

**A COMPARISON
OF THE NERVE IMPULSES OF MAMMALIAN
NON-MEDULLATED NERVE FIBRES WITH
THOSE OF THE SMALLEST DIAMETER
MEDULLATED FIBRES**

BY A. S. PAINTAL

*From the Department of Physiology, V. Patel Chest Institute,
Delhi University, Delhi-7, India*

(Received 5 May 1967)

SUMMARY

1. Filaments were dissected from the aortic nerve of cats and impulses recorded monophasically *in vivo*.

2. The temporal characteristics of impulses of non-medullated fibres were compared with those of medullated fibres with conduction velocities between 4.5 and 12 m/sec. There were no obvious qualitative differences between the two types of fibres and they appeared to belong to a homogeneous sample.

3. In non-medullated fibres the rise time, fall time and absolute refractory period varied inversely with conduction velocity, the relation being similar to that in the medullated fibres. There was practically no difference between the temporal characteristics of the fastest non-medullated fibres and those of the slowest medullated fibres, a result which might throw light on the question why fibres below 1 μ in diameter are not medullated.

4. The mean blocking temperature of sixteen non-medullated fibres was 4.3° C, a value that was significantly different from the mean blocking temperature of sixteen medullated fibres (6.5° C).

INTRODUCTION

It is generally accepted that there are marked differences between the properties of mammalian non-medullated and medullated nerve fibres (e.g. see Davson, 1964). This view has arisen from a comparison of non-medullated fibres with the larger diameter medullated fibres because relevant information is available only concerning the larger diameter medullated fibres (Huxley & Stampfli, 1949; Stampfli, 1954; Tasaki, 1955; Hodgkin, 1964). But since the diameter of non-medullated fibres ranges from 0.4 to 1.2 μ (Gasser, 1950), it would be more meaningful to compare the impulses

of non-medullated fibres with those of the smallest medullated fibres, i.e. with external diameters of about 1–2 μ .

In an earlier investigation (Paintal, 1966) the results were obtained largely from fibres with diameters greater than 2 μ , i.e. with conduction velocities greater than 10–12 m/sec. It was therefore necessary to extend the work to fibres with conduction velocities less than 12 m/sec. Information concerning impulses in single non-medullated fibres recorded at 37° C is also scant. At present it is accepted that the spike duration of non-medullated fibres is about 2 msec at 37° C (Grundfest, 1941; Davson, 1964). This is based (as stated by Gasser, 1950) on what had been recorded in 'single-fiber-like units' of visceral C-fibres by Grundfest & Gasser (1938). Gasser (1950) arrived at approximately the same value in dorsal root C-fibres. However, there are some indications that dorsal root G-fibres may differ from sympathetic C-fibres in certain respects (Gasser, 1950). This makes it desirable to compare sensory non-medullated fibres with medullated sensory fibres. Since the aortic nerve is wholly sensory (Agostoni, Chinnock, Daly & Murray, 1957; Devanandan, 1964) and contains both non-medullated fibres and a considerable number of medullated fibres with conduction velocities less than 12 m/sec (Paintal & Riley, 1966), it proved to be most suitable for this investigation.

It is assumed in this paper that fibres with conduction velocity less than 2.5 m/sec at 37° C are non-medullated. They cannot be medullated if, as is generally supposed, the diameter of the smallest medullated fibres is 1 μ (Duncan, 1934) and if the conduction velocity:fibre diameter ratio for such small diameter medullated fibres is 4.5 (Boyd, 1964, 1965). On the other hand, their conduction velocities are consistent with their being non-medullated; for, as Gasser (1950) showed, the maximum conduction velocity of non-medullated fibres of the dorsal roots is 2.5 m/sec, and it may be presumed this result is applicable to the non-medullated fibres of the aortic nerve since these, like the dorsal root fibres, are sensory. On the basis of the above reasoning, it is also assumed that all fibres with conduction velocities greater than 4.5 m/sec are medullated.

METHODS

Adult cats anaesthetized with chloralose (75 mg/kg) were used. The aortic nerve was identified by the presence of a baroreceptor discharge, and it was separated from the vagus for a few millimetres near the nodose ganglion. Impulses were recorded in filaments dissected from this nerve. Elsewhere, the aortic nerve was not separated from the vagus and sympathetic.

