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Determinants of pattern recognition by cerebellar Purkinje cells

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Many theories of cerebellar function assume that long-term depression (LTD) of parallel fiber (PF) synapses enables Purkinje cells (PCs) to learn to recognize PF activity patterns. According to the classic view, a PC can store and learn to distinguish PF activity patterns that have been presented repeatedly together with climbing fibre (CF) input to the cell. The resulting LTD of the PF synapses is often assumed to lead to a decreased rate of PC simple spike firing, a reduction in the inhibition of their target neurons in the deep cerebellar nuclei and thus an increased output from the cerebellum. We have recently shown by combining computer simulations with electrophysiological recordings in slices and in awake behaving mice that the readout of learned patterns in PCs may operate in a fundamentally different way. Our simulations and experiments predict that the best criterion to distinguish between learned and novel patterns is the duration of a pause in firing that occurs after presentation of a pattern, with shorter pauses in response to learned patterns [1].

Although our previous simulations have used a biophysically detailed PC model that has been tuned to generate realistic behaviours under in vitro and in vivo conditions, we have applied a simplified learning rule where the AMPA receptor conductance of an active PF synapse is halved every time a PF pattern is learned. Moreover, our previous simulations have not incorporated the LTD of inhibitory synapses that can be induced when the PC receives coincident CF input [2], and that could potentially counteract the effect of the depression of the excitatory PF synapses. Here, we study the effect of inhibitory synaptic plasticity on pattern recognition, and we explore a variation of our original learning rule that has been adapted to result in a better match to experimental data on LTD induction in slices [2,3].

To study the effect of plasticity at the synapses between inhibitory interneurons and PCs, we presented the model with feed-forward inhibitory input, which followed the excitatory input with a time delay of 1.4 ms [1,2]. Initially, we chose an inhibition/excitation ratio of one, in the range of experimental observations in vitro [2]. We then introduced LTD at the inhibitory synapses and evaluated the pattern recognition performance for varying numbers of learned patterns. We found that the performance was unaffected by the presence of inhibitory LTD, even in the extreme case when the inhibitory plasticity was restricted to the presentation of learned PF patterns. Our simulations predict that LTD based pattern recognition is very robust in the presence of LTD at inhibitory synapses.

By dividing the synaptic weights of active PFs by two for every pattern that was learned, our original learning rule could result in very small AMPA receptor conductances for large numbers of learned patterns. However, LTD induction in cerebellar slices hardly ever results in the depression of responses to less than 50% of the pre-induction baseline [2,3]. We studied the effect of saturating LTD in our simulations and found that the pattern recognition performance was very sensitive to the value at which the synaptic weights saturated. In contrast to a corresponding artificial neural network, which was unaffected by the value at which LTD saturated, pause based pattern recognition in the PC model deteriorated drastically in the presence of higher saturation values and therefore smaller amounts of LTD. To result in satisfactory pattern recognition, LTD had to depress the AMPA receptor conductances

in the PC model down to at least 70% of their baseline values, and optimal performance resulted from setting the weights to zero and silencing the synapses completely. Interestingly, large numbers of silent PF synapses have been observed in another experimental study [4]. Our simulation results suggest that it will be crucial to explore these discrepancies to understand the connection between PF LTD and pattern recognition.

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