Supplementary information S4 (box): Granular layer

While the recent successes in obtaining intracellular granule cell recordings \textit{in vivo} have produced results that agree on many points, two related issues have arisen that remain to be settled.

Similar versus dissimilar mossy-fibre inputs

Evidence in favour of the view that all mossy fibre inputs to a single granule cell are driven from the same receptive field and submodality has been outlined in the main text and in Fig. 2. However, there is a question of whether the extreme absence of convergence on GCs reported for the cuneocerebellar and lateral reticular nucleus MF systems is characteristic of other MF inputs. For example, different conclusions have been drawn in studies of whisker-related MF input\textsuperscript{1} and head-rotation evoked MF input\textsuperscript{2} to granule cells. However, in neither study were MF inputs systematically analysed, so the possibility remains open that in these systems also, the MF inputs to individual GCs are homogeneous.

Mossy fibres needed to fire a granule cell

There is disagreement about whether granule cell firing can be produced by a single MF. One \textit{in vitro} study has found that intense bursts of firing in a single MF can by itself trigger granule cell spike output (hence the label ‘detonator’ model – the idea was inspired by the observation that MFs \textit{in vivo} were driven to bursts by sensory stimulation)\textsuperscript{1}. However, a previous \textit{in vivo} study\textsuperscript{3} had indicated that the kind of EPSP summation that would be required for a single mossy fibre to be able to trigger the granule cell spike does not occur.

A possible reason for the discrepancy between the results is the different kinetic properties of the synaptic responses \textit{in vivo} as compared to \textit{in vitro} (See the figure). \textit{In vivo}, the distance between the membrane potential and firing threshold of granule cells is very large\textsuperscript{4,3,5}. Activation of the granule cell spike therefore requires summation of EPSPs, which can be achieved either temporally (repetitive activation of the same mossy fibre) or spatially (coincident activation of separate mossy fibre synapses). Both the time course and amplitude of the EPSP will hence be very important determinants for the temporal window of the integration. The fact that mossy-fibre EPSPs have longer decay time constants and larger peak amplitudes \textit{in vitro} as compared to \textit{in vivo}\textsuperscript{3,6} means that the conditions for temporal summation obtained during repetitive activation of a single mossy fibre is much exaggerated \textit{in vitro} (see the figure). Hence, the validity of the detonator model \textit{in vivo} still needs to be confirmed.

This issue is related to the one concerning the nature of MF signals to an individual GC, because if they are very similar there is a very high probability that all of the MFs are activated in relative synchrony. The similar coding model would then maximize the transmission of the weakest mossy fibre inputs, and so ensure that GCs were highly effective transmitters of both discrete events, and the frequency-modulated signals observed in mossy-fibres in behaving animals e.g.\textsuperscript{7,8,9}.
Figure

Schematic illustration of the properties of mossy fibre to granule cell transmission in two different models.

A Granule cell transmission of mossy fibre inputs according to the 'similar coding' model. Synchronized activity in afferent mossy fibres is required for transmission.

B Granule cell transmission of mossy fibre inputs according to the ‘detonator’ model. A single mf can drive the spike of the granule cell if it is intensely activated.

C The different performances of the models arises because model A uses small, fast EPSPs (as observed in vivo) whereas model B uses large, slow EPSPs (as observed in vitro).

D In both cases the EPSPs are summed, and initiate spikes once they reach a threshold. In model A (left hand trace) the maximum summed EPSPs for a single MF input do not reach threshold, whereas in model B they can do so.
References