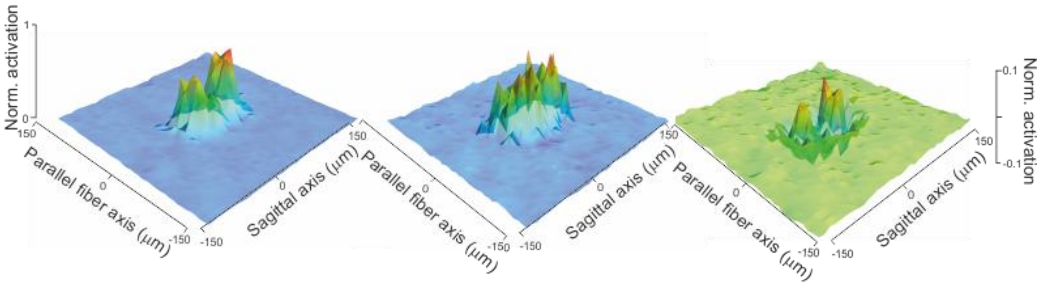
Advanced modelling of the Cerebellum Granular Layer

Sergio Solinas[1], Stefano Casali[2], Davide Allavena[2], Stefano Masoli[2], Egidio D'Angelo[1, 2]
[1] Brain Connectivity Center, Istituto Neurologico IRCCS C. Mondino, Via Mondino 2, I-27100 Pavia, Italy
[2] Department of Brain and Behavioural Science, University of Pavia, Via Forlanini 6, I-27100, Pavia, Italy



Purpose

The cerebellum granular layer is a network formed by granule cells, Golgi cells and mossy fibers organized according to a number of statistical and geometrical rules. Although not all the aspects of this connectivity have been clarified, available information can be used to generate network models integrating neuronal and synaptic dynamics. The main issue is how the granular layer operates internal spatio-temporal transformations of incoming signals. Although a fundamental hypothesis was proposed by Marr, who recognized that this network could perform input signal decorrelation and sparse coding, the original models were only based on topological and statistical considerations but not on geometry and neuronal dynamics. Therefore, it is expected that a radically different mechanism of computation would emerge once these properties are accounted for. A first step in this work was to construct the granular layer network and validate its critical mechanisms of function against experimental recordings.

Methods

We have constructed a biologically realistic computational model of the cerebellar granular layer following previously published principles of network connectivity (Solinas et al. 2010) and using available single neuron models of granule cells and Golgi cells. The signals were reconstructed to yield the equivalent of a voltage-sensitive dye imaging recording (Mapelli et al., 2010a,b). The network model was scalable and was written in NEURON-PYTHON. Simulations were performed on a 60 nodes INTEL computer cluster and on the BlueJene/Q FERMI computer clusterat CINECA (Bologna – ITALY). Simulations have been carried put in the context of HUMAN BRAIN PROJECT, REALNET, CEREBNET, MinSal-GR2009.

Results

We have incorporated the following features:

- advanced models of granule cells (D'Angelo et al., 2001; Diwakar et al., 2009), Golgi cells (Solinas et al., 2007a,b) and synapses (Nieus et al., 2006; Nieus et al., 2014).
- network structural constraints based on *statistics* of convergence/divergence ratios (Solinas et al., 2010)
- network structural constraints based on *3D geometry* of the Golgi cell input/output connections (Sillitoe et al., 2008; Barmack et al., 2007; Cesana et al., 2013; D'Angelo et al., 2013)

The model was able to predict the 3D center-surround (CS) organization of granular layer activity. The network was activated by test trains of 5 pulses at 100 Hz running on a few neighbouring glomeruli. The CS had a size (core radius ~25 μm; surround radius ~25 μm) and a ratio of discharging neurons (~10% in the center, ~0% in the surround) very similar to those measured experimentally with 2-photon microscopy in slices (Gandolfi et al., 2014) or inferred from local field potential reconvolution *in vivo* (Diwakar et al., 2011). Moreover, the CS showed different transmission properties, with higher gain in the center than in the surround (Mapelli et al., 2010a,b). The model predicts that Golgi cell synaptic inhibition, through its specific geometrical arrangement, plays a critical role in shaping the response of the network (Forti et al., 2013).

Discussion

The cerebellar granular layer model is proving a valuable tool to explore intrinsic computational dynamics of the cerebellar granular layer. The model is conceived for a future implementation on the HBP platform.

References : See http://www-5.unipv.it/dangelo/