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Age-related neuromorphological distortion affects stability and robustness in a simulated test of spatial working memory

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Normal aging in humans and nonhuman primates is associated with cognitive decline, particularly in tasks involving working memory function that relies on the prefrontal cortex [1]. Because normal aging is not correlated with widespread neuron death or gross morphological degeneration, the biological substrate of these deficits remains unclear [2]. We have constructed a simulated network of model neurons with sufficient detail to model age-related perturbations to morphology and network connectivity, in order to investigate the extent to which these morphological changes in single neurons could explain the functional degradation.

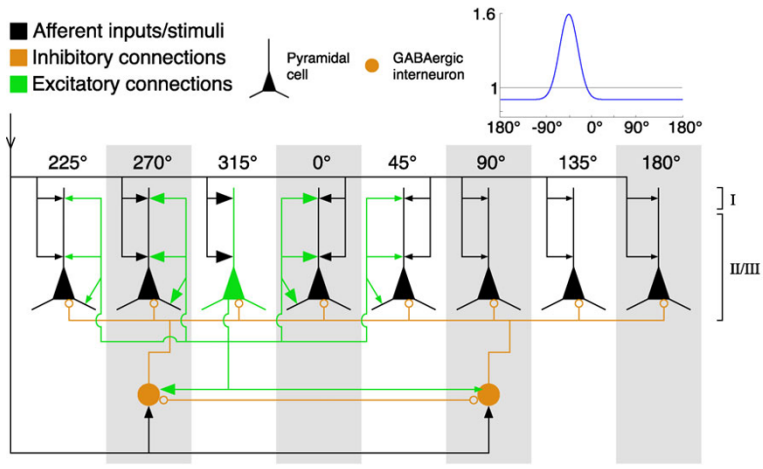

Figure 1
"Bump" attractor network model receiving input encoding the direction '315°' (green neuron), with fully interconnected populations of layer 2/3 pyramidal neurons and GABAergic interneurons. Neurons are arranged in direction-selective columns. Directionally-tuned input arrives along afferent collaterals (black arrows). Excitatory connections project preferentially to cells in similarly tuned columns (weighting in inset, upper right).

Spatial working memory can be modeled with a "bump"-style network of recurrently connected model neurons, characterized by a continuum of dynamical attractor states that provide an analogue of working memory of spatial orientation [3]. A bump-attractor network (Figure 1) was constructed using branching compartmental models of layer 2/3 neocortical pyramidal neurons [4]. Spine number and density are reduced with age in this neuron type [5], a morphological perturbation that was modeled as a reduction in both recurrent network connectivity and equivalent dendritic surface area. Network function was quantified in terms of the dynamical stability of network attractor states during the delay period of a simulated memory task, as well as the robustness of task performance against perturbation of network parameters. Stability and robustness were compared between "young" and "aged" model neuron populations with the multi-dimensional stability manifold method, which has been used in a previous study to examine the dependence of network simulations on modeling methodology [6].

By defining a stability manifold, we demonstrate how stability and robustness can be quantified as a function of biologically relevant perturbations to single cell morphology and network parameters. This provides a novel technique for evaluating the functional significance of local morphological changes, caused by age, disease or injury, upon cognition at the organism scale.

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