The cerebellar microcircuit as an adaptive filter: experimental and computational evidence

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Abstract | Initial investigations of the cerebellar microcircuit inspired the Marr–Albus theoretical framework of cerebellar function. We review recent developments in the experimental understanding of cerebellar microcircuit characteristics and in the computational analysis of Marr–Albus models. We conclude that many Marr–Albus models are in effect adaptive filters, and that evidence for symmetrical long-term potentiation and long-term depression, interneuron plasticity, silent parallel fibre synapses and recurrent mossy fibre connectivity is strikingly congruent with predictions from adaptive-filter models of cerebellar function. This congruence suggests that insights from adaptive-filter theory might help to address outstanding issues of cerebellar function, including both microcircuit processing and extra-cerebellar connectivity.

Purkinje cell
By far the largest neuron of the cerebellum and the sole output of the cerebellar cortex. Receives climbing fibre input and integrates inputs from parallel fibres and interneurons.

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In 1967, Eccles, Ito and Szentagothai published their landmark book *The Cerebellum as a Neuronal Machine*[1], which described for the first time the detailed microcircuitry of an important structure in the brain. Perhaps the most striking feature of the cerebellar cortical microcircuit (BOX 1) is that Purkinje cells (PCs), which provide the sole output of the cerebellar cortex, receive two very different types of input. Each PC is contacted directly by a single climbing fibre (CF) and indirectly by thousands of mossy fibres (MFs). The organization of these inputs, as it was understood until recently, is illustrated in BOX 1. MFs, which convey information from many different sources, contact granule cells, which have a direct excitatory projection to PCs through parallel fibres (PFs). CFs, which arise solely from the inferior olive, have a highly structured projection to PCs, dividing the cerebellar cortex into a large number of distinct zones that can be subdivided into microzones. A microzone is defined as a coherent strip of cerebellar cortex in which the PCs receive CF inputs that are driven by essentially identical peripheral inputs[2–4]; as the PCs in a microzone innervate a specific subset of cells in the deep cerebellar nuclei (BOX 1) with a specific output function, a microzone probably corresponds to the minimal functional unit of the cerebellar cortex. Although microzones differ from one another in their external connectivity, their internal microcircuitry is generally considered to be similar throughout the cerebellum.

Inputs from MFs and those from CFs have different electrophysiological effects in PCs. PCs fire two types of spike (BOX 2). Simple spikes are normal action potentials and are thought to be modulated by the many PFs that contact the PC dendritic tree. By contrast, complex spikes are unique to PCs. The CF input to the PC is one of the most powerful synaptic junctions of the CNS, and complex spikes occur only when the CF fires.

The fact that the cortical microcircuit seems to have the same structure throughout the cerebellum inspired the idea that there must be a 'cerebellar algorithm' with a general signal-transforming capability. Indeed, soon after the first classic description of cerebellar electrophysiology had been published[1], hypotheses about such an algorithm appeared in the form of microcircuit models proposed by Marr[5] and Albus[6]. These models agreed on several points. First, the function of the cerebellum was assumed to be related to motor control (on the basis of the anatomical, clinical and lesion evidence available at the time[7]), implying that PC outputs were related to motor commands. Second, these commands were thought to be conveyed by simple spikes fired by PCs. Third, complex spikes were assumed to fire at too low a rate (1 spike per second; BOX 2) to influence cerebellar output significantly, but instead it was thought that they might act as an error or teaching signal for the PC. Moreover, because this signal formed part of the command sent to the muscles, the function of the circuit as a whole was thought to be motor learning.

The two models also differed in certain respects, but their commonalities gave rise to the 'Marr–Albus

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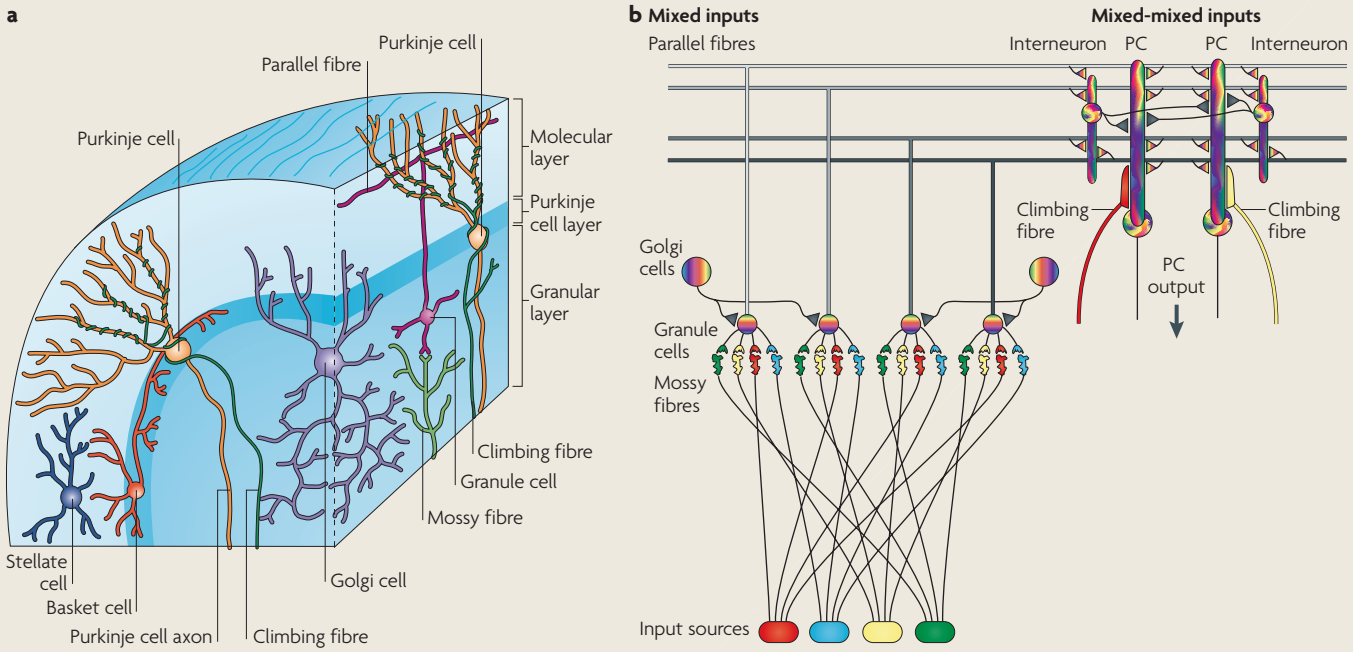
framework' of cerebellar function, which has been extremely influential in driving both experimental and theoretical investigations. Marr–Albus-based models have been applied to a range of behaviours, including smooth-pursuit eye movements[8], ocular following[9], saccades[10,11], the vestibulo-ocular reflex[12–20], classical eye-blink conditioning[13,21–27] and limb control[20,28–34], and in high-level interpretations of cerebellar function, which propose that the cerebellum can act as an internal model[28,35–41], a state estimator[42,43] or a Smith predictor[44] (see also Supplementary information S1 (box)).

However, several recent experimental discoveries concerning cerebellar connectivity, microcircuitry and plasticity indicate that the early descriptions of the cerebellar microcircuitry on which these models are based require revision. Interpretations of the function of the

Box 1 | **View of the cerebellar circuitry in the late 1990s**



Basic structure of the cerebellar cortex

Of the two main afferents to the cerebellar cortex (see the figure, part **a**), climbing fibres (CFs), which are the thick ramifications of the olivocerebellar axons, make direct excitatory contact with Purkinje cells (PCs), and mossy fibres (MFs) make excitatory synaptic contacts with granule cells (and with Golgi cells (not shown)). Each ascending axon of a granule cell branches in a T to form the two ends of a parallel fibre (PF), which in turn make excitatory synaptic contacts with PCs and with the molecular layer interneurons (that is, stellate and basket cells) and Golgi cells. PFs extend for several millimetres along individual cerebellar folia. CFs and MFs also provide collaterals to the cerebellar nuclei *en route* to the cerebellar cortex (not shown). With the exception of granule cells, all cerebellar cortical neurons, including PCs, make inhibitory synaptic connections with their target neurons.

