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REVIEW LECTURE

# THE CEREBELLUM AS A COMPUTER: PATTERNS IN SPACE AND TIME

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## *General considerations of structure and function*

It is generally believed that in some way the cerebellum functions as a type of computer that is particularly concerned with the smooth and effective control of movement. It is assumed that in the cerebellum there is integration and organization of the information flowing into it along the various neural pathways, and that the resulting cerebellar output either goes down the spinal cord to the motoneurones – and so participates directly in the control of movement – or else is returned to the thalamic nuclei and so to the cerebral cortex, there to modify the control of movement from these higher centres. The cerebellum was developed in primitive fishes for the processing of information derived from the vestibular and the lateral line receptors. Throughout evolution the neuronal wiring diagram has been preserved in its basic features, but in the birds and mammals, there have been additions of complex patterns of inhibitory action that presumably give more subtle and intricate performance (Eccles, 1969*a*). With mammalian evolution the cerebellum grows commensurately with the cerebrum, and there are massive communication lines subserving reciprocal linkages. By virtue of its computing capability the cerebellum contributes finesse and skill to actions programmed from the cerebral cortex. For example the marvellous motor controls exercised in musical performance, in ballet, in games, and in craftsmanship and technology are believed to be due to the utilization of remembered cerebellar skills.

Fig. 1 gives a schematic illustration of the principal neuronal pathways in the cerebellum. There is a full account of these anatomical pathways and of their physiological operation in a recent book (Eccles, Ito & Szentágothai, 1967). Since that time the most notable advance has been in four anatomical papers that set new standards in quantitative investigations on the central nervous system (Palkovits, Magyar & Szentágothai,

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1971*a*, *b*, *c*, 1973). The quantitative data of this work has been incorporated in Table 1. Fig. 1 shows the two afferent pathways that convey information to the cerebellum, namely, climbing fibres (cf) and mossy fibres (mf), and also the only pathway out of the cerebellar cortex, which is via the

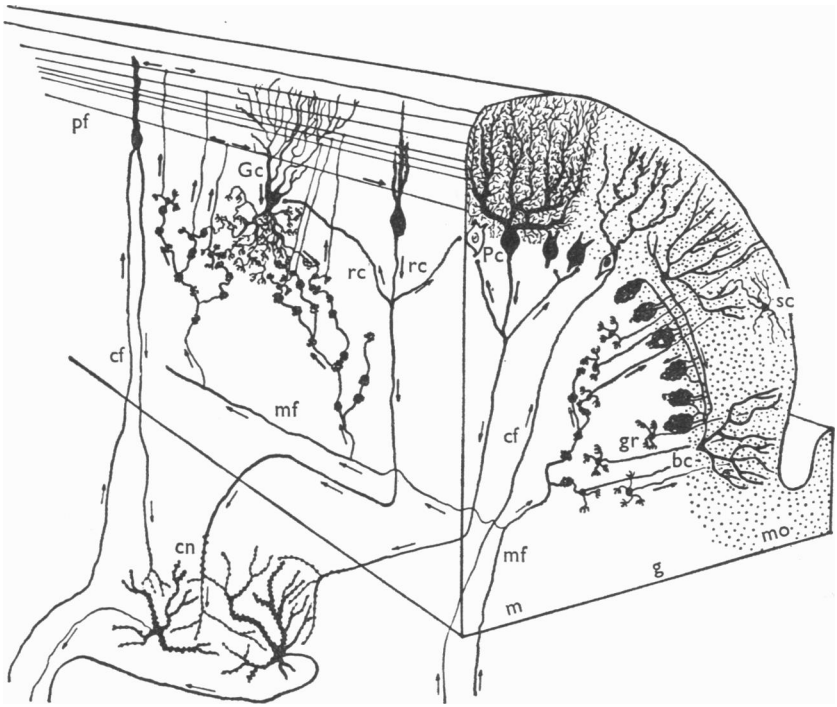


Fig. 1. Schematic diagram showing in perspective drawing the various neurons and neuronal connexions of the cerebellar cortex. mf, mossy fibre; cf, climbing fibre; gr, granule cell; Gc, Golgi cell; bc, basket cell; sc, stellate cell; Pc, Purkyně cell; pf, parallel fibre; cn, cerebellar nucleus; mo, molecular layer; g, granular layer.

Purkyně cell axons. A Purkyně cell is supplied by a single climbing fibre which exerts a powerful excitatory action. On the other hand, the mossy fibre input is characterized by the enormous divergence documented in Table 1, and it has both excitatory and inhibitory actions on Purkyně cells. For our present purpose it is sufficient to outline the two major pathways. The excitatory pathway is by mossy fibres to granule cells, which in turn discharge impulses along their axons, the parallel fibres, that give excitatory synapses to Purkyně cells, the approximate divergence and convergence numbers being given in Table 1. The inhibitory pathway

TABLE 1. Mossy fibre pathway

| Numbers | | Excitatory: Divergence number | Excitatory: Convergence number | | Inhibitory: Divergence number | Inhibitory: Convergence number |
|---|---|---|---|---|---|---|
| $4{\cdot}8 \times 10^6$ | Mossy fibres | | | Mossy fibres | | |
| | ↓ | 460 | 4·2 | ↓ | 460 | 4·2 |
| $2{\cdot}2 \times 10^9$ | Granule cells | | | Granule cells | | |
| | Parallel fibres | | | Parallel fibres | | |
| | ↓ | 45 | 80,000 | ↓ | 20 | 20,000 |
| $1{\cdot}2 \times 10^6$ | Purkyně cells | | | $7 \times 10^6$ Basket cells | | |
| | | | | Basket cell axons | | |
| | ↓ | | | ↓ | 8 | 50 |
| $1{\cdot}2 \times 10^6$ | Nuclear cells | 20–50 | 20–50 | Purkyně cells | | |
| | | | Climbing fibre pathway | | | |
| $1{\cdot}2 \times 10^5$ | Inferior olive cells | | | | | |
| | Climbing fibres | | | | | |
| | ↓ | 10 | 1 | | | |
| $1{\cdot}2 \times 10^6$ | Purkyně cells | | | | | |

is by mossy fibres to granule cells to parallel fibres to basket cells (bc) that give a dense array of inhibitory synapses on the bodies of the Purkyně cells. The approximate divergence and convergence numbers are also given in Table 1 for the sequential neuronal links in this inhibitory pathway.

In contrast, the climbing fibre pathway is very restricted in its distribution, as is documented in Table 1. Each Purkyně cell receives synapses from only one climbing fibre which exerts such a powerful excitatory action that the Purkyně cell responds by a brief repetitive discharge at high frequency. The climbing fibres are axons of cells in the inferior olive that subdivide a few times to give a divergence of about tenfold (Table 1).

Fig. 1 illustrates an important design feature of the cerebellar cortex, namely the rectangular lattice construction with the densely packed parallel fibres running along the folium and through the dendritic trees of the Purkyně and basket cells that have an espalier-like conformation or arber spread transversely across the folium. As pointed out by Szentágothai (1968), this is the optimal design for maximizing the synaptic connectivities of the parallel fibres that extend for about 1 mm in each direction from their origin in a bifurcating granule cell axon (Palkovits, Magyar & Szentágothai, 1971*c*). In its total length of 2 mm a parallel fibre passes through about 200 Purkyně dendritic trees, making synapses only on about 1 in 5 to give the divergence of 45 in Table 1. The convergence of 80,000 signifies that over 400,000 parallel fibres pass through the dendritic arber of each Purkyně cell. Another design feature in Fig. 1 is that the only output line from the cerebellar cortex is via the Purkyně axons that project to the cerebellar nuclei. The basket cell axons extend transversely in either direction for no longer than 600 $\mu$m, making occasional contributions (eight on the average) to the baskets around the Purkyně cell somata, while each basket represents a remarkable convergence from fifty basket cells (Palkovits *et al.* 1971*c*).

The mossy fibres branch profusely so that each innervates about twenty glomeruli and gives synapses to the twenty granule cells that send dendrites to each glomerulus. The resulting divergence number is about 460 because a granule cell usually receives synaptic input from separate mossy fibres on each of its four dendritic claws, as is indicated by the convergence number of 4·2 (Palkovits, Magyar & Szentágothai, 1973). Converging onto these mossy fibre-granule cell synapses in the glomeruli are the profuse axonal terminals of the Golgi cells (Palkovits, Magyar & Szentágothai, 1971*b*).

It is important to recognize that all of the neurones of the cerebellar cortex and nuclei are in continuous activity even under what may be regarded as resting conditions, as illustrated in Fig. 2 for Purkyně and nuclear cells. The 'resting' frequencies of impulse discharges are usually

in the range of 20–100 Hz, and are characterized by a remarkable variability in successive spike intervals (Eccles *et al.* 1967, ch. xi; Thach, 1968, 1970*a*, *b*; Marchesi & Strata, 1971; Eccles, Faber, Murphy, Sabah & Táboříková, 1971*b*; Eccles, Sabah, Schmidt & Táboříková, 1972*b*, *d*; Eccles, Sabah & Táboříková, 1971). This irregular on-going activity can be thought of as the neuronal machine 'ticking-over' in all of its multiple components, so that each is already primed to respond to synaptic input by raising or lowering its firing frequency. It is a general principle of operation of the nervous system that with each neurone the intensity of its excitation is coded as its firing frequency, and in turn the intensity of its synaptic action on other neurones is given by its firing frequency (cf. Eccles, 1964). Inhibitory synaptic action is post-synaptic, counteracting excitatory synaptic action in the typical manner of the so-called algebraic summation in its effect on the firing frequency of a neurone. Thus inhibitory synaptic action is coded as a reduction or even a silencing of the spike discharges.

*Design features of the cerebellum related to computer performance*

The anatomical structure of Fig. 1 has now been given physiological meaning by the identification of each of the component species of neurones and fibres as excitatory or inhibitory, as may be seen in the greatly simplified anatomical diagram of Fig. 3 (Eccles *et al.* 1967). All the species of neurones are inhibitory except granule cells and nuclear cells, and are indicated in Fig. 3 symbolically in black, i.e. Golgi, basket, stellate, and Purkyně cells. Both species of input fibres, the mossy and climbing fibres, are excitatory. It can be seen in Fig. 3 that all input to the cerebellar cortex turns into inhibition in at most two synaptic relays. It was pointed out many years ago (Eccles *et al.* 1967, ch. xv) that this unique design feature is of importance for the effective computer operation of the cerebellum. It eliminates the danger of continuous reverberatory activity in chains of excitatory neurones, such as would occur for example if the Purkyně cells with their recurrent axon collaterals were excitatory. The effects of all excitatory inputs are automatically turned off, so that within 100 msec the neuronal machinery is cleared and ready for a new computation unbiased by the preceding activity. This automatic clearance is of importance for faithful computer operation, as has also been recognized by Perkel & Lewis (1968).

