SCiNDU 2020

Systems & Computational Neuroscience Down Under

Wednesday 29th–Friday 31st January

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

ARC Centre of Excellence for Integrative Brain Function

The University Of Queensland
AUSTRALIA

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SCiNDU 2020

Systems & Computational Neuroscience Down Under

Conference program

Wednesday 29th–Friday 31st January

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

A note about poster presentations

Poster numbers have been assigned sequentially in alphabetical order to the poster abstracts at the end of this booklet.

Odd number posters will be presented at Poster session 1 (Wednesday 4–5.45pm)

Even number posters will be presented at Poster session 2 (Thursday 4.15pm–6pm)

Wednesday 29th January

10am –1pm	Tutorials
Auditorium	**Tatyana Sharpee** *Maximally informative neural coding*
Seminar Room	**Vinod Menon** *Functional organization of the human brain: linking maps, circuits, dynamics and behavior*
1pm	**Lunch for tutorial attendees**

Main conference starts	
2pm	**Barry Dickson** *The neurobiology of Drosophila reproductive behaviours*
2.45pm	**Bruno van Swinderen** *General anaesthesia: linking single molecule effects to whole-brain defects*
3.15pm	**Lucy Heap** *A paradoxical kind of sleep in Drosophila melanogaster*
3.30pm	**Martyna Grabowska** *Reading a fly's mind—Electrophysiological correlates of valence-driven attention in the fruit fly*
3.45pm	**Afternoon tea**
4pm	**Poster session 1**
5.45pm –7pm	**Welcome reception**

Thursday 30th January

9am **Tatyana Sharpee**
Hyperbolic geometry in olfaction

9.45am **Tony Burkitt**
Neural dynamics, time delays and real-time temporal alignment of neural activity in spiking neural circuits

10.15am **Elizabeth Zavitz**
Connectivity for redundancy reduction in neural populations

10.30am **Morning tea**

11.00am **Nicholas Price**
Representing and communicating information in visual cortex

11.30am **Jason Mattingley**
Understanding the role of prediction in sensory encoding

12 noon **Maureen Hagen**
Functional inhibition across a sender-receiver communication channel coordinates looking and reaching

12.15pm **Jativa Vega**
Dissociating the effects of affective salience and signal probability on visual attention

12.30pm **Ali Almasi**
How do stimulus statistics change the receptive fields of cells in primary visual cortex?

12.45pm **Lunch**

2pm **Lucy Palmer**
Auditory input enhances somatosensory encoding and tactile goal-directed behaviour

2.30pm **Juan-Andrés Mucarquer**
Informational-effects quantification of 'hidden hearing loss' using the information bottleneck method

2.45pm **Stephen Williams**
Principles of neuronal circuit computations

3.15pm **Suraj Honnuraiah**
Cellular and circuit mechanisms underlying processing of binocular visual information in visual cortex

3.30pm **Alexandra Tzilivaki**
Challenging the point neuron dogma: FS interneurons as 2- stage integrators.

3.45pm **Afternoon tea**

4.15pm **Poster session 2**

6pm **Conference dinner**
location: Saint Lucy Caffe e Cucina

Friday 31st January

9.00am **Vinod Menon**
Unifying models and theories of human brain function and dysfunction

9.45am **Kai-Hsiang Chuang**
Mapping large-scale network dynamics and plasticity in rodent brain

10.15am **Miriam Matamales**
Functional connectivity of the striatal network and its role in goal-directed learning

10.30am **Morning tea**

11.00am **Linda Richards**
Activity-dependent and molecular mechanisms regulating the development of cortical connectivity

11.30pm **Matilde Balbi**
Activity dependent neuroprotection induced by gamma-range stimulation in the acute phase after stroke improves functional outcome

12.00pm **Amelia Douglas**
Circadian control of food intake

12.15pm **Lunch**

1.30pm **Tobi Delbruck**
Data driven perceptual inference

2.15pm **Moritz Milde**
Time-based computation in cortical recurrent networks

2.30pm **Panel discussion**

3.30pm **Afternoon tea**
conference concludes

Wednesday 29th January 2pm

The neurobiology of *Drosophila* reproductive behaviours

Kaiyu Wang[1], Fei Wang[1], and Barry J. Dickson[1,2]

[1] Janelia Research Campus, Howard Hughes Medical Institute, Ashburn VA, U.S.A.
[2] Queensland Brain Institute, The University of Queensland, Brisbane, Australia

Reproduction in most animal species involves complex rituals for courtship, copulation, and post-mating behaviours. These behaviours are robust, innate, and sexually dimorphic, making them attractive model systems for understanding how neural circuits operate more generally. In *Drosophila*, these behaviours are shaped by the sex-determination genes *fruitless* (*fru*) and *doublesex* (*dsx*). These genes are expressed in ~2000 individual neurons, comprising >200 distinct cell types, many of which have been ascribed specific functions in male or female reproductive behaviours. I will present evidence that these neurons are organized into anatomically distinct but functionally analogous circuits in the two sexes. In both males and females, central brain neurons encode a state of mating arousal, which modulate and coordinate the sensorimotor transformations that underlie each sex's behaviour.

Wednesday 29th January 2.45pm

General anaesthesia: linking single molecule effects to whole-brain defects

Bruno van Swinderen

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

All general anaesthetics produce a loss of consciousness in humans, and a profound loss of behavioural responsiveness in all animals. While it is understood that some anaesthetics such as propofol and isoflurane abolish consciousness by targeting endogenous sleep mechanisms in the brain, it remains unclear how all of these drugs produce a total loss of behavioural responsiveness, albeit at different dosages linked to their lipophilicity. We have recently discovered that clinically-relevant doses of general anaesthetics impair presynaptic neurotransmission, by decreasing the number of active release sites at glutamatergic synapses. Single molecule imaging revealed significant effects on syntaxin1A and munc-18 mobility, which are crucial components of the synaptic release machinery. We have developed an ex-vivo brain preparation for *Drosophila melanogaster* allowing us to image single-molecule dynamics under general anaesthesia, to understand the effects of these drugs on presynaptic function. We propose that the presynaptic target of general anaesthetics causes a failure of brain function, and that this is what renders animals completely unresponsive. To test this requires an understanding of how local effects on single molecules translate to global defects in brain function, for which we developed an in-vivo *Drosophila* brain recording preparation. We imaged calcium activity in thousands of neurons across the fly brain, in behaving animals that were exposed to environmental stimuli such as light flashes and air puffs. We examined whole-brain responses and connectivity during waking, during anaesthesia induction, and during deep anaesthesia, with a view towards uncovering the diverse and complex target processes underlying general anaesthesia.

Wednesday 29th January 3.15pm

A paradoxical kind of sleep in *Drosophila melanogaster*

Tainton-Heap, L. A. L., Kirszenblat, L. C., Notaras, E. T., Grabowska, M. J., Jeans, R., Feng, K., Shaw, P. J. and van Swinderen, B.

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

The dynamic nature of sleep in most animals suggests distinct stages which serve different functions. Genetic sleep induction methods in animal models provide a powerful way to disambiguate these stages and functions. In *Drosophila*, activation of the dorsal fan-shaped body (dFB) promotes sleep, but it remains unclear how the rest of the fly brain is behaving, or if any specific sleep functions are being achieved. Here, we recorded neuronal activity and connectivity across the fly brain during dFB-induced sleep and compared this to a sleep-promoting drug. We found that drug-induced spontaneous sleep decreased brain activity, whereas dFB sleep resembled wakefulness. Prolonged optogenetic dFB activation resulted in similar sleep durations as drug-induced sleep, and both corrected visual attention defects brought on by sleep deprivation. However, arousal thresholds were higher during dFB sleep and visual responsiveness in the brain was blocked. These results suggest that dFB activation promotes a functionally relevant sleep stage in *Drosophila*, which results in wake-like brain activity and connectivity, coupled with a loss of responsiveness to external sensory stimuli.

Wednesday 29th January 3.30pm

Reading a fly's mind—Electrophysiological correlates of valence-driven attention in the fruit fly

Martyna J. Grabowska and Bruno van Swinderen

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

Selective attention describes an animal's ability to prioritize one set of stimuli while ignoring others and depends on past experience as well as in innate preferences. Attended stimuli are usually assigned valence, which can be negative or positive. In animals, valence is typically studied using behavioral assays that measure attraction or aversion, but it is unknown whether these responses exist in the insect brain independent of the corresponding behaviors. In this study we recorded visually-evoked potentials from the central brain of *Drosophila melanogaster* in a closed-loop virtual reality environment, to determine if flies display stereotypical neural responses to visual objects that they found innately attractive or aversive. We found that an attractive object evoked stronger responses in the central brain than an aversive object, even when flies were not in closed-loop control. The valence of objects could however be overturned by optogenetic activation of a reward circuit in the fly brain which was detectable by a switch in neuronal activity towards both visual stimuli. The attentional switch manifested in an amplitude modulation of endogenous 20-40Hz oscillations by the presence of the visual valence cues. This suggests that valence effects in the fly brain reflect attention-like process that are shaped by circuits involved in gain control.

Thursday 30th January 9am

Hyperbolic geometry in olfaction

Tatyana Sharpee

Salk Institute for Biological Studies

Using the sense of smell as an example, I will describe both theoretical reasons and experimental evidence that natural stimuli and human perception can be mapped onto a three dimensional hyperbolic surface. The results are obtained using a combination of tools from algebraic topology and multi-dimensional scaling with a hyperbolic metric.

Although the representation that we derive is obtained purely from the statistics of co-occurrence between mono-molecular odorants in the natural environment, it revealed topography in the organization of human perception of smell. I will conclude with arguments for why hyperbolic metric should be generally applicable elsewhere in the nervous system.

Thursday 30th January 9.45am

Neural dynamics, time delays and real-time temporal alignment of neural activity in spiking neural circuits

Anthony N. Burkitt

Chair of Bio-Signals and Bio-Systems, Department of Biomedical Engineering, Melbourne School of Engineering, The University of Melbourne

The real-time temporal alignment hypothesis postulates that information of sensory signals is transmitted through neural pathways in a manner that compensates for neural transmission delays at each stage of the pathway. These neural transmission delays result from both synaptic delays and the time required for action potential conduction via axons. For sensory inputs that change in a predictable fashion, their representation at higher levels of the processing hierarchy remain aligned with the stimulus. Neural information that is fed backwards from higher to lower levels of the hierarchy is realigned in time through a synaptic plasticity mechanism based upon nonlinear Hebbian learning and normalization at each level of the hierarchically structured network. These predictions from the higher levels of the pathway are thereby able to be fed backwards without becoming increasingly misaligned over time with the incoming sensory input. Examples from visual motion processing indicate that such neural processing is plausible and is consistent with the psychophysically observed results of several known motion-position illusions.