Connectivity of the cerebellar cortical microcircuitry

In the late 1990s, all of the above microcircuitry features were known. However, as shown, this view offered no explanation of how incoming information was channelled through the microcircuitry, so the specific processing carried out by the microcircuit was essentially unknown. In the figure, part **b**, inputs are colour-coded to signify the type of information (somatosensory, auditory and so on) that is conveyed. A mix of colours (for example, in granule and Golgi cells) indicates that the cell or synapse was thought to sample different types of information. In PCs and interneurons, the 'mix of mixes' illustrates that they were thought to receive mixed granule cell input. Also, interneurons were considered to provide inhibition to PCs in a non-patterned fashion in the form of feedforward and/or lateral inhibition. PCs were generally thought to be the sole recipient of CF input.

Also by the late 1990s new information had emerged about patterns of connectivity between specific areas of cerebellar cortex and their CF inputs and deep cerebellar nuclear outputs. The high degree of organization of these connections formed the basis for the concept of the microzone. Microzones seem to constitute the basic functional subunit of the cerebellum and are subdivisions of the previously established sagittal zones (for reviews see REFS 148,149). Microzones are defined as a coherent strip of cortex in which the PCs are activated by essentially identical CF inputs (the figure illustrates PCs in two different microzones, which receive different inputs, as indicated by the colour code of the CFs). Because all the PCs in a microzone have a common innervation territory in the deep cerebellar nuclei, they have a specific output effect — that is, they control one specific movement component or target one specific region in the downstream cerebral cortical areas or brainstem nuclei. A rough estimate of the number of microzones in the cerebellum can be obtained as follows: based on a microzone width of ~5 PCs (50–100 μm) in the C3 zone of the cat[3], a microzone length of ~15 mm, and the sagittal extent of a PC dendritic tree of ~0.3 mm, we arrive at around 200 PCs for a microzone. If the total number of PCs in the cat is ~1,000,000 (REF. 150), then the total number of microzones in the cerebellar cortex would be ~5,000. The concept of the microzones is an important frame of reference for characterizing how incoming information is channelled through the microcircuitry. These figures do not show the unipolar brush cells, which are preferentially located in cerebellar areas with vestibular input[151], or Lugaro cells.

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microcircuit have in the past focused heavily on PCs and their CF and PF inputs, whereas little attention has been paid to other components of the cerebellar microcircuitry (BOX 1). Moreover, newly discovered forms of plasticity indicate that the cerebellar circuitry can adapt its wiring in response to altered functional requirements. The validity of models based on earlier descriptions of the cerebellar microcircuit is therefore called into question. We address this issue first by arguing that almost all of the Marr–Albus-derived models have the core characteristics of an adaptive filter (see Supplementary information S2 (box)). We then describe several recently discovered microcircuitry properties, and show that they are consistent with many of the requirements for fulfilling the basic computational features of adaptive filters. Finally, we indicate how the striking and unexpected congruence between the computational properties of adaptive filters and the cerebellar microcircuitry has crucial consequences for both interpreting cerebellar function and identifying important issues for future research.

Climbing fibre
(CF). Arises from cells in the inferior olive and provides an extraordinarily strong, 'climbing' multi-synaptic contact on Purkinje cells. However, branches of the olivocerebellar axon contact not only Purkinje cells but also other neuron types of the cerebellum. In the latter cases, there is no 'climbing' pattern in the anatomical configuration of the contacts. Nevertheless, for convenience, the input from the olivocerebellar axons to the interneurons is referred to as 'CF' input in the text.

Mossy fibre
(MF). Provides the bulk of the afferent input to the cerebellum and originates from numerous sources in the spinal cord, brain stem and pontine nuclei (the latter mediating input from the cerebral cortex).

Granule cell
Integrates excitatory mossy fibre input from external sources and local inhibitory input from Golgi cells.

Parallel fibre
(PF). Arises from granule cells and provides excitatory input to Purkinje cells and molecular layer interneurons.

Microzone
A narrow longitudinal strip of the cerebellar cortex, just a few Purkinje cells wide but up to hundreds of Purkinje cells long, in which all the Purkinje cells receive climbing fibres driven by the same input.

Vestibulo-ocular reflex
Reflex movement of the eyes elicited by vestibular stimulation. Its purpose is to keep the retinal image stable, preventing degradation of visual processing. The reflex is under the control of the floccular region of the cerebellum.

Box 2 | **Simple and complex spikes**

Properties of Purkinje cell (PC) spikes from intracellular whole-cell recordings *in vivo*
PCs fire simple spikes (see the figure, part **a**, top) at ~40 spikes per second on average. They are standard action potentials typical of neuronal firing throughout the nervous system. By contrast, complex spikes (see the figure, part **a**, bottom), which are characterized by multiple after-discharges and appear at ~1 spike per second on average, are unique to PCs. Complex spikes are generated as a result of the activation of most or all of the PC dendritic tree by the uniquely powerful climbing fibre (CF) synapse (see main text). CF discharge, in turn, is derived from the firing of neurons in the inferior olive. Simple spikes, which do not backpropagate into the PC dendritic tree[152], fire spontaneously in the absence of afferent input. The spontaneous firing rate of simple spikes can be modulated in both excitatory and inhibitory directions by specific inputs (see the figure, part **b**), in a manner consistent with their generation by excitatory parallel fibre (PF) and inhibitory interneuronal inputs, respectively[72,76,85], and with these inputs being summed primarily in a linear fashion[153] (note, though, that other *in vitro* work indicates that PCs use nonlinear summation[154]). The origin of simple spike modulation is still the subject of controversy, particularly concerning the relative roles of PFs and the ascending part of the granule cell axon and whether PC simple spikes operate in a bistable fashion.

PF synapses versus ascending granule cell axon synapses
In recordings from the C3 zone, as shown above, the mossy fibres and granule cells that convey input from the red skin area, which provides excitatory drive to the simple spike activity (see the figure, part **b**), are not located beneath the PCs[72,76]. It is hence clear that the PFs, rather than the ascending granule cell axon, carry most of the excitatory input. This contrasts with the view that the ascending granule cell axon might be a dominating input in PCs, an idea that has received some experimental support[155]. However, many of the supporting experiments *in vivo* were made in anaesthetized animals, and anaesthesia can severely depress the transmission of spiking activity from the granule cell to the PF (also discussed in REFS 85,156). It has also been reported that the synapses made by the ascending axon and by the PFs differ in their susceptibility to long-term depression in PCs *in vitro*[157], but this does not seem to be a prominent trait in PCs *in vivo*, where inputs from granule cells located beneath and from granule cells not located beneath the PC seem equally susceptible to potentiation and depression[72]. Furthermore, a recent *in vitro* study of ascending and PF inputs to PCs using optical stimulation indicates that the two inputs are functionally equivalent[158].

PC bistability
Results from *in vitro* and anaesthetized preparations have led to suggestions that PCs have two states, an up state and a down state, and that the simple spike output of the PC depends mainly on the current state[159]. In this view, CF activation works as a switch between the two states, and the PC essentially becomes a binary element. However, the functional relevance of this bistability has been challenged by the claim that it is rarely observed in awake animals[160] and in studies in which the PC simple-spike firing is related to behavioural parameters in activities such as smooth-pursuit eye movements (for example, see REFS 40,136,161–169).

