Exp. Brain Res. 15, 498—520 (1972)

Integration by Purkyně Cells of Mossy and Climbing Fiber Inputs from Cutaneous Mechanoreceptors

J.C. Eccles, N.H. Sabah, R.F. Schmidt and H. Táborříková

Department of Physiology and Biophysics, School of Medicine, State University of New York, Buffalo (USA)

Received January 3, 1972

Summary. The preceding two papers gave accounts of mossy fiber (MF) or of climbing fiber (CF) inputs to Purkyně cells under conditions where the other input was depressed by the experimental procedure. By utilizing either chloralose anesthesia or decerebration with sparing of the pyramidal tracts it has been possible to study the convergence of MF and CF inputs onto single Purkyně cells. The stimulation of cutaneous mechanoreceptors, the recording procedures for unitary Purkyně cell discharges and the computer averaging techniques were as previously described.

Testing by taps to the footpads evoked a combined MF and CF response more commonly than either response alone, and often both inputs were very effective. There was a tendency for such phasic CF responses to be more frequently observed than the tonic responses to pad pressure, but such responses did occur.

Purkyně cells were located by the usual procedure along the microelectrode tracks later identified in serial sections. Those cells activated by the fast MF inputs from the pad receptors were found to be closely associated in groups or colonies. The delayed MF inputs probably via spino-reticular pathways were more widely dispersed. The topographical relationships of these colonies are displayed on maps of the unfolded cerebellar cortex for lobules II to VI of both vermis and pars intermedia. In general these distributions of Purkyně cells activated from forefoot and hindfoot appear as islands in the larger fields that degeneration procedures exhibit for the cuneocerebellar and dorsal spinocerebellar tracts respectively. The CF inputs from the footpads also project to these same colonies, so that there are conjoint MF and CF colonies.

The several modalities of the cutaneous mechanoreceptors of the forefoot or hindfoot often participate in the receptive fields of individual Purkyně cells. Such a field may be restricted to one or other side of the foot, all tested cutaneous mechanoreceptors then sharing approximately in the same restriction. Finally it is shown how these experimental findings relate to the theories of cerebellar function, particularly to the dynamic loop hypothesis.

Key words: Cerebellum — Cutaneous mechanoreceptors — Mossy fibers — Climbing fibers — Integration — Purkyně cell groups

Already topographical studies have been undertaken for the field potentials generated by climbing fiber and mossy fiber inputs (Eccles, Provini, Strata and

Táboříková, 1968b; Kitai, Táboříková, Tsukahara and Eccles, 1969) and for the excitatory and inhibitory actions as revealed by the impulses discharged by individual Purkyně cells (Eccles, Faber, Murphy, Sabah and Táboříková, 1971c). However all these studies had the shortcoming that nerve stimulation was used to generate the inputs. This limitation was mitigated by applying the stimulation to nerves that were purely to muscles or to skin, and also by studying the effects of careful gradations of stimulus strengths so that the various modalities of the receptor organs were to some extent discriminated, as is often possible with the muscle afferents. No such modality discrimination on the basis of nerve threshold is possible with cutaneous stimulation (Hunt and McIntyre, 1960; Schmidt, 1969), hence the necessity for this present investigation using adequate stimulation of the cutaneous mechanoreceptors. However, imperfect as they were, these earlier investigations on the anterior lobe led to two general concepts: firstly that there is an ill-defined patchy distribution onto the cerebellar cortex of the mossy fiber and climbing fiber inputs from any particular afferent nerve; and secondly that the total input of information to the anterior lobe is broken up into an indefinite number of subsets of diverse composition, there being integration in a piecemeal rather than in a holistic manner.

The dynamic loop hypothesis of cerebellar control (Eccles, 1967, 1969) provides the general conceptual framework around which are organized the diverse observations of this paper and of the preceding papers of this series (Eccles, Sabah, Schmidt and Táboříková, 1972a, 1972b, 1972c). An initial enquiry will be made into the degree to which there is convergence onto the same Purkyně cell of the mossy fiber (MF) and climbing fiber (CF) inputs generated by cutaneous mechanoreceptor stimulation. These receptors will be stimulated in both a phasic and a tonic manner. Finally there will be a comparative study of the receptor fields of the forefoot or hindfoot that project to adjacent Purkyně cells. This study directly relates to the concepts of a patchy distribution of any particular input and the piecemeal integration by the individual Purkyně cells.

Methods

The method of experimentation has been fully described in the previous papers of this series (Eccles, Faber, Murphy, Sabah and Táboříková, 1971a, 1971b, 1971c). It should be noted that differentiation of the recorded potentials enabled the spike potentials generated by a single Purkyně cell to be much more clearly distinguished than would appear from the specimen records in some figures. Continuous monitoring gave assurance that the spike potentials of only a single cell were being averaged to give the PSTHs and the CFDs.

The only exceptional requirement for part of this present investigation is that both the climbing and mossy fiber inputs to the cerebellum be preserved. In the unanesthetized decerebrate cat there is severe depression of the climbing fiber input (Ferin, Grigorian and Strata, 1971; Eccles *et al.*, 1972b), while the mossy fiber input is severely depressed in pentothal anesthesia (Eccles *et al.*, 1972c). Two procedures have been employed in securing effectiveness of both inputs. In one (20 experiments) decerebration was performed by means of an electrode assembly in which two medial coagulating electrodes had a less deep penetration, so sparing the pyramidal tract at least in part. Our other procedure (6 experiments) was to anesthetize by an intraperitoneal injection of chloralose (50 mg/kg). It was usually necessary to give very small repeated intravenous doses of surital or pentothal (2 or 3 mg/kg) in order to control the chloralose seizures that provided disturbing inputs into the cerebellum. Unfortunately even such doses depressed the synaptic relay of mossy fibers to granule cells. It is not claimed that there was a normal level of mossy fiber and climbing fiber input in our experiments, but at

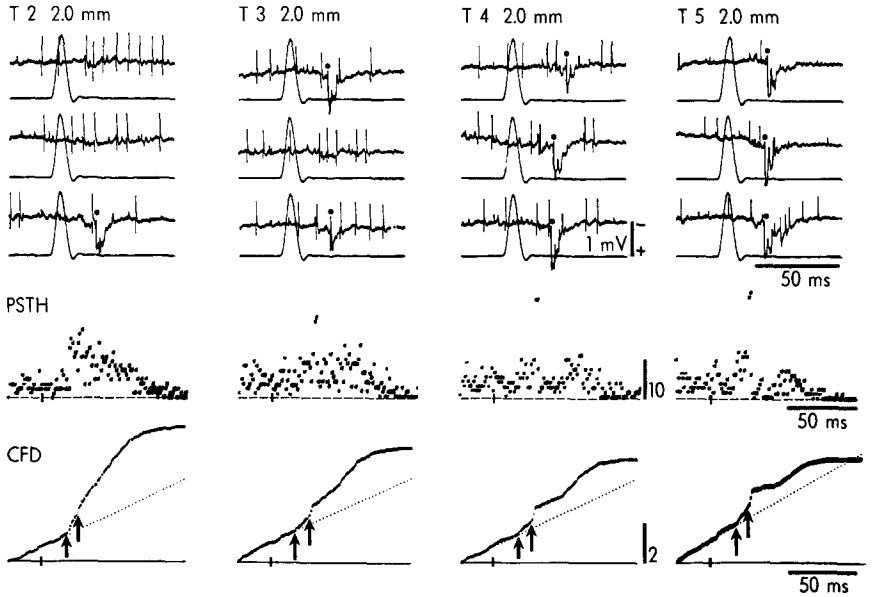


Fig. 1. *Mechanoreceptor input evoking MF and CF responses of a Purkyně cell.* In each of the specimen records of the three upper rows there are unitary responses of a Purkyně cell, and below is the time course of the tap applied to one of the toe pads of the hindfoot. Responses evoked by climbing fiber inputs are identified by a superposed dot. Above each column is indicated the toe stimulated and the size of the tap (2 mm). The two lowest records of each column give the poststimulus time histogram (PSTH) for 64 repetitions, there being averaging in 128 bins of 1 msec duration, and the cumulative frequency distribution (CFD) formed by progressive addition of all bin counts. The short vertical bars give the time of onset of the taps, and the sloping dotted lines of the CFDs give the projection of the initial rate of discharge. Same time and voltage scale obtain for all specimen records. Count scale for PSTH measures the total count per bin, while that for the CFD measures the average count for a single trace. Same time scale for PSTHs and CFDs. Arrows in CFDs mark approximate onsets of the MF and CF-evoked responses. Chloralose anesthesia and recording in lobule IV of lateral vermis

least we have many experiments in which both inputs were effective. All investigations were on the inputs from the ipsilateral forefoot or hindfoot. The most reliable identification of Purkyně cells is provided by the characteristic climbing fiber responses. When these were not present, as in Figs. 6, 7, 9, other criteria for identification were employed, as already described (Eccles *et al.*, 1971b).

