Symposium of Neuroscience

Date: 8th June 2018

Venue: G5317, Yeung Kin Man Academic Building

Time	Speaker	Title
9:30-10:10	Prof Christoph Schreiner University of California, San Francisco	Effects of Noise on Cortical Responses: From Synapses to Behavior
10:10-10:50	Prof Anthony Holtmaat University of Geneva	The role of higher-order thalamocortical feedback in cortical synaptic plasticity
10:50-11:30	Prof Gregg Recanzone University of California, Davis	Age-related effects on the auditory system
11:30-12:10	Prof Daisy Shum The University of Hong Kong	Emerging role of perineuronal chondroitin sulfates and semaphorin 3A on the developing vestibular circuitry.
12:10-14:00	Lunch	
14:00-14:40	Prof Anna Wang Zhejiang University	Laser-fMRI: A new method for studying the columnar connectom
14:40-15:20	Prof Jun Xia The University of Science and Technology of Hong Kong	LHFPL4/GARLH4 is a major binding partner of neuroligin-2 and crucial for inhibitory synapse formation
15:20-16:00	Prof Xiang Yu Insitute of Neuroscience, Chinese Academy of Sciences	Molecular mechanism underlying activity-dependentneural circuit development

Effects of Noise on Cortical Responses: From Synapses to Behavior

Prof Christoph Schreiner
University of California, San Francisco

Abstract
We will discuss the difference between narrow-band and broad-band stimuli on excitatory and inhibitory synaptic responses of auditory cortical neurons. Furthermore, we will examine the effects of different signal-to-noise ratios on the response to foreground sounds and the ability to affect the neuronal and behavioral performance of animals by prolonged noise exposure and detection training. Potential mechanisms of background-noise influences will be discussed.

The role of higher-order thalamocortical feedback in cortical synaptic plasticity

Prof Anthony Holtmaat
University of Geneva

Abstract:
Sensory experience and perceptual learning changes receptive field properties of cortical pyramidal neurons, possibly mediated by long-term potentiation (LTP) of synapses. We have previously shown in the mouse somatosensory cortex (S1) that sensory-driven LTP in layer (L) 2/3 pyramidal neurons is dependent on higher order thalamic feedback from the posteromedial nucleus (POm), which is thought to convey contextual information from various cortical regions integrated with sensory input. Here, we followed up by dissecting the cortical microcircuitry underlying this form of LTP, and by characterizing POm feedback activity during whisker sensory discrimination learning. We found that repeated pairing of POm thalamocortical and intracortical pathway activity in brain slices induces NMDAr-dependent LTP of the L2/3 synapses that are driven by the intracortical pathway. In addition, we found that the simultaneous activation of the two pathways recruits activity of vasoactive intestinal peptide (VIP) interneurons, whereas it reduces the activity of somatostatin (SST) interneurons. VIP interneuron-mediated inhibition of SST interneurons has been established as a motif for the disinhibition of pyramidal neurons. Selective expression of the hM4Di receptor (an inhibitory Designer Receptor Exclusively Activated by Designer Drugs - DREADD) in these two interneuron subtypes, we found that activation of this disinhibitory microcircuit motif by higher-order thalamic feedback is indispensable for eliciting LTP. This suggests that in vivo, this feedback may help modifying the strength of synaptic circuits that process first-order sensory information in S1. To characterize the relationship between higher-order feedback and cortical plasticity during learning in vivo, we adapted a perceptual learning paradigm in which head-fixed mice have to discriminate two types of textures in order to obtain a reward. POm axons or L2/3 pyramidal neurons labeled with the genetically encoded calcium indicator GCaMP6s were imaged during the acquisition of this task as well as the subsequent learning of a new discrimination rule. We found that a subpopulation of the POm axons stably represent textures, even upon a texture-rule change, whereas a relatively large fraction of the L2/3 neurons re-tune their selectivity to the texture that is newly associated with the reward. Altogether, our data suggest that higher-order thalamic feedback shapes synaptic circuits in S1 that may be important for processing of sensory input and texture discrimination.

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Age-related effects on the auditory system

Dr Gregg Recanzone
University of California at Davis

Abstract:
Age-related hearing deficits are the third leading cause of disability among the geriatric population, afflicting nearly everyone aged 80 or older. As the geriatric population increases worldwide, the malady will afflict greater and greater numbers of people. In most cases, these deficits go beyond increased detection thresholds, indeed many individuals with normal audiograms still suffer from these deficits, with the greatest complaint being that it is difficult to understand speech in a noisy environment. Despite its prevalence, very little is understood about the central mechanisms of this hearing loss. Recent studies in the macaque monkey indicate that central changes occur as early as the cochlea and continue to be manifest throughout the ascending auditory neuraxis. At the cortical level there are marked changes in spatial, temporal, and intensity tuning, likely underpinning the age-related changes observed in both humans and non-human primates.