Bio-sketch

Professor Anthony Burkitt holds the Chair in Bio-Signals and Bio-Systems in the Department of Biomedical Engineering at the University of Melbourne since 2007. His research encompasses a number of areas of neuroscience and medical bionics, including computational neuroscience, neuroengineering, retinal-implant vision processing, cochlear-implant speech processing and bio-signal processing for epilepsy. His research has made significant contributions to understanding the behaviour and function of neural information processing in the brain, encompassing both neural coding and spike-timing synaptic plasticity. His work has also been instrumental in the development of visual stimulation paradigms for retinal implants, new cochlear implant speech processing strategies, methods for detecting and predicting seizures, and the use of electrical stimulation for seizure abatement in epilepsy. He was the Director of Bionic Vision Australia (2010-2016), a Special Research Initiative in Bionic Vision Science and Technology of the Australian Research Council (ARC), and he successfully led the project though all of its phases: Project conception, securing $50million in ARC funding, the research and development programs that led to the development of a prototype bionic eye (suprachoroidal retinal implant), the successful implantation in three patients, and the establishment of the company Bionic Vision Technologies (BVT) with US$18million of venture capital for the ongoing commercial and clinical development of the technology.

Thursday 30th January 10.15am

Connectivity for redundancy reduction in neural populations

Elizabeth Zavitz[1], Maureen A. Hagan[1], Brian H. Oakley[1], Yan T. Wong[1,2], Nicholas S.C. Price[1]

[1] Department of Physiology, Biomedicine Discovery Institute, Monash University, Clayton
[2] Department of Electrical and Computer Systems Engineering, Monash University, Clayton

When spiking activity from pairs of neurons is recorded simultaneously, the firing rates tend to be correlated. Pairwise correlations are created when patterns of activity are shaped by the structure of the local network, and changes in pairwise correlations can be used to evaluate the functional architecture of a network. Attention, adaptation and sensory context can all affect correlation structure, but it is not clear how to relate changes in correlations to differences in functional circuits. Natural images contain significant sensory context. They have information across many spatial frequencies, and that information tends to be phase aligned to form edges between surfaces. To test whether these differences cause the distribution of pairwise correlations to change, we made recordings of populations of neurons in area V1 and MT of anaesthetised marmoset. Based on these recordings, we have found that images with a wide range of spatial frequency information aligned across phases evoke activity with the lowest correlations. This suggests that local circuits are specialised so that stimuli with phase alignment across frequencies have a specific role in reducing spiking redundancy. To test whether this is the case, we use model networks of spiking neurons to simulate how activity evoked by stimuli with different structures propagates through a network and produces observed correlated variability. By varying the rules that determine connectivity within the network, we can link stimulus-related changes in correlations to specific wiring principles.

Thursday 30th January 11.00am

Representing and communicating information in visual cortex

Nicholas Price[1], Elizabeth Zavitz[1], Brian Oakley[1], Maureen Hagan[1], Yan Wong[1,2]

[1] Department of Physiology and Neuroscience Program – Biomedicine Discovery Institute, Monash University
[2] Department of Electrical and Computer Systems Engineering, Monash University

The visual system is a complex, hierarchically-organised information processing network. Counter-intuitively, successive areas contain less information about a scene, but neural activity is structured to better represent specific information. For example, neurons in primate area MT convey little colour information, but motion direction can be linearly decoded from their activity. The ongoing activity of individual neurons is highly variable, meaning reliable computation depends on collaborative processing across neural populations. However, it remains unclear how visual information is reliably represented across neurons within an area, and how these representations are transformed between areas to extract specific stimulus properties. To address this, we record visually-evoked activity simultaneously from dozens of neurons in V1 and MT in marmosets.

We use decoding techniques to predict stimulus orientation or direction from activity across a neural population. This has allowed us to show that neural representations are affected by stimulus history: recent motion biases predictions in a manner consistent with perceptual illusions; and luminance and contrast changes affect orientation coding, again in a manner consistent with human sensitivity.

We study inter-area communication by comparing the timing of action potentials in V1 with local field potentials (LFP, a population measure of local dendritic activity) in MT. We have shown that action potentials preferentially occur at specific phases of the LFP, and that motion information is best communicated from V1 to MT at specific phases.

Collectively, this suggests that hierarchical information processing depends on action potentials in privileged subsets of neurons occurring in privileged time windows.

Thursday 30th January 11.30am

Understanding the role of prediction in sensory encoding

Jason B. Mattingley

Queensland Brain Institute & School of Psychology, The University of Queensland

At any given moment the brain receives more sensory information than it can use to guide adaptive behaviour, creating the need for mechanisms that promote efficient processing of incoming sensory signals. One way in which the brain might reduce its sensory processing load is to encode successive presentations of the same stimulus in a more efficient form, a process known as neural adaptation. Conversely, when a stimulus violates an expected pattern, it should evoke an enhanced neural response. Such a scheme for sensory encoding has been formalised in predictive coding theories, which propose that recent experience establishes expectations in the brain that generate prediction errors when violated. In this talk I will present findings from experiments in humans and mice in which we asked whether the encoding of elementary visual features is modulated when otherwise identical stimuli are expected or unexpected based upon the history of stimulus presentation. In human participants we employed electroencephalography to measure neural activity evoked by gratings of different orientations, and used multivariate forward modelling to determine how orientation selectivity is affected for expected versus unexpected stimuli. Using an analogous visual paradigm in awake head-fixed mice, we used two-photon calcium imaging to quantify orientation tuning of individual neurons in the primary visual cortex to expected and unexpected gratings. Results revealed enhanced orientation tuning to unexpected visual stimuli, both at the level of whole-brain responses and for individual visual cortex neurons. I will discuss the implications of these findings for predictive coding theories of sensory encoding.

Thursday 30th January 12 noon

Functional inhibition across a sender-receiver communication channel coordinates looking and reaching

Maureen A. Hagan[1,2] and Bijan Pesaran[3]

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Eye-hand coordination is a natural behavior unique to primates that is controlled by the posterior parietal cortex, a brain structure that expanded substantially in primate evolution. Understanding how natural behaviors like eye-hand coordination are controlled depends on understanding the neural mechanisms of multiregional communication. We investigated whether a sender-receiver communication channel supported multiregional communication between the parietal saccade and reach regions during naturally-coordinated eye-hand movements. Eye movements are central to accurate reaching and grasping due to foveal acuity. Arm and hand movements are less accurate without foveation. Analyzing behavior revealed saccades are transiently inhibited following reaches, termed “gaze anchoring”. The saccade inhibition was revealed by longer saccade latencies, which correlated trial-by-trial with reach accuracy. Gaze anchoring therefore provides a testbed for studying how reach and saccade systems communicate during coordinated movements to influence behaviour.

We trained two macaque monkeys to perform a gaze-anchoring task, while recording cells and local field potentials from reach areas and saccade areas simultaneously in the posterior parietal cortex. During gaze anchoring, beta-frequency (15-25 Hz) neural coherence between the parietal reach and saccade regions revealed the operation of a sender-receiver communication channel. Parietal reach neuron spiking correlated trial-by-trial with the suppression of both saccades, reach accuracy and spiking in the parietal saccade system when the channel was open but not closed. Functional inhibition within sender-receiver communication channels mediated by neural coherence may be a general mechanism that flexibly coordinates our natural behavior.

Thursday 30th January 12.15pm

Dissociating the effects of affective salience and signal probability on visual attention

Jativa Vega M[1], Kryklywy JH[1], Hu S[1], Ransom M[2], Markovic J[2], Fazelpour S[2], Todd RM[1]

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[2] Department of Philosophy, University of British Columbia, Vancouver, Canada

Recent evidence has shown that both a stimulus' association with punishment and the predictability of its occurrence can influence attentional prioritization. Learning about statistical regularities of the environment serves the goal of predicting frequently occurring events required for action, while guidance of attention by punishment serves the goal of acquiring and holding on to sources of physical danger. The goal of this study was to manipulate and dissociate the influences of affective salience and probability as separate sources of attentional guidance. To disembed the contributions of expectation and emotion as separate sources of attentional guidance, we conducted a signal detection task wherein affective salience is manipulated through classical conditioning, and signal probability—the frequency of a signal appearing in a given location—is explicitly stated. We introduce a hierarchical adaptation of the temporal context model (Howard and Kahana, 2002) to describe the dynamical prioritization of competing attentional sources within a priority space. Preliminary behavioral results replicate prior work showing increases in both hit percentage and false alarms with increasing signal probability (Wyart et al., 2012). Furthermore, an increased hit rate for stimuli with high compared to low affective salience was observed. We interpret these findings as evidence for the separate influences of affective salience and expectation on mechanisms of visual attention.

Thursday 30th January 12.30pm

How do stimulus statistics change the receptive fields of cells in primary visual cortex?

Ali Almasi[1,3], Shi Sun[1,2,3], Molis Yunzab[1,3], Michael Ibbotson[1,2,3], Hamish Meffin[1,2,3]

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Recently, mathematical tools have been developed that allow us to estimate the parameters of visual receptive field (RF) models, which are typically a cascade of linear filters that act on the stimulus, followed by static nonlinearities that map the output of the filters to neuronal spike rates. However, how much do these characterisations depend on the choice of the stimulus?

We studied the changes that neuronal RF models undergo due to the change in the statistics of the visual input. We applied the nonlinear input model (NIM) to the recordings of single cells in cat primary visual cortex in response to white Gaussian noise (WGN) and natural scenes (NS). We estimated for each cell the spatial filters constituting the neuronal RF and their corresponding pooling mechanism, while making minimal assumptions about the underlying neuronal processing. The most striking finding was that NS resulted in around twice as many significant filters as WGN. We also compared the identified RF filters under the two stimulation regimes in terms of preferred orientation and spatial frequency: orientation was highly preserved (correlation coefficient $r = 0.97$), as was spatial frequency but to a lesser degree ($r = 0.73$). However, population analysis revealed a statistically significant bias towards higher spatial frequency filters under the NS stimulation regime (*t-test*; p-value < 0.0025). We also found profound differences in the relationship between the filter's output and the cell's spike rate: notably for gain, input scaling, output scaling, or a combination of all three.

Thursday 30th January 2pm

Auditory input enhances somatosensory encoding and tactile goal-directed behaviour

Lucy Palmer

Florey Institute of Neuroscience and Mental Health, University of Melbourne

The capacity of the brain to encode multiple types of sensory input is key to survival. However, how neurons integrate information from multiple sensory pathways and to what extent this influences behaviour is largely unknown. Here, we report the influence of auditory input on sensory encoding in the somatosensory cortex and its effect on tactile goal-directed behavior. Using two-photon Ca^{2+} imaging, optogenetics and electrophysiology *in vivo* and *in vitro*, we show that monosynaptic input from the auditory cortex enhances distal dendritic Ca^{2+} tactile responses and somatic action potential output in layer 2/3 pyramidal neurons of the forepaw somatosensory cortex. During a tactile-based goal-directed task, auditory input increased distal dendritic activity and reduced the behavioural reaction time, which was abolished during photoinhibition of auditory cortex projections in forepaw somatosensory cortex. Taken together, these results indicate that distal dendrites of cortical layer 2/3 pyramidal neurons encode multi-sensory information, leading to enhanced neuronal output and performance during goal-directed behaviour.

