The Dynamic Organism: from Molecules to Cognition – HUJI-UCL joint meeting
November 26-28, 2018
Abstracts

Theme 1: **From molecules to behavior and its disorders**

Alzheimer's disease: synapses, plaques, tangles and microglia, how are they related?

Frances A. Edwards, UCL

Abstract:
Alzheimer's disease presents one of the most pressing health problems of our time and while some treatments help the symptoms, the progression of the disease is poorly understood. Evidence from animal models and from human GWAS studies have, over recent years, revealed the importance of microglia in disease development[1,2] and we suggest that microglia have a protective role, at least in the early stages of the disease. I will discuss some of our recent findings on the earliest effects of rising amyloid beta on synaptic transmission[3] and also compare the effects of plaques on the changes in gene expression in these models and the relative effects on synaptic transmission versus microglial activation in different models. The presentation will outline where this research is taking us into the future, developing new mouse models and comparing mouse and human results to predict future GWAS hits.
Finally I put forward an hypothesis concerning the progression of the disease, linking rising amyloid beta, microglia and the development of Tau pathology and neurodegeneration and why severe cognitive decline is only detected so late in disease progression. Localised damage, caused by the high amyloid beta levels affecting synapses in and around plaques, may initially be limited by microglia removing damaged synapses to prevent wider spread damage to the neurone. This would however only delay the final effect as plaques grow and damage spreads along axons, eventually leading to Tau pathology, cell death and cognitive decline. Plaques, microglia and even tau tangles may delay cognitive decline but, in the end, may be its cause.

References:
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2. Matarin, M., Salih, D. A., et al (2015) A Genome-wide Gene Expression Analysis and Database in Transgenic Mice during Development of Amyloid or Tau Pathology. Cell Reports 10:633-644 (linked to the publically available database of genome wide gene expression www.mouseac.org)
3. Cummings, D.M., et al (2015) First effects of rising amyloidß in mouse hippocampus: synaptic transmission and gene expression. Brain 138: 1992-2004

From single cells to cellular and molecular landscapes of neurodegenerative diseases

Naomi Habib, HUJI

Abstract:
As human longevity rises, the prevalence of aging-related neurodegenerative diseases has dramatically increased and their onset has been observed at younger ages. In particular, Alzheimer's disease (AD) is the most frequent cause of dementia in Western societies, and thus one of the most pressing global medical issues to date. A better understanding of the cellular circuits and molecular mechanism driving disease initiation and progression, will enable the discovery of new and efficient therapeutic strategies. The complexity of the brain with its enormous cellular diversity is challenging the research in the field, however, the emergence of new RNA-sequencing technologies, such as single nucleus RNA-seq (sNuc-Seq), provides a unique opportunity to study cellular circuits and molecular mechanisms in complex tissues with single cell resolution and high-throughput. We have previously shown that sNuc-Seq enables sensitive, efficient, and unbiased classification of cell types and dynamic cell states, and we have applied sNuc-Seq to profile hundreds of thousands of nuclei from healthy and diseased brains of Alzheimer's mouse-models and from post-mortem human brains. We find distinctive molecular and cellular features of the AD brain compared to the healthy brain, showing multiple cell types involved in the disease and distinct cellular pathways associated with each cell type. Specifically, in astrocyte cells, we find a reduction in the population in a homeostatic state and an increase in a reactive toxic state, which combined together can be a driving force in AD progression. Overall, our approach is paving the way for a systemic charting of the unique cellular and molecular landscape of the Alzheimer's brain. These landscapes aided in the identifying of disease-altered cell types and molecular signatures specific to the AD brain, which we expect will lead to better understanding of molecular mechanisms driving disease initiation and progression.