There is recent evidence that in awake cats, around half of PCs show frequent long pauses (mean ~700 ms), and that the transition between pauses and modulated simple spike firing is sometimes (25% of the time) associated with complex spikes[170]. These data are consistent with bistability. However, the issue of functional significance is still unclear. The animals were not engaged in a specific behavioural task (other than sitting quietly), and the occurrence of pauses was not related to behavioural events. The contrast between these findings and those that report correlations between simple-spike modulation and behaviour in awake animals is striking and unexplained.

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Engineering control theory
A branch of engineering science concerned with the control of dynamic systems (including aircraft, chemical reactions and robots).

Silent synapses
Synapses that can be structurally identified but which provide no synaptic currents in the postsynaptic cell.

Adaptive-filter models

In 1982, Fujita introduced the adaptive filter to cerebellar modelling[45], influenced by Ito's suggestion that the cerebellum's role in adaptation of the vestibulo-ocular reflex could be understood in terms of engineering control theory[46,47]. FIGURE 1 shows how a simplified version of the cerebellar cortical microcircuit can be mapped onto an adaptive-filter structure: the (MF) filter inputs are analysed into (PF) component signals, which are then weighted (PF–PC synapses) and recombined to form the filter (PC simple spike) output.

The filter is adaptive because its weights can be adjusted by a teaching or error signal (the CF input), using the covariance learning rule proposed by Sejnowski[48] (FIG. 1). According to this rule, a PF signal that is positively correlated with an error signal has its weight reduced (through long-term depression (LTD)), whereas a signal that is negatively correlated with an error signal has its weight increased (through long-term potentiation (LTP)). This procedure makes sense when correlations represent causal relations, because in that case reducing the impact of PF signals that are correlated with an error signal will reduce the error itself (provided that the system outputs are appropriately directed).

Adaptive filters deal with temporally varying signals of the kind seen in the neural control of movement and have proved to be highly versatile in various applications (BOX 3). Depending on the information contained in the error signal, they can be used for (sensory) signal processing, motor control and learning internal models (see Supplementary information S1,S2 (boxes)).

Close inspection of the Marr–Albus-based models indicates that many of them use time-varying signals, analysis of input signals, and the covariance learning rule[9,11,17–20,26,27,38–41,43,49–55], which are key features of the adaptive filter (BOX 3; FIG. 1; Supplementary information S2 (box)). Although the models themselves are often not explicitly described as such (see BOX 4 for a discussion of how other types of model stand with respect to the adaptive-filter family of models), we argue that treating them as adaptive filters has an important advantage. The relative simplicity of adaptive filters means that their general computational features (BOX 3; Supplementary information S2 (box)) can be analysed to determine whether their success depends on these general features rather than on specific implementation details that vary from model to model.

Recent developments[17,18,20,51,56–59] have indicated that implementing the core computational features of an adaptive filter in the cerebellar circuitry leads to the predictions that symmetrical LTP and LTD, dual pathway plasticity, silent synapses and recurrent architecture occur in the microcircuitry. Below, we compare these computational predictions with recent empirical data, revealing a striking congruence between the two. We also discuss recent findings concerning the cerebellar granule layer

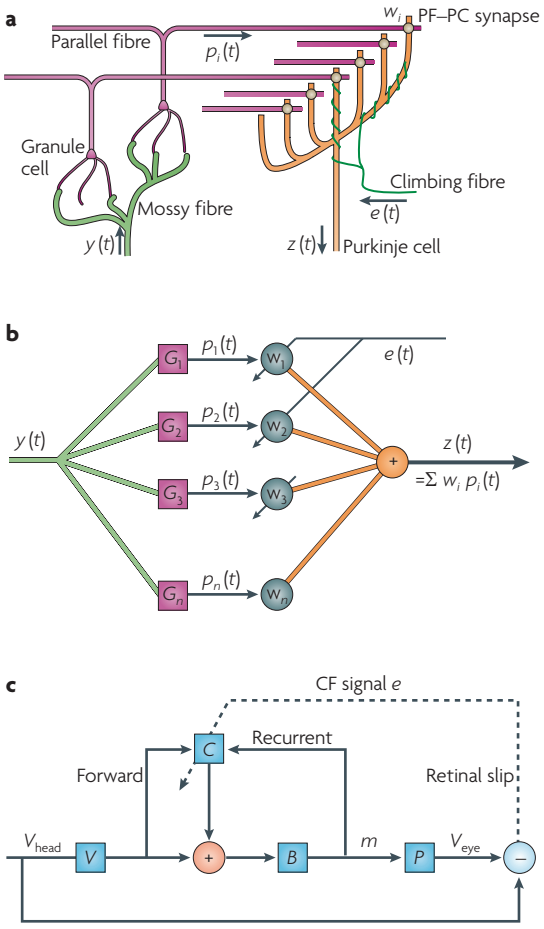

Figure 1 | **A simplified cerebellar microcircuit as an adaptive filter. a** | A mossy fibre (MF) input signal is distributed over many granule cells, the axons of which form parallel fibres (PFs) that synapse on Purkinje cells (PCs). In Marr–Albus-type models, correlated firing of a PF and the single climbing fibre (CF) that winds around the PC alters the strength of the PF–PC synapse. Note that this figure omits a number of the microcircuit features shown in BOX 1, in particular the inhibitory projection from granule cells to PCs via stellate and basket cells. Plasticity in this projection is only rarely included in adaptive-filter models of cerebellar function[8]. **b** | The structure of this microcircuit can be identified with that of an adaptive filter as follows: the processing of a sensory input or motor signal input by the granule cell layer is interpreted as analysis by a bank of filters. PC output is modelled as a weighted sum of these PF inputs, with the weights corresponding to synaptic efficiencies. The CF input is interpreted as a teaching signal that adapts synaptic weights using the covariance learning rule[48]. Formally, the filter weights w_i are adjusted using by $\delta w_i = -\beta\,(ep_i)$, where δw_i is the change in weight, e is the teaching signal, P_i is the signal to the weight and (ep_i) denotes the covariance of e and P_i. The teaching signal e is often performance error, and is in that case referred to as an error signal. The learning rule can then be shown theoretically to minimize mean square performance error (e^2) and is usually called the least mean square rule in artificial systems. **c** | Forward and recurrent architectures illustrated for horizontal vestibulo-ocular reflex (VOR) adaptation. The task of the VOR is to convert the vestibular signal v_{head} into motor commands m to the oculomotor plant P that move the eye so as to exactly compensate for head movements: $v_{eye} = v_{head}$. This adaptable reflex is mediated by a direct pathway through the brainstem B, supplemented by forward and recurrent adaptable pathways through the floccular region of the cerebellum C that carry mainly vestibular information (processed in V) and a motor efference copy, respectively. It has been argued[17] that VOR plant compensation (changes in the adaptive filter C in response to changes in the motor plant P) depend mainly on the recurrent pathway through C. This formulation has the advantage that the required teaching signal is sensory error (retinal slip e) as shown. In more general adaptation problems both forward and recurrent pathways are necessary, with the former used for vestibular compensation (that is, adaptation to changes in V) and the latter for plant compensation[20]. Previous schemes for plant adaptation have used only the forward pathway in a feedback error learning architecture[179]. The advantages of the recurrent architecture for control of nonlinear and redundant systems are discussed in REF. 54. Parts **a** and **b** are reproduced, with permission, from REF. 18 © (2004) The Royal Society. Part **c** is reproduced from REF. 58.

