Reconstruction and simulation of the cerebellar microcircuit: a scaffold strategy to embed different levels of neuronal details

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Computational models allow propagating microscopic phenomena into large-scale networks and inferencing causal relationships across scales. Here we reconstruct the cerebellar circuit by bottom-up modeling, reproducing the peculiar properties of this structure, which shows a quasi-crystalline geometrical patterning well defined by convergences/divergence ratios of dendritic and axonal processes [1]. Therefore, a cerebellum scaffold model has been developed and tested. It maintains scalability and can be flexibly handled to incorporate neuronal properties on multiple scales of complexity. The cerebellum scaffold includes the canonical neuronal types: Granular cell, Golgi cell, Purkinje cell, Stellate and Basket cells, Deep Cerebellar Nuclei cell. Placement was based on density and encumbrance values, connectivity on specific geometry of dendritic and axonal fields, and on distance-based protocols. In the first release, spiking point-neuron models based on Integrate&Fire dynamics with exponential synapses were used. The network was run in the neural simulator pyNEST. Complex spatiotemporal patterns of activity, similar to those observed in vivo, emerged [2]. For a second release of the microcircuit model, an extension of the generalized Leaky Integrate&Fire model has been developed (E-GLIF), optimized for each cerebellum neuron type and inserted into the built scaffold [3]. It could reproduce a rich variety of electrophysiological patterns with a single set of optimal parameters [4].

Complex single neuron dynamics and local connectome are key elements for cerebellar functioning. Then, point-neurons have been replaced by detailed 3D multi-compartment neuron models. The network was run in the neural simulator pyNEURON. Further properties emerged, strictly linked to the morphology and the specific properties of each compartment. This multiscale tool with different levels of realism has the potential to summarize a wide-ranging spectrum of the electrophysiological intrinsic neuronal properties that drive network dynamics and high-level behaviors.

The model has been tested in a sensorimotor loop of EyeBlink Classical Conditioning (EBCC) [5], let emerge fundamental operations ascribed to the cerebellum: prediction, timing and learning of motor commands.

GABAergic interneuron (DCNi)

Electrophysiology and imaging

Single cell and microcircuit recordings in vitro and in vivo in rodents.

MRI and fMRI in humans

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REFERENCES

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