Results

Phasic MF and CF Induced Responses

Particularly favorable conditions for testing the relationships of MF and CF inputs to a Purkyně cell are given in preparations under chloralose anesthesia with the supplement of occasional small intravenous injections of surital or pentothal. Figure 1 illustrates responses to taps of 2 mm amplitude to the four toe pads. In the specimen records for each toe there is evidence of an initial mossy fiber and a later climbing fiber excitation. For example the averaging of all twelve records shows that, at 18—28 msec after the onset of the tap, the single spike frequency was 130/sec as compared to 50/sec in the earlier part of the records. There

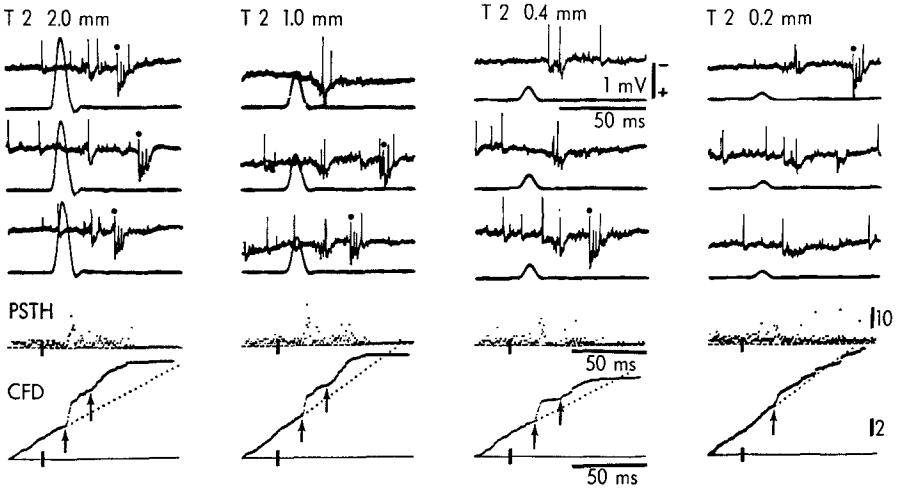


Fig. 2. *Purkyně cell responses to graded mechanoreceptor stimulation.* The three upper rows show specimen records of Purkyně cell responses and mechanical taps as in Fig. 1, but are for a Purkyně cell in a different experiment. The amplitudes of the taps to toe 2 are indicated. The PSTHs and CFDs are formed by summation of 64 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. 1 for PSTH and CFD. Other conventions as in Fig. 1. Chloralose anesthesia and recording in lobule IV of lateral vermis, but in a different experiment from Fig. 1, of responses to the hindfoot taps

is confirmation of this dual input in the averaged records, the poststimulus time histograms (PSTH) and cumulative frequency distributions (CFD), below each series of three specimen records. With taps to toes 3, 4 and 5 nearly all specimen records show a climbing fiber (CF) response. Including the 3 illustrated traces in each series, CF responses were observed as follows: toe 2, 7 recorded traces with 2 CF responses at latencies of 27.5 and 29 msec; toe 3, 5 recorded traces with 3 CF responses at 29—31 msec; toe 4, 10 recorded traces with 6 CF responses at 27—33 msec; toes 5, 13 recorded traces with 8 CF responses at 26—32 msec. In the CFDs of Fig. 1 the first arrows signal the onsets of the MF evoked discharges of the Purkyně cell, the latencies being 18 to 19 msec, while the second arrows indicate the times of the earliest CF-evoked responses as listed above. With toes 3, 4 and 5 the second arrow points to the onset of a second wave, which presumably can be attributed to the averaging of the CF-evoked responses. With toe 2 the CF responses were infrequent and there was no clear second wave in the CFD. These latencies for the MF (18—19 msec) and CF-evoked (26—29 msec) responses are in good accord with latencies recorded in experiments where hindfoot taps evoked either MF or CF responses alone (Eccles *et al.*, 1972b, 1972c). In Fig. 1 the MF and CF inputs would seem to be about equally effective in exciting discharges from the Purkyně cell. In making this estimate the MF-evoked responses have to be recognized as continuing during the CF-responses, as is indicated in the specimen records.

In Fig. 2 there are assembled the responses that were evoked in another experiment when the taps to toe 2 of hindfoot were progressively reduced in

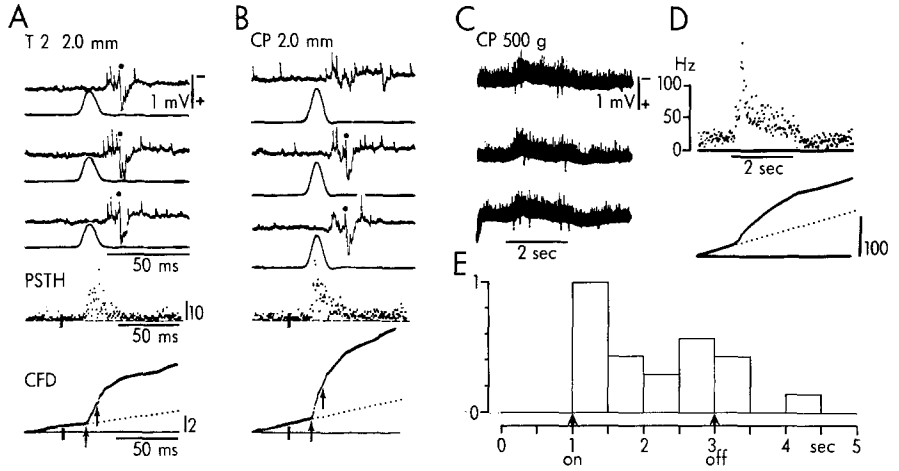


Fig. 3. *Phasic and tonic responses of a Purkyně cell to cutaneous mechanoreceptors.* In A and B are specimen records of responses evoked by taps of 2 mm to toe 2 and the central pad of the hindfoot, as indicated, together with the PSTHs and CFDs. There was summation of 64 repetitions in 256 bins of 0.5 msec. In C are three specimen records of response evoked by pressure on the central pad by 500 g for 2 sec at the time shown by the lower bar. There is fusion of the single spikes at this slow sweep speed, but the CF-evoked spikes appear as large positive-going deflections, as indicated in the specimen records of A and B. In D are the PSTH and CFD for 16 repetitions, there being 256 bins of 20 msec each. The Hz scale on the PSTH measures the average frequency of the Purkyně cell discharge, while for the CFD the scale measures the average count for a single response. E is a histogram formed by the counts of CF responses evoked in 7 traces as in C. The count was made for 0.5 sec sections of the 5.12 sec trace and averaged for a single trace, times of on and off being indicated by arrows. Decerebrate unanesthetized preparation with recording in lateral vermis of lobule III

amplitude. The specimen records show that the MF and CF-evoked responses of this Purkyně cell resembled those observed in Fig. 1, and are well shown by the two excitatory waves in the averaged responses with latencies of 16 and 33 msec (note arrows). With reduction in the size of the toe taps, both these waves were diminished and delayed, but with the weakest tap the CF-evoked response had disappeared leaving only a small MF-evoked response with a latency of 22 msec. Usually the threshold discrimination was in the reverse sense. For example the threshold for a brief tap was sometimes below 0.02 mm for the CF-evoked response (cf. Eccles *et al.*, 1972c).

Figures 1 and 2 give results from two Purkyně cells in two chloralose experiments. Altogether in four chloralose experiments 38 Purkyně cells responded to the inputs generated by taps to the pads of the hindfoot. In 13 of these cells taps to some at least of the pads produced a very effective excitation by both the MF and the CF inputs (cf. Figs. 1 and 2). In 6 others either the MF or CF input was weak, and in 4 others the CF input was good, but the MF input was detectable only by a prolonged inhibitory action, which presumably was effected via the MF input to basket cells or Golgi cells.

In some preparations the CF input from cutaneous mechanoreceptors survived the decerebration, presumably because all of the pyramidal tract had not been destroyed by the decerebrating coagulation. The CF and MF inputs were then

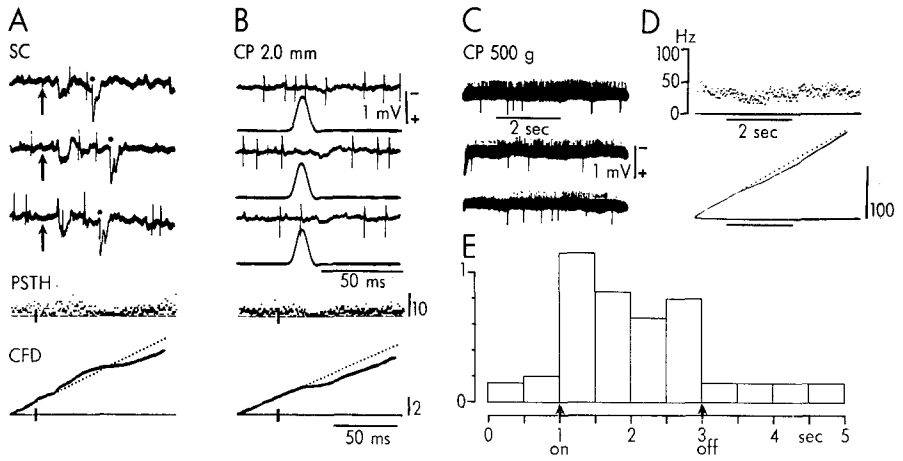


Fig. 4. *Phasic and tonic responses of a Purkyně cell to cutaneous mechanoreceptors of hindfoot.* General conditions of experiment as in Fig. 3, but as a variant there are in A the responses evoked by a stimulus to the sciatic nerve at a strength about 3 times threshold. The Purkyně cell was in the same cerebellum as that of Fig. 3 and was likewise in the lateral vermis of lobule III, but it was in another microelectrode track and about 1 mm distant. The histogram of E was compiled as in Fig. 3E, but was for the average of 20 responses

observed to project to the same Purkyně cell, just as in Figs. 1 and 2. For example in Fig. 3, taps to toe 2 and to central pad were both very effective in generating MF and CF inputs. The onsets of both the MF and CF-evoked discharges are indicated by the arrows in the two CFDs of A and B exactly as in Fig. 1. The respective MF latencies were both 18 msec, whereas both the CF-evoked responses had latencies of 27 msec. This study of phasic mechanoreceptor stimulation can be summarized by the statement that there may be convergence of the MF and CF inputs onto a Purkyně cell as in Figs. 1, 2 and 3. However we have often observed that there may be one input without the other, as for example occurred in 15 of the 40 Purkyně cells in our chloralose experiments.

