

Chapter 5

End-organs, Nerve Impulses and Nerve Cells

A change of scene took place when the vacuum tube made amplification of small electrical changes possible (see p. 58) and the triumphant progress of modern electronics gradually came to be reflected in nerve physiology. The pioneer whose work had the greatest immediate influence on the development of Sherrington's world of ideas was E. D. (since, Lord) Adrian. He and Sherrington were following convergent lines in the sense that both were heading for the properties of the nerve cell as a functional unit. The effect of Adrian's work was soon felt in the better understanding of the nature of the afferent message from sense organs. With several co-workers, among the best known, D. W. Bronk, Rachel Matthews, B. H. C. (since, Sir Bryan) Matthews and Yngve Zotterman, Adrian availed himself of the possibility of amplifying the small electrical changes that corresponded to the passage of impulses in individual afferent nerve-fibres and showed that the sense organs from which they emanated delivered a message coded in terms of a variation of frequency of discharge.

The individual impulse or 'spike' was the well-known action current which now became recorded as an action potential charging the grid of a vacuum tube. It was then stepped up by amplification about a million times in order to deliver the current or potential difference necessary for driving recording instruments. Fig. 14 shows that impulses at the ordinary recording speeds (used in nerve physiology) look like spikes because they are very fast. In any given nerve-fibre they do not vary in size (as the all-or-none law had correctly predicted) but merely in

frequency so that the stronger the sensory stimulus, the greater the frequency at which a sense organ tends to discharge. 'The sensory messages,' said Adrian, 'are scarcely more complex than a succession of dots in the Morse code.'—'How complex must not the central processes then be in order to explain the workings of our mind,' was Sherrington's first comment.

The loudspeaker introduced by Adrian and Bronk made the repetitive discharge of individual nerve impulses more realistic and soon it became impossible to stay aloof if one was interested in sense organs. Adrian in his books, two slender volumes, described the new findings in a most enticing manner: 'The advent of the triode valve, or vacuum tube amplification,' he

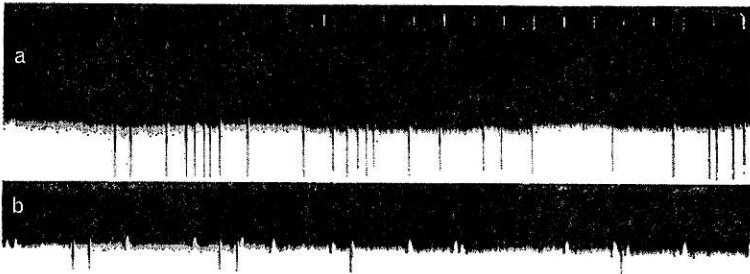


Fig. 14 Discharges in dorsal cutaneous nerves of a frog. (a) shows large rapid impulses due to touching the skin; (b) slow impulses produced by 2 per cent acetic acid on the skin. (Adrian, *The Mechanism of Nervous Action*, University of Pennsylvania Press: Clarendon Press, Oxford, 1932)

said, 'has so altered the whole position that we can compare ourselves to a microscope worker who has been given a new objective with a resolving power a thousand times greater than anything he has had before. We have only to focus our instrument on the field to find something new and interesting.' This was quite true and who could refuse a peep down the tube?

In those days a key-word like 'information' was not yet used in the scientific sense it has since acquired from binary Boolean algebra. One was therefore more likely to speak of impulse patterns in single nerve-fibres and think of them as coding information from sense organs or as eliciting muscle action potentials at end-plates of muscles. Cable theory had played some rôle in the development of nerve physiology and so one

was used to the idea of nerve-fibres being cables joining cells across synapses. Clearly the impulses in the nerve-fibres represented the language in which one cell speaks to another.

From now we move on familiar ground and need not discuss technical details. For some forty years impulses have been recorded from innumerable single cells and single nerve-fibres, in vertebrates and invertebrates, and much of what we know about the nervous system has come from impulse recording. Lord Adrian began his work with sensory or afferent impulses and today it still seems to me true to say that no other branch of vertebrate nerve physiology has gained as much from this technique as the study of sense organs including the projections of their afferents in the central nervous system. The eye, the ear, and the muscle spindles stand as the greatest gainers. In the twenties everything we knew about sight and hearing belonged to the realm of psychophysics. Probable functions and interpretations of histological features of the eye and the ear were deduced from psychological entities such as colour, pitch, threshold quantities of perception, etc. In spite of such limitations many brilliant discoveries had been made, especially in vision and audition, and to this very day these have guided electrophysiological research into the mechanisms that serve as cues for psychological interpretation.