We now come to consider the question of cerebellar computation, asking what is computed and how is the computation carried out (cf. Sabah, 1972). The direct answer to the first question is that the information being computed is simply the input of impulses along the mossy and climbing fibres. There is a 'resting' impulse discharge, usually of 20–100 Hz,

in the mossy fibres, mf (Eccles, Faber, Murphy, Sabah & Táboříková, 1971*a*; Eccles *et al.* 1972*a*), which would give an immense impulse barrage for the $4{\cdot}8 \times 10^6$ mossy fibres in the cat cerebellum for example. In addition there is a much slower firing of the climbing fibres, cf (about 1 Hz) (Eccles *et al.* 1967; Thach, 1968; Marchesi & Strata 1971; Eccles *et al.* 1972*c*) but each impulse generates a brief bursting discharge of about

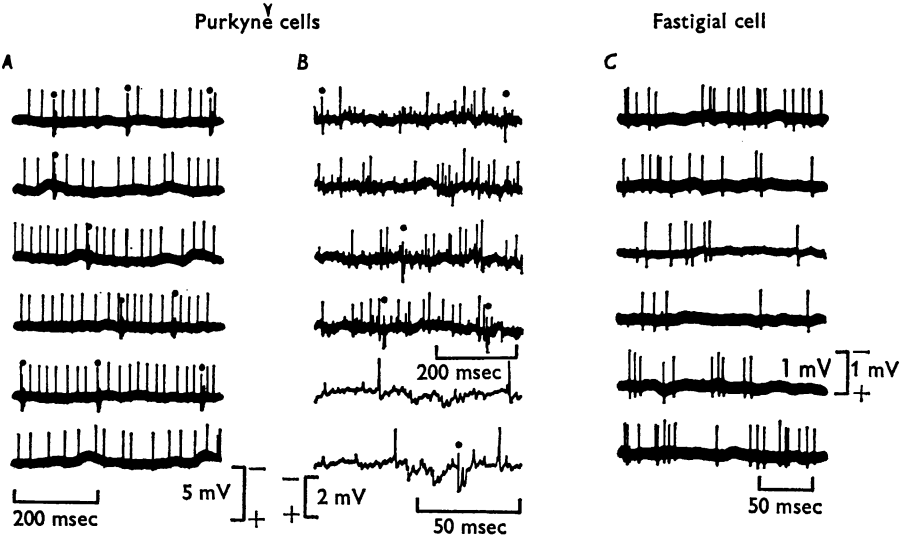


Fig. 2. Spontaneous discharges of two Purkyně cells and a fastigial cell. In *A* the Purkyně cell is seen to discharge simple spikes in an irregular manner and interspersed are climbing fibre spikes as indicated by superimposed dots. *B* shows spike responses from another Purkyně cell in which there was considerably more background complication by other spikes. However, the simple and climbing fibre spikes can be recognized, particularly in the two fastest sweeps below. *C* shows the spontaneous irregular firing from a typical nuclear cell of the cerebellum.

four impulses in its Purkyně cell (Eccles *et al.* 1967, ch. VIII). Together these inputs form the background on which is superimposed the transitory variants in frequency that constitute the signals for computation. I propose to concentrate on the mossy fibre (mf) input because it is much more powerful and differentiated, and also because the manner and significance of its computation is much better understood.

Fig. 3*B* displays the negative feed-back action that the inhibitory Golgi cells exert on the mossy fibre-granule cell synapses. It is important to recognize that this Golgi cell inhibition acts in a widely diffused manner because of the profuse branching of the Golgi cell axons (Eccles *et al.* 1967, ch. I, XII; Szentágothai, 1968; Palkovits *et al.* 1971*b*), each Golgi cell in-

hibiting an immense number of granule cells (up to 10,000). There is some overlap in the territories of granule cells inhibited by adjacent Golgi cells. This Golgi cell inhibition would suppress the discharges from all weakly excited granule cells, and thus would serve to focus the response to those granule cells strongly excited by the mf input (Eccles *et al.* 1967, ch. VII).

Another important control of granule cell response is provided by the mode of action on the granule cell of synaptic input on its four dendritic

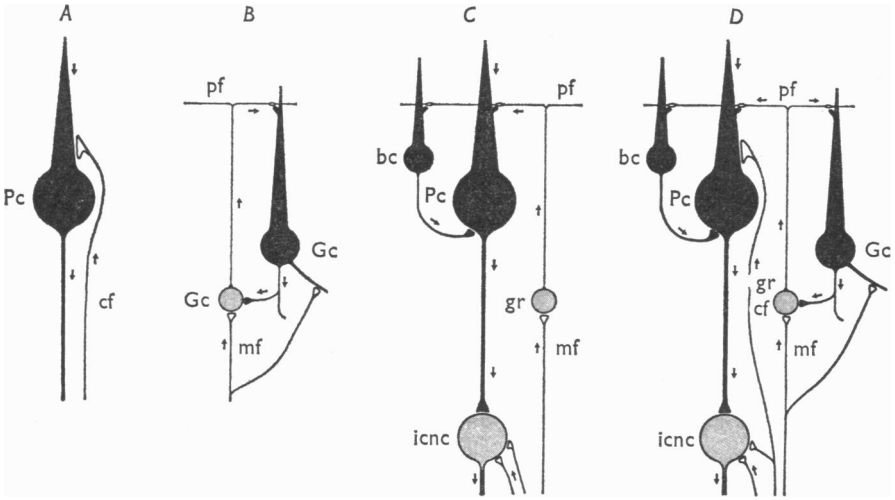


Fig. 3. Diagrams of the most significant cells and their synaptic connexions in the cerebellar cortex. The component circuits of *A*, *B* and *C* are assembled together in *D*. Arrows show lines of operation. Inhibitory cells are shown in black. Pc, Purkyně cell; cf, climbing fibre; gr, granule cell; pf, parallel fibre; Gc, Golgi cell; mf, mossy fibre, bc, basket cell; icnc, intracerebellar nuclear cell.

claws, as discussed by Marr (1969) and Sabah (1971). As a rule each claw is activated by a different mossy fibre, and there is evidence (Eccles *et al.* 1967, ch. vii; Allen, Azzena & Ohno, 1972) that summation of synaptic excitations on at least two claws is required to evoke a granule cell discharge. This design feature also ensures that only a concentrated activation of mossy fibres would be effective in evoking a granule cell discharge. Mathematical treatments of this problem have been developed by Marr (1969) and Sabah (1971). It is sufficient to note that the synaptic connectivities of mossy fibres to granule cells provide a randomizing divergent mechanism for the mf input (cf. Sabah, 1972).

Fig. 3 *C* displays the excitation of both basket and Purkyně cells by the axons of the granule cells (the parallel fibres) and the respective inhibitory actions of these cells on Purkyně cells and nuclear cells respectively. It was

a remarkable discovery (Ito, Yoshida & Obata, 1964) that Purkyně cells act as inhibitors of nuclear cells (cf. Eccles *et al.* 1967, ch. xiii). This inhibition is measured against a background excitation of nuclear cells that we shall discuss later. For the present it can be stated that the whole output from the cerebellar cortex is via the Purkyně cell discharges that provide an inhibitory sculpturing of the nuclear cell discharges. The inhibitory action of basket cells depresses Purkyně cell discharges and so serves to relieve the nuclear cells of Purkyně cell inhibition. This is an

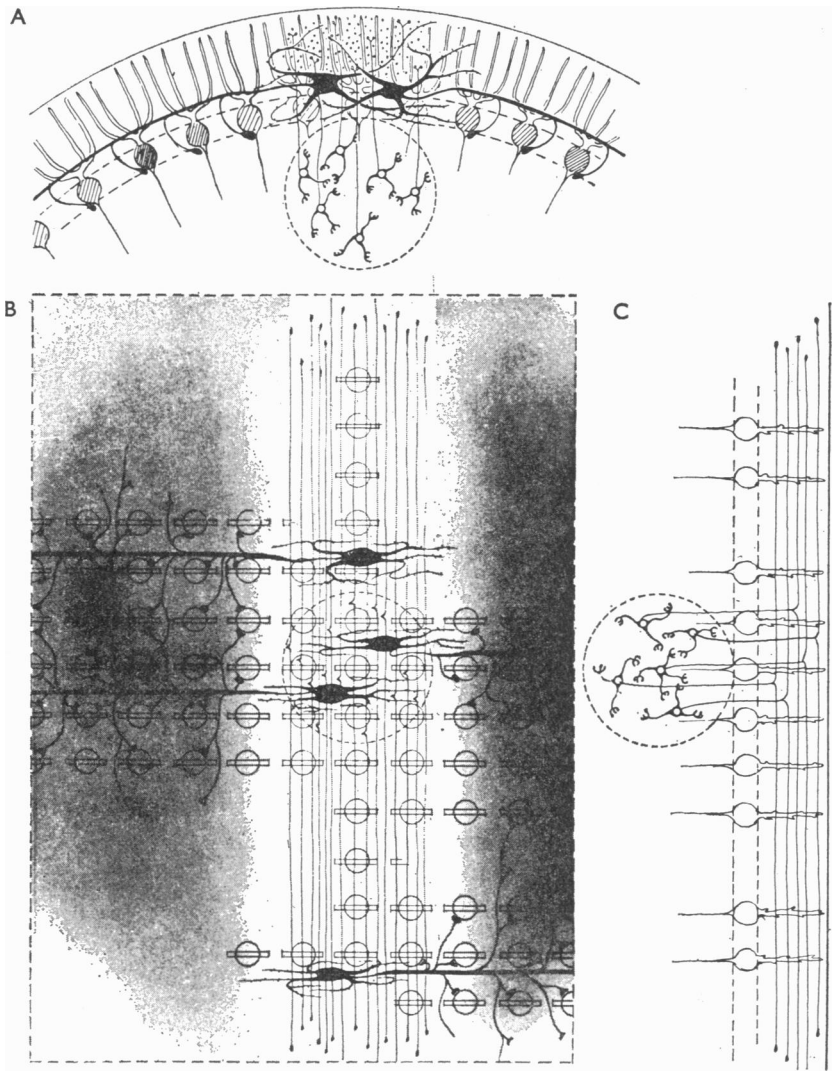


Fig. 4. For legend see facing page.

action termed disinhibition, and operationally it has the properties of an excitation. Fig. 3 *D* is an assemblage of the separate features of *A*, *B* and *C*.

