migration. Current work is focused on 'caging' photoactivatable small-peptide inhibitors of Cdc42, PP1, JNK and Gqα, to control endogenous proteins with light.

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Noise Induced Hearing Enhancement: Clinical and Machine Learning Studies

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The addition of a certain amount of background noise has been shown to improve the hearing of pure-tone sounds. The underlying mechanism of this counter-intuitive phenomenon is believed to be stochastic resonance, where the threshold level of a pure-tone signal is lowered by adding an appropriate amount of background noise. Here, to investigate whether background noise can aid the hearing of more complex sound such as the human voice, we perform hearing tests with Korean syllables, and find that syllable recognition is enhanced with noise for rarely used syllables. Similar tests with a machine-learning speech recognition shows that the same enhancement arises only when the system is insufficiently trained, corresponding to hearing a rare syllable. The overall phenomenon looks similar to the stochastic resonance but any successful model should explain that the enhancement arises in perceptual processes as it depends on the level of training and the syllables.

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Stress-Induced Differential Regulation Leads to Decoupling of the Activity between mPFC and Amygdala

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Exposure to severe stress leads to the development of psychiatric disorders. Clinical studies have shown that three brain areas involved in learning and memory—the hippocampus, amygdala and medial prefrontal cortex (mPFC)—undergo distinct changes with stress disorders. While the hippocampus and mPFC show impairment in structural and functional changes, the amygdala shows an enhancement. Despite these three brain regions having strong anatomical connections, most of these studies focus on individual brain regions. However, recent studies have shown that these connections between regions have strong functional implications. The connectivity between the mPFC and the amygdala has recently been shown to be crucial for fear expression (Likhtik et al., 2014). The effect of stress on the functional connections between these regions is poorly understood. Therefore, we performed in-vivo local field potential recordings from the mPFC and the amygdala in awake behaving rats during fear expression. We found that stress differentially regulates the activity in the mPFC and the amygdala during fear expression. Consistent with cellular findings, the activity in the amygdala is upregulated by stress during fear expression. However, the activity of the mPFC is unaffected by stress during fear expression. We also found that stress causes a decoupling between the activity in the amygdala and mPFC. Interestingly, an earlier study showed that stress strengthens the coupling between the hippocampus and the amygdala (Ghosh et al., 2013). Therefore, although chronic stress impairs structure and function in both the hippocampus and mPFC, the interactions of these two areas and the amygdala appear to be affected in a contrasting fashion. Functional connectivity gets stronger from amygdala to hippocampus but it gets disrupted between mPFC and amygdala. Future studies need to focus on mechanisms involved in these connectivity changes.

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Temperature Sensation and Integration in the *Drosophila* Circadian Clock

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Circadian clocks are entrained by zeitgebers, environmental cues such as light and temperature that adapt living organisms to the physical rhythms of the earth. Although temperature has been shown to be a major zeitgeber and can entrain the circadian clock of *Drosophila*, the neural and molecular mechanisms by which circadian clocks respond to temperature remain poorly understood. In our work, we use *in vivo* calcium imaging to characterize the temperature response of clock neurons in *Drosophila* to temperature modulation. We show that a selective group of clock neurons responds to temperature changes and that dorsal neurons (DNs) are excited by cooling and inhibited by warming. We further investigated the physiological input pathway of temperature sensing into the circadian clock. We find that arista and chordotonal organs are both critical factors that contribute to the response of circadian neurons to temperature modulation. Our work reveals that clock neurons respond to temperature changes through multiple temperature input pathways, suggesting a complex network similar to the entrainment of circadian clocks by light input.

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TRP Channel Function in iPSC-Derived Sensory Neurons

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Using somatic cells to generate induced pluripotent stem cells (iPSC) is an established method in research and has multiple applications and advantages. An increasing amount of cell types have been successfully differentiated from iPSCs, including hematopoietic cells, cardiomyocytes, smooth muscle cells, pancreas, liver and renal tissue. Directing differentiation into neuronal cells has the great benefit of bypassing the problematic isolation of human neuronal cells. Recently, a protocol using dual SMAD inhibition was shown to drive differentiation into sensory neuron-like cells. While expression of canonical markers of sensory neurons has already been validated, an in-depth characterization of sensory TRP channels in these induced neurons is still lacking. In this study, we use qPCR, Fura-2-based microfluorimetry and patch-clamp experiments to evaluate the expression and function of the sensory TRP channels at different time points during the differentiation toward a sensory neuron phenotype. We not only confirm expression of the sensory channels TRPV1, TRPM8 and TRPA1, but also demonstrate for the first time strong molecular and functional expression of TRPM3 in iPSC-derived sensory neurons. Interestingly, we found a temporarily increase of TRPM3 responses at an early time point in differentiation, which might indicate a role for this channel in the development of sensory neurons. To conclude, we were able to produce sensory neurons using iPSCs, and validated functional expression of TRP channels important in somatosensation. This approach has the potential to investigate the development of sensory neurons *in vitro*, and to explore the cellular physiology and pharmacology of TRPM3 and other sensory TRP channels in a human context. Moreover, it may open the door to generate patient-derived neurons for disease modeling and target validation.

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Effect of Spatial Complexity on Dopaminergic Signaling Revealed from Multiscale Simulations

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Efficient clearance of neurotransmitters from the synapse by dopamine transporters (DATs) is critical to regulating dopamine (DA) signaling in the central nervous system. Despite significant advances in the field, we still lack a complete mechanistic understanding of DA transport events. First it is still unclear how molecular structure and dynamics affect cellular neurosignaling events. Second, the structural and stochastic properties of the cellular environment, including the morphology of the synaptic regions, and the heterogeneous distribution of transporters on the cell membrane may affect the efficiency of neurotransmitter transport, and no realistic simulations of the dopaminergic signaling has been carried out to date. We adopted a multiscale methodology to examine the effects of spatial complexity and firing patterns on DA reuptake by DATs. We used a kinetic scheme derived from our earlier molecular, together with high resolution images dopaminergic neurons from fluorescence spectroscopy and electron microscopy, to reconstruct in silico the simulation environment mediating DA signaling. Overall, our model provides a framework to investigate the effect of variations in different neuronal properties to gain a better understanding of the modulation of DA signaling in the central nervous system. Our results highlight the significance of considering the realistic geometry as well as the spatial heterogeneities from experiments as opposed to adopting well-mixed assumptions. The computing platform also permits us for the first time to gain a quantitative understanding of the effect of psychostimulants and antidepressants on DA signaling.