
Input/Output Relationship in CA3 Pyramidal Cells
(1R01AG025633-01-FY04)
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CA3 pyramidal cells (CA3pcs) constitute a central crossroad of synaptic integration in the hippocampus, and play a key role in spatial mapping and memory storage. CA3pcs are monosynaptically excited by the entorhinal cortex, dentate granule cells, and other CA3pcs. The electrophysiological repertoire of CA3pcs includes single spiking and bursting, spanning a broad range of frequencies. Despite a general understanding of the anatomy and physiology of CA3pcs, little is known about the correspondence between a given pattern of synaptic inputs and the resulting firing output. This information, which is essential to relate hippocampal activity and function, constitutes the main goal of this project. First, we will investigate CA3pc dendrite biophysics (passive properties, channel distributions and kinetics), and the unitary synaptic inputs from each pathway. This will be achieved with voltage- and current-clamp recordings, calcium imaging, and the creation of a detailed, data-driven computational model. Next, the firing patterns of CA3pcs will be examined in response to systematic combinations of excitatory inputs. Surgically and pharmacologically isolated pathways will be stimulated extracellularly at various intensities and frequencies, while recording from individual CA3pcs. Corresponding compartmental simulations, implemented and validated against the experiments, will extensively characterize the computational properties of CA3pcs with respect to non-linear summation, pathway specificity, and coincidence detection of synaptic input. The public health relevance of this project directly relates to the mission of the NIA. Malfunction of the hippocampus is linked to devastating age-related conditions such as Alzheimer's disease. The combination of state-of-the-art experimental techniques with the ever-increasing computational power of biophysical modeling will accelerate research progress and help develop highly trained neuroscientists. In addition to the dissemination of results in conferences and peer-reviewed publications, all models will be publicly distributed through internet archives.

Project Website

http://www.krasnow.gmu.edu/L-Neuron