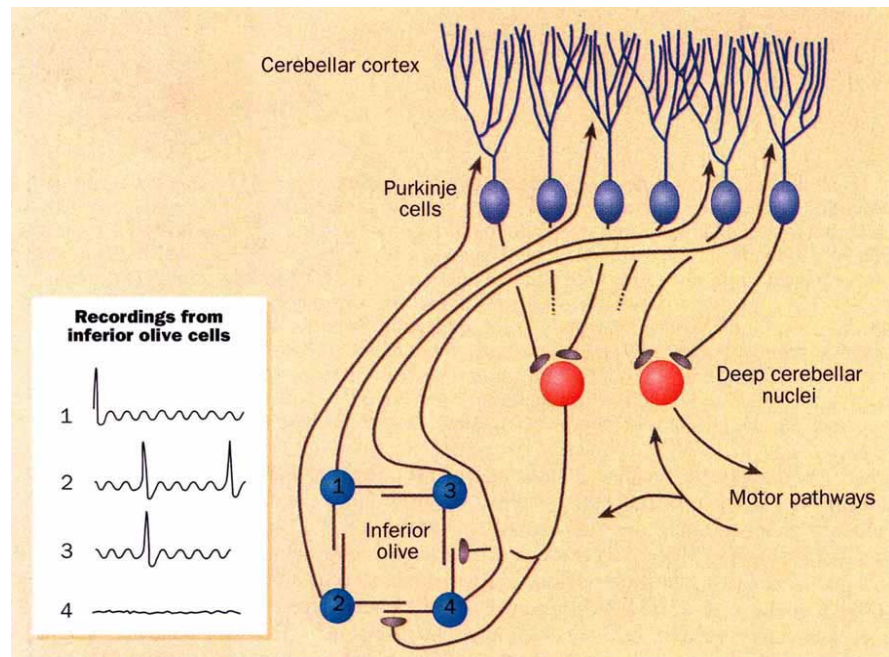


The cerebellar symphony

David A. McCormick

MOST of our daily movements — driving, typing or, for some, playing the violin — are performed with ease and precision. We owe this precision to the cerebellum ('little brain'), for damage to this structure results in imprecise and unsure movements, and sometimes even impaired thoughts about movements¹. So how does the cerebellum achieve this task? In their paper on page 453 of this issue², Welsh, Llinás and colleagues show in rats that dynamic synchronization of ever-

fibre and climbing fibre inputs provide important information concerning what movements are planned and proprioceptive feedback as to the status of those movements. The mossy fibre, granule cell and parallel fibre input pathway is responsible for the continuous tonic discharge of Purkinje cells, while the arrival of an action potential in the climbing fibre results in a 'complex spike' consisting of a high-frequency burst of action potentials generated through the activation of den-



Dynamic synchronization of inferior olivary input to the cerebellar cortex. Cells of the inferior olive collectively generate 'sine-wave' oscillations through intrinsic membrane properties and gap-junction connections between cells^{5,6}. These oscillations synchronize the generation of action potentials in different inferior olivary neurons (for example cells 1, 2 and 3), and the subsequent complex spikes in cerebellar Purkinje cells. The inhibitory cells of the deep cerebellar nuclei are proposed dynamically to segregate inferior olivary cells into functional groups, so that some neurons oscillate in synchrony (cells 1–3) while others do not (cell 4)^{2,8,11,12}. The process is continually varying in order to coordinate movement. (Based on Fig. 1 of ref. 13.)

changing subgroups of inferior olivary neurons may organize cerebellar activity during the performance of well-learned movements, thereby making the inferior olive a conductor of the symphony of cerebellar neuronal activity.

The cortex of the cerebellum consists of only one type of output cell, the Purkinje cell, and two main sources of input, the mossy fibres and the climbing fibres (see figure). The mossy fibre system originates from a variety of sources and provides, through granule cells, a numerically impressive innervation (up to 200,000 parallel-fibre inputs) to each Purkinje cell; by contrast, only one climbing fibre, originating in the inferior olive, innervates each Purkinje cell³. Together, the mossy

dritic Ca^{2+} spikes. The importance of the mossy fibre system in the continual adjustment of Purkinje cell activity during movement has long been recognized. But the role of individual inferior olivary cells has been less clear, with their intermittent activity at a rate of only about 1 Hz seemingly being too slow to coordinate movements in an 'on-line' manner⁴.

One possible reason for the failure to elucidate the role of the inferior olivary inputs is that the inferior olive may use a population code — that is, the ensemble of activity in this structure may be the way in which it contributes to the coordination of movement. By comparing the timing of climbing fibre inputs to 29 simultaneously recorded Purkinje cells, Welsh *et al.* show

that this may indeed be the case. Their results indicate that inferior olivary cells continuously reorganize into varying subgroups of neurons whose discharge is synchronized upon an approximately 10-Hz carrier wave, and that each subgroup synchronizes during the performance of a specific aspect of a well-learned movement, in this case repetitive licking by rats for a water reward (see figure).

