



# Long-term depression and recognition of parallel fibre patterns in a multi-compartmental model of a cerebellar Purkinje cell

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## Abstract

It has been suggested that long-term depression (LTD) of parallel fibre (PF) synapses enables a cerebellar Purkinje cell (PC) to learn to recognise PF activity patterns. We investigate the recognition of PF patterns that have been stored by LTD of AMPA receptors in a multi-compartmental PC model with a passive soma. We find that a corresponding artificial neural network outperforms a PC model with active dendrites by an order of magnitude. Removal of the dendritic ion channels leads to a further decrease in performance. Another effect of the active dendrites is an afterhyperpolarization response to novel PF patterns. Thus, the LTD based storage of PF patterns can lead to a potentiated late PC response. © 2001 Elsevier Science B.V. All rights reserved.

*Keywords:* Cerebellum; Purkinje cells; LTD; Pattern recognition; Learning

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## 1. Introduction

One of the most contentious issues in cerebellar research is whether or not long-term depression (LTD) of parallel fibre evoked excitatory postsynaptic potentials (epsps) in Purkinje cells is the substrate of learning in the cerebellar cortex (e.g. [3]). LTD can be induced by repeated conjunctive parallel fibre (PF) and climbing fibre (CF) input to the Purkinje cell [8]. It has been suggested that a PF pattern that is repeatedly paired with CF input elicits a reduced Purkinje cell response, leading to

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disinhibition of neurons in the deep cerebellar nuclei (DCN) and increased output from the cerebellum. Many theories of cerebellar function assume that PF LTD implements pattern storage and motor learning. However, all previous studies of PF pattern storage use very simplified Purkinje cell models (e.g. [9,1]). In real Purkinje cells, the recognition of stored PF patterns is influenced by various factors, including the spatial distribution of PF inputs over the dendritic tree, the interaction of ion channels and intracellular calcium and the spontaneous simple spike firing that is caused by PF background input. Here, we study the recognition of stored PF patterns by a complex multi-compartmental model of a cerebellar Purkinje cell [4,5].

## 2. The model

We compare the pattern recognition performance of the multi-compartmental Purkinje cell model with the performance of an artificial neural network (ANN). The ANN used is a modified version of an associative net [10] with real-valued synapses and an LTD learning rule (Fig. 1). During the learning phase, each binary input pattern is stored in the ANN by decreasing the weights of all synapses that receive input by a factor of 0.5. During the recall phase, the response of the ANN to a pattern is given by the sum of the weights of all synapses that are associated with active input lines. Thus, the average response of the ANN to stored patterns will be lower than the response to novel patterns. The ability of the net to discriminate between stored and novel patterns can be described by the signal-to-noise ratio (e.g. [7]):

$$s/n = \frac{(\mu_s - \mu_n)^2}{0.5(\sigma_s^2 + \sigma_n^2)} \quad (1)$$

where  $\mu_s$  and  $\mu_n$  are the mean values and  $\sigma_s^2$  and  $\sigma_n^2$  the variances of the response to stored and novel patterns, respectively.

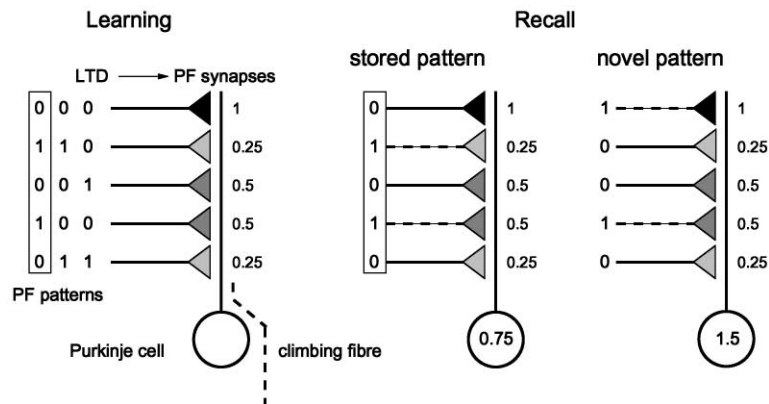


Fig. 1. ANN model of LTD based learning (see text for explanation).