Modelling dementia with human stem cells: progress and challenges

Selina Wray, UCL

Abstract:
The development of human induced pluripotent stem cells (iPSC) and their subsequent differentiation into neurons has provided new opportunities for the generation of physiologically-relevent in vitro disease models, particularly for disease such as Alzheimer's Disease, where it has been difficult to generate in vivo models that recapitulate the pathological hallmarks of the disease (amyloid plaques and intracellular neurofibrillary tangles of of the microtubule associated protein tau) together with neuronal death. Despite the advantages they offer to create "disease in a dish" models of neurodegenerative disease, there are several challenges associated with their use, particularly the fact that aspects of tau biology such as phosphorylation and splicing are subject to developmental regulation. I will discuss our progress using patient-derived iPSC to model Alzheimer's Disease and Frontotemporal Dementia. Specifically, I will discuss our findings that the developmental regulation of tau splicing is conserved in iPSC-

neurons, but disrupted by FTD-associated splicing mutations in MAPT. The developmental phosphorylation of tau is also conserved in our model, and I will discuss our progress using long-term neuronal cultures to understand the earliest pathological changes to tau in cells from patients with mutations in MAPT in 2D and 3D cultures. Finally, I will discuss our work using iPSC from patients with familial AD (APP and PSEN1) and how this is increasing our understanding of the molecular heterogeneity in this disorder.

Theme 2: **Nociception and pain**

Brain-state transitions and pain-free surgery

Marshall Devor, HUJI

Abstract:
Absence of pain and loss of consciousness are the most striking characteristics of surgical anesthesia and anesthesia-like states such as concussion, reversible coma and syncope (fainting). These states also feature immobility, amnesia, a shift to delta-wave EEG pattern, and depressed cerebral metabolism. It is generally presumed that this constellation of changes reflects widely distributed suppression of synaptic action and neuronal excitability due to ubiquitous drug action, or oxygen or nutrient starvation. I will present evidence for a radically different architecture... that a small group of neurons in the mesopontine tegmentum has executive control over the alert status of the entire cerebrum and spinal cord, and can generate loss of pain and loss of consciousness through specific neural circuitry.

Pain, peripersonal space and defensive actions

Giandomenico Iannetti, UCL

Abstract:
The nervous system relates us to the rest of the world through perception and action: environmental information is continuously used to make decisions resulting in actions appropriate to achieve the ultimate objectives of life, survival and reproduction. For this reason, nervous systems are particularly sensitive towards the detection of salient environmental events that need to be rapidly acted upon and imperil survival - a typical example being transient nociceptive stimuli causing pain. These stimuli elicit extremely large brain responses, which have been traditionally used to build models of where and how painful percepts are generated in the human brain, and, more recently, to infer whether an individual is in pain.
I will provide evidence that this dominant view is incorrect. Instead, I will suggest that the largest part of these brain responses reflect a basic mechanism through which the human brain detects and purposefully reacts to behaviourally-relevant sensory events, regardless of their perceptual quality. I will describe a basic physiological mechanism that couples these saliency-related cortical responses with an activation of the motor system, indicating that saliency detection is not merely perceptive but reactive, preparing the animal for subsequent appropriate actions.

I will finally show how stimuli occurring near the body elicit stronger behavioural and physiological responses. This phenomenon, which makes evolutionary sense (a predator within striking distance is more salient than one farther away), led to the concept of peripersonal space (PPS). The common and intuitive description of PPS as a single, distance-based, in-or-out zone, is however contradicted by empirical data. I propose a reconceptualization that incorporates PPS into mainstream theories of action selection and behavior.

Theme 3: **The hippocampus: Development, plasticity, function**

The role of sensory inputs in generating and sustaining cognitive maps

Francesca Cacucci, UCL

Abstract:
The hippocampal formation contains neurons whose firing represents a code for the position and orientation of an animal in space. Collectively, these cells are thought to constitute a neural map of space, or 'cognitive map' (Tolman, 1948; O'Keefe & Nadel, 1978), by means of which an animal can remember locations and navigate to goals. O'Keefe & Nadel (1978) suggested that the hippocampal cognitive map may represent a Kantian synthetic a priori system, not requiring extensive experience of space for its construction, which may therefore emerge early during post-natal development. Research by ourselves and others (Wills, Cacucci et al, 2010; Langston et al, 2010) confirmed that some components of the neural map are indeed set up early during post-natal development (e.g. Head Direction cells, which code for orientation), although others emerge only after extensive experience of exploration (e.g. Grid Cells, which may provide a distance metric for space). I will review recent work from my laboratory, focused on determining which sensory cues support the emergence of spatially responsive neurons, and which aspects of network development may proceed independently of sensory input. I will also discuss recent data relating to the emergence of the mnemonic properties of hippocampal place cell networks.

