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A working memory model based on excitatory-inhibitory interactions and calcium dynamics

Kyle Lyman[1], Robert McDougal[1], Brian Myers[1], Joseph Tien[1], Mustafa Zeki[1], Christopher Fall[2], David Terman[1*]

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Working memory corresponds to our ability to store and manipulate information for a short time in order to carry out complex cognitive tasks. The brain region most closely associated with working memory is the prefrontal cortex; neurons within the PFC show sustained elevated activity that persists after the removal of a stimulus. It is believed that this elevated activity is held in memory during a delay period in order to guide a forthcoming response. Problems with working memory have been implicated in numerous neurological diseases including schizophrenia.

There have been numerous models for persistent activity. Most of these models are based on either intrinsic cellular properties or recurrent excitatory connections, formed during learning, among selective populations coding for a different memory. One problem with this class of models is that they deal with novel stimuli through synaptic learning, which may be too slow to account for the ability to generalize to novel stimuli in unique working memory tasks.

Here, we present a model for persistent activity based on excitatory-inhibitory interactions. The model includes a mechanism that allows for bistability between the resting background state and a persistent state based on calcium dynamics; that is, changes in intracellular calcium in an excitatory projection neuron leads to changes in the excitability of that cell or the cell's ability to respond to inhibitory synaptic input. The model reproduces several important properties of persistent activity. The network is multistable: both a background state, in which all neurons fire at a low firing rate, and persistent states, in which some subpopulation of cells fire at an elevated firing rate, are stable. The network is capable of maintaining a limited number of persistent states at the same time. The persistent activity is robust to noise or distracters; however, one can also reset the network once a 'memory' is no longer needed or switch the network to another memory if, perhaps, it is presented with a more salient cue. During both the background and persistent states, neurons have firing rates constrained by experimental data. In particular, neurons fire irregularly with a coefficient of variation close to one. The network is able to retain completely novel stimuli. Finally, we explore the role of neuromodulators in altering the processing of working memories and how changes in these neuromodulators may lead to neurological disease.

Author details
[1]Department of Mathematics, Ohio State University, Columbus, Ohio 43210, USA. [2]Department of BioEngineering, University of Illinois at Chicago, Chicago, IL 60607, USA.

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* Correspondence: terman@math.ohio-state.edu
[1]Department of Mathematics, Ohio State University, Columbus, Ohio 43210, USA