Physical and Mathematical Principles of Brain Structure and Function Workshop

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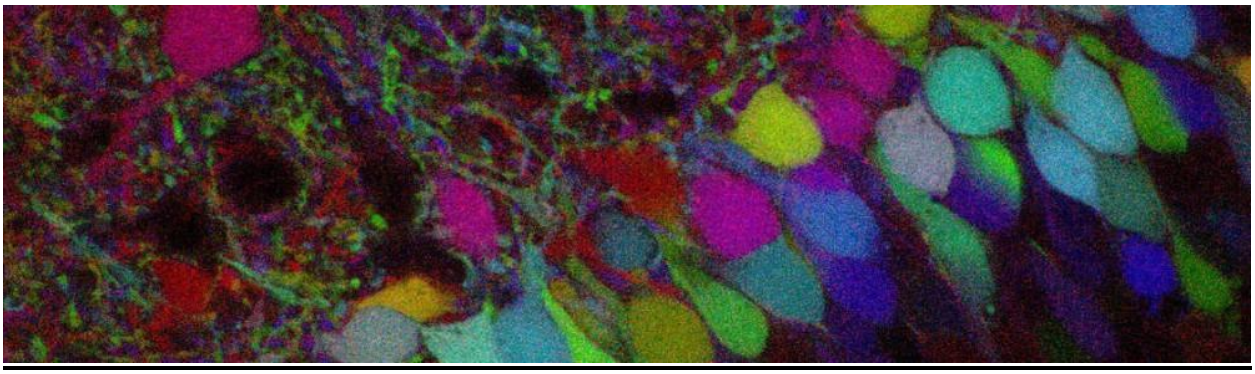
White Papers: Major Obstacles Impeding Progress in Brain Science



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The major obstacle impeding progress in brain science is a dearth of understanding about how information is encoded and represented in the nervous system. This problem drives what technologies need to be developed in order to understand brain function or what information is needed to characterize the “state of the brain”.

The hierarchical structural of both white and gray matter suggests that different length and timescales are involved in neuronal information processing. Understanding information flow and representation of information may involve integrating over various length and timescales and identifying salient networks at various scales. This research may require sociological readjustments in the neuroscience community where those who study circuits, or glia, white matter, etc. may have to leave their silos and adopt a more global, integrative view.

A strong focus should be on understanding neural information processing in simpler organisms such as *C Elegans* or Zebrafish in which we can control gene expression and neural activity in an ethical manner, not possible in humans. A worthy goal would be to develop an *in silico* model of a *C Elegan*s’ 302 neurons that could reproduce all behaviors of this organism subject to various stimuli and predict behaviors when new stimuli are presented. This “virtual worm” would go a long way to helping us discover the integrated nature of the nervous system. The Zebrafish provides another window on nervous system function. Different cells could be targeted with knock in or knock out models, and light scattering and absorption are minimal in limiting penetration depth and resolution. Genetic control over certain pathways could help us systematically

Neuroscience has benefited enormously from lesion studies, helping us understand the function of distinct brain regions. At the gross anatomical scale, we would benefit from developing and using technology to induce non-invasive, reversible, and focal “virtual lesions” to help localize and temporarily disrupt different cortical areas, deep brain structures, and white matter pathways, individually and in a spatially or temporally correlated fashion. Transcranial Magnetic Stimulation (TMS) is probably not focal enough for this purpose. Much recent progress has been made in High Intensity Focused Ultrasound (HIFU) and its combination with MRI. If hybrid HIFU-MRI systems could be adapted for this purpose, and found safe and effective, it may be possible to focus Ultrasound energy (under MRI guidance) in a systematic manner and generate detailed *in vivo* functional brain maps.

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The role of astrocytes in synaptic information transfer and plasticity Short-term presynaptic plasticity designates variations of the amplitude of synaptic information transfer whereby the amount of neurotransmitter released upon presynaptic stimulation changes over seconds as a function of the neuronal firing activity. While a consensus has emerged that the resulting decrease (depression) and/or increase (facilitation) of the synapse strength are crucial to neuronal computations, their modes of expression in vivo remain unclear. Recent experimental studies have reported that glial cells, particularly astrocytes in the hippocampus, are able to modulate shortterm plasticity but the mechanism of such a modulation is poorly understood. It is important to investigate the characteristics of short-term plasticity