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Generation of Gap Models to Assess Impact of Age/Pathology on Neocortical Operations

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It is a challenge to understand or model the impacts of age and pathology on cognitive operations: Alzheimer's disease is especially problematic given its complexity and prevalence. While brain-region level (fMRI) modeling efforts have revealed deficits in functional connectivity, and highlighted compromised brain regions and operations, details of neuronal-circuit level damage are absent. There is thus a huge gap between local-circuit models simulating a few dozen nerve cells vs. fMRI maps that encompass millions of neurons: new approaches are needed.

We introduce Gap Models comprised of specialized neocortical modules that implement computations deemed necessary for simulating cognitive functions that are often damaged by age (such as *word retrieval* and *working memory*). Building upon recent computational results, using e.g. integrate and fire neurons to represent large populations, and spiking-neuron models for finer-grained cellular details, it is possible to emulate network disconnection syndromes, or the degradation of neuromodulation and ion channels, at the cellular level. This allows e.g. the competing etiologies of Alzheimer's disease to be simulated: tau protein dysfunction, amyloid-beta toxicity, inflammation, vascular and white-matter damage and cortical atrophy. By (speculatively) projecting specific damage into the gap models, this framework can quantify potential cellular and network level impacts of defined pathologies. Cortical thinning, for example, is associated with impaired cognition and tau-pathology (Xia et al., 2015; Thaker et al., 2017) and must involve some loss of tissue, such as glial/neuronal loss or shrinkage, demyelination, or loss of spines, dendrites and/or axonal branches. Such pathological changes are imported into Gap Models to assess their impact on network operations: the ensuing network/cognitive failures can then be compared with actual patient deficits.

Mechanistically, this framework is an extension/conjunction of recent computational studies ranging from spiking models (Fiebig and Lansner, 2017), synapse loss/dysfunction (Yadav et al., 2012; Schmid et al., 2016), changes in temporal binding and Hebbian STP (Kastellakis, 2017) and mean-field models (Pereira and Brunel, 2018). The Pulvermuller-Garagnani (2014) approach explicitly tests overall neocortical performance based upon specialized sensory/association area modules. Our poster extends this by incorporating auto-associative nets into neocortical gap models enabling them to utilize stored brain experiences (Rolls and Deco, 2014; Chaudhuri and Fiete, 2016): such experiences are essential for healthy cognitive activity.

keywords: Alzheimer, cognition, computational, autoassociative