1. Introduction

The cortical connectome develops in an experience-dependent manner under the constraints imposed by the morphologies of axonal and dendritic arbors of numerous classes of neurons. In this study, we describe a theoretical framework which makes it possible to construct the connectome of a cortical column by loading associative memory sequences into the structurally (potential) constrained network.

To generate the structural connectivity of the column, we put together axonal and dendritic arbors of 55 neuron classes reconstructed as part of the Blue Brain Project [12] and created a network containing 28,156 neurons interconnected with 1.0±0.4 potential synapses [2]. By loading associative memory sequences into this network [6, 10], we generated its functional connectivity. Many properties of connectivity in the model column are in good agreement with the available experimental measurements. These include correlation probabilities for 24 types of local excitatory and inhibitory projections, the dependence of connection probability on the distance between neurons, correlations between structural and functional connectivity, volume densities of inhibitory synapses in different cortical layers, and the distribution of specific excitatory and inhibitory 5-sequences. Our results contain predictions regarding intra- and inter-layer connectivity between specific neurons classes that can be tested in future experiments.

We conclude that basic properties of connectivity in the cortical column may have resulted from biologically-constrained associative learning in a morphologically constrained neural network.

2. Associative learning model for a cortical column

Virtual column

Axon of L5-1st layer

Dendrites of L5-1st layer

Axon of L6-2nd layer

Dendrites of L6-2nd layer

50 μm

The cortical column consists of 28,156 excitatory and inhibitory neurons, belonging to 55 morphologically defined classes of cells in six layers.

Structural connectivity of the column was calculated based on the neuron positions within the column and the morphologies of their axonal and dendritic arbors.

A structural (potential) connection between two neurons was defined as an apposition of their axonal and dendritic branches at less than 2.0 μm for excitatory-to-excitatory connections and less than 0.7 μm for the remaining three connection types.

We applied soft thresholds to remove connections with few potential synapses. A threshold of 3 was used for excitatory-to-excitatory connections and 1 for other connection types.

3. Structural statistics of the cortical column

- Neuron densities in the model column are consistent with the experimental measurements [1, 3].
- Dendrite length densities agree with the measurements from two cortical systems [7, 8]. However, the length densities of excitatory axon in the model are far below the experimentally observed value (∼40 μm) due to the absence of long-range projections originating from neurons outside the column [9].
- Volume densities of synaptic proteins are much lower than the experimentally measured densities of synapses, which is indicative of high structural plasticity potential of cortical networks.

5. Cell-type specific connectivity

- The average number of synapses between potentially connected excitatory neurons matches well with experimental data.
- The average number of synapses for E = E, E = I, and I = I connections obtained in the model are about 6 times smaller than that reported in experimental studies.

6. Bouton densities on axons and inhibitory synapse volume densities

- Bouton densities in the model are significantly higher than the experimentally measured values.
- Volume densities of inhibitory synapses in the model are generally consistent with the densities of symmetric synapses measured with electron microscopy in different cortical layers.

7. Structural and functional connectomes

- Projections contributing less than 1% of the total synapse numbers were eliminated to avoid clutter.
- Overall, the connectome of the model cortical column exhibits a small-world topology with abundant intra-layer interactions and sparse inter-layer projections.

8. Two- and three-neuron motifs

- Overexpressions of excitatory and inhibitory three-neuron motifs observed in the model are in general agreement with various experimental measurements.
- Overexpressions of motifs 1, 6, 10, and 11 were detected in excitatory L-L-LTPC subnetworks [13], while overexpressions of motifs 3 and 4 in inhibitory subnetworks were reported in [14].

9. References


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