In the upper part of Fig. 4 there is diagrammatically shown a section across a cerebellar folium and below is a surface plan in which the Purkyně cells are depicted with their circular somata and transversely oriented dendrites. The basket cells are in black with their transversely directed axons giving inhibitory synapses to the Purkyně cells. The small cortical area is assumed to be bombarded by a mf input that because of Golgi cell inhibition results in a sharply focused granule cell response. In the lower diagram it is seen that the resulting beam of parallel fibre impulses excites the Purkyně and basket cells on beam. The latter cells in turn inhibit the Purkyně cells on either side of the excited beam, a narrow strip of excited cells between two bands of inhibited cells, as is shown diagrammatically by the dark shading. The excited strip would be about 2 mm long, the length of the parallel fibres (Palkovits *et al.* 1971*c*), while the inhibitory bands would be about 600 $\mu$m across, which is the average length of the transversely directed basket cell axons (Palkovits *et al.* 1971*c*).

It will be appreciated that this arrangement gives excellent opportunities for the integration of the inputs by the many mossy fibres that have overlapping excitatory and inhibitory actions. Effectively this integration is secured by the antagonistic excitatory and inhibitory synaptic actions on individual Purkyně cells. Ideally each focused mf action would have an areal disposition as in the lower diagram of Fig. 4, and one can imagine the overlapping operation of many focused mf inputs in close proximity. For example, the Purkyně cells excited on-beam in one focus may receive convergent inhibitory actions from adjacent foci. But this diagram of Fig. 4

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Fig. 4. Diagram illustrating the concept of the higher order integrative unit of the mossy afferent-parallel fibre neuronal chain. Neurone matrix of folium seen in transverse (*A*) and longitudinal section (*C*), as well as from the surface (*B*). The assumption is made that all granule neurones inside the circles indicated are simultaneously excited and discharge impulses along their axons, the parallel fibres. In this case all Purkyně cells (indicated in *B* as small circles with overlying bars) along a longitudinal strip of about 2 mm length would be excited by the beam of parallel fibre impulses. A powerful inhibition would be exercised by basket neurones situated in the same strip of excitation on all the Purkyně neurones situated on either side of the excited strip. The degree of inhibition, as deduced from the number and strength of connexions (convergence, size of terminal, etc), is indicated by shadowing in *B* and by the density of hatching of Purkyně cell bodies in *A*. The excited region is left white. Only a representative part of the neurone matrix is indicated, for the sake of simplicity, and because of limitation in space not the whole width of the inhibited side fields (ten rows of Purkyně cells, in reality) is shown (Szentágothai, 1965).

illustrates merely an extremely simplified static view. Under what we may call 'real life' operation during complex rapid movements there would be an unimaginable intricacy and intensity of rapidly changing patterns of excitatory and inhibitory interaction, there being many completely different patterns even during 1 sec.

### *Patterns in space*

The most remarkable feature of the computer design of the cerebellar cortex is the number of lines in-parallel that are carrying much the same information (cf. Table 1). At first sight this excess of in-parallel lines may be regarded as a redundancy, but mature consideration reveals that it is essential in ensuring reliability of the computation. The irregularity of the background discharge of the various neurones (cf. Fig. 2) necessarily results in the uncertainty that any transient variation in frequency may be a meaningful signal when evaluated at the unitary level. We may say that the signal-to-noise ratio is very low. When a large number of elements in parallel are converging on to the same neurone, e.g. many parallel fibres on to a Purkyně cell, the averaging of the summed input results in a large reduction in the uncertainty. The divergence and convergence numbers of Table 1 give a measure of the number of in-parallel lines at the various stages of the mf pathway. Usually the redundancy is in the range 20–50, but it may be many thousands. It should be noted that convergence is essential for the integration of signals from diverse sources, as will be described later.

There has now been an intensive investigation of the mosaic patterns formed by the subsets of input from nerves and receptors of the forelimb and hind limb to the anterior lobe of the cerebellum. In the earlier investigations the potential fields in the cerebellar cortex were used in mapping the distribution of inputs from limb nerves (Eccles, Provini, Strata & Táboříková, 1968*a*, *b*; Provini, Redman & Strata, 1968), but with computer averaging techniques it is now possible to obtain very reliable information on the inputs to an individual Purkyně cell, as disclosed by the modulation of its background firing frequency (Eccles *et al.* 1971*b*). Furthermore, nerve stimulation has been replaced by precisely controlled adequate stimulation of skin or muscle receptors (Eccles, Sabah, Schmidt & Táboříková, 1971*a*, *b*, 1972*a*, *b*, *c*, *d*; Faber, Ishikawa & Rowe, 1971; Ishikawa, Kawaguchi & Rowe, 1972*a*, *b*).

The total performance of the cerebellar neuronal machine has to be thought of as being built up by the activities of individual neurones. Since Purkyně cell discharge is the sole output from the cerebellar cortex, it is important to subject this discharge to precise investigation under a wide variety of controlled inputs to the cerebellum. The aim is to understand

the code by which these inputs are converted into neuronal discharges with patterns in space and time. For this purpose we have recorded selectively the impulse discharges of a single Purkyně cell by means of a micro-electrode that is inserted into close proximity to it. The response of this cell is registered against its background discharge by modulation up

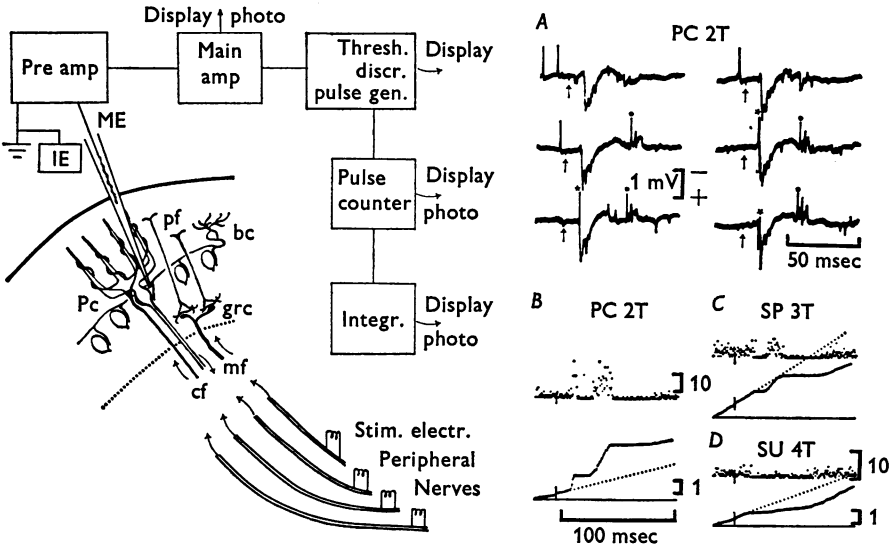


Fig. 5. Recording of histograms of Purkyně cell responses to afferent volleys. Diagram showing micro-electrode ME in position for recording from a Purkyně cell, Pc. There is a climbing fibre, cf, and a mossy fibre, mf, with synapses on granule cells, grc, whose axons are the parallel fibres, pf, of the molecular layer. Other Purkyně cells are shown only in outline of the somata. The basket cell, bc, gives inhibitory synapses to the Pc somata. The potential fields are recorded by ME against an indifferent grounded electrode, IE, on the head of the animal and are fed into a preamplifier (Pre amp). The other recording features are described in the text. Also shown are four limb nerves with stimulating electrodes. *A*, specimen photographs of actual records of a Purkyně cell activated by a plantar cutaneous (PC) volley to discharge simple spikes, with stars superimposed, and climbing fibre spikes with dots superimposed. *B* shows a post-stimulus-time histogram (PSTH) and the cumulative frequency distribution (CFD) produced by successive addition of the histogram values. There is averaging of 128 traces with recording in 256 bins of 0·5 msec. *C* and *D* show similar averaged responses for stimulation of superficial peroneal nerve at three times threshold and sural nerve at four times threshold. The PSTHs of *C* and *D* have the same calibration, that for *B* being different as shown. All CFDs have the same calibration which represents the average number of impulses of a single trace. Dotted lines show the projection of the initial firing frequency of the cell. Vertical bars show times of stimulation.

or down, and it can be revealed with surprising reliability by the averaging technique illustrated in the diagram of Fig. 5.

After the usual arrangements for recording with preamplifier and main amplifier, the signals are fed into the Fabri-Tek 1062 assembly, where there are a threshold discriminator and pulse generator which are utilized under continuous observation to reject the smaller spikes of other Purkyně cells and to convert the spikes from the single Purkyně cell under observation to standard pulses that are fed into the pulse counter whose output gives the post-stimulus time histogram (PSTH). A further stage with cumulative integration of the histogram gives a cumulative frequency distribution (CFD) that is useful for display of particular features of the response.

The upper trace of Fig. 5*B* shows the PSTH and the lower the CFD for 128 repetitions of records illustrated in Fig. 5*A*. The early and late responses in the PSTH and CFD correspond to the early single spikes (stars) evoked by the mf input and the later CF-evoked spikes (dots) of Fig. 5*A*. Volleys in two other cutaneous nerves gave quite different responses in Fig. 5*C* and *D*. The mf input in *D* gave a prolonged inhibition with almost complete silence, which presumably is attributable to basket cell action. This silence can also be seen in *C* with interruption by a CF response smaller than in *B*. Fig. 5 gives a glimpse of the unique character of a Purkyně cell as defined by its responses to three cutaneous inputs. Usually each Purkyně cell of the several hundred of our experimental series was tested by volleys in an array of twelve nerves. A general outcome of this investigation (Eccles *et al.* 1971*b*, *c*) was the disclosure of the surprising individuality displayed by the Purkyně cells with respect to the inputs each receives from the afferent volleys in the array of nerves mounted for stimulation. The response patterns of each cell are of course dependent on the integration of the excitatory and inhibitory influences (as illustrated in Figs. 3 and 4). The conflicting action of these influences must account for the wide range exhibited in the responses of the individual Purkyně cells even in the same zone of the cerebellar cortex. The responses to mf inputs are indeed much more individualized than would have been anticipated from the extensive distribution described in anatomical accounts (cf. Eccles *et al.* 1967, ch. ii, vii; Palkovits *et al.* 1972) of the branches of a single mossy fibre (cf. Fig. 1) and of the further distribution of its input via parallel fibres and basket cells. Presumably it is the interaction of these respective excitatory and inhibitory effects which sharpens the contours and so gives Purkyně cells their individuality of response.