Velocity coupling of grid cell modules in the entorhinal cortex

Yoram Burak, HUJI

Abstract:
How can the brain encode a low dimensional variable such a position with a high dynamical range? Several theoretical works, addressing the encoding of position in the entorhinal cortex, have argued that the grid cell code achieves this goal by splitting the representation of position into different modules, thereby achieving a dynamical range that scales exponentially in the number of modules and neurons. Within each module, neural activity is experimentally observed to lie on a two-dimensional manifold, and it is likely that this restriction to a low dimensional manifold is mechanistically enforced by recurrent connectivity between grid cells. Yet, not much is known about the relationship between the activity of different cells that belong to different modules. I will argue in the talk that coupling between grid cell modules is essential in order to maintain the stability of the neural code for position, in the absence of sensory cues that inform the animal about its absolute position: the state of each module might be perturbed by noise that

arises due to spiking neurons or by noise in the external inputs, leading to gradual drift in the represented position in each module. To avoid catastrophic readout errors and obtain a coherent and continuous joint representation of position over time, the drifts in different modules must be compatible. To address this problem, we recently developed a theory of coupled grid cell modules, in which synaptic connectivity across modules enforces compatible drifts. Thus, the different modules behave dynamically as a joint, two dimensional attractor. However, the coupling only constraints local motion within each module, thus enabling any combination of states of the different modules to be accessed by the joint neural code. Thus, the combinatorial capacity of the code is preserved. Our results suggest that it is functionally beneficial for grid cells from different modules to be synaptically coupled, in a particular circuit architecture that helps stabilize the grid cell representation of position.

The Star Cells of Memory: Hippocampal astrocytes modulate recent and remote memory

Inbal Goshen, HUJI

Abstract:
Memory stands at the basis of cognitive function, and thus attracts major interest in the neuroscience community. Memory disruption is relatively easy to induce, but memory enhancement is a more complicated task that had challenged scientists for many years. We chose to target astrocytic activity as a way to generate synaptic potentiation and enhance recent memory performance. We then inhibited these cells to test their role in remote memory acquisition.
To directly and specifically modulate astrocytic activity we employed a chemogenetic approach: We expressed the Gq-coupled designer receptor hM3Dq or the Gi-coupled designer receptor hM4Di in astrocytes, which allowed their time-restricted activation or inhibition (respectively) by the application of the designer drug clozapine-N-oxide (CNO).
We discovered that astrocytic activation is not only necessary for synaptic plasticity, but also sufficient to induce NMDA-dependent de-novo long term potentiation in the hippocampus, which persisted after astrocytic activation ceased. In-vivo, astrocytic activation enhanced memory allocation, i.e. it increased neuronal activity in a task-specific way, only when coupled with learning but not in home-caged mice. Furthermore, astrocytic activation using either chemogenetic or optogenetic tools during acquisition resulted in memory recall enhancement on the following day. Conversely, directly increasing neuronal activity resulted in dramatic memory impairment.
Astrocytic inhibition during memory acquisition impairs remote, but not recent, recall. We show that this effect is mediated by a specific disrupting the projection from the hippocampus to the anterior cingulate cortex by astrocytes.
Our findings that astrocytes induce plasticity and enhance memory, and are necessary for remote memory, may have important clinical implications for cognitive augmentation treatments.