Thursday 30th January 2.30pm

Informational-effects quantification of ‘hidden hearing loss’ using the information bottleneck method

Juan-Andrés Mucarquer, Jaime Undurraga, David McAlpine

Department of Linguistics, Macquarie University, Sydney, Australia

Cochlear synaptopathy (CS) is a lesion characterised by abnormal synaptic activity between inner hair cells and auditory nerve fibres. Its quantification and specific relationship to hearing loss is unclear, but likely relates to problems listening in noise, with intact hearing thresholds, following exposure to loud sounds (so called ‘hidden hearing loss’, HHL). Here, we address this gap using the information bottleneck method (IBM). The IBM generates reduced representations of random variables, that are maximally informative about another (relevance) variable. Assuming the predictive coding hypothesis, the IBM has been used to yield a set of reduced representations for the time-series of auditory oddball stimuli, enabling the construction of a theoretical prediction error, that is correlated to cortical neural responses. As such, neurons that exhibited significant correlations with the error signal were used to extract parameters of the internal representation (IR) such as, its complexity and predictive power.

We extend the IBM framework for HHL, to quantify and compare several IR’s parameters of noise-induced HHL animals, when exposed to a stimulus composed of broadband noise with time-varying random intensity. First, we express the stimuli capturing its time-varying component, and then derive a Bayesian estimator for the variance (energy) as a function of past information. Next, we obtain reduced representations of the estimator, and calculate a theoretical error signal that we correlate with neural recordings in the auditory midbrain, with the aim of testing the hypothesis that animals exposed to loud sounds exhibit IR with less predictive power or less complexity.

Thursday 30th January 2.45pm

Principles of neuronal circuit computations

Stephen R. Williams

Queensland Brain Institute, The University of Queensland

My laboratory aims to elucidate principles of neuronal and neuronal-circuit function. We use advanced electrophysiological and optical recording techniques to mechanistically dissect physiologically engaged neuronal computations in the microcircuitry of the neocortex and retina. Our work has revealed that active information processing in the dendrites of central neurons plays a cardinal role in neuronal circuit computations.

Thursday 30th January 3.15pm

Cellular and circuit mechanisms underlying processing of binocular visual information in visual cortex

Suraj Honnuraiah, Helena Huang, Robin Broersen, 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 of primary visual cortex plays a critical role in processing visual information received from the eyes. To better understand how binocular information is integrated in binocular visual cortex here we combine optogenetic and electrophysiological methods to identify binocular and monocular neurons *in vitro* and *in vivo* and characterize their active, passive and morphological properties. We have identified two distinct populations of layer 2/3 pyramidal neurons in binocular visual cortex, one that receives long-range monosynaptic excitatory input from the contralateral visual cortex (binocular neurons) and one that does not (monocular neurons). While we found no differences in passive and morphological properties of binocular and monocular layer 2/3 pyramidal neurons, the active properties of binocular neurons were significantly different from monocular neurons. Specifically, the slope of the input/output (f/I) curve generated during somatic current injection was lower in binocular layer 2/3 pyramidal neurons, leading to reduced action potential firing. These data suggest that binocular layer 2/3 pyramidal neurons are intrinsically less excitable than monocular neurons. This difference indicates that binocular layer 2/3 pyramidal neurons may have different cellular integration rules from monocular neurons during synaptic integration. Using a morphologically realistic active model of layer 2/3 pyramidal neurons, we demonstrate that differences in axonal potassium channels likely underlie the difference in f/I curves of binocular and monocular neurons. Consistent with this idea we found that low concentrations of 4-AP (300 μM), which block D-type potassium channels, increased the slope and maximum firing rate of binocular but not monocular neurons. Additionally, using two colour optogenetics we show that layer 2/3 neurons in the binocular visual cortex (V1) receive direct inputs from the lateral geniculate nucleus (LGN) and colocalize with callosal V1 inputs. 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. These findings provide insight into the cellular and circuit mechanisms used by the cortex to process binocular visual information.

Thursday 30th January 3.30pm

Challenging the point neuron dogma: FS interneurons as 2- stage integrators

Alexandra Tzilivaki[1], George Kastellakis[2], Panayiota Poirazi[2]

[1] Einstein Center for Neurosciences Berlin (ECN), Charite Medical School Berlin, NeuroCure Cluster of Excellence, Berlin Germany
[2] Institute of Molecular Biology-Biotechnology (IMBB), Foundation for Research and Technology Hellas (FORTH) Heraklion, Greece

Fast Spiking (FS) basket cells (BCs) constitute one of the main types of inhibitory interneurons. A growing body of literature recognizes their importance in controlling executive functions. However, most studies have focused on their molecular and anatomical features and supported the dogma that these cells passively integrate inputs, completely ignoring dendritic influences. As a result, whether a linear point neuron or a more sophisticated abstraction, like a two-stage integrator, can successfully capture their synaptic integration profile, remains an open question. Towards that goal, we developed a) detailed, biologically constrained biophysical models of hippocampal and mPFC FS BCs, using anatomical reconstructions, b) 2- layer Artificial neural network abstractions (ANNs) and c) a large scale microcircuit model of pyramidal, FS BCs and dendrite targeting interneurons. Synaptic stimulation predicted the co- existence of two distinct modes within the same tree: supralinear and sublinear. Supralinear dendrites supported local, sodium-dependent spikes and were characterized by large volume and low input resistance. Using an array of different activation patterns, we found that spatially dispersed inputs lead to higher firing rates than inputs clustered within a few dendrites. These different activation patterns result are better explained by a 2-layer ANN with non-linear hidden layers rather than a linear ANN. Finally, we trained a circuit network model to encode for a single memory. The outcomes predict that bi-modal nonlinear integration in FS BCs promotes resource savings in the encoding of new memories and the formation of engrams. Our findings challenge the linear point neuron dogma and call for further investigation of the contribution of FS BCs in multiple executive functions such as learning and memory.

Reference:

Tzilivaki A., Kastellakis G., Poirazi P. (2019) Challenging the point neuron dogma: FS basket cells as 2-stage nonlinear integrators. *Nature Communications*. doi: 10.1038/s41467-019- 11537-7

Friday 31st January 9am

Unifying models and theories of human brain function and dysfunction

Vinod Menon

Stanford University School of Medicine

The human brain is a complex system capable of supporting a wide range of adaptive goal-relevant behaviors. These behaviors are thought to be supported by the intrinsic functional architecture of large-scale functional systems that constrain and support diverse cognitive processes in a stable, yet flexible, manner. In this talk, I discuss recent advances in our understanding of the dynamic spatiotemporal organization of the human brain and how this organization supports flexible cognitive control. A unifying triple network model of salience and network switching is proposed and its role in attention and cognitive control examined. I describe how such dynamic spatiotemporal provide a unified framework for understanding key features of several major developmental psychopathologies, including autism, ADHD, and schizophrenia, in which cognitive control is impaired. I conclude by discussing recent progress in characterizing brain network dynamics and transient dynamic functional networks using latent state space models, and demonstrate that these models provide novel insights into (i) how the brain switches flexibly between latent states to meet moment-by-moment changes in cognitive demands, and (ii) how the inability to engage optimal brain states impairs cognition.

Friday 31st January 9.45am

Mapping large-scale network dynamics and plasticity in rodent brain

Kai-Hsiang Chuang

Queensland Brain Institute and Centre for Advance Imaging, The University of Queensland, Brisbane, Queensland, Australia

Resting-state networks of the brain are system-wide large-scale networks that exhibit spontaneous synchronous oscillation during task-free condition. These networks indicate the intrinsic organisation of the functional connectivity of the brain and their alterations have been found in learning, aging and disorders, making them potential markers for tracking the brain plasticity and disease conditions. Despite two decades of research, however, the function and neural basis of these networks are still largely unknown. Using resting-state functional MRI, we identified long-lasting reorganisation of these networks in rodent brain after learning a task. Pharmacological manipulations show that the connectivity strength correlated with behavioural performance. To further understand the specificity of these networks in relation to behaviour, we compared brain networks following the same training but with different intensity. To confirm the functional role of these network plasticity in memory consolidation, we are using optogenetics and chemogenetics for targeted manipulations. Finally, combining calcium recording and ultrafast fMRI would allow us to track the neuronal dynamics and to understand the mechanism of such large-scale neuroplasticity.

Friday 31st January 10.15am

Functional connectivity of the striatal network and its role in goal-directed learning

Miriam Matamales[1], Alice E. McGovern[2,3], Jia Dai Mi[4], Stuart B. Mazzone[2,3], Bernard W. Balleine, and Jesus Bertran-Gonzalez[1]

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Extinction learning allows animals to withhold voluntary actions that are no longer related to reward and so provides a major source of behavioral control. Although such learning is thought to depend on dopamine signals in the striatum, the way the circuits mediating goal-directed control are reorganized during new learning remains unknown. Here, by mapping a dopamine-dependent transcriptional activation marker in large ensembles of striatal projection neurons (SPNs) expressing dopamine receptor type 1 (D1-SPNs) or 2 (D2-SPNs) in mice, we demonstrate an extensive and dynamic D2- to D1-SPN trans-modulation across the dorsal striatum that is necessary for updating previous goal-directed learning. Our findings suggest that D2-SPNs suppress the influence of outdated D1-SPN plasticity within functionally relevant striatal territories to reshape volitional action.

Friday 31st January 11am

Activity-dependent and molecular mechanisms regulating the development of cortical connectivity.

Professor Linda Richards AO

Queensland Brain Institute and School of Biomedical Sciences, The University of Queensland, Brisbane, Australia

Long-range commissural projections are highly conserved in vertebrates and function to integrate information from both sides of the body. Our laboratory studies the development of commissural projections in humans, mice and marsupials to understand the mechanisms regulating the formation of circuits in the brain and how they underpin brain function. Spontaneous activity arises in the cortex in early development and may play a role in the establishment of connections and neural networks in the developing brain. However, exactly how spontaneous activity arises in the cortex and what specific circuit properties control how the circuit develops into a functional network are unknown. We have been investigating the emergence of spontaneous activity in the developing marsupial, the fat-tailed dunnart, *Sminthopsis crassicaudata*. Cortical development in dunnarts closely resembles that of placental mammals, making this an ideal model for studying early mammalian brain development. For example, access to developing joeys in the pouch allows imaging of spontaneous activity using the sensitive calcium indicator GCaMP6S at much earlier stages than can be achieved *in vivo* in placental mammals. We have identified the emergence of various patterns of activity including asynchronous bursts, synchronous bursts, and long-lasting events, as well as specific broader patterns of activity and how they differ across cortical regions. In humans and mice, where the corpus callosum, the major commissural axon tract of the brain, is disrupted, we have evidence for long-range axonal plasticity throughout the brain. These data suggest a considerable degree of variability in precise cortical connectivity between individuals is tolerated in cognitive and behavioural functioning. Overall, this work encompassing cellular, physiological, molecular and genetic investigations together with studies of anatomical and structural brain connectivity at a systems level using MRI, enables micro-macro level analyses of brain wiring mechanisms across multiple species.