Tonic MF and CF Induced Responses

Figures 3 and 4 are from an experiment in which a considerable climbing fiber activity survived the decerebration. In this experiment CF responses were evoked by pad stimulation of the hindfoot in 7 of the 12 Purkyně cells that responded to the MF input, as for example in the cell of Fig. 3. In Fig. 3C the specimen records for the application of a pressure of 500 g give no clear picture of the rapid sequence of single spikes, but the CF-evoked responses are readily visible as the positive spike-like deflections. The single spikes are averaged for 16 traces in the PSTH and CFD of D. There is a brief burst of up to 150/sec at the onset of the pressure, then within 0.5 sec a decline to about 50/sec and thereafter a slow further decline in frequency that terminated in an inhibitory off-effect. Such partly phasic, partly tonic responses have already been illustrated for the MF action on Purkyně cells (cf. Figs. 3, 8B, 10B of Eccles *et al.*, 1972b). The on-line computer was not used to average the CF-evoked responses seen in Fig. 3C, but in these three traces all of the responses occurred during the 2 sec application of the pressure or just after

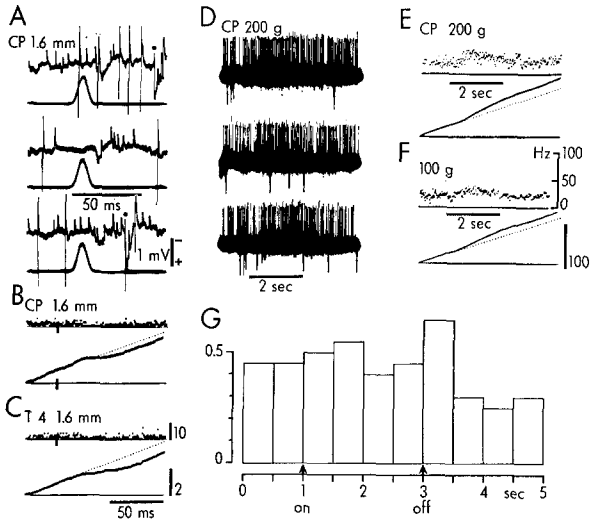


Fig. 5. *Phasic and tonic responses of a Purkyně cell to cutaneous mechanoreceptors.* In general the figure resembles Figs. 3 and 4, but is for a Purkyně cell in another decerebrate preparation. In A there are specimen records and in B the PSTH and CFD for a tap of 1.6 mm to the central pad. In C there are the PSTH and CFD for responses evoked by a tap of 1.6 mm to toe 4. The tonic responses were evoked as indicated by pressures of 200 g and 100 g for 2 sec, there being specimen records in D and PSTHs and CFDs in E and F. In G there is a histogram of the CF-evoked responses compiled as in Figs. 3 and 4, but for the average of 21 responses. The mechanical stimuli were applied to the hindfoot, and the recording was in the pars intermedia of lobule IV

its termination. For the purpose of plotting, the individual CF responses were counted for 0.5 sec bins, the average number per bin in a total of 7 traces being plotted in the histogram of Fig. 3E. Evidently pressure on the central pad evoked an initial phasic and later tonic CF response resembling the MF-evoked responses of Fig. 3D. It will be noted that there were almost no spontaneous CF responses.

In Fig. 4B tapping of the central pad did not evoke any CF responses, but only a MF-induced inhibition with a latent period of 21 msec and with a typical long duration (Eccles *et al.*, 1972b). However in A, stimulation of the sciatic nerve evoked a CF response in every one of the specimen records. The specimen records for the pressure in C resemble those of Fig. 3C in showing a tendency for the positive spikes of the CF responses to occur during the applied pressure to the central pad, and this is substantiated by the plotting in E of a histogram derived from counting 20 traces. E differs from the histogram of Fig. 3E in that there was a small spontaneous discharge and a more sustained effect during the pressure. By contrast the PSTH and CFD for the single spikes in Fig. 4D showed that there was a slight tonic inhibition during the pressure (cf. Figs. 8B and 9 of Eccles *et al.*, 1972b).

There were many different relationships between the MF and CF-evoked responses during a steady pressure. Usually the very low frequency of background CF-evoked responses was not appreciably changed during the pressure. Examples have already been illustrated where the single spike responses of the Purkyně cells gave

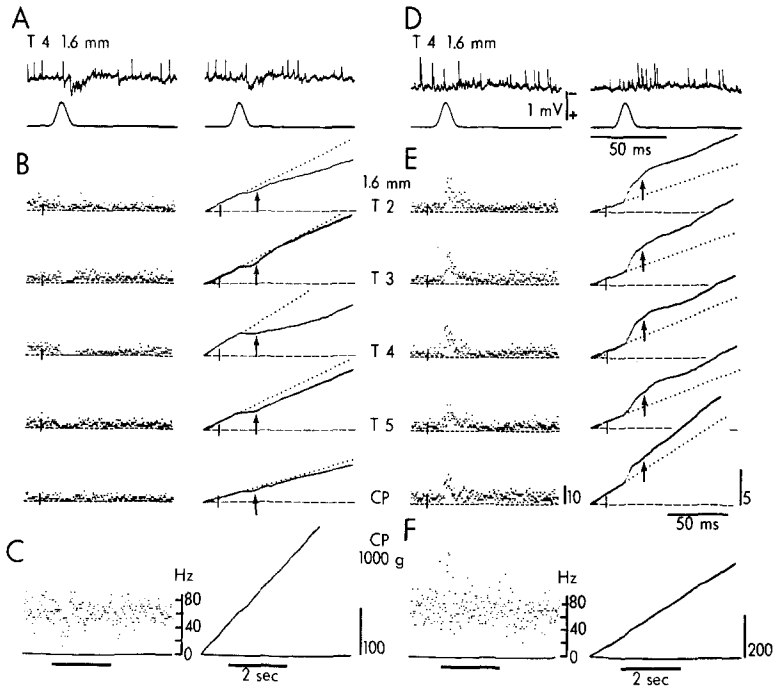


Fig. 6. *Cutaneous mechanoreceptors projecting to adjacent Purkyně cells.* In A are specimen records of responses of a Purkyně cell (cell H of Fig. 8) to 1.6 mm taps of toe 4, while in B are the PSTHs and CFDs of responses evoked in this cell by 1.6 mm taps to all five pads of the forefoot, there being summation of 64 responses in 256 bins of 0.5 msec each. C displays the PSTH and CFD for responses evoked by 1000 g pressure to the central pad for 2 sec, there being summation of 16 responses in 256 bins of 20 msec each. D, E and F are similar to A, B, C, but are for another Purkyně cell (cell J of Fig. 8) 660 μm distant 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, counts and frequencies. In B and E the arrows are at the latency (32 msec) that is used for the measurements in Fig. 8E. Both cells are in lobule V of the pars intermedia as indicated in Fig. 8. Decerebrate unanesthetized preparation

at the most phasic effects at "on" and "off" with no tonic effect (cf. Figs. 1K, 4B of Eccles *et al.*, 1972b). Likewise in Fig. 5D, G pressure did not appreciably change the frequency of the CF responses, which continued throughout the 2 sec pressure at the initial frequency of about 1/sec. This same Purkyně cell responded to taps to the central pad and toe 4 by a predominant inhibition (Fig. 5A, B, C), though in B a mild excitation appeared to precede the inhibition. In E and F pressure by 200 g and 100 g gave a pure tonic excitation.

Topography of Forefoot and Hindfoot Projections to Purkyně Cells by Fast Mossy Fibers as Defined Below

Hitherto the reports in this paper and in the two preceding papers (Eccles *et al.*, 1972b, 1972c) have been concerned with the impulse discharges evoked in individual Purkyně cells by various inputs from the mechanoreceptors of the forefoot and hindfoot. The cells have been treated as isolated units with only general reference to their location in the cerebellum. In this section there will be

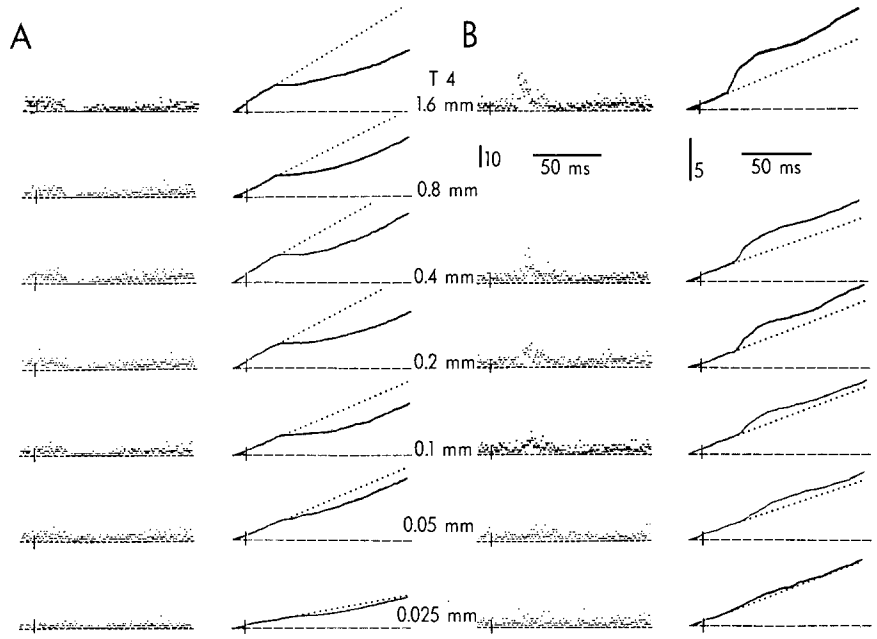
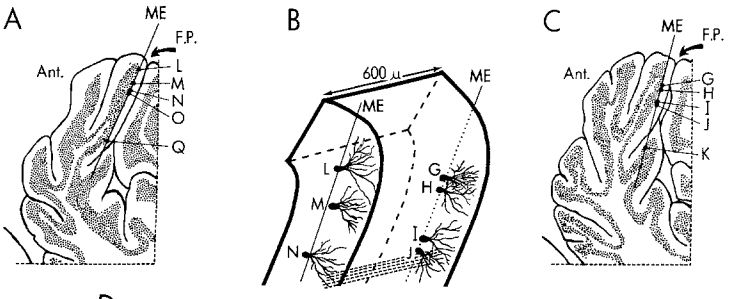


Fig. 7. *Graded stimulation of cutaneous mechanoreceptors projecting to adjacent Purkyně cells.* In A are PSTHs and CFDs for responses evoked in the same Purkyně cell (H) as in Fig. 6A—C, but for graded sizes of taps, 1.6 mm to 0.025 mm, to toe 4 of the forefoot as indicated. B is a similar display for cell J of Fig. 6D—F, except for the ommission of the 0.8 mm tap. All averages are for 64 responses in 256 bins of 0.5 msec. Same time and count scales throughout

an account of the responses of adjacent cells to phasic and tonic inputs and an attempt to view these cells as units in functional assemblages.