Theme 4: **The perceptual brain: olfaction**

Mammalian olfaction is a high bandwidth sense

Andreas Schaefer, UCL

Abstract:
Odours are transported in turbulent plumes resulting locally in highly fluctuating odour concentration. Yet, whether mammals can make use of the ensuing temporal structure to extract information about the olfactory environment remains unknown. Here, we use dual-energy photoionisation recording to simultaneously determine odour concentrations of two odours with >300 Hz bandwidth in air. We show that temporal correlation of odour concentrations reliably predicts whether odorants emerge from the same or different sources in normal turbulent environment outside and in laboratory conditions. To replicate natural odour dynamics in a reproducible manner we developed a multichannel odour delivery device allowing presentation of several odours with 10ms temporal resolution. Integrating this in an automated operant conditioning system we demonstrate that mice can reliably discriminate the correlation structure of odours at frequencies of more than 40 Hz. Consistent with the purely olfactory nature of these tasks already output neurons in the olfactory bulb show segregated responses depending on the correlation of odour stimuli with populations of 10s of neurons sufficient to reach behavioural performance. Our work thus demonstrates that mammals can perceive temporal structure in odour stimuli at surprisingly fast timescales. This in turn might be useful for key behavioural challenges such as odour source separation, figure-ground separation or odour localisation.
I will discuss this work in some detail but also aim to give an overview where my lab at UCL and the Francis Crick Institute is moving towards, including efforts in neurotechnology development and electron microscopy.

Background-dependent dynamics of olfactory figure-ground segregation

Dani Rokni, HUJI

Abstract:
Species that rely on olfaction for everyday functions are constantly faced with the task of detecting and identifying odor-objects over rich and dynamic backgrounds. How the brain achieves such figure-background segregation is not well understood. Several neural processes have been implicated in this task ranging from simple feedforward readouts to more complex networks involving feedback projections (Brody and Hopfield, 2003; Grabska-Barwińska et al., 2017; Li and Hertz, 2000; Mathis et al., 2016). These different proposed networks differ not only in their functional architecture, but also in the temporal dynamics in which they segregate figures from background. Reaction times in behavioral tasks provide useful insight into the relevant time scales for neuronal processing (Hanes and Schall, 1996; Nakayama and Silverman, 1986; STERNBERG, 1969; Treisman and Gelade, 1980). Here we analyzed reaction times in mice performing an olfactory figure-background segregation task (Rokni et al., 2014) to reveal the

relationship between background richness and processing time. Mice were presented with odorant mixtures and were trained to report the presence/absence of target odorants in a 2 choice task. The relationship between reaction time and performance could be described with a logistic function. Increasing the number of mixture components caused a rightward shift of the logistic function, indicating that the neural mechanisms underlying olfactory figure-background segregation require longer processing time for richer backgrounds. Our results argue against a simple feedforward readout for target-odor detection (Mathis et al., 2016) and provide support for iterative mechanisms involving feedforward and feedback projections between the olfactory bulb and olfactory cortex (Grabska-Barwińska et al., 2017; Li and Hertz, 2000).

Stability and plasticity of Mitral Cell connectivity in mothers

Adi Mizrahi, HUJI

Abstract:
The olfactory bulb (OB) is characterized by high numbers local inhibitory networks that synapse onto Mitral Cells (MCs). These networks have been postulated to shape how odor identities are computed and perceived and to contribute to long term circuit plasticity. MC's odor responses can change dramatically based on the experience of the animal, but the mechanisms of such plasticity remain unknown. One possible mechanism – one which we challenged here – is that changes in the connectivity onto MCs underlies their plasticity. We tested this hypothesis in a model of maternal plasticity. In mice, mothers casually depend on odor inputs to trigger and maintain maternal behaviors that supports the survival and wellbeing of their pups. We recently found that MC's undergo plastic changes after parturition and hypothesized that the pre-synaptic landscape onto MC's may be the cause. To test this hypothesis, we screened the pre-synaptic landscape of MCs using monosynaptic rabies virus trans-synaptic tracing (RV). We performed an unbiased RV screen from MC's as starter cells using the T-bet cre mice and described a connectivity index onto MCs. We found that the pre-synaptic landscape of MC's before and after parturition is stable locally but plastic globally. While local interneuron connectivity remained largely intact, we found a ~10 fold increase in the number of presynaptic neurons from the supraoptic nucleus onto MCs in mothers. These findings reveal a previously unknown neural pathway to the OB that is plastic in mothers and may modulate MC activity during maternal behaviors.