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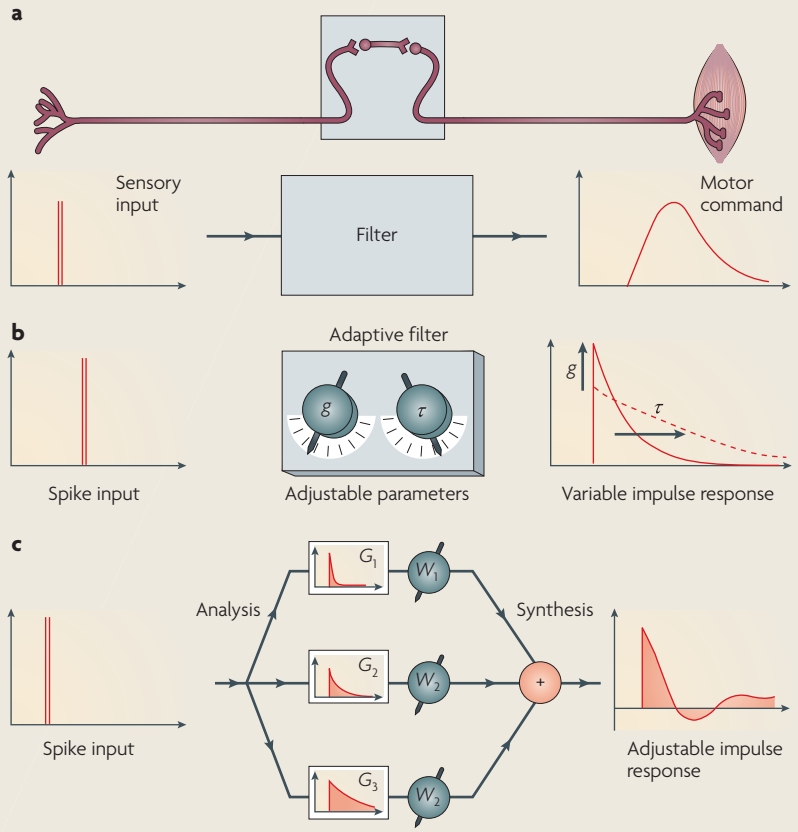
Box 3 | **Application of adaptive filters**

In signal processing terms a filter is a process that transforms an input signal into an output signal. For example, a reflex arc that converts a sensory stimulus into a motor command can usefully be modelled as a filter (see the figure, part **a**). When the filter is linear it can be completely described by its response to a spike input, called its impulse response. Note that although the emphasis here is on temporal transformations, similar considerations apply to spatiotemporal transformations.

An adaptive filter has parameters that can be varied to affect the form of the output. For example, a filter might have an adjustable time constant, so that a spike input produces a prolonged response with an adjustable decay time or an adjustable gain, which varies the amplitude of the response (see the figure, part **b**). The parameters of an adaptive filter can be varied to suit a given task, for example in the case of a reflex to convert an aversive sensory signal into a motor signal that will produce a fast, safe withdrawal movement.

Analysis–synthesis filters form a flexible class of adaptive filters that work by analysing the input into component signals using a bank of fixed filters. In engineering systems these filters might be bandpass filters, which split the input into its various frequency components, or tapped delay lines, which delay the input signal by varying amounts. In biological systems leaky integrators, providing components that are increasingly prolonged over time, provide a plausible analysis method. The components are then recombined to form the output signal, the amount of each component being controlled by adjustable weights (see the figure, part **c**). These are often called linear-in-weights filters; however, the analysis–synthesis input–output relationship does not have to be linear. Nonlinear problems can be solved by including nonlinear operations, such as products of linear filters, or by including more complex filters (such as echo state networks) in the bank of fixed filters.

An important characteristic of the adaptive-filter interpretation is its computational sufficiency. If the cerebellar microcircuit could be shown to implement an adaptive filter, its usefulness for sensory processing and motor control would be clear. Adaptive filters are not just theoretically powerful, they have also been shown to be useful in an enormous range of applications ranging from process control to adaptive noise cancellation in headphones. A particularly relevant application area is the control of humanoid robots[40]; for example, cerebellum-inspired adaptive controllers were extensively used in the ERATO humanoid robot project[171].



that do not fit the earlier predictions from computational analyses but are nevertheless consistent with an adaptive-filter model of the cerebellar circuitry. These developments point the way to a new understanding of the function of the cerebellar granular layer.

Symmetrical LTD and LTP and the covariance rule

Initial studies of cerebellar plasticity showed that paired stimulation of PFs and CFs induced LTD at synapses between PFs and PCs (PF-LTD) (for example, REFS 60–65). Depression at PF–PC synapses had been predicted by Albus[6], and the discovery of cerebellar LTD was accompanied by an interpretation of the Marr–Albus framework that focused on a form of cerebellar learning that used only LTD[39,41,63,66]. However, although usually not made explicit, cerebellar models based on the adaptive filter typically use the covariance learning rule[48], which requires both LTD and LTP (see above). Hence, there was a conflict between experimental and computational descriptions of the learning rule.

More recent investigations of PF–PC plasticity have indicated that LTP (PF-LTP) also occurs at this synapse[67,68]. *In vitro* studies showed that PF-LTP leads to a reversal of the CF-induced PF-LTD in PCs[69–71]. *In vivo*, PF activation in a protocol that mimicked a PF-LTD protocol but omitted the CF activation led to spectacular receptive field expansion in PCs[72], indicating that LTP had occurred (see below). Hence, whether a given PF input causes synaptic depression or potentiation depends on whether a CF input is present. The discovery that LTP also occurs in PF–PC synapses has led to a new view of cerebellar plasticity that is more congruent with the adaptive-filter model than the previous view.

Further computational analysis of the covariance learning rule reveals a possible explanation for why cerebellar LTD was discovered before LTP. The learning rule predicts that temporal coincidence of PF and CF firing produces LTD, whereas PF firing without CF firing gives LTP. This anti-Hebbian type of relationship can be formalized in the form of spike-time-dependent plasticity[73], with pronounced LTD occurring for spikes that coincide in a time window of 100–200 ms[74] and much weaker LTP for non-coincident spikes. LTD might therefore be easier to demonstrate experimentally.

However, the new computational analyses also highlight an important problem for applying the covariance learning rule to the cerebellar microcircuitry: simple adaptive-filter models, as shown in FIG. 1, have weights that can switch between positive and negative values, but real synapses are either excitatory or inhibitory. A solution to this problem would be to include in the models a parallel pathway from granule cells to PCs through inhibitory interneurons. Synaptic weights between PFs and interneurons would then behave as though they were negative weights between PFs and PCs, and these weights would also have to show plasticity (but with the opposite sign). Below we describe a parallel pathway with these properties: the indirect inhibitory pathway from granule cells to PCs through local, molecular-layer interneurons, also known as stellate and basket cells (BOX 1).

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Dual pathway plasticity

For molecular-layer interneurons to contribute to the implementation of the covariance learning rule in the cerebellar cortex, three criteria must be fulfilled. First, CFs must be able to control plasticity at PF–interneuron synapses as they do at PF–PC synapses, and therefore must communicate with interneurons. Second, plasticity at PF–interneuron synapses must have the reverse sign to that of the PF-to-PC input, as the two pathways affect cerebellar output in opposite directions (note that PFs making synapses on interneurons also make synapses on the neighbouring PC). Third, interneurons that receive CF input from one microzone must target PCs in the same microzone, otherwise the specificity of the learning rule would be partly or entirely lost. As we describe below, recent experimental data suggest that all three criteria are met.

Box 4 | **Alternative models of cerebellar function**

Descriptive models

In their pure form, descriptive models are concerned with reproducing aspects of circuit behaviour — for example the firing patterns of various classes of cerebellar cell — without concern for overall function. There are too many descriptive models to list here, but compartmental modelling is increasingly used (for example, see REFS 172–174). Descriptive models are to some extent complementary to the kind of computational model that is the focus of this Review, with the proviso that computational models must not predict circuit behaviour that is incompatible with behaviour predicted by descriptive models.