For studying the effect of temperature on aortic and some vagal nerve fibres and determining their blocking temperature, the experimental procedures described earlier (Paintal, 1965*a, b*) were used. Spike durations and the rising and falling phases of the monophasic spike of aortic fibres were measured according to procedures and criteria used in another paper (Paintal, 1966) except that the distance between the recording electrodes was

0.6 mm and not 1.0 mm. All the precautions and sources of errors described in the earlier papers (Paintal, 1965*a*, *b*; 1966) were taken into account wherever applicable.

Measurements relating to the refractory period were made at 17° C using the basic technique described earlier (Paintal, 1965*b*). However, in the present investigation it was not possible to determine the absolute refractory period after the first impulse (ARP) accurately because of the considerable lag in the second impulse that takes place in the cold pool. This error which is insignificant in faster conducting fibres is sizable in the slowly conducting fibres studied in the present investigation because the second impulse may lag behind the first by 5–20 msec at 17° C owing to the much reduced conduction velocity of the second impulse travelling in the relative refractory period of the first. Consequently, the least interval between the first and second stimuli at the stimulating electrodes (which is what is actually measured) cannot represent the least interval between the two impulses (produced by them) in the pool.

On the other hand since the conduction velocity of the third impulse immediately after the ARP of the second impulse is the same as that of the second impulse immediately after the ARP following the first impulse (Paintal, 1965*b*), the least interval between the second and third stimuli must represent the actual least interval between the second and third impulses in the coldest part of the pool. The least interval between the second and third stimuli therefore represents the ARP after the second impulse. This is what was measured in the present investigation and is referred to as ARP₂. To obtain this measurement the following procedure was adopted: the conduction velocity of a fibre was first determined at 37° C and the temperature of the cold pool (see Fig. 1 in Paintal, 1965*a*) was then brought down to 17° C ± 1° C. When the temperature reading was stable the interval between the first and second stimuli was adjusted so that the second impulse arrived at the coldest part of the pool (i.e. most refractory part) immediately after the ARP following the first impulse. The interval between the second and third stimuli was then adjusted such that the third just failed to yield a response. This interval between the second and third stimuli was then taken as ARP₂. The value was corrected to 17° C using a Q_{10} of 3.5 (Paintal, 1965*b*).

RESULTS

The impulses of thirty-eight fibres with conduction velocities of 0.9–14 m/sec were recorded satisfactorily (cf. Paintal, 1966). These fibres were divided into two groups, the medullated fibres (twenty fibres) with conduction velocities of 4.5–14 m/sec and the non-medullated fibres (seventeen fibres) with conduction velocities less than 2.5 m/sec (cf. Gasser, 1950); three fibres with conduction velocities between 2.5 and 3 m/sec have been included in this group, since their impulses appear to be similar to those of fibres with conduction velocities less than 2.5 m/sec. One fibre with a conduction velocity of 3.2 m/sec has been excluded from both groups but it is shown in Figs. 1–3.

The ARP₂ at 17° C of twenty-six fibres was determined in a different set of experiments. Of these ten fibres were non-medullated with conduction velocities between 1.2 and 2.2 m/sec and fifteen were medullated with conduction velocities between 4.5 and 11 m/sec. Again, there was one fibre with a conduction velocity of 3 m/sec which could not be placed in either category with confidence although it seems to form part of the medullated group (Fig. 4).

Spike duration, rise time, fall time and ARP₂. The relation of conduction

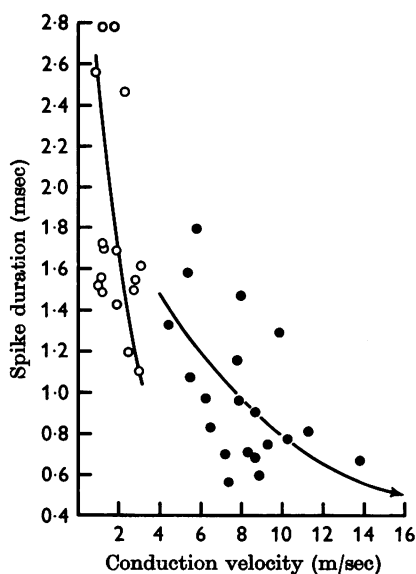


Fig. 1. Relation of spike duration to conduction velocity in medullated —●—●— and non-medullated —○—○— fibres. The lower part of the curve for medullated fibres has been drawn so that it is directed at a point at 16 m/sec whose value was obtained from the earlier paper (Paintal, 1966). Two points with spike durations of 3.4 and 3.6 msec (conduction velocity = 1.2 and 0.96 m/sec) have been omitted.