After having stored varying numbers of patterns with varying numbers of active inputs per pattern in the ANN, the resulting sets of synaptic weights are transferred to the Purkinje cell model and represented as sets of AMPA receptor conductances on the spine compartments. For each binary input pattern in the ANN, the Purkinje cell model is presented with a corresponding pattern of synchronous PF inputs to the spines. The pattern recognition performances are evaluated by calculating  $s/n$  ratios for the ANN and for Purkinje cell models with active and passive dendritic trees. Initially, we restrict ourselves to Purkinje cell models with passive soma compartments and calculate the  $s/n$  ratio by considering the somatic voltage peak as the relevant response.

We use the multi-compartmental Purkinje cell model that has been described in Refs. [4,5]. The model receives excitatory input from 147,400 PFs which activate AMPA receptors on dendritic spines. To increase the computational efficiency, only 1% of the 147,400 spines is represented explicitly. Each of these 1474 spine compartments receives 100 PF inputs. All PFs are activated asynchronously with a frequency of 0.28 Hz, resulting in an asynchronous AMPA receptor activation in each spine compartment with a frequency of 28 Hz. The background excitation is balanced by a tonic background inhibition, and the completely active model fires simple spikes with an average frequency of 50 Hz. All Purkinje cell simulations are performed using the GENESIS simulator [2].

### 3. Simulation results

Figs. 2 and 3 compare the recognition of stored PF patterns in the ANN and the Purkinje cell model with active dendrites and a passive soma. If the maximum of the voltage response in the passive soma is considered as the relevant output, the Purkinje cell model can distinguish 100 PF patterns that have been stored from 100 novel patterns (Fig. 2). There is no overlap between the responses to stored and novel patterns with 1000 or 10,000 synchronously active PFs, but a significant overlap if only 100 out of the 147,400 PFs are active. Thus, in the presence of noise in the form of PF background excitation, stored PF patterns have to contain a sufficient number of active inputs in order to be correctly classified.

Fig. 3 shows the  $s/n$  ratios for varying numbers of stored patterns in the ANN and in the Purkinje cell model with active dendrites. Based on the voltage response in the passive soma, the Purkinje cell model can easily recognize up to 300 stored PF patterns with 1000 active inputs. If the number of active inputs is increased to 10,000, the performance is significantly worse. Low numbers of stored pattern with 10,000 active inputs lead to a saturation of the Purkinje cell response, and the  $s/n$  ratio exhibits a maximum around 50 stored patterns. In all cases, the ANN performs at least an order of magnitude better than the Purkinje cell model.

Previous studies have shown that an active dendritic tree amplifies the postsynaptic response of the Purkinje cell model to distal PF inputs, resulting in a somatic response which is insensitive to the dendritic location of the input [6]. Given that the  $s/n$  ratio increases with a decreasing response variance, active dendrites are expected to result

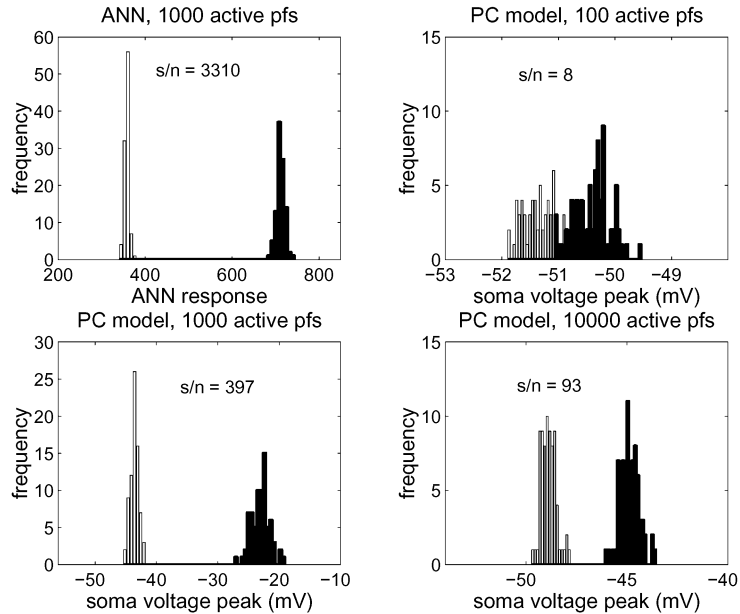


Fig. 2. Distribution of responses to 100 stored patterns (white bars) and 100 novel patterns (black bars) in the ANN and the Purkinje cell model with active dendrites and a passive soma.