Look-up tables

The cerebellar cortex is often regarded as a gigantic memory or look-up table, which stores the desired response to a given set of inputs so that it functions as a pattern classifier or feature detector. The most widely used look-up table is based on Albus's cerebellum model articulation controller (CMAC)[6]. Although the CMAC is rarely used for simulating the role of the cerebellum in behaviour[175], it continues to be applied to certain kinds of adaptive-control problems in artificial systems. The learning rule used by the CMAC for adjusting its weights is of the same form as the covariance rule used by adaptive-filter models, but the key difference between the two types of model lies in input coding. It can be argued that this difference is of secondary importance (Supplementary information S5 (box)) and that CMACs can be seen as a subclass of adaptive filter rather than as a totally separate model. Indeed, the complex control problems that arise in biology might require a hybrid of the two.

Olivary models

In these models (for example, see REF. 176), cerebellar output, as delivered by the excitatory projection neurons of the deep cerebellar nuclei, is determined solely by activity in the inferior olive. Which part of the olive is active is determined by quiescence in the corresponding region of the inhibitory nucleo-olivary pathway. This in turn is generated by Purkinje cell (PC) inhibition, which is switched on by a context request from the mossy fibres in a manner that depends on there being bistability in PC simple-spike firing. This type of model clearly depends on an interpretation of experimental data that differs in fundamental ways from that discussed in this Review. For example, the fact that PCs fire spontaneously is taken as evidence against any role for parallel fibres (PFs) in determining their firing rate — "even if spikes occasionally arise from coincidence of PF inputs, they will be masked by the high rate of ongoing intrinsic activity"[176]. Moreover, although it has been argued that in principle models of this kind could be used for motor control (for example, REF. 177), they have in practice not as yet been used either to simulate biological motor control or to control an artificial device. This is in contrast to the extensive use of adaptive-filter models in both contexts. It is important that olivary models be developed to allow a quantitative investigation of their feasibility for cerebellar tasks. (A recent study of underwater-vehicle control[178] has used a model of six olivary neurons to synchronize the oscillations of its fins. The model includes no features of the cerebellar cortical microcircuit.)

Anatomical and physiological studies have shown that CFs contact interneurons and can evoke an electrical response in interneurons[72,75,76]. This response does not resemble a traditional ionotropic or metabotropic signal[76] and at least *in vitro* seems to be generated by extrasynaptic activation of AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) and NMDA (*N*-methyl-D-aspartate) receptors[77]. PF–interneuron synapses are highly plastic (at least *in vitro*)[78–83], and interneurons seem to have a fundamental role in behavioural adaptation[84], so the key question is whether CF input to interneurons regulates this plasticity.

Evidence supporting the regulation of PF–interneuron synapses by CFs comes from two sets of experiments. First, *in vivo* investigations showed that the cutaneous PF receptive fields of interneurons almost exactly matched the receptive fields of the local CFs. As individual MFs typically have small receptive fields (FIG. 2), an interpretation of this finding is that the interneurons receive active synapses only from the subset of PFs that receive input from the same skin area as the CF, whereas the interneurons' synapses with all other PFs had been rendered 'silent'. In other words, these findings suggested that the PF input onto interneurons is under the control of the CF[85]. A subsequent *in vivo* study combined PF and CF stimulation while simultaneously recording the location of the originally very small PF input from the skin. The combined stimulation resulted in marked increases in the receptive field of the interneuron[72], which later studies showed to be associated with a pronounced increase in the number of active PF synapses onto the interneuron[76]. By contrast, PF activation without CF activation reduced an interneuron's receptive field size, which is compatible with a decrease in the number of effective PF synaptic inputs[72]. These receptive field changes were exactly the opposite of those recorded in PCs and are remarkably congruent with the prediction from the covariance learning rule that plasticity at the interneuron–PC synapse must have the opposite sign to plasticity at the PF–PC synapse.

Second, *in vitro* studies have provided strong, but indirect, support for the idea that CFs control plasticity at PF–interneuron synapses. LTP at these synapses depends on the activation of NMDA receptors[80,82]. However, interneurons have only extrasynaptic NMDA receptors, and normal, low-intensity activation of PFs does not activate them[80]. By contrast, a single CF activation can activate NMDA receptors on interneurons[77]. Therefore, as originally suggested by Szapiro and Barbour[77], the observation *in vivo* that CF input is needed to elicit LTP at PF–interneuron synapses[72,76] probably means that only CF inputs activate the NMDA receptors[77]. Supplementary information S3 (box) discusses why CF dependency of LTP at these synapses has not yet been demonstrated directly *in vitro*.

Although CF input to interneurons might involve glutamate spillover[77], this does not prevent it from providing a reliable, specific error signal. CF responses have a fast onset and a long duration (meaning that the amount of charge carried can be orders of magnitude larger than at a PF–interneuron synapse; the long duration could

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Golgi cell
Inhibitory interneurons in the granular layer that synapse with granule cells. They receive excitatory input from mossy fibres and parallel fibres.

also mean that the CF dependency of PF–interneuron plasticity might have a broad temporal tuning curve similar to that of PCs (see above))[76,77]. Because diffusion signalling is effective only at short distances, glutamate that spills over to an interneuron must be primarily derived from the nearest neighbouring CF–PC synapses or the nearest CF terminals[75]. An interneuron can receive input from two different CFs[77], each of which also contacts up to ten PCs. As a microzone is only around ten PCs wide, the CFs that provide input to an interneuron will primarily or exclusively be located in the same microzone as the interneuron. A microzone can be considered to be the minimal functional unit of the cerebellar cortex (see above), so the interneurons will receive CF input equivalent to that of the PC that the interneurons innervate, even if the CF–interneuron input is mediated by spillover.

The third criterion for the inhibitory pathway to the PCs to implement the covariance learning rule — the microzone-specific inhibition of PCs — has also gained experimental support. For example, all interneurons in a microzone have the same receptive field, which is also identical to the receptive fields of the CFs and the inhibitory receptive fields of PCs in that microzone[72,76,85]. In addition, a study of the vestibulocerebellum[86] reported that interneurons of the molecular layer are driven in phase with the local CFs (that is, the CFs of the same microzone), which is compatible with the view that they are driven by the same inputs as the CFs. By contrast, the neighbouring PCs were driven out of phase but inhibited in phase with the CFs and the interneurons. The authors concluded that the in-phase depression of the PC activity could be explained if these PCs were inhibited by the interneurons that were driven in phase with the CF (and thus were located in the same microzone). Finally, an optimal imaging analysis showed that the inhibition of PCs by interneurons is parasagittally organized (oriented as microzones)[87]. Together, these studies support the idea that inhibition of PCs by interneurons is microzone-specific.

It might seem surprising that the inhibition of PCs is microzone-specific, given that some interneurons have rather long axons. However, these axons seem to follow a strict parasagittal organization[87,88] (which also seems to be true for Golgi cells[86]); that is, they are oriented in congruence with the microzones. Second, any non-microzone-specific connections could be rendered inactive through plasticity in the interneuron–PC synapse: to achieve the microzonal specificity, this plasticity process should lead to a potentiation of the interneuron–PC synapses that are activated in conjunction with the CF input to the PC. At present, such plasticity mechanisms have been investigated only *in vitro*, but the literature is contradictory at this point: CF activation has been shown to lead to either potentiation[89] or depression[90] of this synapse.