Friday 31st January 11.30pm

Activity dependent neuroprotection induced by gamma-range stimulation in the acute phase after stroke improves functional outcome

Matilde Balbi[1], Max Jativa[2], Dongsheng Xiao[1], Hao Hu[1], Matthieu Vanni[1], Louis-Philippe Bernier[1], Jeffrey LeDue[1], Brian MacVicar[1], Timothy H. Murphy[1]

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Stroke is a leading cause of death and disability worldwide. Alterations in gamma-range oscillations have been observed in several neurological disorders, and the entrainment of gamma oscillations has been recently proposed as a treatment for neurodegenerative conditions. Optogenetic stimulation has shown potential to enhance stroke recovery when applied weeks after injury; however, benefits of acute brain stimulation have not been reported. We employed optogenetic stimulation in conjunction with laser speckle imaging, electrophysiology and behavioral tasks to investigate the effects of the gamma-wave modulation in the acute phase—within 1 hr—after stroke. Transgenic VGAT-ChR2 mice were implanted with a transcranial chronic window and subjected to awake, photothrombotic stroke in the motor cortex. Optogenetic stimulation at 40 Hz ipsilateral to the stroke prevented acute disruption of neuronal activity at the theta band in M1 and PTA, and resulted in a significant recovery in blood flow over the course of the first week after stroke. Lesion area and volume were significantly reduced in mice that received the stimulation. Motor function showed a significant improvement over time in mice that received stimulation. In this study, we observed cortical oscillatory dynamics in the acute phase following stroke and describe the beneficial effects of 40 Hz brain stimulation: reduced lesion volume and improved motor function after stroke. Our results suggest that modulation of cortical oscillatory dynamics may serve as a target for neuroprotection.

Friday 31st January 12 noon

Circadian control of food intake

Amelia M. Douglass[1], Hakan Kucukdereli[1], Joseph C. Madara[1], Chen Wu[1], Bradford B. Lowell[1,2]

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Food intake and energy metabolism display strong circadian rhythmicity, allowing animals to optimize foraging strategies depending on food availability and environmental conditions. Although circadian rhythms of food intake are ubiquitous throughout evolution, circadian misalignment is becoming prevalent in humans. Miss-timed food intake is associated with an increase in the incidence of metabolic diseases including diabetes and obesity, demonstrating that an understanding of the neural control of food intake rhythms is imperative.

All mammalian biological rhythms are controlled by the body's internal clock, the suprachiasmatic nucleus, located in the hypothalamus. However, it is unclear how circadian signals influence food intake at the neural circuit level. We have focused on understanding the circadian rhythmicity of a key population of hypothalamic neurons, AgRP-expressing neurons, which orchestrate food intake. Using a novel approach to chronically record neural activity in mice, we have found that the activity of AgRP neurons has robust circadian rhythmicity. This suggests that clock-driven activity of these neurons underlies circadian cycles of food intake. Ongoing work will delineate the circuit mechanism that transmits time-of-day information from the circadian clock to AgRP neurons using viral-based tracing and optogenetic circuit mapping strategies and behaviour studies. Together this work will reveal the neural pathway that underlies the temporal organization of food intake and provide insight into human pathophysiologies resulting from disrupted circadian rhythms

Friday 31st January 1.30pm

Data Driven Perceptual Inference

Tobi Delbruck

Institute of Neuroinformatics

Animals and robots must react sufficiently quickly (i.e. with short-enough latency) to sensory input. Conventional machine vision faces a fundamental latency-power tradeoff, where decreasing latency means increasing sensor sample rate and therefore power consumption. Neuromorphic “event camera” silicon retinas developed by us and now by others can solve this problem by using brain-inspired data-driven spike event output. I will show examples and live demos using our dynamic vision sensor (DVS) event cameras. I will also discuss recent convolutional and recurrent deep neural network hardware accelerators that exploit spatial or temporal sparsity to achieve state of the art power efficiency and throughput.

http://sensors.ini.uzh.ch

Friday 31st January 2.15pm

Time-based computation in cortical recurrent networks

Moritz B. Milde* & Andre van Schaik

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As time progresses, our senses capture features of our surrounding which the neocortex transforms into abstract concepts. The continuous nature of time enables the neocortex to associate different features and concepts on multiple spatio-temporal scales. Time, thus, might act as a binding entity to construct a coherent and stable impression of reality.

Information processing in biological and artificial neural networks, however, is often described by reducing spike-trains to instantaneous Poisson firing rates rather than considering the precise spike-timing, despite an increasing body of research indicating that spike-timing is more reliable than predicted by a Poisson process in the context of natural stimuli. To study the computational implications of precise spike-timing, the underlying processing architecture should feature a routing scheme that naturally represents time. The neocortex's routing scheme is characterised by excitatory-inhibitory subnetworks which are recurrently connected inter- and intra-laminary. This stereotypical organisation allows representing time in ongoing computation due to the hierarchical stacking of recurrent loops at multiple spatio-temporal scales.

Here we propose a cortical-inspired recurrent Spiking Neural Network (SNN) that learns and predicts spatio-temporal patterns from noisy event-based vision sensors. The proposed SNN exploits the precise timing of incoming events to form receptive and projective fields, using local, unsupervised learning rules. The SNN (i) shows balanced and stable activity despite heterogeneous processing elements and (ii) engenders an implicit temporal representation of time in ongoing processing. Our experiments investigate how time can serve as a natural binding entity for learning and demonstrate a potential role of time in neural computation.

Poster number 1: Wednesday 4–5.45pm

Explicit conduction delay learning of spatio-temporal patterns embedded in noise

Joshua Arnold, Peter Stratton, Janet Wiles

The University of Queensland

Current research around building learning neural models is focused on weight-based adaption; however, little work has been done to explore the potential of plastic conduction delays. There is mounting evidence that delays between neurons are not only dynamic over both short and long timescales but could also be a functional computational mechanism for learning. Weight-based systems typically model temporal dependencies between neurons using membrane dynamics or other implicit mechanisms making analysis and control more difficult than explicit temporal representations such as conduction delays. The exact processes controlling delay adaption are still under active research; however, the broad idea has been abstracted and converted into an event-based learning rule called Synaptic Delay Variance Learning (SDVL) (Wright, Wiles 2012). The current study analyses the performance of SDVL for unsupervised detection of spatio-temporal spike patterns. Specifically, we use Leaky-Integrate and Fire neurons with SDVL to detect repeating patterns of different size, pattern presentation frequency, internal pattern variability (jitter), and input spike dropout. Internal pattern variability and spike dropout represent two common classes of noise that neural systems need to be able to handle. We show that plastic conduction delays are capable of detecting recurring patterns using few shot learning under various noise conditions without supervision or weight learning; a key finding of our work being that neurons using SDVL can learn and respond to patterns representing 5% of inputs. Our work enables the explicit study and modelling of temporal dependencies between neurons whilst additionally supporting the hypothesis that plastic conduction delays can be an effective learning rule.

Reference

Wright, P. W., and J. Wiles. "Learning Transmission Delays in Spiking Neural Networks: A Novel Approach to Sequence Learning Based on Spike Delay Variance." In The 2012 International Joint Conference on Neural Networks (IJCNN), 18, 2012. https://doi.org/10.1109/IJCNN.2012.6252371.

Poster number 2: Thursday 4.15–6pm

Organization of a neural ensemble in rodent basolateral amygdala

Madhusoothanan Bhagavathi Perumal[1], Benjamin Latimer [2], Li Xu[1], Peter Stratton[1], Satish S. Nair [2], Pankaj Sah[1]

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Neural circuits in Basolateral amygdala (BLA) generate oscillatory network activity to facilitate emotional memory consolidation. Network oscillations emerge from synchronous activity in neural circuits within specific time-windows. Hebb postulated circuits with intrinsic connections to generate synchronous activity form a functional unit called cell assembly or neural ensemble, and mediate memory. However, what types of neurons and circuits form a neural ensemble is unknown. BLA circuits spontaneously generate a characteristic form of oscillatory activity *in vitro*. We hypothesized BLA neurons formed neural ensembles and generated oscillatory activity. We tested the hypothesis and investigated intrinsic circuits using *in vitro* electrophysiology, spike triggered Ca^{2+} imaging, chemo-genetic inhibition and computational modelling and simulation. We found that synchronized activity among Principal neurons and Interneurons generated Sharp wave and ripple oscillations (SWRs)—a signature for neural ensembles. During SWRs, both Pns and Ints recruited through GABAergic and glutamatergic mechanisms, respectively, and orchestrated by a rare subset of Interneurons, the Chandelier neurons (Chns). Chns controlled modules with feedback and feedforward circuit motifs in BLA. Interaction between modules formed a neural ensemble and generated SWRs. In this study, we provide evidence for cellular and circuit organization inside Hebb's ensemble like network in BLA that generated SWRs.

Poster number 3: Wednesday 4–5.45pm

Optimal dendritic processing of spatiotemporal codes

Brendan A. Bicknell and Michael Häusser

Wolfson Institute for Biomedical Research, University College London, London, UK

Neural information processing relies on the transformation of patterns of synaptic input to meaningful action potential output. For every neuron, this operation is shaped by the morphology and biophysics of the dendritic tree. As the filter through which cells communicate, dendritic integration thus presents both fundamental constraints and additional opportunities for computation. How biological or artificial networks may capitalise on this layer of processing remains an open question. A key challenge is to quantify the interplay between synaptic input statistics and dendritic dynamics, and how these interactions can be shaped by learning. However, most previous work has been limited to restricted input regimes, or reduced models that lack the constraints of dendritic physiology. Here, we show that dendritic processing is maximally effective when information is embedded in both the spatial and temporal structure of stochastic input patterns. We augment a model of a layer 2/3 pyramidal neuron with a set of variational equations that reveal how the somatic voltage depends on the history of synaptic activity. We use this to construct a learning algorithm with which we train the model to perform a nonlinear feature-binding task across diverse input conditions. In the optimal regime, sparse bursts of synaptic input provide a substrate for computation far exceeding the capacity of purely rate or temporally coded schemes. This enhancement requires both a branched morphology and voltage-dependent NMDA receptors, predicting a mechanism for conjunctive stimulus selectivity through summation of dendritic spikes.

Poster number 4: Thursday 4.15–6pm

Onset, early dynamics, and cortical-area specificity of neural activity in the developing neocortex revealed by *in vivo* two-photon imaging of marsupial joeys

Tobias Bluett[1]*, Rodrigo Suarez[1]*, Lilach Avitan[1], Annalisa Paolino[1], Laura R. Fenlon[1], Geoffrey J. Goodhill[1,2], & Linda J. Richards[1,3]

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Spontaneous and evoked neural activity plays key roles in the formation and refinement of cortical circuits. This activity is characterised by transient patterns that engage spatially distinct regions in age-dependent fashions, and can be detected in postnatal rodents *in vivo*. While *in vitro* evidence indicates that these patterns begin prenatally in rodents, precise studies of embryonic cortical activity have been hindered by a lack of experimental paradigms *in vivo*. Here, we exploit marsupial development to characterise the onset and early dynamics of cortical activity starting from stages equivalent to intra-uterine rodents and humans. We overexpressed the calcium indicator GCaMP6s in pyramidal cortical neurons, via in-pouch electroporation, in the Australian marsupial fat-tailed dunnart (*Sminthopsis crassicaudata*), and performed two-photon imaging of the developing cortex across the joeys' translucent skull. Neural activity begins at stages equivalent to prenatal rodents (embryonic day 16.5 mice), as low amplitude, infrequent, but highly synchronised events within cortical areas. More complex features such as travelling waves and non-propagating patchwork-type activity appear towards stages equivalent to perinatal rodents. Importantly, somatosensory and visual cortices show different spatiotemporal patterns and developmental dynamics of activity, similar to findings in rodents, suggesting that they may represent an evolutionarily conserved phenomenon of mammalian neocortical development. These experiments highlight the versatility of dunnarts as experimental models of brain development and evolution. We anticipate this imaging paradigm will open the way for future investigations into the neurophysiology of early cortical activity and the role of such activity in the formation of functional circuits.