This investigation utilizing nerve stimulation was preparatory to a more physiological investigation in which Purkyně cell responses were tested by

adequate stimulation of cutaneous mechanoreceptors or muscle stretch receptors. Many hundreds of Purkyně cells have been tested and here again their responses revealed their individuality in a remarkable manner (Eccles *et al.* 1971, 1972*b*, *d*; Ishikawa *et al.* 1972*a*).

In Fig. 6 the averaged post-stimulus time histograms of two adjacent Purkyně cells have been plotted so that there can be a ready comparison of the responses evoked by brief mechanical stimuli (taps of 16 msec

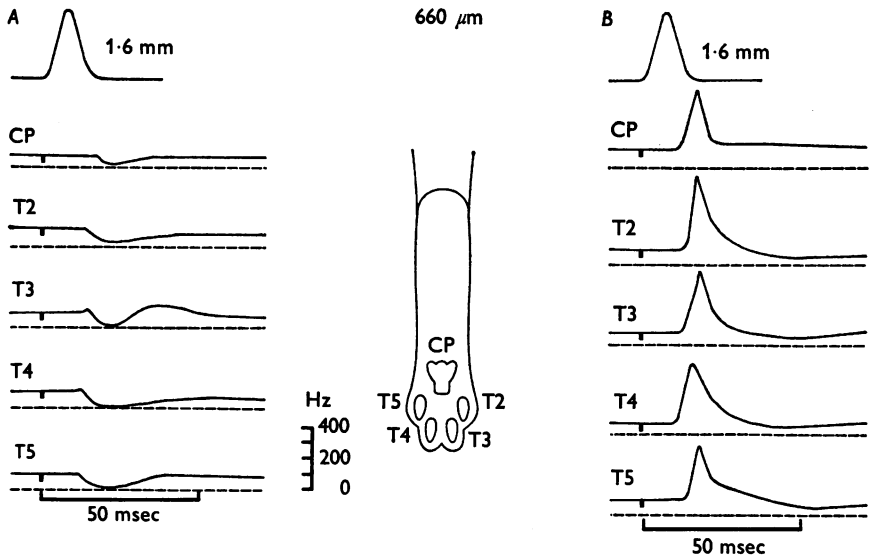


Fig. 6. Cutaneous mechanoreceptors projecting to adjacent Purkyně cells. In *A* are the averaged responses (PSTHs) of a Purkyně cell evoked by 1·6 mm taps (see upper trace) to all five pads of the forefoot, there being summation of sixty-four responses in 256 bins of 0·5 msec each. *B* is similar to *A* for another Purkyně cell 660 μm distance transversely across the same folium. Note that identical mechanical stimuli were employed in the two series and that there are the same scales for time and frequencies. Both series are in lobule V of the pars intermedia. Decerebrate unanaesthetized preparation.

duration) to the forefoot pads. The background frequency of both cells was about 100 Hz, but otherwise the cells were very different. With Purkyně cell *A* the taps caused an inhibitory slowing of the discharge for 20–40 msec with perhaps traces of excitation before and after for the toe 3 response. With Purkyně cell *B* the same taps to all pads powerfully excited the Purkyně cell for 10–20 msec. Since cells *A* and *B* were separated by 660 μm transversely, a single focused mossy fibre input could be responsible for both types of response, as can be seen from Fig. 4. The beam of excited parallel fibres responsible for the excitatory responses of cell *B*,

would also excite basket cells that could give the inhibition of cell *A* 660 $\mu$m laterally. Such a simple spatial relationship in accord with predictions from Fig. 4 has been observed only rarely. Presumably there usually are many diverse foci of mossy fibre inputs that result in complex patterns of parallel fibre activation.

The two cells of Fig. 6 responded similarly to taps to the five foot pads. In contrast, the two cells of Fig. 7 gave discriminatory responses. Taps to the central pad and to toes 2 and 3 excited Purkyně cell *A*, while taps to the pads of toe 4 inhibited it, and toe 5 was ineffective. Yet toe 5 was most

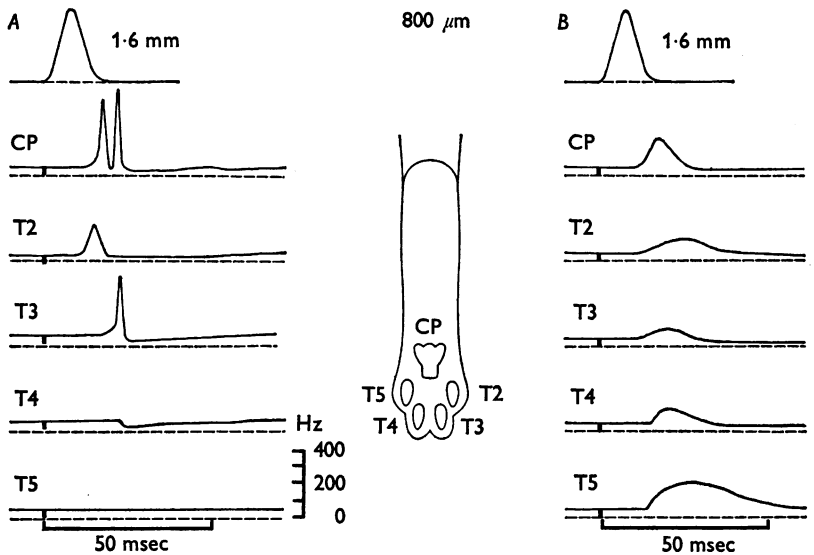


Fig. 7. Phasic responses of two adjacent Purkyně cells to cutaneous mechanoreceptors. This series is similar to that of Fig. 6 but is for two cells that are located along the same micro-electrode track 600 $\mu$m lateral to the track of series *A* and *B* of Fig. 6. The two cells in this figure are 800 $\mu$m apart transversely across the same folium. There was summation of sixty-four responses in 256 bins of 0·5 msec each. Same time and frequency scales for all records. Decerebrate unanaesthetized preparation.

effective on to cell *B*, and all pads were excitatory. Evidently the effects of mossy fibre inputs are more individualized than would be expected from the widely diffused distribution of the branches of a mossy fibre axon in the cerebellar cortex (cf. Szentágothai, 1968). As already suggested, the Golgi cell inhibition presumably is important in giving a sharper focus to this disparate mossy fibre input. Furthermore, the basket cell inhibition also would be effective in giving the much more individualized responses of some Purkyně cells, as in Fig. 7, than would be expected from the widely dispersed branching of a mossy fibre.

The inset of Fig. 8 shows a parasagittal section of the anterior lobe of the cerebellum. Two micro-electrode tracks (ME) are indicated by interrupted lines, the dots on these tracks indicating the locations of Purkyně cells whose responses were investigated. The large diagram shows an approximate map of the unfolded vermis and pars intermedia of the anterior lobe and adjacent posterior lobe with the positions of the sulci drawn in (cf. Provini *et al.* 1968; Voogd, 1964). Note the scale indicating a 10 to 1 reduction for longitudinal *vs.* transverse dimensions. The filled circles plot the positions of Purkyně cells, some of which were at the locations dotted on the ME tracks of the inset. The three sizes of the filled circles symbolize the intensity of the responses evoked by taps to the pads of the forefoot. The three open circles indicate positions of unresponsive Purkyně cells. It is seen that there are two foci of responsive Purkyně cells, a strong focus in the pars intermedia and a weaker focus more posteriorly in the lateral vermis. In *B* there are shown in lobules III and IV at least four foci of Purkyně cells responding to hind foot taps with many zero responses in between. In lobules V and VI forefoot taps evoke responses in many Purkyně cells, which appear to be clustered in at least three foci, there being again many zero responses in between.

These results show diversification of the input to foci of Purkyně cells, which presumably will be sites for integration of different subsets from the total afferent input. For example, during some complex movement, there would be input to the cerebellum from a wide range of receptors in a limb or limbs and with the diverse modalities of cutaneous, muscle, joint and fascial receptors. Our sampling of Purkyně cells by several micro-electrode insertions into the cerebellum in any one experiment gives but fragmentary glimpses of the immense number of colonies constituted by similarly behaving neurones. However we had earlier made a comprehensive study of the responses evoked in single Purkyně cells by afferent volleys from many nerves, both cutaneous and muscular, and had found remarkable examples of convergence (Eccles *et al.* 1971*b*, *c*).

In our adequate stimulation studies we have identified only those Purkyně cells influenced by cutaneous inputs from the foot pads and adjacent hairy skin. In order to preserve and develop the integration of information occurring in colonies having somewhat similar inputs, it is postulated that any such colonies of neurones would project to a common target of neurones. This arrangement would give averaging of inputs from many neurones, so reducing noise, as already described, and giving opportunity for further integration of different subsets of the total input to the cerebellum. If there were randomized projection, there would be a loss of all specificity of information. It is the diversified convergence that enhances the pattern generating capability of the neuronal machinery of

the cerebellar cortex. This postulate of organized projection from Purkyně cells to the nuclear cells has been investigated by a systemic investigation of nuclear cell responses.

*The cerebellar nuclear cells*

When considering the responses of nuclear cells (cf. Figs. 1, 3), two questions arise with respect to the spatial patterns of these responses. First, we may ask, how selective are these responses when tested for a wide range of inputs, and secondly, if there is this significant selectivity, are those neurones giving similar responses arranged in colonies? In answering these questions the responses of almost 1000 neurones have been investigated in the fastigial and interpositus nuclei (Eccles, Sabah & Táboříková, 1971; Eccles, Rosen, Scheid & Táboříková, 1972).