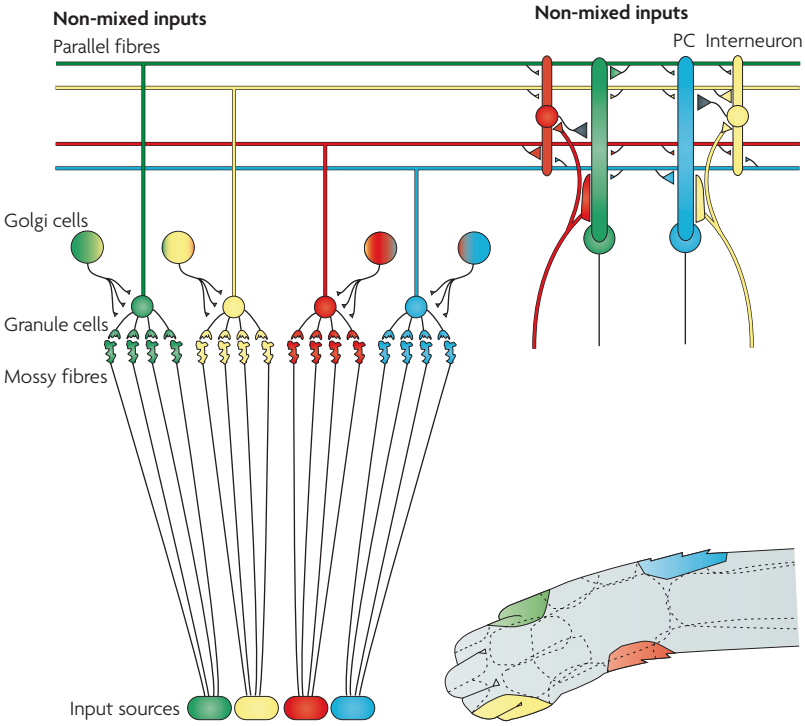

Figure 2 | **Updated view of the physiological wiring of the cerebellar cortical circuitry.** Summary of microcircuitry organization, based mainly on findings for the cuneocerebellar mossy fibre (MF) system of the C3 zone, for which the microcircuitry characterization is most complete. Here, the information 'quantum' equals input from small receptive fields on the skin. The bottom right part of the figure shows the location of sample MF receptive fields (dotted lines) and defines the colour code for the four sample inputs with illustrated distribution in the microcircuitry: granule cells receive inputs from the same skin location on all of their four synapses. This means that the receptive fields of the downstream neurons are the summed receptive field of the granule cells from which they receive their input. Golgi cells have the same receptive fields as the surrounding MFs and granule cells. For both granule cells and Golgi cells, this is a natural consequence of cuneocerebellar MFs with the same receptive field terminating in close proximity to each other in sagittal strips of the cerebellar cortex[85,94]. However, presumably because they combine local MF and granule cell inputs, Golgi cells' receptive fields are larger and consequently less specific than those of individual granule cells and MFs[85,94,102], as indicated by the colours. The MFs carry precise information, and although this precision is lost in the Golgi cells, its core parts are preserved. The Golgi cell axons are distributed primarily in the sagittal plane[86] and thereby follow the MF 'microzones'[85,94] so that the inhibition of granule cells comes from roughly the same input source as the MF excitation[95]. The climbing fibres (CFs) define the microzonal banding pattern of PCs[3] as in BOX 1. However, we now know that interneurons also receive the local CF input and mainly inhibit PCs within the same microzone. Although the entire repertoire of the MF–granule cell inputs is available to both PCs and interneurons through the synapses they make with PFs, most of these synapses are normally 'silent', providing no effective input. Instead, the PF inputs to both interneurons and PCs are specific to the CF input (and therefore the microzonal identity). Note that the input patterns shown are those recorded in the normal, adult animal, but these are readily altered by appropriate stimulation[72,76] and can be expected to change under conditions that induce cerebellum-dependent learning.

Silent synapses in the cerebellum

Silent synapses seem to be a ubiquitous feature of the hippocampus and neocortex[91], but recent discoveries indicate that this phenomenon is probably carried to its extreme in the adult cerebellar cortex, where as many as 98% of PF synapses might be silent.

The first indication that most of the PF–PC synapses are silent came from a study using electrical PF stimulation and glutamate uncaging[92]. Further, direct evidence for silent PF–PC synapses was obtained by recording synaptic currents evoked in PCs by stimulating single granule cells *in vitro*[93]. Despite the fact that the granule cells almost certainly formed PF synapses on the PCs, controlled activation of the granule cells in most cases

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Glutamate uncaging
The process by which chemically caged glutamate can be released by focal light. It is used to study the effects of postsynaptic activation with high temporal and spatial control.

Beam
A bundle of parallel fibres (PFs). A term typically applied to experiments using electrical stimulation of PFs in which the local population of PFs around the stimulating electrode is activated.

failed to elicit an excitatory response at the corresponding PF–PC synapse. The presence of silent synapses was also suggested by evidence from *in vivo* circuitry analysis using receptive field mapping[85] in the C3 zone: although the cutaneous receptive fields of individual MFs and granule cells are very small[94,95], the PFs that innervate a single PC together carry a complete representation of the skin[3,94]. However, only a fraction of the available skin inputs, and therefore only a fraction of the PF inputs, provide input that activates the PC[3,72], leading to the conclusion that most inputs must be silent or otherwise non-effective. The estimated proportion of silent synapses on PCs in the *in vitro* and *in vivo* studies were remarkably similar (85% and 95–98%, respectively), even though the studies involved different species and different functional cerebellar subdivisions.

Further evidence for silent synapses is provided by the nature of the changes that occur in the receptive fields of PCs and interneurons when the purported silent synapses are made effective. LTP protocols applied to the PFs resulted in receptive field increases of several thousand per cent in both cell types[72]. An explanation for this finding is that the activated population of (previously silent) PF synapses carries a representation of more or less the entire body skin. This would in turn indicate that a PF beam contains PFs carrying input from different receptive fields[72,76].

The large number of PF synapses on an individual PC suggests that a high proportion of PFs carry signals that are irrelevant to any particular learning task; that is, they transmit noise. Silent synapses are a natural consequence of the covariance learning rule in this situation[58]. Imagine a PC that is driven by a single PF with a synaptic weight. The learning rule always adjusts the value of the synaptic weight until it minimizes the error signal. If the PF firing represents noise, then by definition it can produce only erroneous output. Consequently, this PF input will continuously drive CF activation until the synaptic weight becomes zero and the synapse has become 'silent'. This effect is shown in simulation (FIG. 3). Any noise (both intrinsic noise and signals providing information that is irrelevant to the current task) that is reflected in cerebellar output produces errors; the PF discharge positively correlates with the error as signalled by CF spikes. This positive correlation produces LTD through the covariance learning rule, eventually driving the synaptic weights on PFs that convey a weakly relevant signal to small values, and on those with no relevant signal to zero.

The covariance rule predicts that the parallel, inhibitory pathway also has silent synapses because the PF–interneuron synapses in this pathway are also plastic (see section on dual pathway plasticity above). The (noise) signal transmitted from the PF to the PC through the inhibitory interneuron has the opposite sign to the (noise) signal that is transmitted to the PC through the direct pathway. Hence, the PF discharge that is transmitted through the indirect pathway will be negatively correlated with error (as signalled by CF spikes). However, the indirect pathway has a learning rule that is opposite to that of the direct pathway, so this negative correlation produces LTD, which eventually drives the PF–interneuron synapse to silence. In the case that both the PF–PC and PF–interneuron synapses are non-zero, the covariance rule produces LTD in the larger of the two weights and LTP in the smaller, driving the weights to equal intermediate values so that the opposite effects of the two pathways cancel each other out. However, the covariance learning rule predicts that this balance is unstable, and intrinsic noise in each pathway will eventually drive both weights to zero (a similar effect is shown in FIG. 3). Note that only correlated noise in PF and CF discharges drives weights to zero; uncorrelated, spontaneous CF discharges do not have this effect[96].