Investigation of the electrophysiological properties of the inferior olive reveals that these neurons possess the intrinsic propensity to generate rhythmic activity at 8–10 Hz through the interaction of specialized ionic currents, namely low- and high-threshold Ca^{2+} currents and Ca^{2+} -activated K^+ currents⁵. Gap-junctions in between the neurons allow them to act as functional groups in the generation of synchronized, yet subthreshold, membrane oscillations, also in the 8–10-Hz frequency range⁶. Anatomically, small regions of the inferior olive innervate rostral–caudal oriented bands of Purkinje cells, in perpendicular organization to many of the folia of the cerebellar cortex⁷. Recordings of the spontaneous activity of inferior olivary input to cerebellar Purkinje cells in anaesthetized rats show that this input is synchronized in rostral–caudal bands, and that administration of tremorgenic agents acting directly upon inferior olivary neurons increases their propensity to generate synchronized oscillations⁸. Synchronization of climbing fibre input is further enhanced by fine adjustments in the conduction velocity of the axons running from the inferior olive to the cerebellum⁹.

Work on the other main input to the cerebellar cortex, the mossy fibres, has revealed a so-called 'fractured somatotopy', in that neighbouring regions of the cerebellar cortex often correspond to non-contiguous points on the animal's body¹⁰. The question then arises as to how rigid the rostral–caudal bands of inferior olivary input are, and how they are related to the fractured somatotopy of the mossy fibre system. One possibility, suggested by Llinás¹¹, is that the cells of the inferior olive are dynamically rearranged into functional subgroups based upon the output of the cerebellum itself. Inhibitory, GABA-ergic neurons of the cerebellar deep nuclei send connections to the inferior olive and synapse directly upon the regions of gap-junction formation between inferior olivary cells. Llinás proposes that, through activation of these GABA-ergic inputs, the coupling between inferior olivary cells can be 'shunted', allowing the inferior olive to be dynamically broken into variable subgroups of synchronously oscillating neurons, with the members of each subgroup being determined by the output of the cerebellum itself.

The new recordings of Welsh *et al.*

support this hypothesis. They show that the activity of inferior olivary neurons is dynamically organized during a movement into various synchronous subgroups; and that these subgroups are not strictly limited to rostral-caudal bands in the cerebellar cortex. Rather, the subgroups may form functional units that may be in register with other inputs to the cerebellar cortex. Through ascending and descending connections to the red nucleus, thalamus and brain stem ('motor pathways'), the deep nuclei of the cerebellum then contribute to the refinement and control of the various muscle groups involved in performing the learned task. The possible contribution to synchronization made by the numerous inputs to the inferior olive from sources other than the deep cerebellar nuclei remains to be explored.

Taking a wider perspective, these results reinforce the notion that synchronization of neural activity is one of the main ways in which cell groups throughout the nervous system interact, yielding an interesting mechanism in which neural networks may exhibit dynamic, and plastic, function. Possible tests of this seductive hypothesis for the cerebellar system include examining the effects of GABA antagonists applied directly to the inferior

olive¹², or temporary interruption of the cerebellar-olivary pathway, on the climbing fibre input to the cerebellum and the performance of skilled movements. We eagerly await further news. □

David A. McCormick is in the Section of Neurobiology, Yale University School of Medicine, 333 Cedar Street, New Haven, Connecticut 06510, USA.

- Holmes, G. *Brain* **62**, 1–30 (1939).
- Welsh, J. P., Lang, E. J., Sugihara, I. & Llinás, R. *Nature* **374**, 453–457 (1995).
- Palay, S. L. & Chan-Palay, V. *Cerebellar Cortex. Cytology and Organization* (Springer, Berlin, 1974).
- Brooks, V. B. & Thach, W. T. in *Motor Control* Vol. 2 *Handbook of Physiology* 877–946 (American Physiological Society, Maryland, 1981).
- Llinás, R. & Yarom, Y. *J. Physiol., Lond.* **315**, 549–567 (1981).
- Llinás, R. & Yarom, Y. *J. Physiol., Lond.* **376**, 163–182 (1986).
- Azizi, A. A. & Woodward, D. J. *J. comp. Neurol.* **263**, 467–484 (1987).
- Sasaki, K., Bower, J. M. & Llinás, R. *Eur. J. Neurosci.* **1**, 572–586 (1989).
- Sugihara, I., Lang, E. J. & Llinás, R. *J. Physiol., Lond.* **470**, 243–271 (1993).
- Shambes, G. M., Gibson, J. M. & Welker, W. *Brain Behav. Evol.* **15**, 94–140 (1978).
- Llinás, R. in *Motor Control: Concepts and Issues* (eds Humphrey, D. R. & Freund, H.-J.) 223–242 (Wiley, New York, 1991).
- Llinás, R. & Sasaki, K. *Eur. J. Neurosci.* **1**, 572–602 (1989).
- Llinás, R. & Welsh, J. P. *Curr. Opin. Neurobiol.* **3**, 958–965 (1993).