In the nuclear cell illustrated in Fig. 9, taps to the forefoot pads evoked an initial excitation and a later powerful inhibition that produced a complete silence for 20–40 msec. There was but little discrimination between the five pads. Taps to hind foot pads were also effective on this neurone, but had a much weaker excitatory and inhibitory action. Again there was no significant difference between responses evoked from the five pads. In general we have found that with nuclear cells the discrimination between the toes of a foot is less than with Purkyně cells. It is important to recognize that the Purkyně cell action on nuclear cells is inhibitory, and that the initial excitation usually observed is generated by the excitatory input shown in Fig. 3*C* and *D* and more specifically in Figs. 14, 15 and 16. A further complication in the interpretation of the nuclear cell response is that inhibition of Purkyně cells by basket cells as in Fig. 6*A* would give by disinhibition an excitation of the nuclear cells with a duration comparable to the inhibition in Fig. 9.

When searching for cells in the fastigial nucleus that were activated from the cutaneous mechanoreceptors of the forefoot and hind foot, it was found that they were concentrated in the extreme lateral zone of the fastigial nucleus. Fig. 10 shows symbolically the inhibitory responses evoked in cells of the fastigial nucleus by taps to footpads in two experiments. In *A* there were nineteen cells in three tracks and in *B* twenty-one cells in four tracks. As shown by the convention for forefoot and hind foot there is a general tendency for hind foot dominance in cells located anteriorly and dorsally. With *B* most of the activated cells were either hind foot or forefoot, there being only four with convergent inhibitory actions as in Fig. 9. In *A* most cells exhibited hind foot–forefoot convergence. With Purkyně cells such convergence was only rarely observed, hence it may be concluded that there is projection on to nuclear cells of Purkyně cells that are exclusively oriented to forelimb or hind limb. This convergence is an

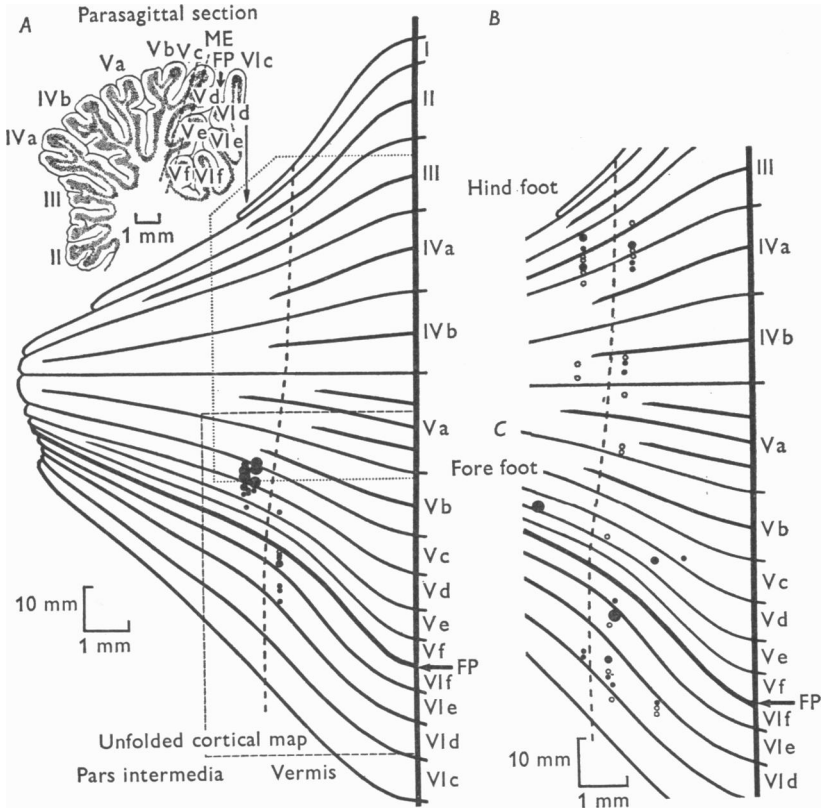


Fig. 8. Maps on unfolded cerebellar cortex of mossy fibre inputs from forefoot pads to Purkyně cells. The inset in *A* shows a parasagittal section at a medial position of the pars intermedia, and on it are marked the lobules II to VI and sublobules with the Larsell (1953) designations and the fissura prima, FP. Also shown are 2 micro-electrode tracks (ME) with eight Purkyně cells marked thereon. The large drawing of *A* represents an unfolded map of the vermis and pars intermedia for lobules I to V and part of VI on the left side (cf. Provini *et al.* 1968), the paravermal sulcus being indicated by an interrupted line, and the mid line by the thick line to the right. As described in the text, the Purkyně cells are located in this map and denoted by four symbols with respect to their excitatory or inhibitory response to the fast mossy fibre input from the forefoot pads. The three small open circles signify zero response, and the three sizes of filled circles give an approximate measure of the sizes of the excitatory or inhibitory responses. *B* and *C* give similar maps for two other experiments with hind foot and forefoot pads respectively. The hind foot observations were all made on Purkyně cells rostral to those of the forefoot. All experiments were on unanaesthetized decerebrate preparations.

example of a spatial pattern concerned in the integration of information from forelimb and hind limb, which doubtless is of importance in the control of movement involving the whole animal. There are several examples in Fig. 10 of cells in close proximity giving similar responses. Such cells are to be regarded as members of a colony that may be presumed to have a considerable population. With our recording procedures it was possible to examine only a small fraction of the constituent cells of any presumed colony.

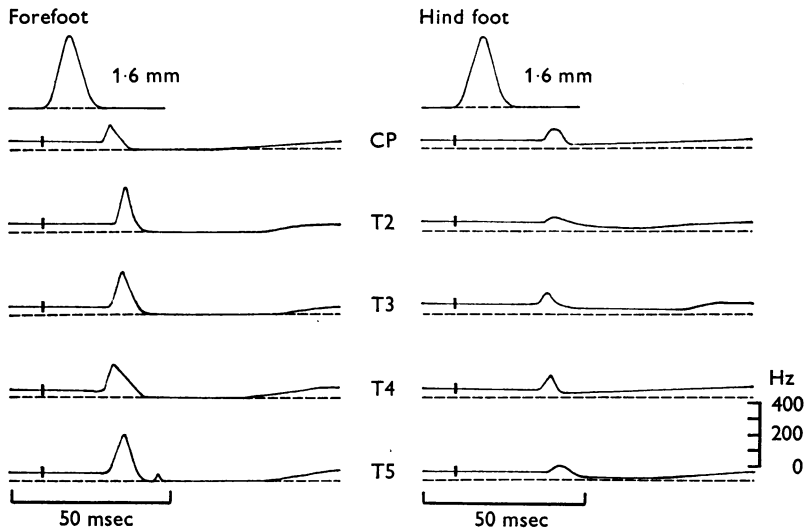


Fig. 9. Effects on a fastigial cell of taps to toes of forefoot and hind foot. These series resemble those plotted in Figs. 6 and 7, but are for single responses of a fastigial cell (cf. Fig. 2*C*). Again the taps are 1·6 mm and are applied to all pads of the forefoot and hind foot, as indicated by the top traces. The plotted records show the averaged PSTHs for sixty-four traces, there being 256 bins of 0·5 msec each. Same frequency and time scales for all traces.

## *Patterns in time*

### *The timing of responses to mossy fibre input*

A convenient display of mossy fibre evoked responses is illustrated in Figs. 11 and 12. In Fig. 11 a nerve stimulus typically evoked a triple burst of mossy fibre responses with a latency of about 6 msec. Two different types of Purkyně cell responses are illustrated, one purely excitatory with a latency of about 12 msec, the other a small initial excitation at 12 msec with a later strong inhibition. Finally, two quite differently responding fastigial cells are illustrated with latencies of about 16–18 msec: a double excitatory followed by inhibition; and a pure inhibitory response. All these various types of response and their latencies are readily explicable on the

simplified circuit diagram of Fig. 3 *D* except for the long latency (16 msec) of the fastigial cell discharge. This discharge should be at 7–8 msec if it were produced by synaptic excitation via collaterals of the fast mossy fibres, as is indicated in Fig. 3 *D*. Certainly it should occur before the Purkyně cell excitation, and not after it as in Fig. 11. On the right side of Fig. 11 mechanical stimuli applied to the pads by the brief tap shown above are

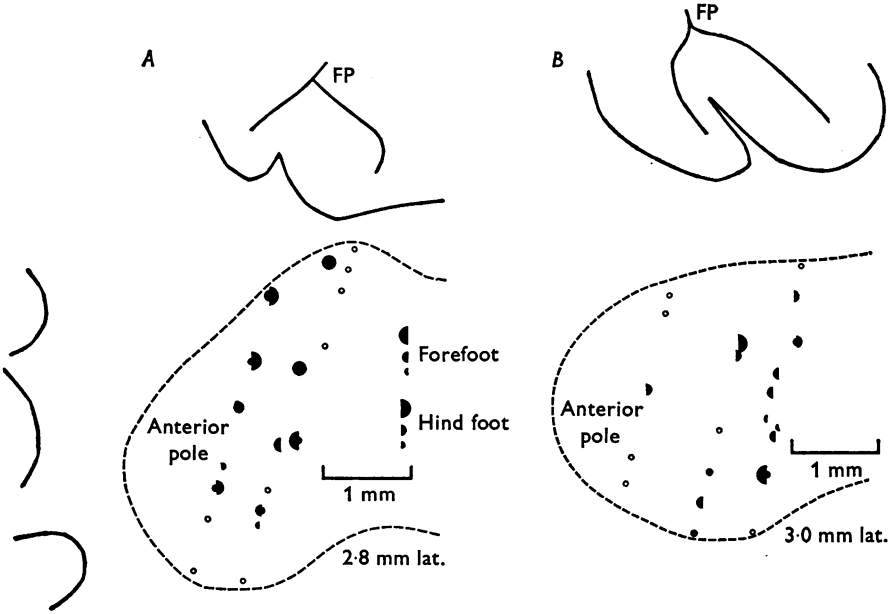


Fig. 10. Fastigial neurone locations with sizes of their responses from forefoot and hind foot. In experiment *A* there were three micro-electrode tracks through the fastigial nucleus (outlined with interrupted line) along which there were nineteen fastigial neurones. FP is bottom of fissura prima. The sizes of the inhibitory responses evoked from taps to forefoot and hind foot are symbolized, as large, medium or small by half circles as shown in the key between *A* and *B*, forefoot facing forwards, hind foot backwards. The tracks were in a parasagittal plane 2·8 mm lateral to the mid line. *B* is similar to *A* but in another experiment with four tracks as shown in a plane 3·0 mm lateral to the mid line.

seen to evoke responses comparable to those on the left side if allowance be made for the additional delay of at least 4 msec involved in transduction from tap onset to nerve impulses. Again there is the unexpectedly long latency of the fastigial cell excitation.

