11 Biophysical Mechanisms of Brain Plasticity: From Molecular Dynamics to Network Adaptation in Learning and Memory

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Optogenetic Emulation of In Vivo-like Up States

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Experimental neuroscience faces a fundamental trade-off between in vitro (e.g., slice electrophysiology) and in vivo experiments in the intact brain and behaving animal. Although in vitro experiments offer a highly controlled environment, the neurons do not experience the same conditions as in the intact brain, where thousands of synaptic inputs impinge on the dendritic tree when the network is active. Rather, the lack of network activity leaves the cells in a down state, which does not fully reflect their physiological behavior in vivo.

Here, we develop a novel technique to emulate the in vivo-like conditions in vitro using 'optical clamping'. We combine spatial light modulators and an optogenetic dual-wavelength probe for excitation and inhibition, creating in vivo-like patterns of synaptic conductances over the entire dendritic tree - similar to an in vivo "up state". In combination with pharmacological manipulations, optical clamping can be used to probe the biophysics of dendritic spike generation during emulated network activity.