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Realistic circuit modeling: large-scale simulations of the cerebellar granular layer

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The granular layer network structure was generated on the basis of anatomical and functional information to a high level of detail and using detailed "realistic" models of neurons and synapses, which include biophysical details at the membrane, channel and receptor level [1-4]. The cerebellar granular layer has been proposed since far to perform spatio-temporal transformations on incoming signals to be relayed to Purkinje cells. However, the nature of such operations remained elusive. Here, by combining advanced observations at the molecular/cellular level with a detailed description of the network structure, we have developed a realistic computational model of the granular layer network and explored its internal dynamics. The network implemented the feed-forward and feed-back inhibitory loops formed by mossy fibers, granule cells and Golgi cells respecting specific connectivity rules and yet allowing for a certain degree of randomness. The network generated noisy background spontaneous activity and was activated using patterns inspired to those recorded in vivo. The response of the model to input bursts consisted in new granule cell bursts composed of a few high-frequency spikes limited in time (time windowing effect) and space (center-surround effect) by network inhibition. Due to the presence of NMDA receptors and other ionic mechanisms, this burst-burst transmission process showed a marked frequency-dependence generating a high-pass filter with a cut-off frequency around 50 Hz. The specific connection geometry, which includes overlapping and clustering of the multiple inhibitory fields of Golgi cells, determined activation of specific granule cell subsets enhancing time-windowing and center-surround. When the model was bombarded with a random mossy fiber discharge, it showed the emergence of sustained coherent oscillations in the theta-frequency band. Thus, the simulations match the most relevant experimental observations reported so far and predict the contribution of various elements to network activities. It is of relevance that, in these simulations, granule cell activation remained sparse not just at rest but also during burst-burst transmission and during coherent population activity. This model represents the basis for investigating the spike codes transmitted through the cerebellar granular layer to Purkinje cells and for further extensive simulations of cerebellar network processing.

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References

1. D'Angelo E, Nieus T, Maffei A, Armano S, Rossi P, Taglietti V, Fontana A, Naldi G: **Theta-frequency bursting and resonance in cerebellar granule cells: experimental evidence and modeling of a slow K^+-dependent mechanism.** *J Neurosci* 2001, **21**:759-770.
2. Nieus T, Sola E, Mapelli J, Saftenku E, Rossi P, D'Angelo E: **LTP regulates burst initiation and frequency at mossy fiber-granule cell synapses of rat cerebellum: experimental observations and theoretical predictions.** *J Neurophysiol* 2006, **95**:686-699.
3. Solinas S, Forti L, Cesana E, Mapelli J, De Schutter E, D'Angelo E: **Computational reconstruction of pacemaking and intrinsic electroresponsiveness in cerebellar golgi cells.** *Front Cell Neurosci* 2007, **1**:2, doi10.3389/neuro.03.002.2007.

4. Solinas S, Forti L, Cesana E, Mapelli J, De Schutter E, D'Angelo E: **Fast-reset of pacemaking and theta-frequency resonance patterns in cerebellar golgi cells: Simulations of their impact in vivo.** *Front Cell Neurosci* 2007, **1**:4, doi10.3389/neuro.03.004.

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