From the point of view of Sherrington's earlier work the sense organs in the muscle were the most interesting ones because there was no relevant psychophysical science to tell us about the properties of the length-meters and tension-meters that he had postulated. To be sure, there was an old literature, mostly in German, about 'Kraftempfindungen' but already at the time good reason could be adduced for locating the appropriate end-organs at the joints (their ligaments). The only hope for advance lay in objective methods of recording the messages from the muscular end-organs themselves. This method was destined to solve many of the riddles that Sherrington faced when he tried to understand the interrelations between proprioceptive impulses and muscle tone. A separate chapter (7) will be devoted to these questions.

Let us now recall that a large fraction of Sherrington's experimental life had been spent in quest of the neurone. In this field he was greatly rewarded when in 1929 Denny-Brown

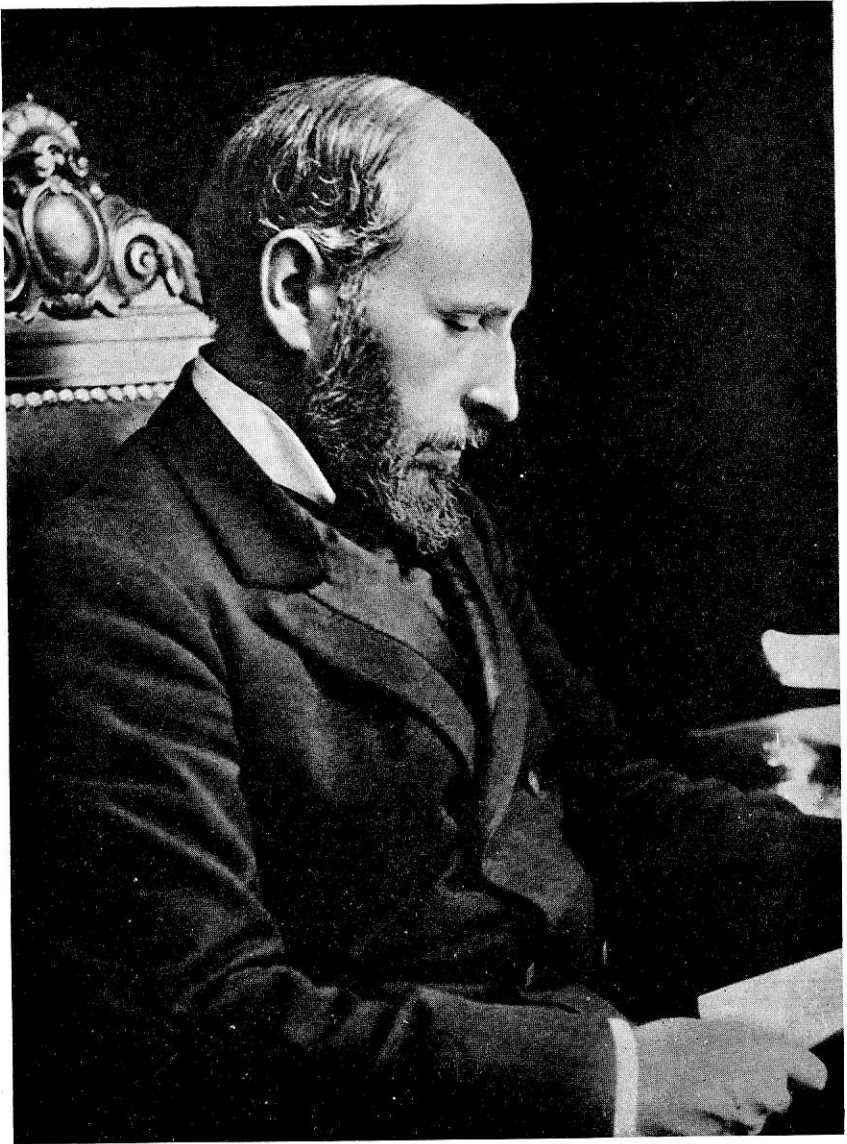


Plate 5 Santiago Ramón y Cajal. (From Sherrington's obituary in *Obit. Notes Roy. Soc.*, 1935, No. 4)

