
Mechanisms of Persistent Neural Activity
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The long-range goal of this research is to identify the cellular and circuit mechanisms responsible for persistent neural activity: a sustained change in sodium action potential firing related to short-term memory. Our collaborative research program combines experimental and theoretical studies of the oculomotor integrator, where persistent neural activity is related to a short-term memory of the current eye position. The experimental preparation is the goldfish, which is particularly advantageous for a cellular and computational analysis of mechanisms. Persistent neural activity in awake goldfish will be measured and perturbed by intracellular recording to test hypothetical cellular mechanisms of persistent activity. The intrinsic and synaptic conductances of integrator neurons will be studied in vitro, and a numerical model will be constructed from the results. Synaptic connectivity will be determined by intracellular fills in vivo and dual recording in vitro, and incorporated into a network of conductance based model neurons. The effects of pharmacological reagents on behavior and neural activity will be compared with model predictions. The properties of correlated neural activity will be measured with microelectrode recordings and compared with network models. Finally, the physiological properties of integrator neuron dendrites will be studied in vivo using two photon laser scanning microscopy. There are several reasons why the proposed research should have broad significance for neuroscience. Firstly, the concept of a neural integrator is a very general idea in motor control and many other neural integrators have been proposed. Secondly, transient inputs or commands cause sustained changes in neural firing in many brain areas. The leading theoretical models of this persistent neural activity are recurrent networks in which the sustained activity is produced by net positive feedback, the same mechanism studied in our network models of the oculomotor integrator. Many of the hypotheses in this proposal are generic to recurrent networks; hence the results of testing them may shed light on the function of other brain areas showing persistent neural activity. Persistent neural activity has consistently been observed in brain areas important in short-term memory, a central component of many cognitive abilities. Some mental disorders, such as schizophrenia, may involve deficits in short-term memory.

PI Website

http://genomics.princeton.edu/tank/research.htm

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