Large-scale, anatomically-constrained simulation of the visual hierarchy

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Experimental and modeling efforts map the relationship between nervous system structure and function in complementary ways. Impairment studies, i.e. experiments in which specific brain areas are lesioned and the resulting behavioral deficits measured, can offer compelling evidence that brain network *X* is *necessary* for function *Y.* On the other hand, minimal mathematical models can demonstrate that *X* in isolation is *sufficient* for *Y.* While the modeling approach offers certain advantages, incorrect simplifying assumptions or parameter values can lead to model misspecification; thus it is critical that model-building be constrained by biological evidence. Fortunately this is becoming increasingly possible with the influx of neuroinformatics tools. Here we utilize three tools in particular: CoCoMac 2.0 (Bakker et al., 2012), a database of axonal connections from 459 antero/retro-grade tracer studies in the macaque; the Scalable Brain Atlas (SBA; http://scalablebrainatlas.incf.org), a collection of several macaque brain atlases registered to a common space; and NeuronDB (http://senselab.med.yale.edu/NeuronDB/), a database of compartmental neuron models.

Using the aforementioned tools and a system of first order differential equations to model neural membrane potential and spike generation, we construct a neural network that balances realism and simplicity. Construction of the network proceeds in four steps: (1) after specifying a list of brain areas (e.g. V1, IT), we use NeuronDB to find the general cell types present in each area; (2) for each cell type we find model parameters consistent with neurobiological dynamics; (3) we estimate the relative number of cells in each region from volumetric data in the SBA and also provide a first order estimate of inter–areal sampling size; (4) we choose the cells' inter–areal coupling based on tracer evidence from CoCoMac. Finally, to evaluate the network, we simulate lesions by removing various connections and compare the model output to *in vivo* electrophysiological recordings. Where possible, we test sensitivity to model misspecification by exploring dynamics over a range of parameter values.