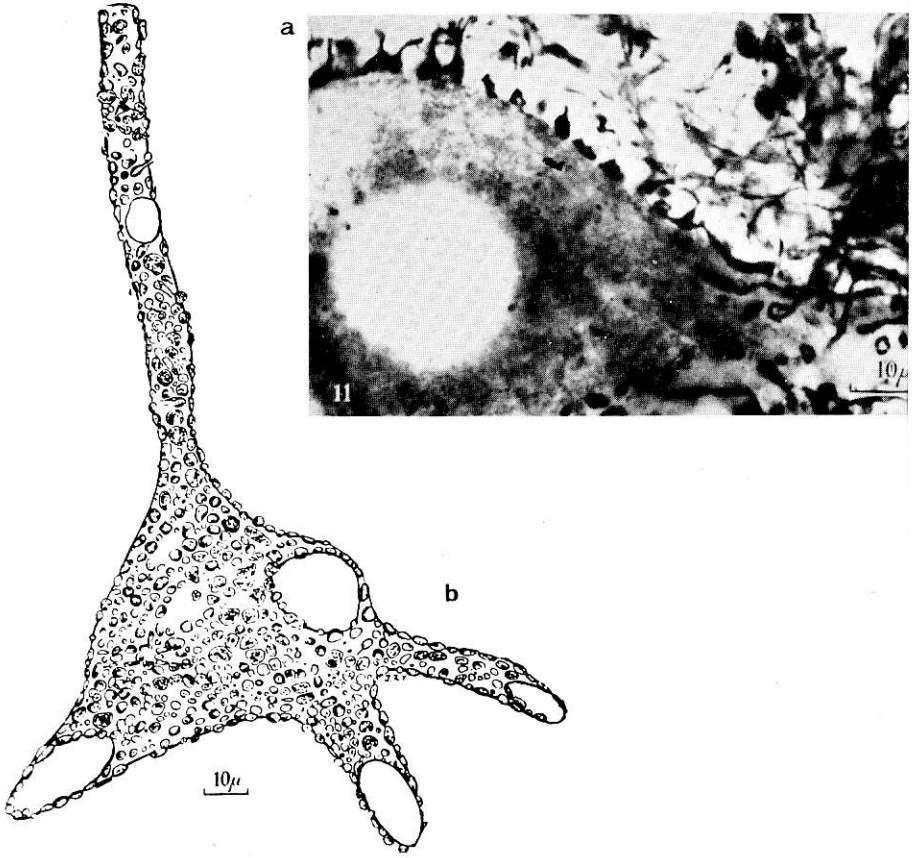


Plate 6 (a) Neurone of the ventral horn (motoneurone) of the thoracolumbar region of the cat (Cajal's block silver method). Fixed with formol, embedded in carbo-wax. Note the end-feet, stained deep black, along the margin of the cell. The afferent terminals from which they originate are broken. (b) The motoneurone surface. *Camera lucida* drawing of part of a neurone from the ventral horn of a cat. Fixed with formol, postchromed, embedded and sectioned in carbo-wax and stained with Bielschowsky-Gros stain. The surface of the cell body and dendrites is almost entirely covered with terminal end-feet. (Wyckoff and Young, *Proc. Roy. Soc.*, 1955, *B144*, 440)

in his own laboratory and Adrian and Bronk at Cambridge independently demonstrated that the motor neurone—his final common path—behaves like a sense organ and fires all-or-none spikes at frequencies which increase when afferent stimulation becomes more intense. Many other facts of importance were unearthed in those papers but the fundamental analogy between sensory end-organs and neurones is of especial significance.

‘The most remarkable point which arises from this paper,’ said Adrian and Bronk, ‘is that the discharge of a motor nerve cell can scarcely be distinguished from the discharge of a sense organ. . . . Clearly more work must be done before we can accept the view that all nervous messages are of the same general type, but some of the consequences of this view may be pointed out. In the first place it would mean that we must abandon the idea that central inhibition can be explained on the lines suggested by Lucas, Forbes, and Adrian, i.e. by the depressant effects produced by high-frequency impulse discharge. Various heroic assumptions might overcome the difficulties which would arise, but they are scarcely worth making. We must therefore revert to the view that two qualitatively different processes can occur in the synapses to account for the inhibitory and excitatory effect.’ Adrian and Bronk, of course, referred to Sherrington’s ideas about the central excitatory and inhibitory states, discussed in previous chapters.

The recording of impulses in single motor neurones may not seem much of a feat to the young electrophysiologists of today who have so many means of solving the technical problems involved, but an older generation of workers need not search their memories for very long to remember the situation in the mid-twenties. The existence of reflex muscle action potentials was, of course, well known. There were, for instance, Miss Florence Buchanan’s (1907) studies of strychnine spasms in frogs with the aid of the capillary electrometer, and Piper’s extensive work in Germany (1912) on voluntary contraction in man for which he used the Einthoven string galvanometer. Miss Buchanan had continued her teacher’s work at Oxford (Sir John Scott Burdon Sanderson). Many others had followed in their path with contributions which described the electrical oscillations obtainable from the surface of contracting muscle—

the electromyogram—among them Dusser de Barenne, Adrian and Cooper, Paul Hoffmann, Preisendörfer, and Wachholder. Rhythms of frequencies up to 500 per sec. had been observed but it is clear, in the light of what we know today (and had reasons to suspect at the time), that these results could merely prove the existence of impulses in the muscles as electrical interference phenomena whose individual components were unknown. Von Kries, in 1923, had summed up the situation in the statement that 'for skeletal muscle we now regard the rhythmic nature of the motor innervation as certain'.