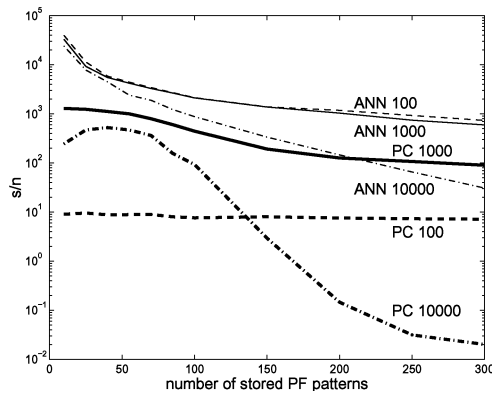


Fig. 3. Signal-to-noise ratios ( $s/n$ ) of the ANN (thin lines) and the Purkinje cell model with active dendrites and a passive soma (thick lines) for the recognition of varying numbers of patterns with 100 (dashed), 1000 (solid) and 10,000 (dot-dash) synchronously active PFs.

in a better pattern recognition performance than passive dendrites. Fig. 4 compares the pattern recognition performance of Purkinje cell models with active and passive dendrites. Although there is no difference in performance for more than 150

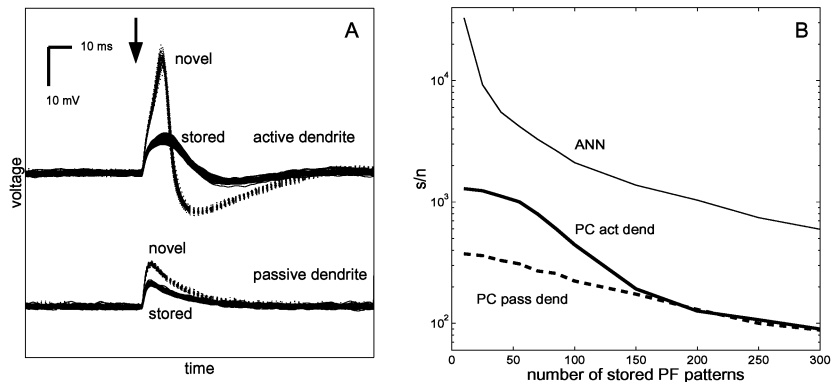


Fig. 4. Pattern recognition performance of Purkinje cell models with active and passive dendrites. (A) Response to 100 stored and 100 novel PF patterns. (B)  $s/n$  ratios for the recognition of varying numbers of patterns.

stored patterns, for smaller numbers of patterns the existence of dendritic ion channels increases the  $s/n$  ratio by up to 300%. Another effect of the active dendrites is a pronounced afterhyperpolarization response to novel PF patterns (Fig. 4A).

#### 4. Conclusions

It has been suggested that long-term depression (LTD) of parallel fibre (PF) evoked excitatory postsynaptic potentials (epsps) enables a cerebellar Purkinje cell to store and specifically respond to a subset of PF patterns. We have studied the recognition of patterns of synchronous PF inputs that were stored by LTD of AMPA receptor conductances in a multi-compartmental Purkinje cell model with a passive soma and active or passive dendrites. We found that the pattern recognition performance was significantly better for inputs with approximately 0.7% active PFs than for 7% or 0.07% active PFs, and that a corresponding artificial neural network with an LTD learning rule performed an order of magnitude better than the Purkinje cell model with active dendrites. For less than 150 stored patterns, the removal of dendritic ion channels resulted in a further decrease in performance. In addition to amplifying the Purkinje cell response and improving the pattern recognition performance, an effect of the active dendrites was a strong afterhyperpolarization response to novel PF activity patterns. As a consequence, the response of the Purkinje cell model to stored PF patterns was first depressed and then potentiated when compared to the response to novel patterns. We are currently studying the effect of this dual response modulation on pattern recognition based on the simple spike response in Purkinje cell models with an active soma.

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**Erik De Schutter** (born 1959) received his medical degree from the University of Antwerp in 1984 where he went on to do a clinical residency in neuropsychiatry and a Ph.D. in medicine. In 1990 he became a postdoctoral fellow at the California Institute of Technology. In 1994 he returned to the University of Antwerp to start the Theoretical Neurobiology group. He is a computational neuroscientist with a research focus on the function and operations of the cerebellar cortex. He played a seminal role in starting and directing a series of European summer schools on computational neuroscience (Crete, Trieste).