Theme 5: **The changing brain in health and disease**

From choice architecture to choice engineering

Yonatan Loewenstein, HUJI

Abstract:
Choice architecture uses qualitative psychological principles in choice design. The recent development of quantitative models of choice can revolutionize this discipline. To launch this

field, which we term choice engineering, we initiate a large-scale competition in which the effectiveness of qualitative principles and quantitative models will be compared.

A computational approach to understanding motivational symptoms in depression
Jonathan Roiser, UCL

Abstract:
Motivational symptoms of depression are debilitating and associated with poor clinical outcome, but the mechanisms underlying them are poorly understood. This talk will present data examining how motivational processing, assessed using a cognitive task, relates to depressive symptoms, using a computational approach. Results from two studies, including 250 participants (healthy volunteers, unmedicated depressed patients, first degree relatives and remitted depressed patients), will be presented. Participants completed cognitive measures of motivation, and symptoms were assessed through questionnaires. Data were analysed using a hierarchical computational approach, with model parameters estimated in a Bayesian framework using sampling. In an initial non-clinical study (N=90), general depressive symptoms were associated with a reduction in reward sensitivity, while anhedonia was specifically related to higher effort cost. In a clinical study (N=50 depressed patients, N=30 first-degree relatives, N=30 remitted patients, N=50 healthy volunteers), the same model was associated with the highest evidence, and in the MDD subjects anhedonia was again associated with greater effort cost. Preliminary results from an experimental medicine study investigating the impact of L-DOPA administration on motivational processing in depression will also be presented. These findings illuminate the cognitive mechanisms contributing to depressive symptoms relating to disrupted motivational processing.

The Claustrum supports resilience to distraction
Ami Citri, HUJI

Abstract:
A barrage of information constantly assaults our senses, of which only a fraction is relevant at any given point in time. However, the neural circuitry supporting the suppression of irrelevant sensory distractors is not completely understood. The claustrum, a circuit hub with vast cortical connectivity, is an intriguing brain structure, whose restrictive anatomy, thin and elongated, has precluded functional investigation. Here, we describe the use of Egr2-CRE mice to access genetically defined claustral neurons. Utilizing conditional viruses for anterograde axonal labeling and retrograde trans-synaptic tracing, we validated this transgenic model for accessing the claustrum and extended the known repertoire of claustral input/output connectivity. Addressing the function of the claustrum,weinactivatedCLEgr2+neurons,chronically as well as acutely, in mice performing an automated two-alternative forced-choice behavioral task. Strikingly, inhibition of CLEgr2+ neurons did not significantly impact task performance under

varying delay times and cue durations, but revealed a selective role for the claustrum in supporting performance in the presence of an irrelevant auditory distractor. Further investigation of behavior, in the naturalistic maternal pupretrieval task, replicated the result of sensitization to an auditory distractor following inhibition of CLEgr2+ neurons. Initiating investigation into the underlying mechanism, we found that activation of CLEgr2+ neurons modulated cortical sensory processing, suppressing tone representation in the auditory cortex. This functional study, utilizing selective genetic access, implicates the claustrumin supporting resilience to distraction, a fundamental aspect of attention.

Dichotomous function of hippocampal sub circuits
Andrew Macaskill, UCL

Abstract:
The hippocampus is one of the most studied brain regions, and has been implicated in spatial and memory processes, reinforcement learning, and in numerous disease states such as anxiety disorders, depression and addiction. However, our understanding of the hippocampal circuit, what calculation it performs and how it performs it is still surprisingly limited. Recent studies have highlighted the enormous complexity of the hippocampus, where the canonical tri-synaptic circuit is composed of multiple parallel circuits with distinct functions and very little crosstalk. The overall aim of our lab is to try and break down the hippocampal calculation into these parallel components.

Our current focus is on a population of neurons that together form the projection from ventral hippocampus to prefrontal cortex. This projection has been shown to be crucial for flexible behaviour, value-based decision making and working memory. In my talk I will discuss some recent, unpublished experiments that show that this projection appears to be formed of two dichotomous elements with opposite effects on downstream prefrontal cortex circuitry. This dichotomy could underlie conflicting accounts of the mechanistic basis of hippocampus to prefrontal cortex circuit function.