Poster number 5: Wednesday 4–5.45pm

Stability of spontaneous activity depends on synaptic delays in spiking network models

Thomas Burns, Tomoki Fukai

Okinawa Institute of Science and Technology Graduate University, Japan

Computational models of spiking neural networks with recurrent excitatory lognormal weight distributions can generate and maintain spontaneous activity states in the absence of external input. Such models have been used to study memory, sensory systems, and spontaneous activity dynamics. We adapt a known spiking neural network model consisting of 10,000 excitatory and 2,000 inhibitory exponential integrate-and-fire neurons to study how variable synaptic delays and failure probabilities affect spontaneous activity stability. We simulate this network for 1s of simulation time and calculate the average last simulated spike time from 10 simulations for each combination of parameters tested. This provides an indication of spontaneous activity stability. We tested six parameters for the networks' synaptic delays with three probabilities of synaptic failure. We find that network stability (as measured by loss of continued dynamics) is highly sensitive to synaptic failure. Networks which include longer delays end prematurely, even in cases where such networks also include shorter delays. We additionally tested the same parameters with the same network structure using adaptive exponential integrate-and-fire neurons. Although adaptive exponential integrate-and-fire neurons successfully replicate many biological phenomena of neurons, they fail to generate spontaneous activity states in this model. We hypothesize this may be due to the neurons' slower sub-threshold integration dynamics. How to overcome this difficulty with adaptive exponential integrate-and-fire neurons is currently under investigation.

This work is partly supported by KAKENHI (nos. 18H05213 and 19H04994) from MEXT, Japan.

Poster number 6: Thursday 4.15–6pm

Development of emotion regulation circuits in the human adolescent brain

Islay G. Davies*[1], Lachlan T. Strike[1], Narelle K. Hansell[1], Katie L. McMahon[3], Margaret J. Wright[1,2]

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Adolescence is an emotionally volatile period that coincides with when the brain is changing and re-modelling. Yet little is known about the development of brain connectivity associated with emotion regulation during this period. Here, using resting-state functional Magnetic Resonance Imaging (rsfMRI), we investigated the pattern of functional connectivity (FC) between brain regions implicated in emotion regulation in typically developing adolescents (n=338, 52% female; mean age=11.38, SD=1.35). In a seed-based analysis we used the ventral striatum (VS) and amygdala (AMY) as seeds, and six subregions of the prefrontal cortex (PFC) as regions of interest. As expected, we found strong positive FC between the VS and AMY, and between each seed and the ventral regions of the PFC. However, contrary to expectations, we did not find a shift in strength between each seed and the ventral anterior cingulate cortex (vACC), suggested by studies in children and adults. In addition, we did not find a general pattern of negative FC between each seed and the dorsal regions of the PFC. This was only evident with the dorsal lateral PFC. These findings are in line with the hypothesis that positive FC between subcortical regions, and these and ventral regions of the PFC, remain through adolescence. However, the hypothesis that FC between the subcortical regions and the ventral (affective) and dorsal (control) subregions of the PFC develop in a linear and opposing way through adolescence was not supported. Our findings suggest a more complex process of FC development between these circuits from childhood to adulthood.

Poster number 7: Wednesday 4–5.45pm

Modelling bidirectional bioelectric pelvic nerve interfaces in EIDORS

Calvin D. Eiber[1], Martin Bertrand[1,2], Peregrine B Osborne[1], and Janet R Keast[1]

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[2] Department of Digestive and Oncologic Surgery, Nîmes University Hospital, Nîmes, France

Micturition (urination) and continence are controlled by the autonomic nervous system; the pelvic nerves provide the primary source of autonomic innervation to the bladder and are prime targets for electrical stimulation to treat over- or under-active bladder. The pelvic nerves in both human and rat are fasciculated, but differ from other well-studied nerves such as the vagus or sciatic nerves in that they largely lack a resistive epineurium. Finite-element models of the pelvic nerves and electrode array were implemented in SIM4LIFE and EIDORS to simulate electrical stimulation and recording, based on measurements of the functional composition of the different fascicles of the pelvic nerve in male rats. Biophysical models for myelinated and unmyelinated axons were adapted to small-diameter pelvic nerve axons and implemented in NEURON (neuron.yale.edu). Parameter sensitivity was established using Sobel' sensitivity analysis for different fascicle arrangements and orientations. Extracellular stimulation thresholds depend on both the macro- and micro-anatomical properties of the pelvic nerve; Within-fascicle selectivity is enhanced in the largest fascicles of the pelvic nerve, and overall thresholds are reduced in the smallest fascicles. Stimulus thresholds and conduction velocities depend on the ultrastructural geometry of the nodal and internodal regions. Extracellular recordings could be computed in NEURON+EIDORS and validated in SIM4LIFE for predicting spontaneous and electrically evoked activity recordings. Extracellular recording sensitivity and stimulus thresholds were both most closely correlated with axon-electrode distance. In conclusion, EIDORS can be used to accurately simulate extracellular recording in complex, heterogenous neural geometries.

Poster number 8: Thursday 4.15–6pm

Development of simultaneous calcium photometry and fMRI of the mouse brain

Shabnam Khorasani Gerdekoohi[1], Hsu-Lei Lee[1,2], Helena Huang[1], Pankaj Sah[1], Kai-Hsiang Chuang[1,2]

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Optical recording of neural activity, such as calcium, provides versatile and important information for understanding the neural dynamics, however, it has limited field of view for mapping the activity across the whole brain. Combining calcium recording with functional MRI could overcome this limitation and improve the interpretation of hemodynamic fMRI measures. Combining both modalities in the mouse brain remains challenging due to image artefact and low fMRI signal in the mouse brain. In this study, we adopted a camera-based photometry that allows multi-channel recording of GCaMP6f responses in the visual cortex and the lateral geniculate nucleus of the visual pathway. 4-6 weeks after viral injection, fMRI was conducted on a 9.4T MRI with 1s and 0.3s temporal resolutions, and GCaMP signal measured with an excitation light (470nm) alternated with a reference light (410nm) sampled at 20Hz frame rate (10Hz per wavelength). Strong calcium and BOLD activation can be detected under visual stimulations, though fMRI signal around the optic fiber implant was highly attenuated due to larger field change over the small mouse brain. Further study is ongoing to reduce the susceptibility artefacts (signal dropout and distortion) from the optic fibre implant and dental cement by optimizing materials, pulse sequences, etc. Besides, deconvolution between calcium and fMRI activities would allow us to infer underlying neural activity from fMRI signals.

Poster number 9: Wednesday 4–5.45pm

Neural circuits for backward walking in *Drosophila*

Kai Feng

Queensland Brain Institute, The University of Queensland

The Moonwalker Descending Neurons (MDNs) are command neurons for backward walking in *Drosophila* (Bidaye et al, 2014). MDNs are known to receive input from visual and mechanosensory pathways that signal threats or obstacles in the fly's path (Sen et al., 2017; Sen et al., in press), but the downstream motor circuits that implement backward walking remain unknown. High-speed video recording and limb tracking on MDN-activated flies indicated that backward walking is driven by the hind legs, with mechanical coupling ensuring coordinated movements of the mid- and forelegs. Tibia flexion and femur levation are the most prominent movements of the hindleg during stance phase. In order to uncover the neural circuits that implement this complex motor program, we used two complementary methods, functional imaging and trans-synaptic labelling (trans-tango), to systematically identify neuronal types that are receiving inputs from MDN. We found more than 50 cell types that were positive by either methods, distributed throughout the ventral nerve cord. Consistent with the behavioural data suggesting that backward walking is driven by the hindlegs, we found that MDNs preferentially activate neurons in the third (metathoracic) segment. Of the 32 types of neurons we found to be either activated or inhibited by MDN, 19 are likely direct synaptic partners indicated by trans-tango. We could generate driver lines to specifically target these cell types for functional analysis. An initial behavioural screen found that silencing many of these neurons rendered flies defective in MDN-driven backward walking. One such cell type, a metathoracic-specific neuron we call Arch, mediates tibia flexion through the tibia-reductor motor neuron. Upon silencing Arch, MDN-induced stance-phase power stroke has a reduced speed and amplitude. Another cell type, Kitten Ear (KE), is present in all three segments but only the metathoracic neurons are strongly activated by MDN. The KE neurons mediate the motor sequence resembling ground searching during swing phase. Silencing KE renders MDN-activated flies delayed swing phase and fewer steps. In conclusion, we have systematically mapped out the neural circuits for backward walking and identified key neuron types controlling the stance (Arch) and swing (KE) phases. Our results and reagents provide an important inroad for understanding the neural mechanisms and principles of walking in legged animals.

Poster number 10: Thursday 4.15–6pm

Effects of variation of sodium and potassium voltage gated ion channel conductances on PING network oscillatory properties

Chris Olteanu[1], Forough Habibollahi Saatlou[2], Chris French[3]

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Introduction – Voltage gated ion channels underlie action potential discharges and rhythmic firing of individual neurons, and might be expected to influence the oscillatory behavior of networks of these neurons. We explored the effects of alterations in amplitude of several potassium and sodium conductances in a pyramidal-interneuron gamma ("PING") network consisting of 40 excitatory E cells, and 10 interneurons consisting of 5 fast spiking neurons (I cells) and 5 dendritically connected oriens lacunosum moleculare (O cells).

Methods – A PING network based on a model described in Kopell et al (2010) was augmented with a persistent sodium current (I_{Nap}) and implemented in the NEURON modelling environment. Currents included for testing were an inactivating potassium conductance (I_A), a delayed rectifier potassium conductance (I_{KDR}), a hyperpolarization activated mixed cation current (I_H) a persistent sodium current (I_{Nap}), in addition to a conventional fast inactivation sodium current (I_{Na}). All conductances were implemented as modified analytic forms of the Hodgkin-Huxley equations. 5 second long simulations were performed, and the results of 10 simulations for each parameter variation were averaged. Local field potential activity was sampled from a point in the network. Conductances were changed individually from 0 to 2x baseline amplitudes in seven increments. Spectral properties of the local field potentials were measured with the *spectrum.periodogram* procedure of MATLAB after initial high and low pass filtering at 0.5 and 100Hz respectively.

