Regulation of inhibitory circuits in the dentate gyrus: role on temporal coding and pattern separation

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Electrophysiological recordings in the hippocampus revealed a tight control of inhibitory interneurons over the Granule Cells (GCs) of the Dentate Gyrus. In *in-vivo* experiments of Long-Term Potentiation (LTP) of the Perforant Pathway, it is found that the expected potentiation of glutamatergic synapses is also accompanied by a reduction of the feed-forward inhibitory activity, facilitating activity propagation in the circuit. To further investigate this phenomenon, we built a population model where neurons were described by Izhikevich's equations and synapsis mediated by AMPA, NMDA and $GABA_A$ receptors. The results obtained from the numerical integration of the model equations, before and after the application of the LTP, support both the counterintuitive experimental observation of synaptic depression in the feed-forward inhibitory connection after LTP induction as well as the change in the correlation between excitatory and inhibitory inputs over GCs. We find that LTP increases the efficiency of the glutamatergic input to recruit the inhibitory network of the hilar region, resulting in an average reduction of the basket cell population activity. The predictions of the model were experimentally corroborated by intracellular patch-clamp recordings in an in vitro preparation, after *in vivo* LTP induction in mice. To gain insight into the functional role of the feedforward inhibition reduction over GCs, we built a neuronal model of GCs including their dendritic arbor. The results obtained from this model predict that the reorganization induced by the LTP increases the occurrence of bursts in GCs and improves the temporal coding and information transmission from the entorhinal cortex to the CA3 via GCs. This finding is supported by previous experiments where it was observed that the activity of CA3 pyramidal cells is tremendously facilitated upon high-frequency presynaptic GCs activity while producing minor changes on the inhibitory neurons' activity.