Rather dominant in the discussion was the so-called Piper rhythm, large waves at approximately 50 per sec. seen in voluntary contraction, and much worry was caused by the absence of electrophysiological signs of activity in tonic contractions until small oscillations were described independently by Dusser de Barenne and Buytendijk; in fact, one used to speak of the 'Dusser de Barenne-Buytendijk vibrations'. Little is to be gained now by discussing forgotten disputes and interpretations of tone. This brief impression from memory should suffice to give an idea of the background against which the new results stood out as revelations.

In order to interpret the Dusser de Barenne-Buytendijk vibrations in the tonically contracting soleus muscle of the decerebrate cat, Denny-Brown used the established technique of leading off from muscle but started cutting down the efferent roots cautiously until he finally had a preparation in which one or two single spikes or muscle action potentials responded by firing when the soleus was pulled out slowly. This is illustrated in Fig. 15. Now here was the stretch reflex visualized in terms of the output of a single motoneurone and with this preparation Denny-Brown made two fundamental observations. One was the curious fact that although he pulled harder and harder on the muscle, the functionally isolated motoneurone fired at much the same frequency. Yet there was every reason to assume (Adrian and Zotterman) that the muscular end-organs would stimulate their motoneurons at increasingly higher discharge frequencies. Why was this effect not reflected in the rate of firing of the motoneurone? The other new result consisted in a full vindication of the correctness and value of Sherrington's concept of recruitment. As the muscle was extended, fresh motoneurons

were 'recruited' into activity (as a rule it was impossible to cut down the efferent root to one fibre only).

The Dusser de Barenne-Buytendijk vibrations now lost their relevance as a specific muscular accompaniment of tone because it was evident that they were merely the sign of a highly asynchronous reflex discharge of motoneurons, recorded in the ordinary way as muscle action potentials. The individual motoneurons were found to discharge at very slow rates, from 5 to 25 impulses per sec. The asynchronism and slow recruitment of fresh motoneurons simply gave a low-voltage interference picture beyond the resolving power of the string galvanometer, as used in combination with non-selective recording. The

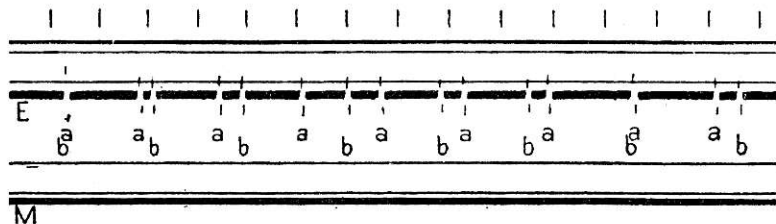


Fig. 15 Electrical response (impulses) in two soleus motor units of the decerebrate cat. The muscle is under a steady slight pull to deliver the stretch reflex shown by the activity of units *a* and *b*. The former fires seven times a second, the latter five to five and a half times a second. Time 0.1 sec. (Denny-Brown, *Proc. Roy. Soc.*, 1929, *B104*, 252)

unknown *x* that still remained to be explained concerned the regulative processes by which the motoneurons were held in check and forced to fire at such slow steady rates independent of extension in stretch. In defining recruitment Sherrington had assumed that the recruiting reflex fought its way against inhibition because pull on the muscle would mobilize both excitatory and inhibitory end-organs. Thus their rivalry would determine the outcome. While this is true, it is not a sufficient explanation of the observed stabilization of the rate of firing because recruitment was there to prove that excitation got the upper hand during increasing pull on the muscle. Stabilization must therefore be something connected with firing as such from a motoneuron, and we shall return to this point in Chapter 7. Technical improvements, which made both muscular end-organs

in the periphery, and motoneurons at their sites within the spinal cord, directly accessible to analysis, in the end supplied the full explanation of stabilization of discharge rate in tone.

Adrian and Bronk had started with the phrenic nerve to the diaphragm. This supplied for study a rhythmically recurring 'natural' event. The frequency of respiratory discharge in individual motor fibres was found to be from 25 to 30 impulses per sec. in normal breathing, rising to 50–80 per sec. in forced respiration when sometimes motoneurons also began to fire in synchrony. They went on to investigate a large number of reflexes, confirming Denny-Brown's observations on the stretch reflex of the decerebrate animal, and, in general, finding rates of discharge which were adapted to the contractile properties of the muscles on which the motor fibres terminate. Rates below 50 per sec. were typical for maintained contractions but initially the frequency of discharge—just as in sense organs—might be twice that rate. Reflex action was found to be graded both by the frequency of discharge and by the number of motoneurons mobilized, the stretch reflex being unique in mainly employing a variation of number alone, as described above.