Results – All conductance types influenced gamma and theta power or frequency over the range tested. The effects were complex, often with both enhancement and inhibition of spectral properties over the ranges tested. I_A strongly affected theta and gamma power with a 25% change reducing power by 80%, and 50% respectively with little influence on peak frequency. I_H also reduced theta power from 33 to 90% and gamma power by 12.5 to 50%, but increased theta frequency peak from 5 to 300% and approximately doubled gamma peak frequency over the tested range. Small changes in I_{KDR} produced strong suppression of theta power (66 to 90%), with little effect on gamma power or frequency. Increases in I_{Nap} beyond the baseline value of $2e^{-8}$ S/cm^2 had a strong suppressant effect on theta power but little change in frequency and minor effects on gamma power or frequency.

Conclusion – Relatively small changes in a range of potassium and sodium conductances produced significant changes in network rhythmicity. These changes might realistically be expected to occur with CNS active drugs, and may contribute to therapeutic effects as well as unwanted side effects.

Poster number 11: Wednesday 4–5.45pm

Spatiotemporal differences in the axon guidance systems of marsupial and placental mammals underlie divergent neocortical commissure formation

Elizabeth H. Haines[1], Laura R. Fenlon[1], Annalisa Paolino[1], Peter Kozulin[1], Linda J. Richards[1,2], Rodrigo Suárez[1]

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A defining feature of all mammals is the organisation of their telencephalon into a six-layered neocortex, with conserved organisation of projection neurons. Over one hundred million years ago, placental and marsupial mammals diverged evolutionarily, demonstrating a striking anatomical difference in the main connection between left and right neocortical hemispheres. In marsupials, interhemispheric neocortical axons turn laterally, before crossing the midline alongside olfactory axons in the anterior commissure. Exclusively in placental mammals, this population of axons turns medially to form the corpus callosum. Using an Australian marsupial, the fat-tailed dunnart, and the placental mouse, we compare similarities and differences in brain development to elucidate evolutionary steps that led to the emergence of the corpus callosum. Here, we uncover key features of marsupial neocortical commissure formation, demonstrating conservation of a neocortical neurogenic gradient initiating rostro-laterally and proceeding medio-caudally, similar to mice. This neurogenic gradient also has a conserved relationship with the order of crossing of neocortical commissural axons in dunnarts, indicating that this mechanism preceded callosal evolution. However, our data show that cingulate axons do not pioneer the commissural route in dunnarts. An analysis of axon guidance molecule expression in the dunnart brain suggests that marsupial neocortical axons use ‘callosal-like’ cues rather than those used by the anterior commissure to cross the midline. Crucially, we identify candidate spatiotemporal differences in the expression of some of these cues, such as an inverted expression, which may underlie medial (placental) versus lateral (marsupial) turning of neocortical commissural axons and the emergence of the corpus callosum.

Poster number 12: Thursday 4.15–6pm

Genetic and environmental distinctiveness and covariation among hippocampal subfield volumes in 2,148 young adult twins and siblings

Hansell NK, Strike LT, van Eijk L, O'Callaghan V, de Zubicaray GI, McMahon KL, Thompson PM, Wright MJ

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The extent to which overlapping, or distinct, genetic and environmental sources influence variation in the hippocampal subfields remains unclear. However, this can be an important consideration in study design. Here we combine twin and sibling data from two independent young adult cohorts to explore covariation among hippocampal subfield volumes in the largest twin study of these measures to-date. Analyses included data from 2,148 individuals, comprising 1,073 individuals from 627 families (mean age = 22.3 years) from the Queensland Twin Imaging (QTIM) Study, and 1075 individuals from 454 families (mean age = 28.8 years) from the Human Connectome Project (HCP). Hippocampal subfields were segmented using Freesurfer software. Multivariate classical twin modelling was conducted in OpenMx, using the combined sample, to decompose variance into genetic and environmental sources. For the majority of subfields, sources of variance were mostly overlapping, with 32-83% of total variance for individual subfields identified as being influenced by sources influencing multiple subfields. Still, variance unaccounted for by shared sources, and thereby considered distinct in terms of the other subfields, was substantial for some variables (i.e. 68% for Parasubiculum, 64% for Fissure, and 53% for Fimbria). Distinct, or specific, sources of influence had both genetic and environmental components (as did the overlapping sources of influence). However, while specific environmental components were found to be significant (accounting for 10-37% of total variance for the subfields), the specific genetic components (accounting for 6-31% of variance) did not reach significance. Nonetheless, in terms of genetic and environmental influences, results support the continued investigation of sub-regions of the hippocampus, as novel insights may be gained compared to studying the hippocampus as a single volume.

Poster number 13: Wednesday 4–5.45pm

The interplay of anxiety and hunger in anorexia nervosa

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Anorexia nervosa (AN) is an eating disorder characterized by voluntary self-starvation, extreme weight loss, and negative body image. It is a potentially life-threatening psychiatric disorder with the highest mortality rate. Furthermore, AN has high comorbidity with other psychiatric conditions such as severe depression and chronic anxiety. Unfortunately, treatments remain inadequate and do not restore healthy eating behavior. A major obstacle to developing more effective treatments is lack of understanding of the underlying circuits and their pathology. Several important brain areas involved in stress and learning of cues may be implicated in the altered reactions to food cues and aversive cues in patients with AN. One such region where stress and learning of food cues coincides is the basolateral nucleus of amygdala. We are using cutting-edge neuroscience imaging techniques to test the hypothesis that natural and artificial hunger (i.e. direct optogenetic stimulation of hypothalamic AgRP neurons) may suppress aversive cue responses in neural circuits involved in stress and anxiety in basolateral amygdala. Together, these experiments will provide novel approaches to understanding the neural circuits underlying learned behaviors that promote sustained food restriction in AN.

Poster number 14: Thursday 4.15–6pm

Automated tracking and quantification of prey capture behaviours in larval zebrafish

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Bridging the gap between neural computation and behavioural output requires meaningful quantitative descriptions of how animals interact with their natural environments. Larval zebrafish are a useful vertebrate model for the study of naturalistic behaviours in the context of neural development. In addition to the possibility for whole-brain imaging and manipulation of neural activity at single cell resolution, larval zebrafish exhibit a rich repertoire of complex goal-oriented behaviours from a young age including visually guided prey capture. While certain highly stereotyped behavioural markers of prey capture such as eye convergence are well established, behaviours on finer scales—for example relationships between action selection and the target trajectory—are not well understood. Furthermore, the analysis of naturalistic behaviour imposes the challenge of variability which may not be under the experimenter's control, for instance due to the position and orientation of the animal and its target, or other unobserved internal states including hunger and stress. Such variability necessitates the collection of large samples and therefore scalable methods for extracting relevant behavioural measures. We addressed this challenge by developing custom image processing software that automatically tracks behaviour from 500 frames per second video recordings of zebrafish prey capture. Our software comprises correlation filter-based tracking using histogram-of-oriented-gradients features in combination with a range of traditional image processing techniques. With minimal user input and as few as 10 training frames our method achieves robust tracking of locomotion, tail kinematics and prey trajectories. This method therefore facilitates high-throughput analysis and subsequent modelling of complex naturalistic behaviours in larval zebrafish, which in turn may help to reveal characteristic changes in hunting behaviour over development or between genotypes.

Poster number 15: Wednesday 4–5.45pm

Diffusion Tensor Imaging reveals extensive white matter alterations in the aftermath of traumatic brain injury and post-traumatic stress disorder in Vietnam War veterans

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[@] Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf
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Background: To date, Diffusion Tensor Imaging (DTI) studies have revealed structural changes in major white matter (WM) tracts shortly following traumatic brain injury (TBI) and in patients with post-traumatic stress disorder (PTSD), but the long-term persistence of these changes is unknown. We utilized DTI to investigate WM alterations in TBI and/or PTSD survivors, five decades after the trauma.

Methods: Data from 167 Vietnam War veterans recruited by the US Department of Defense Alzheimer's Disease Neuroimaging Initiative, underwent a neuropsychological Assessment, structural MRI, and DTI, and were divided into TBI (n = 23), PTSD (n = 53), TBI+PTSD (n = 39), and control (n = 52). We tested for group differences in WM's fractional anisotropy (FA) and mean diffusivity (MD) (tract-based spatial statistics), and calculated correlations between WM alterations with neuropsychological scores (Voxel-wise).

Results: The PTSD and TBI+PTSD groups showed greater neuropsychological and cognitive impairments as compared to the TBI and control groups. Compared to controls, decreased FA and increased MD were observed in major WM tracts including the corpus callosum, external and internal capsule, inferior longitudinal fasciculus, cingulum, and superior longitudinal fasciculus. Furthermore, FA alterations correlated positively with the Boston Naming Test and Montreal Cognitive Assessment, while MD correlated negatively with Boston Naming Test and Mini-Mental State Exam scores, implying a relationship between disruption of WM axons and present cognitive performance.

Conclusion: DTI detected distinct patterns of WM changes in veterans with TBI and PTSD almost half a century post-trauma, and the extent of WM alterations correlated with poor clinical outcomes.

Poster number 16: Thursday 4.15–6pm

Inheritance of a *Draxin* mutation determines the severity of interhemispheric fissure remodelling defects and interhemispheric tract malformations in the BTBR mouse strain

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Axon tract formation occurs through a series of developmental events under the regulation of gene expression networks. Single gene mutations are thought to underlie disrupted interhemispheric tract formation in humans with neurodevelopmental disorders, but how variable phenotypes arise in individuals carrying the same gene mutation is not well understood. We therefore investigated the cellular and genetic correlates for variable interhemispheric tract malformations in BTBR inbred and outcrossed mice.

Remodelling of the interhemispheric fissure by astrocytes provides a substrate for axons of the corpus callosum and hippocampal commissure to cross between hemispheres, thus facilitating formation of these interhemispheric connections. We identified defects in astroglial development and failed remodelling of the interhemispheric fissure in BTBR mice, and the severity of these defects is directly correlated with the severity of callosal and hippocampal commissure malformations. Moreover, we identified that BTBR mice carry an eight base pair mutation in *Draxin*, which truncates the encoded axon guidance protein and disrupts its expression *in vivo*. Surprisingly, inheritance of the *Draxin* mutation is the main driver of interhemispheric fissure remodelling defects and subsequent corpus callosum and hippocampal commissure malformations. We therefore conclude that *Draxin* is a major determinant of cortical connectivity by regulating the extent of midline substrate formation for callosal and hippocampal commissures to cross the telencephalic midline.

Our study provides cellular and genetic correlates underlying variable phenotypes of disrupted interhemispheric connectivity in a mouse model. This work provides a foundation for further investigation into the developmental basis of variable phenotypes in humans with neurodevelopmental disorders.