The preponderance of silent synapses is a further reason why a parallel, inhibitory pathway from granule cells to PCs is required for implementing the covariance learning rule: without it, silent synapses could not be used for learning that requires a decrease in PC output[58] (which involves an active inhibitory process). Thus, the dual pathway plasticity described in recent experiments

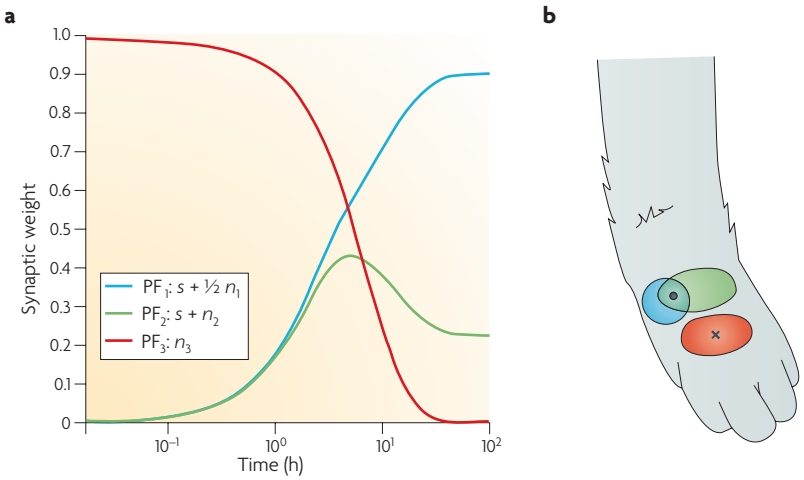

Figure 3 | **Learning dynamics with covariance learning rule. a** | Optimality of synaptic weights and learning hysteresis illustrated in a simulation of vestibulo-ocular reflex adaptation (for details see REF. 58). The time course of synaptic learning is shown for two parallel fibres (PFs) (PF_1 and PF_2) carrying equal levels of a relevant signal (in this case a motor efference copy), with the first having lower noise; a third PF (PF_3) carries noise alone. In the early stage of learning the weights on PF_1 and PF_2 (initially zero) are driven to the same value because they carry equal amounts of signal. Later in learning the noise carried by each PF drives these weights to their optimal values, with a higher weight eventually assigned to the lower-noise input PF_1. Meanwhile, the weight on the all-noise channel PF_3 (which was initially set to be non-zero) is driven to its optimal value of zero. **b** | The optimality principle applies both to 'genuine' noise, for example intrinsic noise in PF signals, and to situations in which noise is an irrelevant sensory signal. For example, the weight histories shown on the left also apply to an idealized learning task requiring a spatially localized skin sensory input. Before training, the relevant location (black cross) lies in the receptive field of PF_3 (red), so that this input has high synaptic weight. Weights on the irrelevant PF_1 and PF_2 (blue and green, respectively) will be zero. If the task is modified so that the relevant input is now located at the black dot, then the input from PF_3 is irrelevant (effectively all noise). Relevant inputs now come from PF_2 (large green receptive field: always responds to a correct stimulus but often responds to irrelevant stimuli, hence also has a high noise content) and from PF_1 (small blue receptive field: also carries the relevant signal but rarely responds to irrelevant stimuli, hence has low noise content). The weight for PF_3 will be driven to zero by long-term depression, whereas PF_2 and PF_1 both learn through long-term potentiation and eventually stabilize at values that maximize the overall signal-to-noise ratio.

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is exactly what is required by an adaptive filter with noisy inputs and weights that are restricted to either positive or negative values.

Recurrent architecture

It has recently been suggested that cerebellar microzones typically receive MF inputs that are related to the microzone's own outputs. For example, studies using transneuronal transport of neurotropic viruses have shown that the area of cerebral cortex that receives projections from a cerebellar region also sends projections back to that region[97]. The nature of the computations performed by the cerebellar microcircuit in this recurrent architecture is an important theoretical question[97,98], to which the adaptive-filter framework provides a compelling answer.

A vital clue to this answer was provided by computational analysis of a well-understood region of the cerebellum, the flocculus (FIG. 1c). This region is concerned with the control of eye movement and receives a massive MF input related to eye movement commands[19]. It also receives, through its CF input, an error signal related to image slip across the retina. Applying the covariance learning rule to these two signals (FIG. 1) points towards a function for the recurrent projection of the eye movement motor command[17,18]. The rule indicates that synaptic weights cease to change when there are no longer any correlations between the PF inputs and the CF error signal (BOX 3; FIG. 1; Supplementary information S2 (box)). As the adaptive filter continues to learn until this state is achieved, its goal is effectively that of decorrelating its inputs from some measure of the undesirable effects of its output. The implicit logic behind this procedure is that the correlation between PF firing and the error signal provided by the CF is evidence of a causal relationship. In the case of motor commands and retinal slip, successfully decorrelating the two leads to new motor commands that do not cause inaccurate movements[17,18,59]. In effect, the system learns the most accurate available motor commands — an important goal of models of cerebellar function.

This proposed role for the recurrent architecture addresses a long-standing problem in adaptive motor control, namely that in autonomous systems the correct motor commands might not be known in advance and so cannot be used to generate error signals. However, in systems with a recurrent architecture the sensory consequences of inaccurate commands (for example, movement of the image across the retina in the vestibulo-ocular reflex) can be used as an error signal, solving the so-called motor error problem (or distal error problem)[54]. In general terms, the recurrent architecture allows the cerebellum to compensate for changes in downstream structures (the eye muscles in the example of the flocculus above), whereas the forward projections allow compensation for changes in structures upstream of the cerebellum (the semi-circular canals in the example above)[20].

Compensation for changes in downstream structures is especially important for motor control, and demonstrating how it can be achieved by decorrelation control is particularly relevant to the idea of the cerebellum as a motor structure[99,100]. Indeed, appropriate recurrent connections have been observed wherever they have been looked for, including in the oculomotor vermis (involved in saccade control)[101,102] and regions of the cerebellum involved in controlling limb movement[103,104]. This downstream compensation need not be limited to motor control but could have more general applicability, which might prove to be relevant for cerebellar functions in sensory or cognitive processing[41,105].

Granule cell function

A central feature of signal processing in adaptive filters is the breakdown of input signals into different components (BOX 3), which in the cerebellum has been assumed to take place in the granular layer[13,21–23,45] (BOX 1). These assumptions, which are related to Marr's ideas about 'expansion recoding' in the granular layer[5], are in part based on the observation[1] that MFs branch into several terminals, so that the number of granule cells is greater than the number of MFs; according to recent estimates, the number of granule cells per MF is in the order of 400–800 (REF. 106).

The technical difficulties associated with recording from granule cells *in vivo* have only recently been overcome[95,107–110], but the initial results of these recordings do not support the idea that the granule layer performs complex signal decomposition[95,108,110]. In some studies, granule cells seemed to receive functionally equivalent MF inputs on all four dendrites (FIG. 2), indicating that they might function as coincidence detectors with a pronounced noise-filtering capability accompanied by simple linear integration for suprathreshold synaptic input[95,111]. Moreover, in some experimental systems granule cells seem to receive modality- and receptive field-specific input from all afferent MF inputs[95], and there is even evidence that granule cell inputs might be submodality-specific (for example they respond to either skin hair deflection or stimulation of tactile skin receptors; they can be activated by either phasic or tonic tactile skin input, et cetera)[95]. In addition, it has been reported that MFs that are driven by the same modality but which code the input in different ways terminate on separate sets of granule cells (FIG. 2), and that granule cells only receive MF inputs with similar coding[110]. These findings are consistent with evidence that MFs from the same functional systems[106,112–117] or carrying the same input[94] colocalize to terminate in the same parts of the granular layer[118–121]. If MFs carrying different information terminate in different parts of the granule layer, it is unlikely that a granule cell can integrate the different sets of information because granule cell dendrites are typically very short.

Although there is disagreement about whether granule cells always receive similar MF inputs, and about whether granule cell firing can be triggered by a single MF or requires multiple MF inputs (for further details, see Supplementary information S4 (box)), the recent recording data suggest that the granular layer transmits MF inputs with relatively modest alterations — certainly far more modest than those required by typical adaptive-filter models.

Image slip
Movement of the entire image across the retina, usually produced by movement of the eyes.