Adrian and Bronk's introduction of the concentric needle electrode for recording the muscle action potentials in voluntary contraction in man became of considerable clinical importance. Wachholder (1923) in Germany had continued Piper's work and replaced the pad leading off from the surface by two needles thrust into the contracting muscle. With this technique, making use of feeble contractions, he had seen individual muscle action potentials. With stronger contractions an oscillatory interference picture was obtained. When Adrian and Bronk, by cutting down the nerve and recording from functionally isolated fibres, had proved that the efferent message did not differ in principle from its afferent counterpart, they went back to the old method of picking up the reflex efferent message after it had been translated into muscle action potentials at the motor end-plate. Their new electrode consisted of an injection needle (of the kind used with a syringe) whose shield was earthed while from the inside protruded the bared tip of a thin wire enamelled for insulation and connected to the grid of the amplifier. Single spikes were obtained between tip and shield, and by this technique they could satisfy themselves that the complex

oscillatory responses characterizing strong voluntary contractions were merely caused by the activity of more and more fibre groups. Sherrington's concept 'motoneurone' had now been subjected to rigorous tests and emerged unscathed.

'Reading some of the early papers of that time,' said Adrian, 'one cannot help remembering what a pleasure it was to find that most of the inferences had been correct. Impulses arising in sense organs or nerve cells were accompanied by action potentials like those in a nerve trunk stimulated electrically. They followed the all-or-nothing rule inferred from Keith Lucas' work on the frog's dorso-cutaneous muscle. They appeared where and when we had reason to expect them, in sensory and in motor nerve. In fact there was no need to revise the accepted theories of the nature of nervous communication. It was carried out by impulses of the familiar type' (1953). However, the insight into function that the new techniques gradually engendered was new, and from now on the discharging cell was destined to receive an ever increasing share of the attention of nerve physiologists. By different means Sherrington and Adrian had been striving to make the nerve cell an analytical unit. This had been, as I said above (p. 29), Sherrington's 'first great notion' and for him, in a sense, it was journey's end. In 1932 Adrian and Sherrington shared the Nobel prize.

In speaking of nerve impulses in a single fibre being translated into muscle-action potentials across the motor end-plates which it innervates, nothing has so far been said of the highly specialized end-plate structure. This is really a synapse, located in the periphery instead of within a centre, and much of our basic information on synapses has come from the detailed study of events at the motor end-plate. The fast spike in the nerve-fibre is there translated into a slow electrical change, the end-plate potential (Göpfert and Schaefer, 1938), which in its turn is responsible for the muscle spike. For the understanding of synaptic events the motor end-plate proved to be a touchstone making possible a decision between the two leading theories of synaptic transmission, the chemical and the electrical hypothesis. As briefly alluded to above, the late Otto Loewi of Graz in Austria had shown, in a series of papers from 1921 onwards, that the effect on the heart of the two nerves, the vagus and the accelerans, which, like the rein and the whip,

control its rhythm, is produced by two chemical mediators, the *Vagusstoff* and the *Acceleransstoff* respectively. After the extended studies of Loewi and of Dale there could be little doubt that the *Vagusstoff* was acetylcholine. Loewi had found the *Acceleransstoff* to be an adrenaline-like substance. Along independent lines U. S. von Euler many years later—in the late forties—provided evidence which led to the acceptance of one of the candidates, noradrenaline, for the rôle of transmitter substance at sympathetic nerve-endings.

The chemical theory of synaptic excitation, based on the motor end-plate as model, became firmly established when Sir Henry Dale with G. L. (now, Sir Lindor) Brown and W. Feldberg in the early thirties showed that acetylcholine was the transmitter substance responsible for the end-plate potential. The nature of the latter has since been elucidated in detail by Bernard Katz and his co-workers but a review of their results would lead us too far away from our theme. Sherrington could not on the basis of his own findings advocate any specific theory of synaptic excitation and preferred to be non-committal. For our purposes the end-plate potential can be described as a process released by the nerve impulse in order to deliver the energy needed for setting up a muscle-action potential.

Application of this model to central synapses with the motoneurone as prototype would imply that the terminal knobs of the afferents there, too, would require a chemical mediator in order to be able to depolarize the cell to the extent of making it discharge impulses down its axon. It was fairly generally and for good reasons believed that excitation led to depolarization of the cell receiving excitatory impulses, and soon there was evidence from Sir Bryan Matthews working with D. H. Barron (1935-38) to the effect that the depolarization ensuing upon activation of motoneurons could actually be led off electrotonically from the ventral roots. ('Electrotonus' is a physiological spread of current from the cell into its axon.) The idea that a synaptic potential corresponding to the end-plate potential is produced by afferent bombardment of the ventral horn cell was also strengthened by the observations that Sir John Eccles and his co-workers made in the late forties with small electrodes stuck in among the motoneurons themselves, a technique mentioned above in connection with Lorente de Nó's studies of

synaptic delay (p. 59). A focal potential corresponded to activation of motoneurons, and analysis suggested that it was of cellular origin. Graded slow potentials had also been seen by Gasser, recording from the surface of the spinal cord, and work by Bremer contributed to the canonization of the general idea of a synaptic potential (depolarization of the cell membrane) being an essential link in the excitation of nerve cell bodies (including ventral horn cells). This notion was so well founded that to Eccles it seemed natural, at the time, to elaborate an electrical theory of synaptic excitation in spite of evidence to the contrary from the motor end-plate (and from the ganglions of the vagus and the sympathetic nerves). This theory need not be reviewed here as Eccles himself abandoned it some years later (see next chapter).