In Fig. 6 there are illustrated the responses of two Purkyně cells (labelled H and J in the serial order of this experiment) in the same microelectrode track and 660 μm apart (Fig. 8C). Specimen records in A and the PSTHs and CFDs of B show that taps of 1.6 mm to the forefoot pads induced inhibition of cell H with a latency of 17 msec, toe 4 being the most potent in this respect. By contrast these same inputs induced excitation in cell J (D, E) with a latency of 15 msec, toes 2, 3 and 4 being the most potent. C and F reveal that neither cell gave the slightest tonic response to pressure of 1000 g to the central pad. In Fig. 7 there are displayed responses of these two cells to graded mechanical stimulation of toe 4. There is a remarkable parallel between the sizes of the respective inhibitions (A) and excitations (B) as the toe 4 taps were diminished from 1.6 mm to 0.025 mm. The threshold was below 0.025 mm for both responses. It would appear that the MF input from the footpad is channelled to the two Purkyně cells in an equivalent but opposite manner.

Figure 8C is an enlarged tracing of a parasagittal section of the pars intermedia of the anterior lobe. The microelectrode track in Fig. 8C was identified in the subsequent histological examinations and was in lobule V just anterior to the fissura prima. Cells H and J are marked along with the three other cells (G, I and K) also recorded from in this track. In the Table labelled E there are entered the



D

	CP	T 2	T 3	T 4	T 5
L	0.7	1.3	0.7	1.1	2.5
M	1.3	0.6	0.5	0	0
N	1.2	0.5	1.5	1.2	1.6
O	-0.8	-0.2	-	-0.2	0
Q	-0.8	-0.5	-	-	-0.8

E

	CP	T 2	T 3	T 4	T 5
G	0.4	0.3	-	-	0.2
H	-0.5	-0.7	-0.8	-1.3	-0.8
I	-0.5	-0.6	-	-	-0.8
J	1.7	2.7	2.7	2.5	2.0
K	-0.1	-0.2	-0.1	0	0

Fig. 8. *Locations and responses of Purkyně cells along two microelectrode tracks.* In A and C the microelectrode tracks (ME) are drawn on two parasagittal sections of the same cerebellum in the pars intermedia of the anterior lobe, the plane of A being 0.6 mm lateral to that of C. The tracks were in the same transverse plane just anterior to the fissura prima (FP) and fortunately ran along the Purkyně layer so that several cells were recorded from in the same folium. In B is a perspective drawing with diagrammatic representation of cells L—N of track A and G—J of track B. This drawing shows how a beam of parallel fibers could excite the Purkyně cell N of A and J of B. At the same time this beam would also induce inhibition in cells I and H by virtue of the transverse distribution of the axons of basket cells excited in the region of J. In Tables D and E are the measurements of the excitatory or inhibitory actions of taps of 1.6 mm to the five forefoot pads. The measurements were made on the CFDs at a latency of 32 msec from the onsets of the taps, as indicated by the arrows in Figs. 6 and 9. The numbers give the average increase (+) or decrease (—) in the number of impulses up to that time, as calculated from the CFD scales of Figs. 6 and 9. The values for L and M of Table D are derived from Fig. 9, and those of H and J in Table E from Fig. 6. Short bars in Tables D and E signify that this action was not tested

responses evoked in these five cells by pad taps of 1.6 mm for each of the pads of the forefoot. The positive numbers refer to the average numbers of cell discharges evoked per trace, while the negative numbers are the deficits in cell discharges due to inhibition. All measurements were made at 32 msec after the onset of the tap, as indicated in Fig. 6B and E. Zeros indicate no response. Short horizontal lines signify that no test was made. The principal interest of this Table is in showing that cell J was in a strong focus of parallel fiber excitation. The inhibition of cells I and H presumably can be attributed to the basket cells also activated by that parallel fiber excitation. The distance of 660 μm across the folium is well within the transverse traject of basket cell axons in their inhibitory action on Purkyně cells (Eccles, Sasaki and Strata, 1966; Eccles, Ito and Szentágothai, 1967). There is a sharp contour between cells J and I, which is a strong topographic feature because the reversal of response occurs within 50 μm. Though only 70 μm from cell H, cell G gave small excitatory responses, which presumably are attributable to another excitatory parallel fiber beam. Finally cell K gave only slight responses, as might

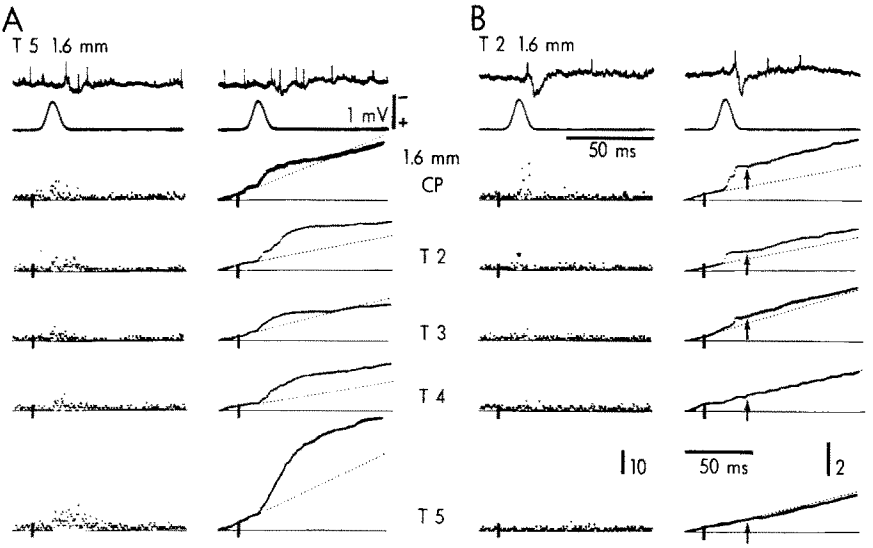
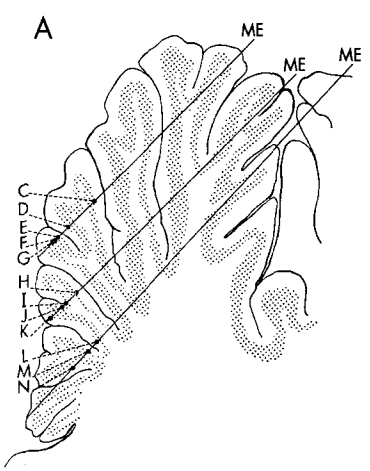


Fig. 9. *Phasic responses of two adjacent Purkyně cells to cutaneous mechanoreceptors.* In A are specimen records of responses of a Purkyně cell (L of Fig. 8) to taps of 1.6 mm to toe 5 and the PSTHs and CFDs evoked by taps of this amplitude to all pads of the forefoot. In B is a similar series but for another Purkyně cell (M of Fig. 8) 0.8 mm deeper in the same microelectrode track. The specimen records are for taps of 1.6 mm to toe 2. The arrows on the CFDs of B are at the latency (32 msec) that is used for the measurements in Fig. 8D. The locations of these cells are illustrated in Fig. 8 (L and M), being in the pars intermedia of Lobule V in a track 600 μm lateral to the track for cells H and J of Figs. 6 and 7. All PSTHs and CFDs have the same time and count scales. Decerebrate unanesthetized preparation

be expected because it was in another sub-folium far removed from the action centering on cells H and J.