Theme 6: **The aging organism**

Deciphering the proteostasis network's response to dissimilar challenges
Ehud Cohen, HUJI

Abstract:
The ability to maintain proper protein homeostasis (proteostasis) is critical for organismal functionality and viability. Cells have developed sophisticated mechanisms that act in concert to maintain the integrity of the proteome. These mechanisms, which are known as "the proteostasis network", assist protein folding, supervise the integrity of mature proteins and direct damaged polypeptides for degradation. Nevertheless, subsets of aggregation-prone proteins challenge the proteostasis network by escaping degradation and forming insoluble aggregates. In some cases,

such aggregates underlie the development of late-onset neurodegenerative disorders such as Alzheimer's disease (AD) and Huntington's disease (HD). How the proteostasis network responds to dissimilar challenges and whether the nature of the aggregating protein or the cell type where aggregates accumulate, shape this response, are largely unanswered questions. Here, we employed nematodes that express neurodegeneration-linked, aggregative proteins, and found that Torsin chaperones (Torsin 1 and 2) protect model worms from the aggregation of the HD-causing, long poly-glutamine (polyQ) stretches and of a mutated super oxide dismutase 1 (sod-1) which leads to the development of Amyotrophic lateral sclerosis (ALS). In contrast, the same chaperones expose nematodes to the toxicity of the AD-causing peptide, Aβ. These opposing effects were observed in both, neurons and muscles cells, indicating that the nature of the toxic polypeptide rather than the tissue of expression shapes the proteostasis network to dissimilar aggregative proteins. These opposing effects on proteotoxicity that stem from the knockdown of tor-2, are accompanied by differential modulations of gene expression. Our results indicate that the proteostasis network differentially responds to dissimilar proteotoxic challenges and highlight the importance of understanding the accurate response to specific aggregative proteins, to design specifically tailored therapies to neurodegenerative maladies

New discoveries about ageing in *C. elegans*

David Gems, UCL

Abstract:
Arguably, *C. elegans* ageing studies have stalled slightly in recent years. Life span genetics continues to identify interesting new genes and pathways, yet the proximate mechanisms of ageing that such genes influence remain largely unclear. Recent work in my lab is using new ideas from M.V. Blagosklonny to develop and test novel hypotheses about the primary causes of ageing in *C. elegans*. These ideas link G.C. Williams' evolutionary concepts (particularly antagonistic pleiotropy) with recent findings on the role of insulin/IGF-1 signaling in ageing. They suggest that senescent pathologies that limit lifespan may be driven primarily by late life run-on of wild-type biological programs, rather than damage accumulation (e.g. due to reactive oxygen species). They motivate a new, pathology-centred approach to understanding senescence, particularly via the study of how pathologies develop ("developmental pathology"), and how they cause mortality[1]. This has enabled the discovery of several new mechanisms by which senescent pathologies originate in *C. elegans*, including intestinal and gonadal atrophy, yolky pool formation (a form of senescent obesity), and uterine tumours[2,3]. These mechanisms provide clues to the origins of several senescent pathologies in humans. It has also yielded insights into the causes and mechanisms of organismal death in *C. elegans*[4,5].

1 Zhao, Y. *et al. Nature Comm.* **8**, 15458 (2017). 2 Wang, H. *et al. NPJ Aging Mech. Disease* **4**, 6 (2018). 3 Ezcurra, M. *et al. Curr Biol* **28**, 2544-2556 (2018). 4 Galimov, E. R. *et al. Cell Reports* **22**, 2730–2741 (2018). 5 Coburn, C. *et al. PLoS Biol* **11**, e1001613 (2013).