Sherrington's central excitatory state (Fig. 13, p. 79) was a concept that seemed supported well enough by the observations just mentioned. Further elaboration began at the Rockefeller Institute and the new approach originated in the late Herbert Gasser's interest in the conduction velocity of nerve-fibres (p. 59). Erlanger had suggested at an early date (1927) that specificity of the sensory message might well hinge upon differentiations connected with fibre size and hence with conduction velocity. The electrical technique had undergone great advance since the early days when Gasser and Erlanger measured conduction velocities in nerve-fibres with a primitive cathode ray oscillograph. Sweep and relay circuits connected to the stimulating shock made it possible by turning a knob to start any impulse at will and to visualize the electrical events on the screen with any chosen time base. It was now possible to study the temporal course of the effect of a synchronous volley of impulses. Eccles and Sherrington had, indeed, been able to execute rather complex experiments on the timing of reflexes in the early thirties but a decade of technical advance had reduced the amount of labour involved in such work and thereby pushed the experimenters on to problems requiring great precision in stimulation and recording.

In the present era one has the impression that electronic engineering has made the technical element 'foolproof' to the extent of attracting workers to this field who are ignorant of and uninterested in conceptual developments of the kind which

the physiology of the central nervous system urgently demands. Sherrington's work should serve as a perpetual reminder of the necessity of long-range planning accompanied by ceaseless attempts to penetrate experiments and results with leading ideas. In this field the life of an experimenter is too short to be spent merely on *ad hoc* notions.

Eccles and Sherrington had traced the time course of the central excitatory state (see Fig. 13, p. 79) by measuring with

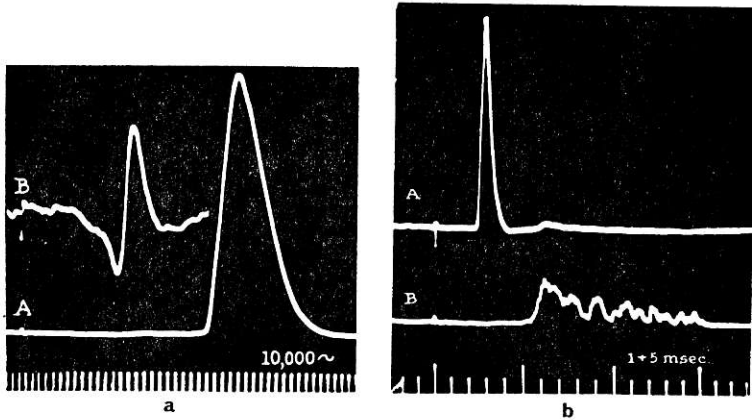


Fig. 16 (a) Monosynaptic reflex *A* recorded from the first sacral root on stimulation of the *gastrocnemius* nerves. The white mark is an artifact caused by a single electric shock, and record *B* shows when the impulse volley enters the spinal cord (on which leads have been placed). Time in 10,000 cycles per second. (b) Another similar experiment, but greater shock strength in *A* has brought in the polysynaptic reflex component from afferents of thinner calibre. *B* is a reflex to stimulation of sural nerve (a skin nerve) causing polysynaptic reflexes only. (Lloyd, *J. Neurophysiol.*, 1943, 6, 111, 293)

a test shock the effect left by a conditioning shock in the flexor centre. As defined by this experiment the time course found refers to a situation in which polysynaptic components of the afferent input have been activated and in which the relative amounts of excitatory facilitation contributed by the various neural circuits are unknown. The monosynaptic reflex made it possible to measure the time course of excitability at one specific set of synapses by the same technique (Lloyd), namely, those which represent the terminal knobs of the largest and

fastest muscular afferents, as explained above (p. 65). The synchronous volley elicited in a group of such fibres undergoes little dispersion with time and finally emerges on the ventral side as the monosynaptic response illustrated in Fig. 16. Use of a weak electrical conditioning shock restricted stimulation to the largest fibres.

In agreement with Sherrington's principle of graded excitation in a 'subliminal fringe' the conditioning volley would set up an excitatory state even if the shock was too weak to excite any neurone supraliminally (above threshold). This state of facilitation would rise and fall according to some curve which the test shock would measure by the number of motoneurons (size of response) that in any given interval could be raised to firing level. Monosynaptic testing, as elaborated by Renshaw and Lloyd, is therefore a technique that depends upon the existence of a fringe of subliminally excited motoneurons. The state of facilitation obtained in this manner is seen in Fig. 17 to drop exponentially to zero in about 14 milliseconds.