Emerging role of perineuronal chondroitin sulfates and semaphorin 3A on the developing vestibular circuitry

Prof Daisy Shum
The University of Hong Kong

Abstract
Perineuronal nets (PN) are implicated in controlling the postnatal period of plasticity during neural circuit formation in the CNS. The emergence of negative geotaxis with postnatal maturation of the vestibular circuitry for gravity detection offers a behavioral readout in tests for roles of PN molecules in vestibular plasticity. Using rat as model, we found that negative geotaxis was mature by postnatal day (P) 9, in correlation with consolidation of PN around GABAergic neurons in the vestibular nucleus (VN). Treatment of the VN with chondroitinase ABC (ChABC) at P6 cleaved chondroitin sulfate (CS) moieties of PN and delayed emergence of negative geotaxis to the end of the second postnatal week. Similar delay was observed when the VN was treated with a $GABA_A$ receptor antagonist. The results support a crucial role of perineuronal CS for maturation of GABAergic transmission in the VN circuit for graviception. In the postnatal VN, CS moieties of PN were found to colocalize with semaphorin 3A (Sema3A), a secreted protein recently shown to impact on dendrite arborization. The expression of Sema3A in the VN was confirmed by in-situ hybridization and immunocytochemistry. In VN explant cultures, exogenous Sema3A and/or ChABC was found to alter the dendritic pattern of VN neurons, suggesting involvement of CS and Sema3A in controlling structural plasticity of VN neurons in the growth phase. The dynamic changes of immature dendrites implicate delayed efficacy in formation and maturation of synapse during circuit formation. Taken together, our results suggest that retention of Sema 3A by CS moieties of the consolidated PN limits the participation of Sema3A, as a putative plasticity-inducing factor, in dendritic/synaptic modulation of GABAergic VN interneurons, thereby contributing to the hardwiring of the central pathway for vestibular behaviour.
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"Laser-fMRI: A new method for studying the columnar connectome"

Prof Anna Wang
Zhejiang University

Abstract
Establishing connection patterns between cortical columns is essential for understanding brain networks. However, currently, there is no method to systematically map at this scale. Here, we combined pulsed infrared neural stimulation (INS) with high field fMRI. When applied to cat and monkey brains, we found that single site INS stimulation produces (1) reproducible, intensity-dependent activation, (2) connections between cortex and subcortical locations, (3) long-range cortico-cortical connections, and (4) local cortical connections. We suggest that INS-fMRI is a new *in vivo* functional tract tracing technique that can map networks with high spatial resolution.

LHFPL4/GARLH4 is a major binding partner of neuroligin-2 and crucial for inhibitory synapse formation.

Prof Jun Xia
The Hong Kong University of Science and Technology

Abstract
Synapses are sites of neuronal communications. Abnormal synapse formation and function could lead to brain disorders such as autism, schizophrenia and epilepsy. Our understanding of the molecular mechanism governing synapse formation, especially the inhibitory synapses, is limited. Neuroligin-2 (NL2) is a transmembrane protein capable of initiating inhibitory synapse formation. In an effort to search for NL2 binding proteins and the downstream mechanisms responsible for inhibitory synapse development, we identified LHFPL4/GARLH4, a four-transmembrane-domain protein, as a major NL2 binding partner. LHFPL4/GARLH4 was exclusively expressed in the nervous system and specifically enriched at inhibitory postsynaptic sites. Significant proportions of LHFPL4/GARLH4 and NL2 were associated with each other in the brain, and they regulated the protein levels and synaptic clustering of each other. Moreover, deficiency of LHFPL4/GARLH4 in mice resulted in profound impairment of inhibitory synapse formation as well as prominent motor behavioral deficits and increased seizure susceptibility, highlighting the essential role of LHFPL4/GARLH4 in inhibitory synapse formation and function.

Molecular mechanism underlying activity- dependentneural circuit development

Prof Xiang Yu
Insitute of Neuroscience, Chinese Academy of Sciences

Abstract
Natural sensory experience is critical to activity-dependent neural circuit development and plasticity. To uncover the molecular mechanisms underlying these processes, we established various sensory deprivation and enrichment paradigms. Using these models, we identified an early form of global crossmodal plasticity in the mouse sensory cortices, where deprivation of sensory input into one sensory modality crossmodally reduce excitatory synaptic transmission in all sensory cortices. We further demonstrate that this effect is mediated by the neuropeptide oxytocin and can be rescued by increased natural sensory experience through environmental enrichment. In other work, we showed that an acute injection of LPS or Poly(I:C), manipulations that mimics bacterial or viral infections, result in elevated level of the cytokine CCL2, secreted by the mural cells of the microvessels in the brain. This CCL2 can rapidly elevate excitatory synaptic transmission in multiple cortical and hippocampal regions. We propose that this mural cell secreted CCL2 could act as an early sentinel during systemic injection. Together, that there are global and crossmodal forms of plasticity in the brain, especially during early development. Developmental neurological disorders, including mental retardation, autism and schizophrenia, may have defects in these forms of plasticity