Project Summary

The hippocampus plays a critical role in the formation of episodic memories. The current predominant hypothesis is that memories are gradually consolidated across distributed cortical networks under the influence of hippocampal activity. However, the nature and impact of hippocampal influences on cortical circuits remains unknown. One of the main challenges has been that hippocampal inputs result in subthreshold changes in the membrane potential of cortical neurons which are invisible to extracellular recordings, the tool used in the vast majority of previous studies. To overcome this challenge we propose to use *in vivo* whole-cell recordings of cortical neurons in combination with 2-photon imaging and optogenetic control of the hippocampal-cortical projections to directly measure the functional coupling between hippocampal and cortical networks, and characterize its modulation by brain state and learning. These experiments have only recently become feasible, and will also enable the first direct *in vivo* characterization of the plasticity rules governing hippocampal-cortical synapses across different brain states. Optogenetic control of the hippocampal inputs to cortex will enable pin pointing the key neural events underlying the memory consolidation process during awake behavior and sleep, and selective boosting of hippocampal inputs around these key events can guide the development of brain implants for cognitive enhancement or restoration of compromised memory function. These experiments will bring us closer to a mechanistic understanding of the processes used by the brain to extract information and embed it across cortical circuits. This may inspire novel machine learning approaches that leverage brain circuit learning rules and dynamics to extract structure from data, and enable tackling problems beyond the reach of current approaches, such as unsupervised learning, one-shot learning, and complex dynamic scene analysis. This will enable the design of neurally inspired learning systems that can operate reliably in real-world conditions.