A further exploration of the topography of forefoot projection to this same pars intermedia is illustrated by the responses of Purkyně cells L and M in a microelectrode track shown in a parasagittal section (Fig. 8A) 600 μm more lateral than that of Fig. 8C. In Fig. 9A and B are displayed specimen records and the averaged responses for cells L and M respectively. There were large differences in the responses of these two cells to inputs from the different pads. For example toe 5 had the largest excitatory input to cell L and zero action on cell M, as also had toe 4. The central pad had the largest input to M, but its input to cell L was relatively small. There was no inhibitory action from any pad. There was still another pattern of input to cell N, whose responses were illustrated in an earlier paper (Fig. 2 in Eccles *et al.*, 1972b), there being large excitatory inputs from all pads except that of toe 2. The whole ensemble of the responses of cell L, M and N as well as of two additional cells O and Q are shown in the Table of Fig. 8 labelled D, all cell locations being marked in the track of Fig. 8A. It is to be noted that there were mild inhibitory actions or no action at all from the pads onto cell O although it was in very close proximity to N. The zero for toe 5 input to O is in strong contrast to its large excitatory input to N. Possibly the zero for toe 5 is due to a balance of excitatory and inhibitory action. Cell Q is so remote from the M, N, O cluster



B

		CP %TO	CP PH	T 2	T 3	T 4	T 5	Sc
	C	-15	0.8	-0.6	-0.3	0.5	0	0.4
	D	-35	-0.7	0.2	-	-	-0.2	2.1
	E	10	0.6	0	-	-	0.5	1.0
	F	10	-0.3	0.3	-	-	0.3	1.6
	G	0	0.4	-	-	-	-	1.7
C	H	-	-0.2	0	-	-	-0.3	1.0
	I	65	0.5	0.4	-	1.0	0.6	1.6
	J	-50	-0.2	0	0.2	-0.6	-0.3	0.6
	K	-75	1.5	0.7	0.5	1.1	1.3	3.0
D	L	-40	1.1	0.4	0.2	0	0	0.5
	M	0	0	-	-	-	-	1.2
	N	0	0	-	-	-	-	0

Fig. 10. *Locations and responses of Purkyně cells along three microelectrode tracks.* In A the microelectrode tracks are drawn on a parasagittal section (cf. Fig. 8A, C) that was approximately between vermis and pars intermedia, and on these tracks are marked Purkyně cells C to N. Actually the track for C to G was about 800 μ m. more lateral than the other two tracks. B to D give measurements of the excitatory (+) or inhibitory (—) actions on Purkyně cells C to N to taps of 1.6 mm to the five pads of the hindfoot, the measurements being made exactly as for those of Fig. 8D, E. In addition the first column gives the percentage changes in frequency (+ or —) of discharge at 1.5 sec after onset of 500 g pressure on the central pad, and the last column gives the excitatory or inhibitory action by stimulation of the sciatic nerve, the measurements being made at a latency of 25 msec, in contrast to 32 msec for the pad taps. Short bars signify that no test was made

that the observed inhibitory inputs must give indication of a quite separate mossy fiber input to granule cells and so to basket cells.

In Fig. 8B is a perspective drawing of the folium of pars intermedia just anterior to the fissura prima. The two microelectrode tracks with their associated Purkyně cells are shown. The dominant excitatory actions for the foot pads onto cells N and J are in good agreement and are explicable by the same beam of excited parallel fibers which easily could extend for the 600 μ between the two tracks as indicated in Fig. 8B (cf. Eccles, Ito and Szentágothai, 1967, Chapt. VI). Despite this satisfactory relationship for cells N and J, it can be anticipated that it would be a rarely observed phenomenon because of the complexity of the mossy fiber distribution in the granular layer (cf. Eccles *et al.*, 1967, Chapts. II and VII). The situation obtaining for a mossy fiber input from peripheral stimulation would be much more complex than with the generation of a beam of parallel fiber impulses by direct stimulation (Eccles, Sasaki and Strata, 1966). A good illustration of this complexity has already been provided by the sharp difference between the receptive fields for cells N and O despite their close proximity.

In the sagittal section of Fig. 10A there are shown three tracks in the zone between vermis and pars intermedia that pass down into lobules IV and III. Altogether in these three tracks 12 Purkyně cells were recorded from as individual units, and most were very effectively influenced from the mechanoreceptors of the

hindfoot. The responses of three of these cells have already been illustrated in preceding papers (I in Fig. 3A, B, C, and K in Fig. 10 of Eccles *et al.*, 1972b; I and J in Fig. 2, Eccles, Sabah, Schmidt and Táboříková, 1971). In Tables B, C and D of Fig. 10, the responses to taps were measured at 32 msec from their onset as in Figs. 6, 8 and 9. Cells C to G had small phasic excitatory and inhibitory inputs from the hindfoot mechanoreceptors, with also some mild tonic inhibition to cells C and D. There were much stronger influences on the cells I to K that gave mixed excitatory and inhibitory phasic responses. However, the tonic influences were more remarkable because a strong excitation to I passed over to a strong inhibition with cells J and K (Figs. 2 of Eccles, Sabah, Schmidt and Táboříková, 1971; and 10 of Eccles *et al.*, 1972b). Cell L in another track responded by a phasic excitation and a tonic inhibition, thus resembling cell K but with weaker responses. The still deeper cells M and N gave no responses to cutaneous mechanoreceptors. Hence in Fig. 10 there is evidence for a group of Purkyně cells I, J, K and L that have good inputs from the mechanoreceptors of the hindfoot, particularly the tonic mechanoreceptors. This input shows a sharp transition from tonic excitatory for cell I to tonic inhibitory for cells J and K. As with the excitatory-inhibitory transition in Fig. 6, this reversal can likewise be interpreted as due to a tonically excited beam of parallel fibers that directly excites cell I and also in that location basket cells which send their axons transversely to inhibit tonically cells J and K. Since cell K is over 1 mm transversely from cell L, it is doubtful if the basket cells responsible for the tonic inhibition of cell K can also function in tonically inhibiting cell L. Conceivably there are subsidiary mossy fiber inputs between cells K and L in addition to the input that caused such a powerful tonic excitation of cell I and inhibition of cells J and K. The last column of Tables B, C and D in Fig. 10 gives the responses evoked by a single stimulation of the ipsilateral sciatic nerve at about 3T strength. The measurements were made as for the taps to the toes, but at an interval of 25 msec after the stimulus. As would be expected from the much larger and more diversified input, the evoked responses were usually larger than for the taps, and strongly involved some cells such as G, H and M that were little if at all affected by the toe taps or the pressure.

The extreme folding of the cerebellar cortex makes it difficult to convey in a diagram the topographical relationships of Purkyně cells that are encountered in a series of microelectrode tracks. The illustration in Fig. 8 was possible because of the very fortunate circumstance in which two tracks ran tangentially along the cortex of the same folium. As a consequence there was unitary recording from 8 Purkyně cells that lay in the same plane of cerebellar cortex, as is illustrated in Fig. 8B. It was thus possible to account in part for the responses of these Purkyně cells by reference to the excitatory action of a beam of parallel fibers running along the folium and to the transversely distributed inhibition by basket cells excited by that beam.

In order to represent all the Purkyně cells investigated in an experiment on such a planar cortical map, it is necessary to construct a map of the unfolded cerebellar cortex, as has been done, firstly by Braitenberg and Atwood (1958) and then by Voogd (1964) and by Provini, Redman and Strata (1968). The map of Fig. 11A is derived from that drawn by Provini *et al.* with minor modifications. As an inset there is a parasagittal section of the cerebellar cortex in the medial zone

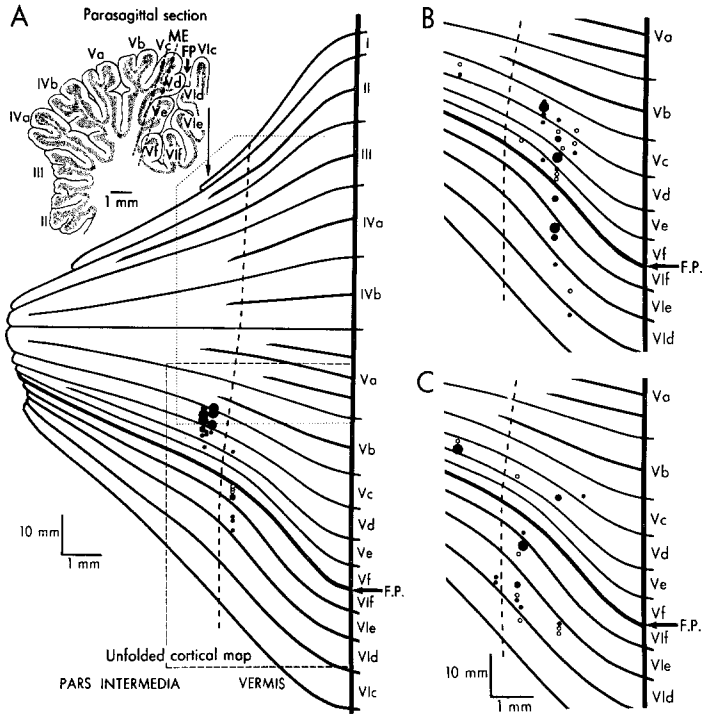


Fig. 11. *Maps on unfolded cerebellar cortex of mossy fiber inputs from forefoot pads to Purkyně cells.* The inset in A shows a parasagittal section at a medial position of the pars intermedia, and on it are marked the lobules and sublobules with the Larsell (1953) designations. Also shown are 2 microelectrode tracks with 8 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 a broken line, and the midline 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 fiber input from the forefoot pads. Small open circles signify zero response, and the three sizes of solid circles give an approximate measure of the sizes of the excitatory or inhibitory responses. For example the largest size is scored by excitatory responses of 1 or more in the Tables of Fig. 8D, E or 10, or by inhibitory responses that silenced the discharge. B and C give similar maps for two other experiments with forefoot pads, but only part of the unfolded map is reproduced, namely the part enclosed by the broken line in A. All experiments were on unanesthetized decerebrate preparations

of the pars intermedia, at the site on the unfolded cortex approximately shown by the vertical arrow. The unfolded cortex is so enormously extended in the longitudinal direction that it is convenient to draw the map on a 10 to 1 scaling as indicated. The various lobules and sublobules are given the Larsell (1953) nomenclature in the section, and this labelling is reproduced on the medial side of the map. The curved lines denote the foldings at the depths of the sulci, that for the fissura prima, FP, being intensified. Also a broken line gives the paravermal sulcus which is the demarcation between the vermis and the pars intermedia.