MARINE GEOLOGY

Of Hess crust and layer cake

Jonathan E. Snow

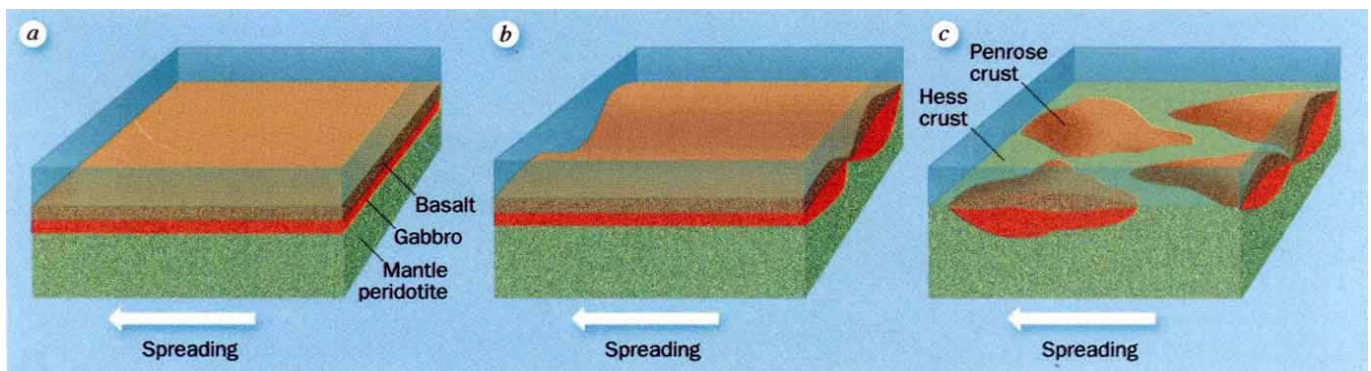
FOR over 35 years, the ocean floor has been of prime interest to geologists because of its role in plate tectonics. Today, basalt and gabbro (extrusive and intrusive volcanic rocks) are regarded as the primary constituents of the oceanic crust, a view largely brought about by the students and colleagues of Harry Hess in the 1960s^{1,2}. Hess himself, on the other hand, believed that serpentinite (mantle peridotite altered by reaction with sea water) was the dominant rock type³, but the geological community had largely discounted this view by the time he died in 1969, and had

relegated serpentinites to major (large-offset) oceanic fracture zones. M. Cannat, C. Mével and collaborators⁴ now bring this argument full circle by demonstrating the widespread occurrence of serpentinite crust far from fracture zones in the North Atlantic ocean. Combined with geophysical evidence⁵, this new 'old' geological interpretation neatly synthesizes a large body of recent geological, geophysical and geochemical observations of the ocean floor at slowly spreading ridges^{6–15}. The new model has deep implications for the geology of the Earth as a whole, as altered

rocks at mid-ocean ridges account for much of the material recycled into the mantle at subduction zones and, through alteration, for a large portion of the chemical budget of sea water.

From a geophysical point of view, the ocean floor has a layered structure of increasing seismic velocity and density with depth. Combined with geological observations from ophiolites (thought to be ocean crust fragments emplaced on land), and the natural affinity of geologists for layered structures, these observations led to a 'layer-cake' model of ocean crust structure^{1,2}. This structure of sediments underlain by basalts, sheeted dykes, gabbros, and finally mantle peridotite (part *a* of the figure) was enshrined by a Penrose Conference in 1972 (ref. 2). It is so fundamental to modern marine geology that it colours our way of thinking about nearly every aspect of the evolution of the sea floor. The Penrose layer-cake model implies that nearly all exposed ocean crust has basaltic composition, and hence that all chemical fluxes involving crustal alteration can be approximated by interactions between basalt and sea water alone^{6,7}.

Geologists and geophysicists soon began to realize that a purely layered structure did not fit some aspects of ocean-floor geology. For example, mid-ocean ridges are interrupted not only by fracture zones but also by 'zero-offset' zones where tectonism dominates over magmatism. Ocean-ridge magmatism is also segmented^{8,9}, because of an inferred three-dimensional focusing of melts into magmatic centres along mid-ocean ridges⁹. By the mid-1980s, the ocean floor was thought to retain essentially the Penrose structure, but with a thinner basaltic crust in the regions away from magmatic centres (part *b* of the figure). However, near large-offset fracture zones, the crust is thinned to the extent that areas of tectonically excavated lower crust are found together with sparse eruptive basalts piped in laterally from distant magmatic centres¹⁰. Although axial magma undersupply and serpentinite emplacement were known¹¹, their signifi-



Three views of slowly spreading ocean crust, with axial valley perpendicular to spreading direction. *a*, Penrose 'layer-cake' stratigraphy^{1,2}.

b, Variable crustal thicknesses due to magmatic focusing^{8–11,14}. *c*, Discontinuous magmatic focusing and Hess crust emplacement^{4,5}.