Poster number 17: Wednesday 4–5.45pm

Elucidating a phylogenetic switching model of sleep, vision & mental health with computational biology and complex network analyses

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Bistable oscillator models have long been investigated by chemists, physicists & biologists to elucidate a range of phenomena from chemical reaction networks and predator-prey cycles through to sleep/wake rhythms and brain activity dynamics. In visual neuroscience, dichoptic presentation of orthogonal gratings in fruit flies, hawkmoths, cats, macaque monkeys and humans induces bistable switches in perception, i.e., binocular rivalry (BR). Remarkably, optomotor BR switching behavior in *Drosophila* engages left-right interhemispheric alternations in LFP activity (Tang & Juusola, 2010). Other examples of such switching activity include alternations between: (i) relative left & right nasal patency (the nasal cycle) in several mammalian species; (ii) left- & right-hemispheric activity during birdsong and sleep; (iii) independent eye movements in the sandlance & chameleon (Pettigrew et al., 1999); and (iv) left & right SCN electrophysiological activity and *Per* mRNA expression in rodents. This independent converging evidence supports a phylogenetic switching model of brain & behaviour. Here we will present a research program characterising this fundamental brain switching mechanism in humans with: (i) complex network analyses of sleep EEG data; (ii) genome-wide association analysis of BR rate data from a large sample of healthy adolescent twins (N=1091); and (iii) studies of slow BR rate in bipolar disorder as a putative mental health biomarker. This work aims to lay the foundation for elucidating bistable approach/avoidance choice behaviour across taxa such as in neurogenetic models (e.g., *E. coli*, *C. elegans*, *Drosophila*, fish, mice), with implications for understanding the evolution of biological (locomotor) rhythms, cognition and neuropsychiatric states.

Poster number 18: Thursday 4.15–6pm

Spikes representing motion direction are phase-locked to the LFP within and between areas MT and V1 in anaesthetised marmosets.

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Visual perception relies on communication between distinct cortical areas, each of which serves a specialised role in visual processing. This communication depends primarily on action potentials or "spikes", but the role of the local field potential (LFP) in coordinating this spiking remains unclear. In awake primate area V1, spikes are phase-locked to the LFP and orientation selectivity is modulated by the phase of the gamma-band oscillations. This is consistent with the theory that communicating areas may rely on transient increases in coherence, to ensure the propagation of signals from one area to another. In awake macaques, attention has been shown to determine which of two visually stimulated V1 populations entrains a downstream area, though it is not known whether this entrainment occurs in the absence of attentional modulation. We test this by recording from connected visual areas V1 and MT, in anaesthetised marmosets. As previously seen in V1, we found that both V1 and MT spiking is phase-locked to the LFP, and the strength of information about the direction of motion varies with phase. Surprisingly, this phase-locking is strongest in the alpha/beta bands, rather than gamma as previously shown. We also found that spikes were phase locked to the LFP between areas as well, and tuning strength in the spiking of one area is modulated by the phase of the LFP in the other area. These results suggest phase-locked stimulus information is present even in the absence of attentional modulation, and therefore represents a fundamental characteristic of inter-area communication.

Poster number 19: Wednesday 4–5.45pm

Depression, daytime sleepiness, and the default mode network in adolescent twins

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Depression and daytime sleepiness have a bidirectional relationship and have critical consequences for adolescents' behaviour, academic performance, and other mental health concerns. The reason for this association is underexplored in adolescents; however, previous research in adults suggests genetic effects may play a role. Furthermore, it is also unknown whether experiencing both depression and daytime sleepiness during this critical period can have implications for brain development, in particular for the development of the default mode network. We aimed to investigate the genetic covariation between depression and daytime sleepiness in a community sample of 390 adolescent twins (96 monozygotic and 99 dizygotic pairs; 49% female) aged 9–14 from the Queensland Twin Adolescent Brain (QTAB) project. Depression and Daytime Sleepiness were measured using the Short Mood and Feelings Questionnaire (SMFQ) and Paediatric Daytime Sleepiness Scale (PDSS), respectively. Additionally, we collected rs-fMRI images on a 3T Siemens PRISMA whole body scanner. A classic twin design with a bivariate cholesky decomposition model was used, with age and sex controlled for. Twin modelling estimated that the genetic influence on depression accounted for 40% of genetic variance in sleepiness with the remaining variance (60%) unique to daytime sleepiness. Additionally, the covariation between depression and daytime sleepiness was due to roughly equal parts of genetic (49%) and environmental factors (51%). These preliminary results confirm that genetic factors also play an important role in the link between depression and daytime sleepiness in adolescents. Results will be extended in a future study to investigate the effect of depression and daytime sleepiness on the development of the default mode network in adolescents.

Poster number 20: Thursday 4.15–6pm

Using deep learning to automate analysis of zebrafish behaviour

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How nervous systems generate complex behaviours is one of the outstanding mysteries of neuroscience. Zebrafish provide an important model system in this regard since they are transparent at the larval stage allowing optical imaging of neural activity, can model human genetic disorders, and display complex natural behaviours such as hunting that can be studied in a lab environment. Eye convergence is a known marker for when zebrafish are actively hunting. Here we propose a method for automatic identification of hunting events from high speed video recordings of free swimming behavioural experiments, using a deep convolutional neural network for semantic segmentation of the eyes followed by ellipse fitting to track the eye angles. We used the pretrained neural network ResNet18 adapted to fit the requirements of the DeepLabv3+ architecture for semantic segmentation. This network was trained on 140 randomly selected, manually segmented frames from a video of zebrafish hunting. Threshold based classification of hunting events from automatically detected eye angles revealed no false negatives and very small levels of error in event timings when benchmarked against expert manual annotations. These results suggest that deep neural networks provide a promising technique for automatically segmenting zebrafish hunting behaviour.

Poster number 21: Wednesday 4–5.45pm

Estimating transfer entropy in continuous time for spike trains

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Transfer entropy (TE) [1] is a measure of the flow of information between components in a system. It is defined as the mutual information between the past of a source and the present state of a target, conditioned on the past of the target. It has received widespread application in neuroscience [2, 3], both for characterizing information flows as well as inferring effective connectivity from data sources such as MEG, EEG, fMRI, calcium imaging and electrode arrays. Previous applications of TE to spike trains have relied on time discretization, where the spike train is divided into time bins and the TE is estimated from the numbers of spikes occurring in each bin. There are, however, several disadvantages to estimating TE from time-discretized data [4]. First and foremost, as time discretization is a lossy transformation of the data, it will result in an underestimate of the TE. Thus, any estimator based on time discretization is not consistent. Secondly, whilst the loss of resolution of the discretization will decrease with decreasing bin size, this requires larger dimensionality of the history embeddings to capture correlations over similar time intervals. This results in an exponential increase in the state space size being sampled and therefore the data requirements. The increase in the data requirements renders the estimation problem intractable for the typical dataset sizes present in neuroscience.

Recently, a continuous-time framework [4] for transfer entropy was developed. This framework has a distinct advantage in that it demonstrates that, for spike trains, the TE can be calculated solely from contributions occurring at spikes. This presentation reports on a newly developed continuous-time estimator for transfer entropy for spike trains which utilizes this framework. Importantly, this new estimator is a consistent estimator of the TE. As it does not require time discretization, it calculates the TE based on the raw interspike interval timings of the source and target neurons. Similar to the popular KSG estimator [5] for mutual information and TE, it performs estimation using the statistics of K-nearest-neighbour searches in the target and source history spaces. Tests on synthetic datasets of coupled and uncoupled point processes have confirmed that the estimator is consistent and has low bias. Similar tests of the time-discretized estimator have found it to not be consistent and have larger bias. Further tests on Izhikevich neurons driven by Poisson sources have demonstrated that the continuous-time estimator is far superior in distinguishing between coupled and uncoupled sources when these sources are correlated with one another. Finally, the continuous-time estimator has been found to require substantially lower computational resources, both in terms of memory and CPU time.

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Poster number 22: Thursday 4.15–6pm

Convolutionary, evolutionary, revolutionary: What's next for bodies, brains and AI?

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The flexibility, adaptability and resilience of even simple brains are unmatched by any current technology. Recent unexpected difficulties in realizing truly autonomous vehicles, making reliable medical diagnoses, detecting offensive online content, creating useful chat-bots and even just recognizing faces, show that brains remain significantly functionally more capable than we can currently emulate. In recent years we have made significant progress identifying computational principles that underlie neural function. We are beginning to dispense with the overly-simplistic stimulus-driven encode/transmit/decode doctrine. Instead we must embrace the brain's inherent dynamic complexity and emergent properties, and explain how plasticity moulds the dynamics to capture useful couplings across brain regions and between the brain, the body and the world. While certainly not complete, we have sufficient evidence that a synthesis of these ideas could result in a deeper understanding of neural computation, and which could potentially be used to construct new AI technologies with unique capabilities. I discuss the relevant principles, the advantages they have for computation, and how they can benefit AI. Limitations of current AI are now generally recognized, but fewer people are aware that we understand enough about the brain to immediately offer novel AI formulations.

Poster number 23: Wednesday 4–5.45pm

Neural encoding models for multivariate optical imaging data

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The brain must integrate external sensory information with internal factors that regulate circuit function, cognitive state, and behaviour. Such internal factors give rise to spontaneous neural activity, and can substantially affect measurements of stimulus-evoked responses, especially in calcium imaging data where the temporal dynamics of calcium indicators is markedly slow. Here we develop an approach to modelling these data that simultaneously accounts for patterns of neural activity evoked by sensory stimuli and ongoing spontaneous activity driven by hidden internal factors. In this framework, low-dimensional patterns of spontaneous activity can be computed as the maximum *a posteriori* estimate under the latent variable model and easily separated from evoked responses. This decomposition allows us to numerically quantify how neurons are differentially driven by sensory input and internal factors. We then further develop the model in a more tightly constrained Bayesian framework by incorporating spike-and-slab sparse priors that better model deconvolved calcium dynamics, latent Gaussian processes that govern ongoing fluctuations in excitability, and stochastic gradient variational methods for tractable posterior inference. Application of the model to the zebrafish optic tectum identifies smooth changes in excitation across the neural population that modulate the influence of evoked and spontaneous activity.

Poster number 24: Thursday 4.15–6pm

Understanding the interactions between sleep and prediction in *Drosophila*

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Different stages of sleep play distinct and yet equally important roles for the brain, and these are associated with behavioural as well as electrophysiological signatures. In mammals, deep sleep is associated with delta wave (1-4Hz) activity and regular breathing, while during REM sleep the brain appears awake and some body parts (notably, the eyes) move or twitch. Invertebrates such as the fruit fly *Drosophila* melanogaster also appear to sleep in stages of varying intensity, but it is unclear whether this is also associated with distinct microbehaviours, or whether similar functions are being subserved.

To identify possible markers of sleep stages in *Drosophila*, we tracked microbehaviours such as antenna movements and proboscis extensions during sleep using video recordings. We identified the presence of periodic, low-frequency motion of the antennae during sleep bouts in the fly, along with a phasic occurrence of proboscis extensions over the course of the night, suggesting that these could be indicative of distinct sleep stages in flies.

Our working hypothesis is that proboscis extensions occur during deep sleep stages whereas antennal movements might predominate during wake-like or paradoxical sleep.

To test for potential roles of wake-like sleep in optimising attention-like processes for animals we have developed a closed-loop visual paradigm to quantify fly locomotor behaviours in response to predictable and unpredictable events. By integrating our recordings of sleep micromovements and quantitative behavioural measures of predictive capacity we hope to uncover how the quantity and content of sleep for a fly affects their capacity for prediction.