Shown on the section are two of the microelectrode tracks, identified in histological section, and marked thereon by dots are the locations of 8 Purkyně

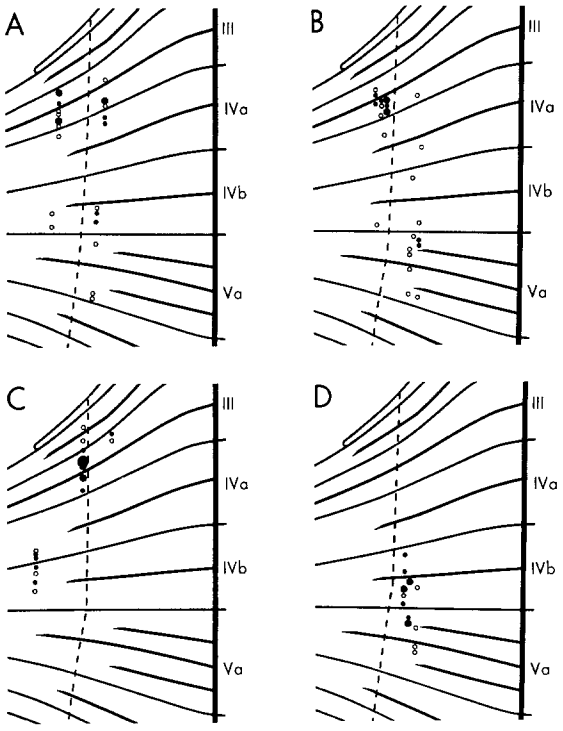


Fig. 12. *Maps on unfolded cerebellar cortex of mossy fiber inputs from hindfoot pads to Purkyně cells.* Only part of the unfolded map is reproduced, namely that outlined by the dotted line in Fig. 11A. A to D give the maps for Purkyně cells in four experiments, all being decerebrate and unanesthetized. The same conventions are employed as in Fig. 11

cells. These locations can be converted into coordinates formed on the one hand by distance from the midline and the paravermal sulcus, and on the other by the site in the Larsell lobule configuration. Then each Purkyně cell can be plotted in the unfolded map, as shown in Fig. 11A, each cell being given a size approximately representing the size of the average response evoked by a tap of 1.6 mm to the foot pads, much as in the Tables of Figs. 8D, E and 10B, C and D. In the first place our efforts were concentrated on mapping the distribution of the mossy fiber input carried by the fast pathways from the footpad receptors, which would be the exteroceptive divisions of the dorsal spinocerebellar and cuneocerebellar tracts. In our experience this discrimination could be achieved by restricting our measurements to Purkyně cell discharges that had a latency from the onset of the tap not in excess of 20 msec for the hindfoot and 18 msec for the forefoot. Since our objective was to display on the map the sizes of the mossy fiber inputs to the Purkyně cells, the sizes of the excitatory and inhibitory actions were plotted for each cell on the same convention of three sizes of filled circles. In Fig. 11A there is seen to be a major focus of action from forefoot pads onto cells of lobules Vc in a medial zone of the pars intermedia with a weaker action on cells of lobules Vd and e. However there was also a subsidiary focus in the lobules VI f and e in the lateral vermis.

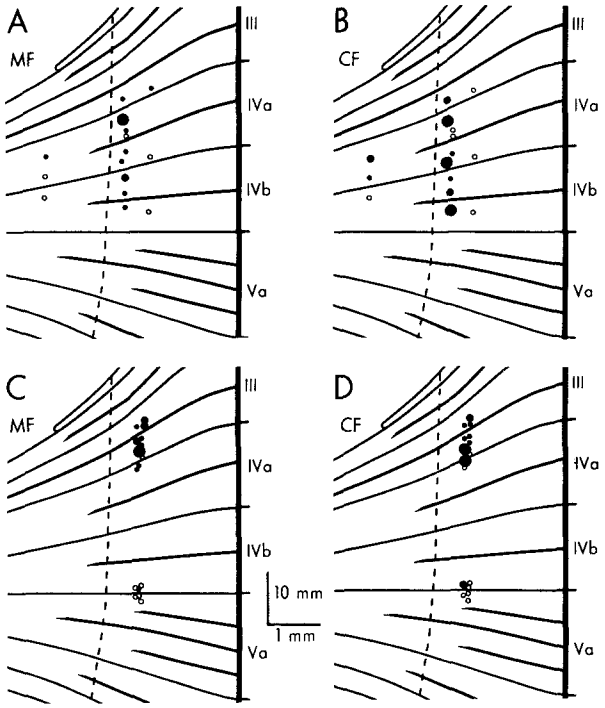


Fig. 13. *Maps on unfolded cerebellar cortex of mossy fiber and climbing fiber inputs from hindfoot pads to Purkyně cells.* All maps are for the part of the unfolded cortex outlined by the dotted line of Fig. 11A. In A and B are the maps for MF and CF inputs respectively in a preparation anesthetized by chloralose with slight additional pentothal. C and D are likewise for MF and CF inputs in another experiment which was decerebrate and unanesthetized with partial sparing of the pyramidal tracts. The same conventions are employed as in Fig. 11

In Fig. 11B and C are similarly enlarged maps of the Purkyně cell locations for fast mossy fiber action in two other experiments on forefoot pads. B was our most extensive investigation, there being 15 microelectrode tracks and recording from 25 Purkyně cells. In C the respective numbers were 8 and 18, and in A, 8 and 21.

The three maps of Fig. 11A, B and C have several common features. Firstly, in each there were several distinct foci of mossy fiber action, at least 4 in B and C, separated by Purkyně cells with zero input. Secondly, in every case, there were foci in lobule VI as well as lobule V. Thirdly, there were always foci in both the pars intermedia and the vermis.

Figure 8 illustrates the only other experiment on the forefoot pads of a decerebrate unanesthetized animal in which there were many microelectrode tracks (6) with subsequent histological identification. There was no exploration of lobule VI, but otherwise there was good agreement with Fig. 11A, B and C.

There has been a more intensive investigation of the topography of the fast mossy fiber input from the hindfoot pads. In Fig. 12 the Purkyně cells responding in four experiments are plotted on the unfolded cerebellar cortex as depicted in Fig. 11A, where the dotted lines outline the areas shown in Figs. 12A to D. The maps of the fast mossy fiber inputs in 12A and B show clearly two foci, one very

anterior, mostly in lobule III of the pars intermedia and vermis, and another much more posterior in lobule IVb or Va of the vermis. In C there was also the very anterior focus, and a subsidiary focus more posteriorly in lobules IVa and IVb of the pars intermedia. D may seem exceptional in that there was only the posterior vermal focus in lobules IVb and Va. However, there was no exploration of lobule III. Closer inspection reveals that separation by Purkyně cells with zero response defines 2 foci in D and probably 4 in A and 3 in C.

Altogether we have carried out investigations on hindlimb inputs via fast mossy fibers in 14 experiments on decerebrate unanesthetized preparations. The same general features recur in experiment after experiment. Firstly, there are the multiple foci of mossy fiber input with the distribution to a very anterior focus in lobule III or IVa and to a posterior focus in lobule IVb or Va. Secondly the foci are both in the lateral vermis and in the medial zone of pars intermedia. We have made no systematic attempt to explore medially in the vermis or laterally in the pars intermedia. There could well be additional foci in lobules IV or III of the pars intermedia. Recently it has been found that the fast mossy fiber inputs from the forefoot and hindfoot converge onto the same Purkyně cells that lie in a deep focus between lobules IVb and Va (Eccles, Sabah and Táboříková, unpublished observations).

Topography of MF and CF Projections to Purkyně Cells from Footpad Receptors

As illustrated in Figs. 1—5, taps to the footpads or pressure on the pads may activate by MF and CF input the same Purkyně cell. This occurs under the favorable experimental conditions provided by chloralose anesthesia or by the unanesthetized decerebrate with sparing of part of the pyramidal tracts. Figure 13 illustrates locations of Purkyně cells on the unfolded cerebellar cortex in two experiments in which taps to the hindfoot pads excited both MF and CF inputs. A and B are identical maps for 15 Purkyně cells that were isolated in a preparation under chloralose anesthesia, A giving the fast MF responses and B the CF responses under the same conventions as in Figs. 11 and 12. This figure serves to illustrate the earlier statement that there tended to be convergence of MF and CF inputs onto the same cells — in 8 out of 15 in Fig. 13A, B. There is a comparable convergence in Fig. 13C and D for a decerebrated unanesthetized preparation in which apparently there was sparing of at least part of the pyramidal tracts. Convergence of the two inputs occurred onto 8 out of the 16 Purkyně cells examined. The proportion is even higher, 8 out of 11, when the calculation is restricted to the cells that were activated by the pad taps.

Discussion

Focal Distribution of the Mossy Fiber Input to Purkyně Cells

The principal interest of Fig. 8 is that it displays a zone of Purkyně cells (L, M, N, H, I, J) that were all strongly influenced by the fast MF input from the cutaneous mechanoreceptors of the forefoot. Our sampling by two microelectrode tracks suggests that, in the relatively large area of the cerebellar cortex shown in Fig. 8B, there is a cluster of Purkyně cells with closely related mossy fiber inputs. This area would be at least 0.4 sq mm in area with a population of over 100 Purkyně cells (Palkovits, Magyar and Szentágothai, 1971) of which we sampled

only six. The membership of such a cluster or colony of Purkyně cells does not imply that these cells have identical receptive fields, but rather that there is much overlap in these fields so that individual Purkyně cells are each performing a related integrative function.

Similarly Fig. 10 illustrates for the hindfoot at least two colonies of Purkyně cells with related functions. The cells C, D, E, F, G were not strongly influenced from the foot pads, but each had a small fast MF input that in most cases was excitatory. There was some discrimination in the receptive fields of these cells (Table B in Fig. 10) and C and D were distinctive in that both had a mild tonic inhibitory input from the central pad. The other colony (I, J, K) was in a separate folium (cf. Fig. 10A), the inputs being quite distinctive for these three cells. This is shown in Table C of Fig. 10 for the phasic inputs from the foot pads, which were almost ineffective on H. However it was in the response to pressure on the central pad that this colony best displayed discriminative responses, tonic excitation for cell I, and tonic inhibition for cells J and K (first column of Table C). It has already been surmised that, though cell L also had a tonic inhibition, it was so remote from cells J and K that a separate MF input is probable, i.e. that L belongs to a separate colony at the base of the folium. In Fig. 12C cells K, J, I of Fig. 10 can be recognized as the three largest plotted points from above downwards, while cell L is the smaller point slightly above that cluster.