Theme 7: **The perceptual brain: vision**

Extending the "active vision loop": The role of memory

Yoni Pertzov, HUJI

Abstract:
We see via our eyes. While this statement seems trivial, much of the vision research has been neglecting this simple fact. To complicate things, our center of gaze moves approximately 3 times a second. The landing position of each movement is determined by the visual input, but the visual input is also dependent on the exact position of gaze. This reciprocal dependency is at the basis of the "active vision loop" framework that has been guiding recent research endeavors (as well as my PhD). However, this framework neglects a critical component: observers move their gaze differently, even when presented with identical stimulus. Thus, the link between visual input and gaze behavior depends on the observer. I will describe our effort in exploring this missing component and focus on memory. I will demonstrate how observers' specific memories influence their gaze behavior and how this modulation prevails even when they try to conceal their memory. I will conclude by demonstrating how these insights could contribute to applied settings in which concealed information is to be detected using eye movements.

Neural circuits for selection of behaviourally relevant visual input in mouse visual cortex during learning and task-switching

Jasper Poort, UCL

Abstract:
We found that neural responses in the mouse primary visual cortex (V1) become increasingly selective when animals learn the behavioural relevance of novel visual stimuli, by repeatedly imaging cells using 2-photon calcium imaging while mice learned a visual discrimination task (Poort et al., 2015, Neuron). However, it is unclear how learning reorganises the activity of different cell types, including excitatory pyramidal neurons and different classes of GABAergic interneurons. Although pyramidal cells provide the output from the local circuit to other cortical areas, different interneuron classes can inhibit pyramidal cells as well as each other, and thus exert a powerful influence on circuit activity. We therefore simultaneously measured responses in V1 of pyramidal cells and parvalbumin, somatostatin and vasoactive intestinal peptide expressing interneurons. Our recent results show that learning leads to changes in the selectivity and co-activation patterns across multiple cell classes, and that increased stimulus-specific inhibition, especially in parvalbumin cells, can contribute to selective processing of relevant objects (Khan et al., 2018, Nature Neuroscience). To determine whether these changes were specific to learning, we trained the same mice to switch between a visual and an olfactory discrimination task to compare neural responses when animals were attending or ignoring the same visual stimuli. We found that the effects of learning and attentional switching on the response selectivity of the same cells were largely uncorrelated. Furthermore, learning and attentional switching differentially affected the interactions between different cell classes. These

results suggest that there are distinct mechanisms underlying the increased discriminability of relevant sensory stimuli across longer and shorter time scales.

Dynamics of adaptation in visual cortex
Samuel Solomon, UCL

Abstract:
In humans and animals adaptation is a perceptual reflex that changes how the world looks – for example, looking out of a moving train's window for a long time causes the world to appear to 'move backwards' when the train stops. This reflexive aftereffect is due to the effects of adaptation on nerve cells in the visual cortex, a form of short term plasticity which occurs automatically during exposure to visual scenes. Adaptation is a nearly ubiquitous phenomena in sensory systems and we are interested both in how adaptation induces changes in the sensitivity and selectivity of sensory cells, and whether adaptation can be used to better understand unhealthy brains. Here I present recordings from cortical neurons that suggest that adaptation's effects may arise in the same circuits that cortical neurons use to interact with each other ('normalization'). I then provide evidence for a temporal dissociation between adaptation's effects on neural sensitivity and selectivity. Finally I present preliminary evidence that adaptation's effects may provide an early indicator of cortical dysfunction in a common mouse model of neurodegeneration.

Rhythmic motifs in cognition: the case of rhythmic sampling
Ayelet Landau, HUJI

Abstract:
Rhythmic temporal structure is a recurring theme in the field of cognitive neuroscience. It spans physiology as well as behavioral performance and provides interesting brain behavior links. In my talk I will describe work focusing on one aspect of rhythmic cognition: Rhythmic sampling. When subjects monitor a single spatial location, target detection depends on the pre-target phase of an ~8 Hz brain rhythm. When multiple locations are monitored, performance decrements suggest a division of the 8 Hz rhythm over the number of locations. This suggests that different locations are sequentially sampled. In my talk I will survey evidence for rhythmic sampling in behavior and in non-invasive physiology. Together with published work, I will present new findings supporting the notion that rhythmic sampling may, in fact, be a domain general principle in the architecture of perception and attention.