The excitatory state shown in Fig. 17 is not identical with its namesake in Sherrington's conceptual world. It should preferably be called a purified version of the latter because of the weeding out of complex accessory circuits which would deliver delayed impulses capable of restoring the dwindling state of excitation. This purification of Sherrington's original concept was based on the following new analytical elements: (i) knowledge of the synaptic delay (above, p. 59); (ii) knowledge of conduction velocity of the fastest muscular afferents whose fibre size had already been measured by Sherrington in 1894; (iii) knowledge of the fact that by carefully grading stimulus strength these afferents could be selectively excited. The 'purified concept' is limited by the assumption that synchronous monosynaptic stimulation is free from specific effects depending upon the site of the monosynaptic synapses (likely to be on the cell body). Assuming that one could initiate a monosynaptic effect selectively from the dendritic portion of the motoneurone, would it follow the same curve? This point is raised merely to indicate the need for still more selective techniques (Chapter 6), which are already being employed (Fadiga and Brookhart).

It will be remembered that on Sherrington's principle of reciprocal innervation, excitation of the extensors would coincide

with inhibition of the flexors and so the question arose as to whether monosynaptic excitation in one of the pair would also correspond to monosynaptic inhibition in the other. This, in fact, is what Lloyd assumed to be the case, but later work by Eccles and his colleagues has shown that inhibition is actually disynaptic. Lloyd's inhibitory curve can be roughly visualized by turning the curve of Fig. 17 by 180° around an axis formed by

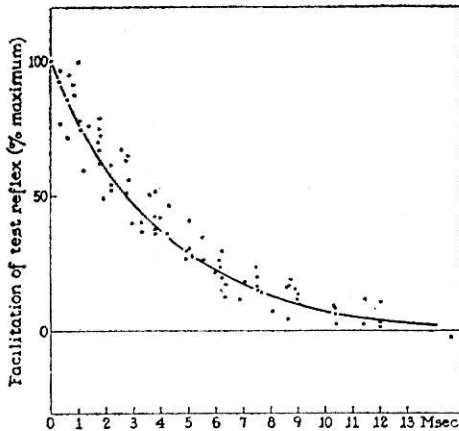


Fig. 17 The period of facilitation after a monosynaptic activation. Facilitation of motoneurons by impulses in primary afferent fibres. Points from seven experiments are scaled on the ordinates to coincide at the time of maximum facilitation. Relative facilitation, expressed in a percentage of maximum, is plotted as a function of time. The plotted curve is an exponential regression having successive half-values at 2.8, 5.6, 8.4, 11.2, and 14 msec. In four experiments, facilitation in flexor nuclei was examined; the remaining three were concerned with extensor nuclei. (Lloyd, *J. Neurophysiol.*, 1946, 9, 421)

the abscissa (see Fig. 18 (b)). For the theory of inhibition it was important at the time to possess a set of purely inhibitory monosynaptic terminals, but now, twenty years later, when inhibition has been studied by the intracellular technique (Chapter 6) in several cells of vertebrates and invertebrates, the point raised is perhaps a little academic. It created some interest because one imagined (Dale's principle) that the inhibitory and excitatory terminals of the afferent fibre, if transmission be chemical, would have to make use of the same

chemical agent. For this reason it seemed natural to postulate an internuncial neurone serving as a 'commutator' to introduce a fresh set of terminals with different chemical properties specializing in inhibition. Tauc (1962) has since found that in some nerve cells of a mollusc, *Aplysia*, acetylcholine produces inhibition at some synapses, excitation at others, and, if this is verified, the effect evidently depends upon a subsynaptic elaboration at the cell membrane itself. This actually was the hypothesis that Sherrington thought most likely.

Knowledge of conduction velocity of the active fibres which proved so clarifying in the experiment just described has since served as a useful characterizing property of the type of fibres engaged and, for sensory fibres, it can only be supplanted by specifications accruing from precise use of the adequate stimulus for the end-organ itself. Unless either method of characterization of the afferent input be attempted, it is fair to say that a piece of work in this field has to offer exceptional compensations in order to possess survival value in the present age.

The relation between stimulus strength and fibre size (conduction velocity) which Gasser and Erlanger had explored so carefully suggested to Lloyd that the monosynaptic curve of facilitation (Fig. 17) could be modified by delayed excitation or inhibition in a characteristic way, depending upon stimulus strength, nature of the afferent nerve, and number of intercalated synapses, and this also proved to be the case. Examples are given in Fig. 18. Such work also led him to a general subdivision of afferent fibres into groups (Table I) according to fibre size. For the myelinated fibre in Groups I-III size is approximately proportional to conduction velocity.

TABLE I

Fibre group	I	II	III	IV
Diameter in μ	20-12	12-6	6-1	unmyelinated or C-fibres

For approximate conduction velocities in metres per second, multiply by 6.