It may be surprising to apply the term colony to a group of cells such as H, I, J, N of Fig. 8 and I, J, K of Fig. 10 with such differences in their responses. The justification lies in the fact that they have much the same receptive fields, the differences in responses depending on the relative sizes of the excitatory and inhibitory effects that a mossy fiber input achieves by operation through the neuronal circuits in the cerebellar cortex (cf. Eccles, Ito and Szentágothai, 1967, Chapt. XII).

Figures 11 and 12 show that the fast MF inputs from the pads of forefoot and hindfoot have quite different locations in the cerebellar cortex. These different locations accord well with the distributions of the cuneocerebellar tract (CCT) and the dorsal spinocerebellar tract (DSCT) that were demonstrated by degenerative studies (Grant, 1962a, 1962b). This technique revealed that the MF input from CCT was to lobules V and the rostral slip of VI fronting the fissura prima, i.e. to lobules VIf and e, while the DSCT input was to lobules II, III, IV, and a rostral slip of Va. Since our study was concentrated on a very restricted component of the total limb input, namely footpad mechanoreceptors, the MF inputs in Figs. 11 and 12 would be expected to be to localized zones of the total limb input, as indeed was the case. For example the last column of Tables B, C and D of Fig. 10 shows that, in response to stimulation of the whole sciatic nerve, the fast MF input was much more widely and uniformly distributed than was the input generated by taps to pads. In two respects the fast MF input from the pads was distributed beyond the zones defined by Grant (1962a, 1962b) and Voogd (1964): there was the distribution from the hindfoot to the lateral vermis of lobule Vb and c, and from the forefoot to lobule VId and c (Fig. 11C, D).

It must be appreciated that our experimental procedures allow a sampling of only a few cells of any particular colony; nevertheless, from our observations on almost 1000 Purkyně cells in about 100 experiments, we have derived the general

impression that cells with related receptive fields tend to be assembled in colonies separated by zones in which cells were poorly, if at all, activated (cf. Figs. 8, 10). In the anterior lobe there appear to be several such colonies receiving input from the mechanoreceptors of the hindfoot in lobules III and IV and from the forefoot in lobule V and VI, and these colonies occur both in the lateral vermis and in the pars intermedia.

The colonies of cells relating to the fast MF input from forefoot and hindfoot as illustrated in Figs. 8, 10, 11 and 12 are small relative to the total Purkyně cell population of the anterior lobe. At the most two to four colonies have been recognized in any one experiment, and there was considerable variation in position, so that their discovery often entailed an initial exploration by several microelectrode insertions. It must be appreciated that the experiments illustrated in this paper and the two preceding papers (Eccles *et al.*, 1972b, 1972c) were orientated in relation to Purkyně cells whose receptive fields had representation by the cutaneous mechanoreceptors of the forefoot and hindfoot. We have attempted to locate the microelectrode tracks so that they would be optimal for finding Purkyně cells with these special inputs. However the surface pattern of vessels restricted the sites at which we could insert microelectrodes. In this respect the paravermal vein precluded exploration of areas that often would have been optimal for Purkyně cell responses. In the earlier systematic study of the field potentials generated by climbing fiber input from peripheral nerve volleys (Eccles *et al.*, 1968b; Kitai *et al.*, 1969) there were large silent areas of the anterior lobe, particularly the medial zone of the vermis. It was assumed that these areas were related to the body, neck and tail, but much more topographical study remains to be done before even crude somatotopic maps can be constructed. The situation is much more confused than in the cerebral cortex for which there are reliable somatotopic maps. The difficulties arise partly because of the extreme folding of the cerebellar cortex in the complexly branched foliations and partly because there is multiple representation of any particular receptive area in ill-defined scattered patches.

If the scope of the observations were extended to include delayed MF inputs, there was a wider dispersion of the input from the footpads. Many good scores would replace the zeros plotted in Figs. 11, 12 and 13. Presumably these delayed MF inputs were mediated via the widely dispersed spino-reticular cerebellar pathways (Oscarsson and Rosén, 1966; Bloedel and Burton, 1971). Reference should also be made to the very wide dispersal of cerebellar potentials evoked by nerve or cutaneous stimulation in the decerebrate unanesthetized cat (Combs, 1954).

The Congruence of the MF and CF Inputs

We suspect that there has been only limited success in our best efforts to observe simultaneously the normal level of MF and CF inputs onto Purkyně cells. In the decerebrate preparation there was probably always a depression of the CF input despite the attempted sparing of the pyramidal tract. In chloralose anesthesia there would be depression of the MF input by the small additional doses of surital or pentothal used to control the seizures. Nevertheless there were remarkable examples of cutaneous mechanoreceptors acting upon a Purkyně cell by both MF and CF inputs, as illustrated in Figs. 1, 2, 3, 4, and 5. Moreover the

cortical maps of Figs. 13 show that Purkyně cells with convergent MF and CF input were more numerous than those with only one such input. Evidence for this convergence of MF and CF inputs onto single Purkyně cells has also been obtained by Thach (1967, 1970) and by Ferin *et al.* (1971).

The demonstration of congruence of MF and CF inputs onto the same Purkyně cell in Figs. 1—5 and 13 is at a much more significant level than the earlier demonstration by means of field potentials (Eccles *et al.*, 1968a; Kitai *et al.*, 1969). Two problems thus arise in an acute form. Firstly, what factors guide the ingrowth of mossy and climbing fibers so that this approximately congruent distribution is achieved? This is a special problem in the field of developmental neurobiology. Evidently there must be subtle factors, as yet undetermined, guiding the growth of mossy fibers and a climbing fiber that project to a Purkyně cell from similar receptive fields. Secondly, what is the functional significance of this congruence? One possible answer is that the mossy and climbing fiber inputs are providing the Purkyně cell with different varieties of sensory information. There is some evidence that the MF input is weighted towards tonic input from slowly adapting receptors, while the CF input is more activated by fast adapting receptors, such as Pacinian corpuscles, and the rapidly adapting receptors of the footpads and the hair receptors (cf. Eccles, Sabah, Schmidt and Táboříková, 1972d). However Figs. 3 and 4 show that this is not always the case. A second possible answer is that the congruence of CF with MF input is concerned in the synaptic modifications involved in learning, as has been suggested by Szentágothai (1968) and Marr (1969). However preliminary investigations (Eccles, Marr, Sabah, Schmidt and Táboříková, unpublished observations) have failed to disclose any long term (up to 1 hour) potentiation of the MF-evoked response when CF and MF inputs to a Purkyně cell were activated hundreds of times in conjunction; however it was not practicable to make significant observations for more than one hour.

The Receptive Fields of Individual Purkyně Cells

It was surprising to find that quite minute mechanical stimulation provided such effective inputs to Purkyně cells, there being thresholds as low as 20 μm both for mossy fiber (Fig. 7; and Eccles *et al.*, 1972b, Fig. 2) and climbing fiber inputs (Eccles *et al.*, 1972c, Figs. 1, 3, 5). These extreme sensitivities were observed for the centers of the receptive fields of Purkyně cells. Usually the thresholds were about 10 times larger, but even that sensitivity entails a remarkable efficiency in the transmission mechanisms to the cerebellum. It must be envisaged that, in the ordinary running or exploring movements of the foot, the Purkyně cells possessing this receptive field must be subjected to the most intense and varied inputs by mossy and climbing fibers. Again the range of sensitivity for tonic excitatory and inhibitory action (Figs. 3, 4, 5 and Eccles *et al.*, 1972b, Figs. 3, 9, 10) corresponds well with the pressures exerted on the foot pads during the standing and walking of the cat.

By utilizing stimulation of digital nerves and recording the evoked MF and CF potentials in the anterior lobe (Kitai *et al.*, 1969), it was possible to show that there were discriminative inputs from the nerves innervating the foot pads and adjacent regions. In this present series of investigations there have been examples

of large differences between the pads of a foot. This signifies that there may be quite sharp contours in the receptive field that projects to a Purkyně cell. It was remarkable that, when there was a sharp contour for pad receptors excited by taps, the same contour obtained for the hair receptors (cf. Eccles *et al.*, 1971c, Fig. 5).

It would seem that the receptive fields of Purkyně cells include several modalities of cutaneous mechanoreceptors. There have also been several illustrations showing that a Purkyně cell had in its receptive field both the phasic (via Pacinian and rapidly adapting receptors) and the slowly adapting receptors of the central pad (Eccles *et al.*, 1972b, Figs. 3, 9, 10). However the convergence on the Purkyně cell may be oppositely directed — excitatory from the tonic group of receptors and inhibitory from the phasic (Fig. 5; and Eccles *et al.*, 1972b, Fig. 9C, D); and this opposition may even occur for the same receptors from different pads (Eccles *et al.*, 1972b, Fig. 8). In fact it must be recognized that there may be a mixed excitatory and inhibitory action on a Purkyně cell even from functionally "pure" inputs such as those evoked by weak adequate stimulation of cutaneous mechanoreceptors in a single footpad. Indeed, such antagonistic action on individual Purkyně cells is to be expected from the known excitatory and inhibitory action of cutaneous mechanoreceptors on the mossy fiber input to the cerebellar cortex (Eccles *et al.*, 1972a) and from the known action of the mossy fiber input on the complex neuronal machinery there — the granule, Golgi, basket and stellate cells (cf. Eccles, Ito and Szentágothai, 1967).

Implications of the Observations for Theories of Cerebellar Action

The arrangement of Purkyně cells in colonies is of importance in the events subsequent to the impulse discharges from Purkyně cells. It would be expected that the axons of adjacent cells would tend to converge onto the same target neurones, where there occurs the first stage in the integration of the output from the cerebellar cortex. If there is not a highly specific projection from Purkyně cells to these neurones, for example if there is a randomization in the projection, there will be a smudging in the transmission process with a consequent irretrievable loss of information. Preliminary studies of the responses of the principal target neurones (the fastigial nuclear cells) have shown that there is a very effective transmission of integrated information (Eccles, Sabah and Táboříková, 1971, and unpublished observations), and it is suggested that in the first place this is accountable to the colonial arrangement of Purkyně cells.