Poster number 25: Wednesday 4–5.45pm

Antidepressant and antimanic effects of deep brain stimulation of the ventral tegmental area

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Background: DBS for treatment-resistant unipolar and bipolar depression has preliminary efficacy signals, however, few studies include patients with bipolar disorder (BD). A concern for DBS in BD is the observation of induced psychiatric side-effects in isolated cases (eg, changes in mood, induced hypomania). Further studies on the effects of different patterns of stimulation in this condition are needed.

Methods: We utilised rat models of treatment resistant depression and mania induced via chronic administration of adrenocorticotropic hormone (ACTH; 100µg/day; 14 days) or methamphetamine (2mg/kg/day; 14 days), respectively. Effects of two patterns of ventral tegmental area (VTA) stimulation on behaviour were tested: 1) intermittent low frequency stimulation (Frequency: 10Hz; 2 burst/sec; 300µA; n=8-12); and 2) continuous high frequency stimulation (130Hz; 200µA; n=8-12). Following 20 mins stimulation, ACTHtreated animals underwent the forced swim test (6 mins) and amphetamine-treated animals were observed in the open-field test (20 mins). Quantification of VTA-evoked nucleus accumbens dopamine was performed using fast-scan cyclic voltammetry (n=4).

Results: Low frequency stimulation reduced immobility time in ACTH-treated animals only, whereas high frequency stimulation decreased immobility time in both saline and ACTH groups ($p<0.05$). High frequency, but not low frequency DBS, decreased locomotion in methamphetamine-treated animals ($p<0.05$). Both parameters significantly increased and decreased dopamine release in ACTH- and methamphetaminetreated animals, respectively, with high frequency stimulation more effective in both instances ($p<0.05$).

Conclusions: These results suggest DBS modulates both depressive and manic symptoms in a frequency-dependent manner. One mechanism through which this may be mediated is direct modulation of perturbed mesoaccumbens dopamine neurotransmission.

Poster number 26: Thursday 4.15–6pm

Large-scale calcium imaging of spontaneous activity in larval zebrafish reveals signatures of criticality

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Neural networks in the brain may self-organise such that they operate near criticality, that is, poised on the boundary between phases of order and disorder. Models of neural networks tuned close to criticality are optimal in terms of dynamic range, information transmission, information storage and computational adaptability. However, experimental evidence for criticality in the brain has been limited to investigations of: (i) neuron spiking data from *in vitro* tissue cultures or in anesthetised animals using microelectrode arrays which under-sample the neural population, or (ii) mesoscopic-scale neural activity from large populations of neurons *in vivo* using magnetic resonance imaging or electroencephalograms which under-sample spatial resolution. Here we exploit the unique properties of the larval zebrafish which enable imaging of large populations of neurons *in vivo* using 2-photon calcium imaging. We report evidence of critical dynamics in populations of approximately 10000 neurons observed at single-cell resolution from 3-dimensional volumetric recordings of spontaneous neural activity in the optic tectum and cerebellum of larval zebrafish with pan-neuronal expression of GCaMP6s. Neural avalanche statistics revealed power-law relationships consistent with crackling noise dynamics simulated in a three dimensional random field Ising model – an archetypal model of critical dynamics. This result provides the first evidence of criticality in the brain from large-scale *in vivo* neural activity at single cell resolution and demonstrates the potential of larval zebrafish as a model for further investigation of critical phenomena in the context of neurodevelopmental disorders such as autism that may perturb the brain away from criticality.

Poster number 27: Wednesday 4–5.45pm

A frequency-dependent requirement for PICK1 in synaptic vesicle endocytosis

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Neuronal communication relies on the rapid release of neurotransmitters following the fusion of synaptic vesicles with the plasma membrane. Following exocytosis, these vesicles are retrieved through endocytosis, a process that is crucial to replenish the finite number of vesicles available in order to maintain synaptic transmission. The Protein Interacting with C-Kinase 1 (PICK1) is a BAR (Bin/amphphysin/Rvs) and PDZ (postsynaptic density-95/disc-large/zona-occluden-1) domain-containing molecule that regulates the vesicular trafficking of many postsynaptic neurotransmitter receptors and transporters. Interestingly, PICK1 is also expressed in the presynaptic terminals where its function remains unknown. To determine whether PICK1 regulates synaptic vesicle recycling, we employed a live-cell imaging technique to monitor the recycling of a resident synaptic vesicle protein, synaptophysin that is tagged with a pH-sensitive green fluorescent protein (SypHy), in primary hippocampal neurons. PICK1 loss of function specifically slows the kinetics of SypHy endocytosis without affecting its exocytosis when neurons are stimulated at 50 Hz, but not at 10 Hz. In addition, shRNA-mediated knockdown of PICK1 also causes surface stranding and mislocalisation of SypHy along the axon. Structure and function analyses reveal that a functional PDZ domain of PICK1 is required for the proper targeting of SypHy along synaptic boutons, whereas the interaction between PICK1 and clathrin is responsible for synaptic vesicle retrieval. Surprisingly, mutations in the lipid-binding BAR domain have little effect on SypHy localisation or recycling at synapses. Taken together, our data has uncovered a role for PICK1 as a novel regulator of presynaptic vesicle recycling through clathrin-mediated endocytosis in mammalian central neurons.

Poster number 28: Thursday 4.15–6pm

Global transcriptional profiling of deep brain stimulation in an animal model of antidepressant treatment-resistance

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Background: Deep brain stimulation (DBS) is an emerging therapy being evaluated for treatment resistant depression. The current study aimed to identify antidepressant mechanisms of DBS in an animal model of antidepressant resistance.

Methods: Male Sprague-Dawley rats received saline (0.9%) or adrenocorticotropic hormone (ACTH) (100μg; i.p.) for 14 days and were allocated to stress-naïve or forced swim test (FST) stress conditions. An additional ACTH/FST group received DBS of the infralimbic cortex (IL) (n=7-8 per group). The IL was dissected and global gene expression profiles obtained (Agilent). Gene set enrichment analysis was performed (DAVID) following Bonferroni correction and KEGG pathways identified (Fisher exact score p<0.05). Pivotal genes were validated in independent groups (n=4-5) by RT-PCR and/or immunoblotting.

Results: Key sensors of energy demand, cell division/growth, apoptosis, protein synthesis and glucose/glycogen regulation were significantly altered. Phospho-AMPK and phospho-AKT levels were decreased in ACTH/FST animals compared with ACTH/naïve by 45 and 40% (p<0.05), respectively, and not reversed with DBS. In contrast, mRNA level of genes that respond to oxidative stress, hypoxia, ER stress, pro-inflammatory cytokines, nutrient deprivation and DNA damage, such as *Gadd45β Gadd45γ*, *HIF1α*, *CHOP* and *p53*, were increased in ACTH/FST compared with ACTH/naïve, and were restored with DBS (p<0.05).

Conclusions: Antidepressant responsive versus resistant animals demonstrate disparate responses to stress, underscoring importance of studying therapeutic mechanisms of DBS in an appropriate model. Data indicate that DBS is reversing the effects of the genes involved in the control of cellular stressors rather than those involved in energy/glucose regulation.

Poster number 29: Wednesday 4–5.45pm

Ultrafast fMRI differentiates timing differences in hemodynamic responses in the mouse visual pathway

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Better characterization of hemodynamic response function (HRF) is not only essential for fMRI analysis but also important for understanding the dynamics of underlying brain processing. However, it has been difficult to resolve HRF in mouse fMRI due to the very low blood oxygenation level dependent (BOLD) signal. In this study, we took advantage of increased sensitivity and temporal sampling of a novel ultrafast fMRI we developed [1] to measure the event-related activation of the mouse visual system in 9.4T MRI scanner. Strong bilateral BOLD responses to the visual stimulus were identified in the visual system brain regions, which allowed HRF to be measured with high fidelity. By resolving HRFs in different brain regions, we found regional variation of HRFs that the delay time of HRF reflected the known sequence of information flow in the visual pathway. The timing difference can only be differentiated using short event stimuli but not from longer ones. Using this ultrafast fMRI and event-related design, more naturalistic stimulations can be applied in rodent fMRI studies to avoid neural adaptation and allow flexibility in the design, such as mixing events and randomization. The individually characterized HRF can be used to improve detection accuracy and infer dynamics of neural processes.

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Poster number 30: Thursday 4.15–6pm

Normalised tectal coding does not rescue behaviour deficits in a zebrafish model of fragile X syndrome

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Fragile X syndrome (FXS) is the most common inherited form of autism spectrum disorders (ASDs), and is caused by a mutation of the fragile X mental retardation 1 (*fmr1*) gene. Some of the key characteristics of FXS include visual processing abnormalities, visual-motor function deficits and social deficits. However, little is known about the developmental trajectory of FXS, particularly early visual processing and its effect on visually driven behaviours. Utilizing the unique advantages of the zebrafish model system, here we used behavioural recordings of zebrafish hunting events combined with *in vivo* 2-photon calcium imaging of the optic tectum expressing GCaMP6s, to assess functional changes between *fmr1-/-* and *fmr1+/-* larval zebrafish at 5 and 9 days post-fertilisation (dpf). We found that *fmr1-/-* fish were less successful in hunting at both ages. *fmr1-/-* fish also showed delayed development of spatial representations of visual information in the optic tectum at 5 dpf, but no difference with *fmr1+/-* fish at 9 dpf. Furthermore, *fmr1-/-* fish had higher pattern similarity between spontaneous and evoked activity at 5 dpf, and higher co-activity level upon visual stimulation at 9 dpf. We also assessed social behaviour at 28 dpf, and found that *fmr1-/-* fish had increased social preference compared to wild-type fish. Together these results suggest that, while some early visual processing deficits in *fmr1-/-* fish are subsequently corrected, loss of functional *fmr1* gene nevertheless causes long-term impacts on behaviour.

Poster number 31: Wednesday 4–5.45pm

Understanding resting-state network dynamics after a spatial learning task

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Understanding the functional integration underlying learning and memory remains a major goal in neuroscience research. Increasing evidence indicates that learning-induced plasticity in functional network is detectable by resting-state functional magnetic resonance imaging (rsfMRI) under task-free or even anesthetised condition. However, the exact function and neural basis of these network are still largely unknown. To address this question, we conducted fMRI after spatial learning at two time points (1 day and 8 days after training) to determine the dynamics of the functional networks in memory consolidation. We examined how training intensity affect network organization by comparing two training paradigms which have same number of training trials but different inter-trial intervals. To identify the key network hubs involved in this process, we hypothesised that the key network hubs fulfil the following criteria: 1) identified in both training paradigms; 2) increase global efficiency in the network graph; 3) correlate with behavioural performance. We observed that multiple functional areas are involved in both paradigms and intensive training induced more cortical networks, particularly related to sensorimotor function. Moreover, the brain connectivity was reorganized after 1 week of consolidation in both paradigms to be less hippocampal dependent, which is consistent with a theory of long-term memory consolidation. Based the three criteria, we found different key nodes which may be explained by that each criterion focuses on different aspect of the dynamics of functional network induced by the learning task. To further understand the specific role of these key nodes in memory consolidation and verify the accuracy of the three screening criteria, targeted manipulations using techniques such as optogenetics and chemogenetics are ongoing.