Here was a set of specifications which has served as a useful

standard of reference in reflex work. It required knowledge of fibre size in different afferent nerves from skin, muscles and ligaments (in the joints), and several laboratories hastened to contribute information of this kind (Lloyd and Chang, Rexed and Therman, Fernand and Young, Hagbarth and Wohlfarth). Synaptic excitation, rather than the physiological rôle of the

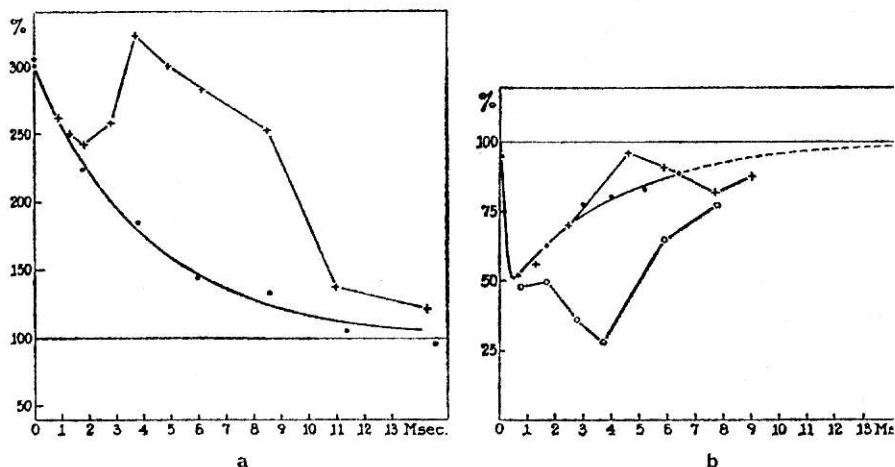


Fig. 18 (a) The period of monosynaptic facilitation has been obtained by activating large Group I muscular afferents alone, as in Fig. 17. The curve deviating from it at moment 2 msec. represents the effect of adding an interneurone. This has been done by increasing stimulus strength to include Group II afferents, i.e. by using a stronger conditioning shock. (b) The period of inhibition by Group I afferents is represented by the smooth curve. The secondary inhibitions and facilitations have been obtained by activating interneurons which have afferents of lower conduction velocity and hence have required stronger conditioning shocks (Lloyd, *J. Neurophysiol.*, 1946, 9, 421)

end-organs, became the ultimate focus of that line of research logically culminating in the intracellular studies of reflex activity inaugurated in 1952 by Sir John Eccles and his co-workers (Dunedin, New Zealand and then at Canberra, Australia). From 1949 onwards my own laboratory started pursuing questions of organization and motor control connected with the nature of the muscular end-organs. These problems had been neglected by the research groups interested in synaptic

transmission and in the analytical possibilities of timing central events.

In summing up the work which put conduction velocity of the afferent fibres to such good use in studies of central excitation and inhibition, let us finally consider the general question—the one that Erlanger raised—of how well specific sensory functions correlate with definite fibre groupings. To answer it, one must distinguish between statistical aspects of excitation and inhibition and the more precise correlations required to ascribe a set of fibres from one type of end-organ to one narrowly defined group of conduction velocities. In a statistical sense Lloyd's approximation, or any other classification for that matter, may often be valid and valuable as a tool in the analysis. So far it has proved most useful with the muscular afferents. But even with them there are exceptions (Bianconi and Van Der Meulen, 1962). In the ankle extensors, for instance, there is a considerable degree of overlap between fibres from tendon organs and fibres from muscle spindles with regard to conduction velocity (Hunt and Kuffier, 1951). It is also well known from the early work of Zotterman (1939) that touch is carried in both very fast and very slow fibres. In recent times Yves Laporte's group at Toulouse has devoted special attention to the relation between fibre size and function in the limb nerves. Gasser himself (1943) always advocated some caution in inferring from conduction velocity to specific sensory effects.

It remains a moot point why Sherrington, who was so interested in sense organs and at the turn of the century wrote those excellent summaries of the early work in this field in Schäfer's *Text-Book*, never himself contributed more than one study of sensory functions (as apart from end-organ anatomy), the last chapter in his *Integrative Action* dealing with fusion of binocular flicker. I can suggest no other answer than that he found reflex work more profitable from the motor point of view. No doubt he was right, and moved by the notion which he also expressed in print, that definite problems ripen for attack at definite times. The developments to which this chapter has been devoted had to come before much could be done in the sensory field. I can, however, testify to Sherrington's lively interest in sensory physiology, even at the time when the work on the spinal cord was remunerative beyond expectation. The Linacre

Lecture on *Muscular Activity* (quoted p. 76), is one instance, and when, in 1928, I turned up with a dominating interest in the retina, he told me that he had always wanted someone specializing on vision in his laboratory. Nearly all my work on the retina was carried out during his lifetime and many letters of kind encouragement from Sherrington accompanied its progress.