The responses of Purkyně cells to cutaneous mechanoreceptors represent but a small fraction of the performance of that part of the cerebellum oriented to limb movements. Nevertheless their detailed study is important because it discloses principles of operation that are in general agreement with the hypothesis of dynamic loop control (Eccles, 1967, 1969). There is firstly the evidence that ill-defined patchy assemblages (colonies) of Purkyně cells receive specific subsets of the total information input from the limb receptors. Secondly there is the evidence of wide variance of responses even within a colony, there being as a consequence opportunity for the most varied integrational operation, particularly in relation to the Purkyně projection to the cerebellar nuclei. Thirdly there is the evidence that the cutaneous mechanoreceptors of the receptive fields project to

individual Purkyně cells by both mossy and climbing fibers. There are thus the connectivities postulated in the conjunction theory of learning (Marr, 1969).

It can be claimed that the investigations reported in this paper and in the preceding three papers of this series (Eccles *et al.*, 1972a, 1972b, 1972c) present what we may term "hard data" on the input of information to the cerebellar cortex, on the integration of this input, and on expression of this integration in the temporal patterns of impulse discharge from individual Purkyně cells. This data will be essential in the attempts to model the mode of operation of the cerebellum in the control of posture and of movement, functions which are associated in particular with the vermis and pars intermedia of the anterior lobe. An addition to this "hard data" has been provided by a similar study of the responses of fastigial neurones to cutaneous mechanoreceptors (Eccles, Sabah and Táboříková, 1971). Furthermore, parallel studies are being made on the responses of Purkyně cells and fastigial neurones to inputs from adequately stimulated muscle receptors of the fore and hind limbs (Faber, Ishikawa and Rowe, 1971; Ishikawa, Kawaguchi and Rowe, 1972).

Acknowledgments: This work was supported by a grant from the National Institute of Neurological Diseases and Stroke, Grant No. R01NB0822101,2,3 and by generous research support by Dr. Henry C. and Bertha H. Buswell Fund to J.C. Eccles, R.F. Schmidt and H. Táboříková. We wish to thank Miss Tecla Rantucci for her technical assistance and Mr. J. Waldron for the photography.

References

Bloedel, J.R., Burton, J.E.: Electrophysiological evidence for a mossy fiber input to the cerebellar cortex activated indirectly by collaterals of spinocerebellar pathways. J. Neurophysiol. **33**, 308—320 (1970).

Braitenberg, V., Atwood, R.P.: Morphological observations on the cerebellar cortex. J. comp. Neurol. **109**, 1—34 (1958).

Combs, C.M.: Electro-anatomical study of cerebellar localization. Stimulation of various afferents. J. Neurophysiol. **17**, 123—143 (1954).

Eccles, J.C.: Circuits in the cerebellar control of movement. Proc. nat. Acad. Sci. (Wash.) **58**, 336—343 (1967).

— The dynamic loop hypothesis of movement control. In: Information processing in the nervous system. Ed. by K.N. Leibovic. Berlin-Heidelberg-New York: Springer 1969.

— Faber, D.S., Murphy, J.T., Sabah, N.H., Táboříková, H.: Afferent volleys in limb nerves influencing impulse discharges in cerebellar cortex. I. In mossy fibers and granule cells. Exp. Brain Res. **13**, 15—35 (1971a).

— — — — — Afferent volleys in limb nerves influencing impulse discharges in cerebellar cortex. II. In Purkyně cells. Exp. Brain Res. **13**, 36—53 (1971b).

— — — — — Investigations on integration of mossy fiber inputs to Purkyně cells in the anterior lobe. Exp. Brain Res. **13**, 54—77 (1971c).

— Ito, M., Szentágothai, J.: The cerebellum as a neuronal machine. Berlin-Heidelberg-New York: Springer 1967.

— Provini, L., Strata, P., Táboříková, H.: Analysis of electrical potentials evoked in the cerebellar anterior lobe by stimulation of hindlimb and forelimb nerves. Exp. Brain Res. **6**, 171—194 (1968a).

— — — — Topographical investigations on the climbing fiber inputs from forelimb and hindlimb afferents to the cerebellar anterior lobe. Exp. Brain Res. **6**, 195—215 (1968b).

— Sabah, N.H., Schmidt, R.F., Táboříková, H.: Cerebellar Purkyně cell responses to cutaneous mechanoreceptors. Brain Res. **30**, 419—424 (1971).

— — — — Cutaneous mechanoreceptors influencing impulse discharges in cerebellar cortex. I. In mossy fibers. Exp. Brain Res. **15**, 245—260 (1972a).

— — — — Cutaneous mechanoreceptors influencing impulse discharges in cerebellar cortex. II. In Purkyně cells by mossy fiber inputs. Exp. Brain Res. **15**, 261—277 (1972b).

Eccles, J.C., Sabah, N.H., Schmidt, R.F., Táboříková, H.: Cutaneous mechanoreceptors influencing impulse discharges in cerebellar cortex. III. In Purkyně cells by climbing fiber input. Exp. Brain Res. **15**, 484—497 (1972c).
— — — — A study of the cutaneous mechanoreceptors modalities projecting to the cerebellum. In: The somatosensory system. Ed. by H.H. Kornhuber. Stuttgart: Thieme 1972d.
— — Táboříková, H.: Responses of fastigial neurones to stimulation of cutaneous mechanoreceptors. Brain Res. **35**, 523—527 (1971).
— Sasaki, K., Strata, P.: The profiles of physiological events produced by a parallel fibre volley in the cerebellar cortex. Exp. Brain Res. **2**, 18—34 (1966).
Faber, D.S., Ishikawa, K., Rowe, M.J.: The responses of cerebellar Purkyně cells to muscle vibration. Brain Res. **26**, 184—187 (1971).
Ferin, M., Grigorian, R.A., Strata, P.: Mossy and climbing fibre activation in the cat cerebellum by stimulation of the labyrinth. Exp. Brain Res. **12**, 1—17 (1971).
Grant, G.: Spinal course and somatotopically localized termination of the spinocerebellar tracts. An experimental study in the cat. Acta physiol. scand. **56**, Suppl. 193, 5—42 (1962a).
— Projection of the external cuneate nucleus onto the cerebellum in the cat. An experimental study using silver methods. Exp. Neurol. **5**, 179—195 (1962b).
Hunt, C.C., McIntyre, A.K.: An analysis of fibre diameter and receptor characteristics of myelinated cutaneous afferent fibres in cat. J. Physiol. (Lond.) **153**, 99—112 (1960).
Ishikawa, K., Kawaguchi, S., Rowe, M.J.: Actions of afferent impulses from muscle receptors on cerebellar Purkyně cells. I. Responses to muscle vibration. Exp. Brain Res. **15**, 177–193 (1972).
Kitai, S.T., Táboříková, H., Tsukahara, N., Eccles, J.C.: The distribution to the cerebellar anterior lobe of the climbing and mossy fiber inputs from the plantar and palmar cutaneous afferents. Exp. Brain Res. **7**, 1—10 (1969).
Larsell, O.: The cerebellum of the cat and the monkey. J. comp. Neurol. **99**, 135—199 (1953).
Marr, D.: A theory of the cerebellar cortex. J. Physiol. (Lond.) **202**, 437—470 (1969).
Oscarsson, O.: Functional significance of information channels from the spinal cord to the cerebellum. In: Neurophysiological Basis of Normal and Abnormal Motor Activities, pp. 93—108. Ed. by M.D. Yahr and D.P. Purpura. New York: Raven Press 1967.
— The sagittal organization of the cerebellar anterior lobe as revealed by the projection patterns of the climbing fiber activation. In: Neurobiology of Cerebellar Evolution and Development, pp. 525—537. Ed. by R. Llinás. Chicago: Am. Med. Assoc./Educ. Res. Found. 1969.
— Rosén, I.: Response characteristics of reticulocerebellar neurones activated from spinal afferents. Exp. Brain Res. **1**, 320—328 (1966).
— Uddenberg, N.: Somatotopic termination of spino-olivo-cerebellar path. Brain Res. **3**, 204—207 (1966).
Palkovits, M., Magyar, P., Szentágothai, J.: Quantitative histological analysis of the cerebellar cortex in the cat. I. Number and arrangement in space of the Purkinje cells. Brain Res. **32**, 1—13 (1971).
Provini, L., Redman, S., Strata, P.: Somatotopic organization of mossy and climbing fibres to the anterior lobe of cerebellum activated by the sensorimotor cortex. Brain Res. **6**, 378—381 (1967).
Schmidt, R.F.: Spinal cord afferents: Functional organization and inhibitory control. In: The Interneuron, pp. 209—229. Ed. by M.A.B. Brazier. Los Angeles: UCLA Forum in Medical Sciences 1969.
Szentágothai, J.: Structure-functional considerations of the cerebellar neuron network. Proc. of the I.E.E.E. **56**, 960—968 (1968).
Thach, W.T.: Somatosensory receptive fields of single units in cat cerebellar cortex. J. Neurophysiol. **30**, 675—696 (1967).
— Discharge of cerebellar neurons related to two maintained postures and two prompt movements. II. Purkinje cell output and input. J. Neurophysiol. **33**, 537—547 (1970).
Voogd, J.: The cerebellum of the cat. Assen: Van Gorcum & Comp., N.V. 1964.

Prof. Sir John C. Eccles
Laboratory of Neurobiology
State University of New York at Buffalo
4234 Ridge Lea Road
Amherst, N.Y. 14226 (USA)