The forelimb responses of Fig. 12 are similar to those of the hind limb, but mossy fibre responses are not shown. There is a shorter latency for all responses, which is attributable to the shorter conduction distances. Again the excitatory fastigial cell responses evoked by the nerve volley had an

unexpectedly long latency – about 12 msec. In Fig. 12*A* the excitation was so delayed in one of the traces for a fastigial cell that it arose from an initial inhibition that had the very short latency of about 10 msec. The responses evoked by pad taps (Fig. 12*B*) resembled those for the hind limb in Fig. 11, but tended also to have shorter latencies in accord with the shorter conduction distances. Note also the two examples where the excitation arose from an initial inhibition.

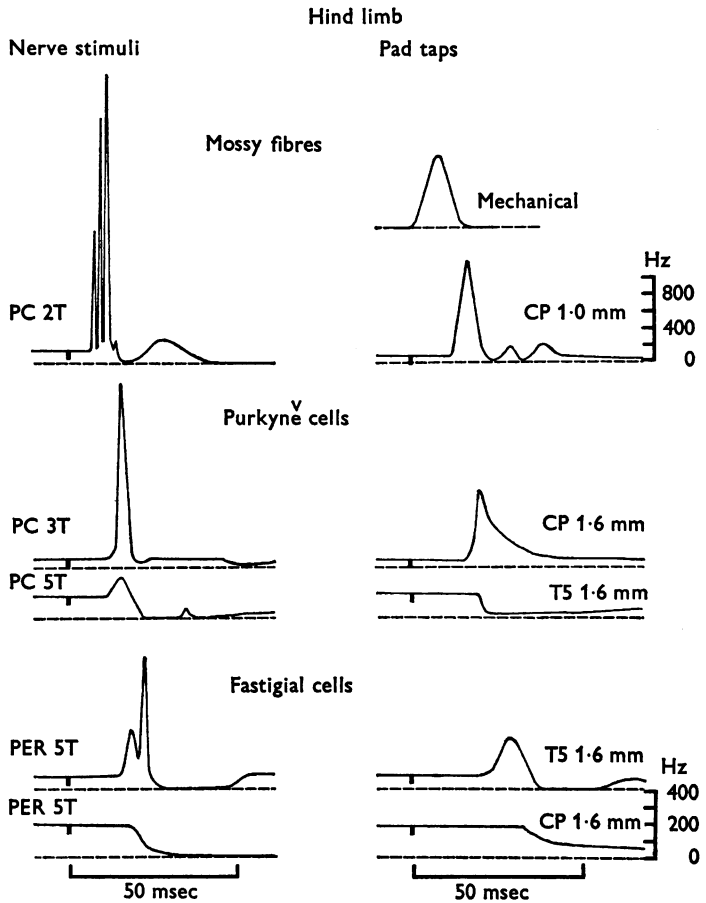


Fig. 11. Assembled plots of post-stimulus time histograms from a series of representative experiments on hind limb nerves and footpads, and for responses of mossy fibres, Purkyně cells and fastigial cells as indicated. In the left column are the responses to nerve stimuli to either the plantar cutaneous (PC) or peroneal nerves (PER) at the indicated strengths of stimuli relatively to threshold (T). In the right column are the responses to taps to the footpads, CP or T5. All records of the Purkyně and fastigial cells have the same time and frequency scales. For the mossy fibres there is a different frequency scale.

On rare occasions a small fastigial or interpositus excitation was seen at the latency (6–8 msec) expected for its production by impulses in the fast mossy fibres (Eccles *et al.* 1972). One can therefore have confidence in concluding that the fast mossy fibres of the dorsal spinocerebellar and cuneocerebellar tracts pass by the nuclei and give only a very few axon collaterals to the nuclear cells. For the synaptic excitation of nuclear cells by the mossy fibre input to cerebellum, a delayed mossy input has to be

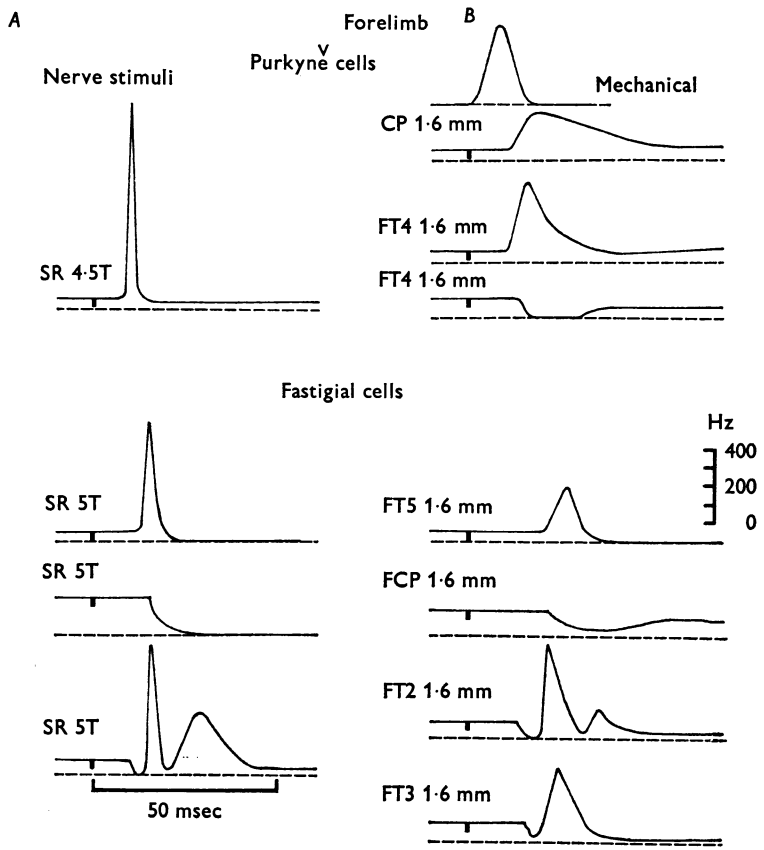


Fig. 12. Assembled plots as in Fig. 11, but for Purkyně and fastigial cell responses to forelimb stimuli as indicated. SR is superficial radial nerve. No mossy fibre responses are shown. There are the same time and frequency scales for all traces.

invoked, namely that by the spino-reticular cerebellar pathway. In response to limb nerve stimulation the input to the cerebellum via this pathway is rather dispersed in time with a major input in the range of 10–20 msec (Grant, Oscarsson & Rosén, 1966; Oscarsson & Rosén, 1966).

The most direct experimental test for this proposed excitatory action on fastigial and interpositus cells was to stimulate the lateral reticular nucleus directly through an inserted electrode and record from single nuclear cells as in Fig. 13. In *A* are three specimen records showing that in every case the stimulus evoked a single nuclear cell discharge at a very short latency. This is further illustrated in the averaged PSTH and CFD records of *B*. By contrast in *C* and *D* there are the long latency (about 15 msec) responses of the same cell to forelimb and hind limb nerve volleys. In *E* there are fast specimen records of the responses evoked from the

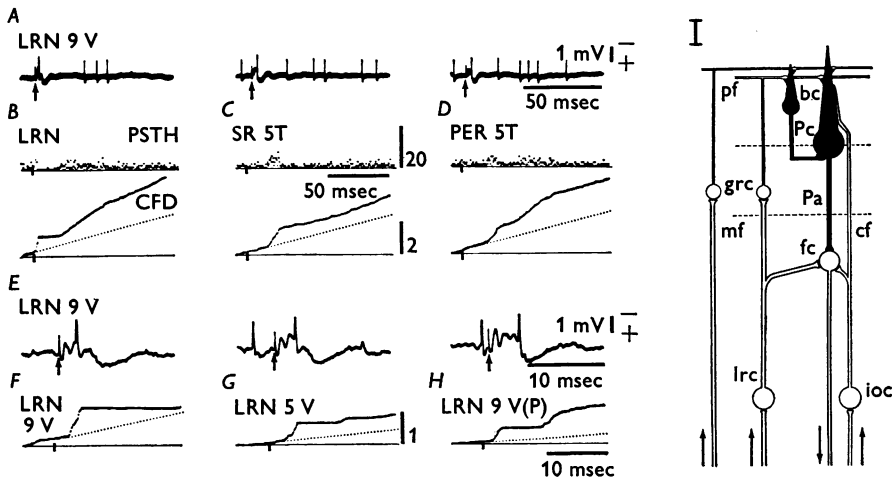


Fig. 13. Responses of fastigial neurone to stimulation of lateral reticular nucleus (LRN). *A*, specimen records of responses of a fastigial neurone to stimulation of LRN (9 V, 0·05 msec duration, 2 mm tip separation). *B*, PSTH and CFD for average of sixty-four responses as in *A* (cf. Fig. 5 *B*). *C* and *D* are PSTHs and CFDs similarly recorded but for responses evoked by stimulation of superficial radial (SR) and common peroneal (PER) nerves. *E* is similar to *A* but recorded at much faster sweep speed, *F* being the CFD. *G* is the CFD when the stimulus was reduced to 5 V and *H* when the stimulus of 9 V was applied slightly more posteriorly in the LRN. PSTHs and CFD of *B* to *D* have same scales, as also do the CFDs of *F* to *H*. I illustrates diagrammatically the essential features of the pathways to a fastigial neurone by cutaneous mechanoreceptors as modified in the light of the present investigation. Pc, Pa, Purkyně cell and axon; bc, basket cell; grc, granule cells; pf, parallel fibres; mf, mossy fibres; cf, climbing fibre; fc, fastigial cell; lrc, lateral reticular cell; ioc, inferior olive cell.

lateral reticular nucleus. The stimulus at the arrow evokes an impulse discharge in 2·3–3·8 msec, being later when there was an immediately preceding spontaneous discharge. The averaged record in *F* confirms the short latency (2·3–3·8 msec) of the nuclear cell response, which was also

observed with a weaker stimulus (*G*), or by a stimulus through another electrode in the nucleus (*H*).