Distal error problem
The natural error signal for learning motor commands is the difference between actual and correct commands ('motor error'). However, in autonomous systems the correct command is typically unknown; only information about the sensory consequences of incorrect commands is available, such as the position of a pointing finger relative to a target ('distal error'). How to use this information to drive motor learning is the distal error (or motor error) problem.

Coincidence detector
A neuron that acts as a coincidence detector responds only when two or more of its synaptic inputs are activated together.

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If this is the case, then the diversity of PF signals that is required by adaptive-filter models would have to be supplied by the MF inputs themselves. The MF inputs to a given microzone seem to be highly diverse (for example, see REFS 102,110,122), as are Golgi cell responses (which are driven by MFs as well as granule cells) that have been recorded in different parts of the cerebellum[85,102,123–125]. Although MF diversity has long been noted, and Yamamoto *et al.*[9] have described an adaptive-filter model of the flocculus that relies on it, the implications of such reliance for adaptive-filter models in general have not been considered. Two fundamental questions it raises are, first, whether it is possible to obtain PF responses that outlast the input stimulus or that start only after a substantial delay (as for example in classical conditioning[126,127]) and, second, how nonlinear combinations of input components (such as polynomials or radial basis functions; see Supplementary information S2,S5 (boxes)) could be achieved.

A further problem is that a simplified granular layer could not learn the efficient input codes that have been assumed to be necessary for individual sensorimotor problems[128–130]. These are codes that are complete but sparse, in order to ensure rapid learning at PF–PC synapses. In theoretical accounts of the role of granular layer processing in adaptive-filter models of the cerebellum, the above problems are typically solved by incorporating inhibitory feedback from Golgi cells[25,131] (see also REFS 132,133). Conversely, some recent data suggest that the role of feedback from Golgi cells might be relatively modest (see below). The implications of these findings for future research are considered below.

Conclusions and future directions

The experimental findings reviewed above indicate that earlier conceptions of the cerebellar microcircuit should be changed with regard to both its internal and external connectivity and the functionality and plasticity of its components. Computational analysis indicates that most of these changes fit extremely well with the adaptive-filter version of the original Marr–Albus theoretical framework. In the case of granule cell electrophysiology, recent findings indicate that the original proposals concerning the details of adaptive-filter signal decomposition need to be re-examined. We now consider the implications of these conclusions for our understanding of cerebellar function and for future research.

First, considering the cerebellar microcircuit as an adaptive filter could reconcile different views of cerebellar function. An adaptive filter is a signal processing device that seeks to decorrelate its main inputs from a teaching or error signal. As such it can be used for motor control, for sensory processing (for example, see REF. 105) and for learning internal models[40,41,134–136] (Supplementary information S1 (box)). The versatility of adaptive filters corresponds to the many uses of adaptive filters in engineering contexts (for example, see REF. 137); it also emphasizes that the cerebellar microcircuit cannot be described as intrinsically having a sensory or motor function, and that the function of a particular microzone is determined by its external connections (that is, its MF and CF inputs and its PC output targets). Although these points about the cerebellum have been made previously in a general context (for example, see REFS 39,41,63,138), the adaptive-filter model gives them specific computational credibility. Recent findings therefore bring into question the original assumptions of the Marr–Albus framework that the cerebellum is involved exclusively in motor control through motor learning, but they support the framework's assumptions that simple and complex spike firing convey output commands and teaching signals, respectively.

Second, this Review has shown that the computational principles that underlie many functional models of the cerebellar microcircuit are those of an adaptive filter, and that these principles fit well with several recent findings related to microcircuit properties. This indicates that the adaptive-filter interpretation of microcircuit function could be more important than hitherto realized for guiding future research, and below we give three examples of how this might be the case.

The first example concerns the functional implications of having two pathways. As outlined above, MF inputs reach the PC through a direct, excitatory PF pathway and an indirect, inhibitory PF–interneuron pathway. In both of these pathways, the PF synapses are subjected to bidirectional plasticity under the control of CFs, resulting in complementary (or reciprocal) plasticity effects, as required for implementing an adaptive filter. What remains to be investigated is whether the learning rates in the two pathways are different. Different learning rates would lead to learning rate asymmetry for different cerebellar tasks[58], as has been described for gain adaptation of the vestibulo-ocular reflex[139] or in systems with hysteresis in which acquisition and reacquisition occur at different rates, such as in classical conditioning[126,140].

A further implication of having these two pathways follows from the observation that in both pathways most of the PF synapses are silent. Learning new tasks is therefore likely to be initiated primarily through LTP (although previously relevant PF input would become depressed through LTD, as shown in FIG. 3a). Furthermore, specific learning tasks might prove to rely initially or primarily on LTP in only one of the two pathways. Identifying such possible selective pathway plasticity is an important goal for future research, not least to provide an interpretational framework for the molecular analysis of cerebellar learning[141,142].

The second example concerns the modularization of cerebellar microcircuitry. Many of the recent discoveries concerning the properties of the cerebellar microcircuit relate to plasticity processes and how these shape the wiring in the cerebellar cortex. Importantly, because many of these processes seem to be related to CF activation, and because the CF system divides the cerebellar cortex into modular compartments (microzones), plasticity-dependent changes in the wiring tend to make the entire cerebellar microcircuitry extremely modularized. For any individual microzone, the CF signal is the primary driver of input plasticity[143,144] and will therefore determine which signal processing task the microzone performs. This central role of CF

Hysteresis
A system has hysteresis when its current behaviour depends on its history. An example of hysteresis in learning is the phenomenon of savings, in which relearning takes place much more quickly than first-time learning.

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input mirrors the role of the 'error' or 'teaching' signal in cerebellar adaptive-filter models. This signal drives the decorrelation process and so determines the function of each individual cerebellar module (as described above). The identification of the exact nature of the CF signal is therefore crucially important for understanding all cerebellar subsystems and remains one of the main outstanding challenges for researchers working on cerebellar function[145].

The final example concerns signal processing in the granular layer. Relating the new experimental findings on granule cell electrophysiology to adaptive-filter function raises several questions. One is the extent to which the absence of convergence on granule cells — as reported for the cuneocerebellar and lateral reticular nucleus MF systems — is characteristic of other MF inputs (see Supplementary information S4 (box)). This is particularly important inasmuch as the PF signal properties of a given microzone might depend mainly on the coding in its MF inputs. Another question concerns the contribution of Golgi cells to signal processing in the granular layer, which recent data suggest[95,146,147] could be relatively modest. Golgi cell inhibition of granule cells primarily consists of persistent tonic inhibition with few distinct fast inhibitory postsynaptic potentials[95,146,147]. Accordingly, granule cells producing burst responses to skin stimulation show little sign of Golgi cell inhibition, even though the Golgi cells are relatively strongly activated by this stimulation[95]. However, considering the diversity of MF inputs and the diversity of activation modes of a single MF (both bursts and more tonic firing can be provoked in MFs with input from the skin; for example, see REF. 95), it is conceivable that during episodes of more moderate MF input (which barely manages to push the granule cell above the firing threshold) Golgi cell inhibition could have more influence over the transmission of MF input. The signal processing role of the granular layer and the variety of MF signalling urgently require experimental and theoretical investigation.

In conclusion, the multitude of recently discovered plasticity mechanisms and microcircuitry features represent a substantially evolved view of the original ideas of the cerebellum as a neuronal machine[1], which in general fits well with the adaptive-filter family of cerebellar models. This congruence of experimental and theoretical models strengthens the view that the cerebellum is especially suitable for studying general principles of brain function. Its organization at the microcircuit level has been investigated at a unique level of detail while the overall, general functional organization of connections has been characterized. In addition, parts of the cerebellum are engaged in well-understood tasks, which makes it possible to understand the specific contribution of a component of the microcircuitry to a given task. The cerebellum therefore offers a unique opportunity for relating specific synaptic modifications to systems-level intelligent behaviour.

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Competing interests statement
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