anaesthetised marmosets. We recorded neural activity while presenting motion with different spatial structure: dots, sine waves, square waves, and phase randomised square waves. These patterns evoke strong responses in MT, but recruit distinct VI populations. We found that response variability in single neurons (Fano factor), and pairwise spike count correlations between neurons were lowest during broadband, phase aligned stimulation in both VI and MT. This suggests that the network architecture in both areas is optimised to represent broadband, phase aligned contours.

# Age-related differences in network topologies associated with sleep ECG signals

#### Guohun Zhu<sup>1</sup>\*, Fangrong Zong<sup>2</sup> and Ying Jiang<sup>3</sup>

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Deceleration capacity of heart rate during sleep will be affected by age. However, age related network changes in sleep ECG signals are poorly understood. This study measures network changes based on sleep ECG signals from 23 subjects to investigate the age-related changes of ECG signals.

Our approach employed differential visibility graphs to analyse ECG signals from three sleep databases with three difference sampling frequencies: 100Hz, 128Hz and 250Hz. The networks topology: clustering coefficient (cc), and mean degree (md) features are extracted with four sleep stages: wake, light sleep, deep sleep and rapid eye movement (REM) stages, from two age groups: younger (<=45) and old group (>45).

Firstly, the network topologies of sleep ECG signals exhibits higher cc and md in deep sleep stages than those of wakeful. However, the cc of younger is significant higher than those of old adults (p<0.001). In addition, the standard deviation of cc in younger of deep sleep stages are always less than 0.02, but the range cc of old people are higher than 0.07. Secondly, the md in deep sleep of younger is significant higher than those of light sleep (p<0.01) conversely, it has weakly difference in older group (p=0.025). However, the md of REM in younger has no significant difference from those of deep sleep, whilst the REM in old group shows higher md than those of deep sleep.

These results shows that the network topologies of differential visibility graph associated with the sleep ECG signals can represent the age-changes. In addition, higher clustering coefficient in REM sleep stage potential imply an increased cardiovascular risk in old age.

# Phase changes in neuronal postsynaptic spiking due to short term plasticity

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The postsynaptic response of a neuron to time-varying inputs is determined by the interaction of presynaptic spike times with the short-term dynamics of each synapse. For a neuron driven by stochastic synapses, synaptic depression results in a quite different postsynaptic response to a large population input depending on how correlated in time the spikes across individual synapses are. Here we show using both simulations and mathematical analysis that not only the rate but the phase of the postsynaptic response to a rhythmic population input varies as a function of synaptic dynamics and synaptic configuration. Resultant phase leads may compensate for transmission delays and be predictive of rhythmic changes. This could be particularly important for sensory processing and motor rhythm generation in the nervous system.

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Notes