This investigation has been carried out on more than two hundred nuclear cells and has led to the postulate of a schema of neuronal connectivities represented in Fig. 13*I*. The fast mossy fibre pathway is shown as giving no collaterals to the nuclear cell (fc), which receives its excitatory input via collaterals from the slow mossy fibre pathway in the bVFR tract that transverses a synaptic relay in the lateral reticular nucleus (lrc). Also

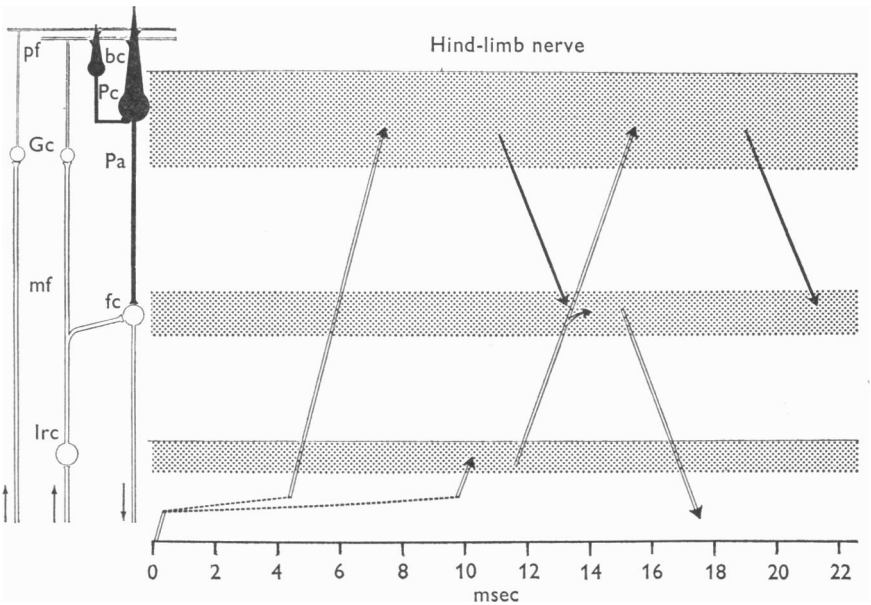


Fig. 14. Spatio-temporal plot of impulse transmission to and from the cerebellum for responses evoked by stimulation of a hind limb nerve. The horizontal bands symbolize the areas of neurones and synapses, from below upwards the lateral reticular cells (lrc), the fastigial cells (fc) and the cerebellar cortex, as illustrated in the diagram to the left, which is identical with that in Fig. 13*I*. Further description in text.

shown is a collateral from another delayed pathway, that for the climbing fibre (cf) that comes via a synaptic relay in the inferior olive (ioc). Evidently there is some special design feature in this diagram of neuronal pathways. Figs. 14 and 15 have been drawn to give the temporal pattern of operation of these neuronal pathways, and to illustrate the operational significance of this pattern.

Fig. 14 displays the time of impulse discharges and impulse propagations in the various pathways illustrated to the left. Nerve stimulation at

zero time results in a fast mossy fibre volley via the dorsal spino-cerebellar tract that reaches the cerebellar cortex in about 7 msec. It is shown with an intercept by an interrupted line that signifies the long traject up peripheral nerve and spinal cord. The slower mossy fibre pathway via the bVFR tract is shown also with an intercept, finally reaching the latera reticular nucleus at about 10 msec latency and evoking a discharge that propagates up to the cerebellum and also via a collateral to the fastigial nucleus. Synaptic excitation by this collateral evokes from the fastigial

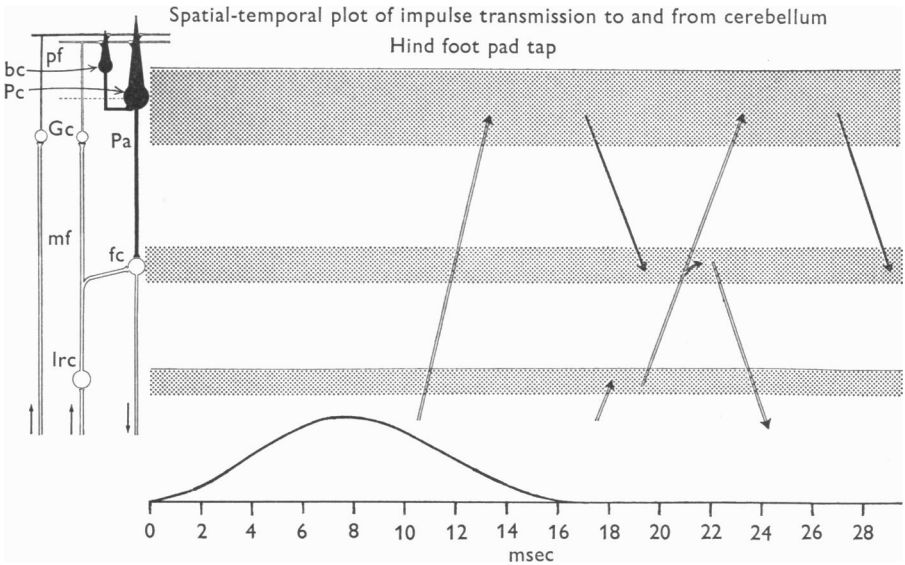


Fig. 15. Similar plot to that of Fig. 14, but for the approximate spatio-temporal co-ordinates of impulses generated by a tap to a hind foot pad that is shown in time course below.

cell a discharge after a delay of a millisecond or so, that is plotted as the downward sloping arrow. This is the postulated pathway for the fastigial cell discharges in Fig. 11. Meanwhile the fast mossy fibre input to the cerebellum will have produced a Purkyně cell discharge to the fastigial nucleus, as shown by the solid downward sloping arrow. The plotted times of discharge correspond with the average values for a large number of experiments and reveal that the Purkyně cell discharge arrives at the fastigial nucleus at approximate simultaneity with the lateral reticular discharge. This is the optimal timing for the interaction of these two opposed synaptic actions. Fig. 14 thus displays an excellent design of the pattern in time that is concerned in the operation of the cerebellum as a computer.

Fig. 15 displays a similar plot to that of Fig. 14, but for the responses to a brief tap the time course of which is drawn below. The fast mossy fibre volley is shown arriving at the cerebellum 5–6 msec later than with nerve stimuli, and evoking a Purkyně cell discharge at a similar delayed timing. The slight differences in relative timing from Fig. 14 are in accord with the averaged values for many experiments, but there is still the close temporal relationship of the Purkyně cell inhibition of nuclear cells and their excitation by the delayed mossy fibre pathway.

Figs. 14 and 15 show clearly that, if the fast mossy fibre pathway had effective excitatory action on the nuclear cells by axon collaterals, some sharp peripheral stimulation, as, for example, a tap to the toe pads, would have evoked a discharge from the nuclear cells many milliseconds before the arrival of any controlling influence from the cerebellar cortex, for example a Purkyně cell discharge counteracting the excitatory influence of the collaterals. Such an eventuality would relegate the whole neuronal machinery of the cerebellar cortex to a minor role in cerebellar function. Several recent theoretical papers (Blomfield & Marr, 1970; Ito, 1970; and Thach, 1972) have emphasized the pathway from fast mossy fibres to nuclear cells as the principal operative circuit for cerebellar function, relegating the output from the cerebellar cortex via Purkyně cells to a secondary modulating role, as illustrated in Fig. 16*B*. In part this proposal arises because it was recognized that axon collaterals from the fast mossy fibres would cause a discharge from the nuclear cells before the arrival of any controlling influence evoked from the cerebellar cortex by the mossy fibre input.

The theoretical position is now radically changed by the discovery that the fast mossy fibre input does not cause a significant excitation of the nuclear cells. In fact it is reversed in the light of the patterns in time illustrated in Figs. 14 and 15. Evidently the neural connectivities are designed so that the delayed mossy fibre input to the nuclear cells arrives at approximately the same time as the Purkyně cell inhibitory control. This control represents the expression of the computation carried out in the cerebellar cortex in response to the fast mossy fibre input. For the effective computational performance of the nuclear cells it is desirable that there be approximate simultaneity of the Purkyně inhibition and the axon collateral excitation, so that there is, as it were, a closely timed clash of these opposed influences. And this is ensured by the design illustrated in Fig. 13*I*. Thus the hypothesis illustrated in Fig. 16*B* has to be rejected in favour of that in Fig. 16*A*, and the cerebellar cortex is reinstated to the position of dominance in the cerebellar computations.

*The relative timing of the mossy fibre and climbing fibre inputs evoked by peripheral or cortical stimulation*

The clear separation in time between the mossy fibre (mf) and climbing fibre (cf) evoked responses of Purkyně cells was first reported by Eccles, Provini, Strata & Táboříková (1968*a*) and is illustrated in Fig. 5*A*, *B* for a peripheral nerve stimulation. Usually the cf response was at least 10 msec later than the mf response, the interval being 18 msec in Fig. 5*B*.

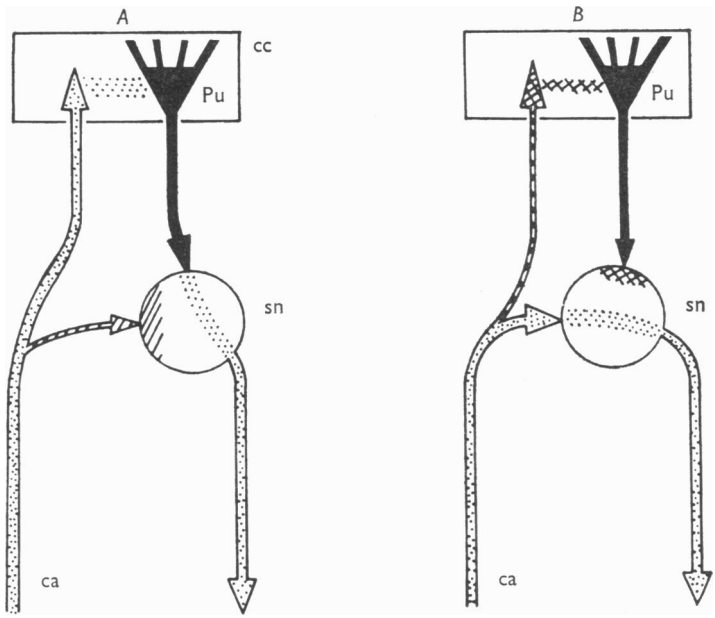


Fig. 16. Diagram showing two possible modes of interaction of the cerebellar cortex (cc) and the cerebellar nuclei (sn). In *A* the cerebellar afferent (ca) has a major influence on cc and on the Purkyně cell (Pu) response, the nuclear action being subsidiary. In *B* the nuclear action is paramount, the pathway through the cerebellar cortex and out by Pu being subsidiary. Further description in text (Ito, 1970).

In Fig. 17 there is similarly a temporal differential of about 19 msec for the responses evoked by the mf and cf inputs resulting from taps to toe 2. The first and second arrows mark the onsets of the mf and cf-evoked responses. The weakest stimulus (0·2 mm) evoked only mf responses. Similarly it has been found (Provini *et al.* 1968; Kitai, Oshima, Provini & Tsukahara, 1969; Allen *et al.* 1972) that there is a differential of about 10 msec between the mf and cf responses evoked by stimulation of the sensori-motor cortex in the cat. In all these cases the principal cause of the

delay in the cf response is the delay in discharge of the inferior olivary cells that appear to be the sole cells of origin of climbing fibres (Eccles *et al.* 1967; Armstrong, Harvey & Schild, 1969; Faber & Murphy, 1969).

It can now be asked, what is the operational significance of this temporal pattern that seems so ubiquitous? One answer is that the climbing fibre axons also give excitatory collaterals to the cerebellar nuclei (Fig. 13*I*), and their delayed response has the advantage of ensuring an approximate

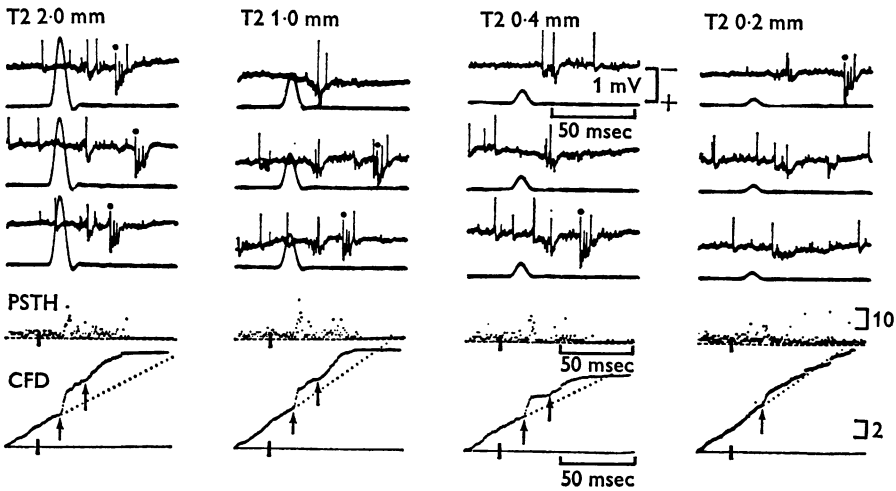


Fig. 17. Purkyně cell responses to graded mechanoreceptor stimulation. The three upper rows show specimen records of Purkyně cell responses and mechanical taps (cf. Fig. 5*A*), the climbing fibre responses being indicated by dots. The amplitudes of the taps to toe 2 are indicated. The PSTHs and CFDs are formed by summation of sixty-four traces in 256 bins of 0·5 msec each. The upper time scale obtains for all specimen records, and the other time scales for all PSTHs and CFDs. Count scales as in Fig. 5 *B* for PSTH and CFD. Other conventions as in Fig. 5. Chloralose anaesthesia and recording in lobule IV of lateral vermis.

synchronism with the delayed mossy fibre excitation. However, one suspects that this temporal pattern has a further operational significance. In this connexion the suggestion of Szentágothai (1968) and Marr (1969) may be of significance. If, as they suggest, a climbing fibre impulse acts on a Purkyně cell dendrite as an instruction to modify the parallel fibre synapses active at about that time, a precise temporal relationship should be of importance. The observed differential of about 10 msec between the mf and cf inputs might be the optimal timing for producing a modification that is postulated to be an elemental learning response. Unfortunately experimental testing of this hypothesis has failed to discover any significant

modification even after some hundreds of parallel fibre-climbing fibre inputs to Purkyně cells with a 10 msec time discrimination (J. C. Eccles, D. Marr, N. H. Sabah, R. F. Schmidt and H. Táboříková, unpublished observations). There has been much discussion of the role of the cf input in relation to the operational performance of the cerebellar cortex, but as yet there has been no clear experimental testing of the diverse theories. The challenging observations are that a localized peripheral or central stimulus often evokes both mf and cf responses of the same Purkyně cell, as in Fig. 17 (Eccles *et al.* 1972*d*; Thach, 1972; Ferin, Grigorian & Strata, 1971), and that these responses have a temporal differential that usually is about 10 msec.

### *Conclusions*

It has been stated earlier that reliability of computation by the cerebellum is secured by having many neuronal lines more or less in parallel, with at each stage divergence and convergence so that there is an automatic averaging, and this will ensure reliability. In our experimental investigations on single neurones reliability was secured by averaging many successive responses – 128 in Fig. 5 and 64 in Figs. 6, 7, 9, 11, 12, 13. Such sequential averaging is inadmissible in the normal operational performance of the cerebellum in the control of movement. The computation has to be done on the basis of single inputs that are generated, for example, by some movement. An approximate equivalence to such sequential averaging can be secured by the neural design with many operational lines in parallel, as is indicated by the divergence and convergence numbers in Table 1. Fig. 18 shows diagrammatically the anatomical basis for averaging on successive target neurones. For example the four Purkyně cells (*A*) converge on one nuclear cell (*a*), and likewise for the Purkyně cells in rows *B*, *C* and *D* and the nuclear cells *b*, *c* and *d*. In the attempt to simplify the diagram an equivalent divergence of the Purkyně cell by axonal branching has been omitted. A further convergence is shown for axonal projections of nuclear cells *a*, *b*, *c* and *d*.

At the most this diagram serves to indicate the manner in which a cluster or colony of cells with similar responses can converge on the same target neurones and so effect averaging with the resultant reliability of the computation. In this context it is important to recognize that the neural cost of this reliability is prodigious. The only biological justification for the immense numbers of neurones in the cerebellum must be in terms of the reliability of the cerebellar computations. However, we have but little understanding of the way in which such enormous numbers of neurones can be effectively organized to enhance reliability. For example, we can give no operational meaning to the immense population of granule cells –

$3 \times 10^{10}$ in the human and $2{\cdot}2 \times 10^{9}$ in the cat cerebellum. One tenth of even one hundredth would appear to be adequate in terms of our limited understanding.

The cerebellum offers remarkable opportunities for experimental investigation: there is a relative simplicity of the neuronal connectivities;

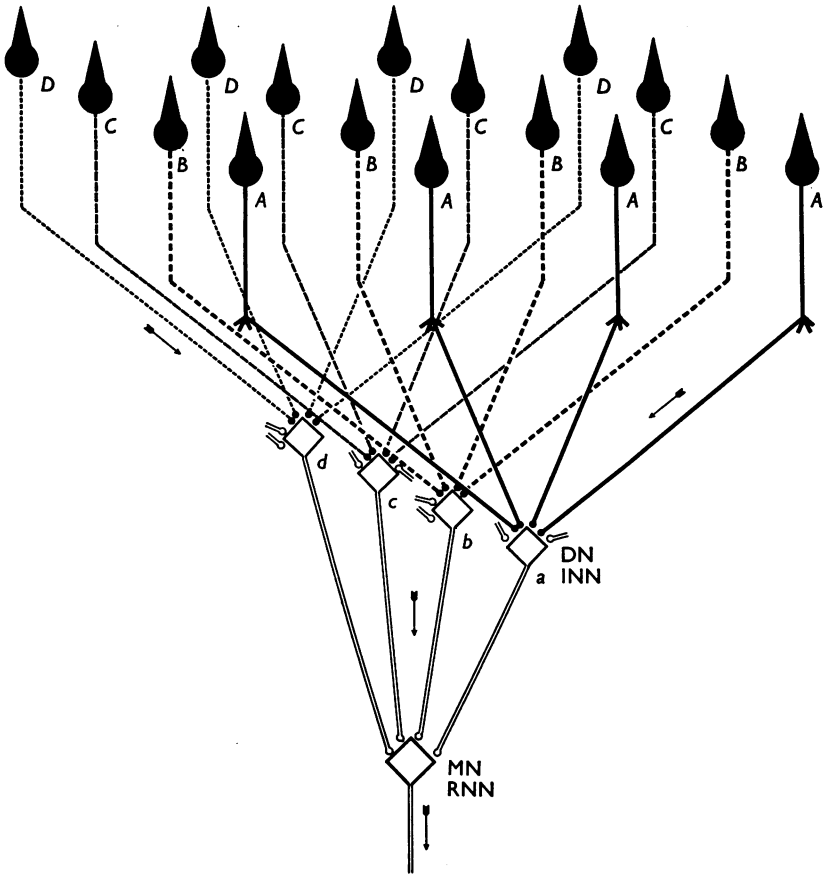


Fig. 18. Diagram showing convergent operation of Purkyně cells. An array of sixteen Purkyně cells in four groups, *A*, *B*, *C*, *D*, project to four target neurones, *a*, *b*, *c*, *d*, that in turn project to one neurone next in the transmission line. The target neurones can be, for example, Deiters' neurones or interpositus nucleus neurones, DN or INN, the former projecting to motoneurones, MN, the latter to red nucleus neurones, RNN. The existence of other branches of the first transmission lines is indicated. It is to be noted that the diagram is highly schematic, and completely neglects all the overlapping connectivities that there would be for the original four groups, *A*, *B*, *C*, *D*. The Purkyně cells are all inhibitory, hence are symbolized in black as also are their synapses. All other cells and transmissions are excitatory, and are shown open.

the five neuronal species have been functionally identified and their main operational properties have been defined; the functions of the two input lines (mossy fibres and climbing fibres) have been identified; the only output line is from the Purkyně cells, that thus have the role of reading out the computation by the neuronal machinery of the cerebellar cortex and transmitting their coded message to the nuclear cells; the operational features of the nuclear cells are now defined with their background excitation being sculptured by the inhibitory Purkyně cells, or enhanced by the disinhibitory action of these cells. In the attempt to understand the mode of operation of the cerebellum a further advantage is that it can be regarded as a computer and so it should be a rewarding project to design models based to some extent on known properties of computers. For all these reasons it seems likely that the cerebellum may be the first fragment of the higher levels of the nervous system to be understood in principle, all the way from peripheral input to peripheral output. In this connexion the concept of the dynamic loop operation of the cerebellum would seem to be particularly apposite (Eccles, 1967, 1969*b*; Eccles *et al.* 1972*e*). According to this concept the computational machinery of the cerebellum is engaged in a continuous ongoing correction of movements in much the same way as occurs for a target-finding missile.

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