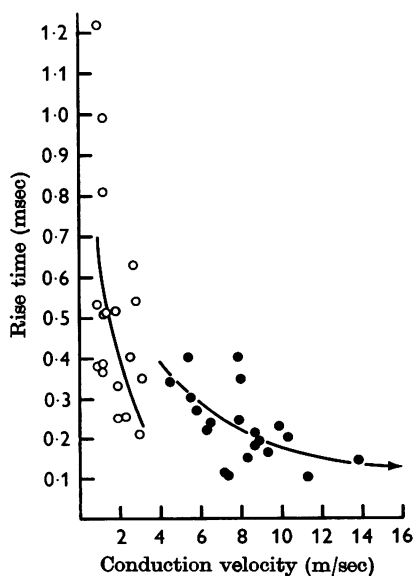


Fig. 2. Relation of rise time to conduction velocity in medullated —●—●— and non-medullated —○—○— fibres. Arrow for medullated fibres is directed at a point at 16 m/sec (cf. Fig. 1).

velocity to spike duration, rise time, fall time and ARP_2 in medullated and non-medullated fibres are shown respectively in Figs. 1-4. These results are in agreement with, and an extension of, those published earlier concerning fibres conducting faster than 12 m/sec (Paintal, 1965*b*; 1966). In

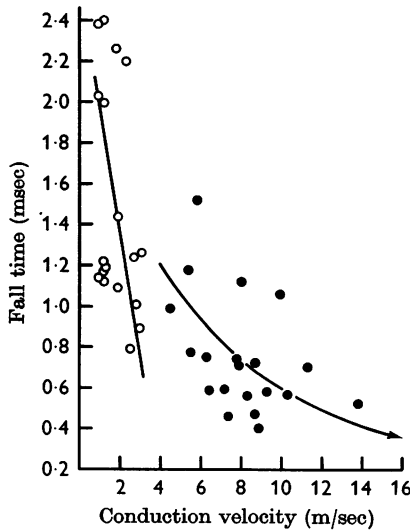


Fig. 3. Relation of fall time to conduction velocity in medullated —●—●— and non-medullated —○—○— fibres. Arrow in curve for medullated fibres is directed at a point at 16 m/sec (cf. Fig. 1).

all four figures the main point that stands out clearly, provided no distinction is drawn between medullated and non-medullated fibres, is that all the points seem to form part of a homogeneous sample, i.e. there is no evidence of any obvious qualitative difference between medullated and non-medullated fibres. However, if the two types of fibres are considered separately then two separate curves result (Figs. 1-4). Both curves were drawn by eye; that for the medullated fibres was drawn so that it passed through the point at 16 m/sec (Figs. 1-3). The points at 16 m/sec in Figs. 1-3 were obtained from the results of the earlier investigation (Paintal, 1966).

As in the case of the faster fibres (Paintal, 1966) spike duration varies inversely with conduction velocity. Figure 1 shows that the spike durations of several non-medullated fibres is between 1.1 and 1.7 msec, i.e. they are the same as or less than those of some medullated fibres with conduction velocities between 4.5 and 8 m/sec. It is therefore not possible to use spike duration as a means of distinguishing non-medullated fibres from slowly conducting medullated fibres. It is also noteworthy that the ARP_2 of some non-medullated fibres is equal to or less than the ARP_2 of medullated fibres with conduction velocities between 4.5 and 8 m/sec (Fig. 4).

Figure 2 shows that in about half of the non-medullated fibres the rise time is 0.2–0.4 msec. This is the same as that of the majority of medullated fibres with conduction velocities between 4.5 and 8 m/sec. This may be of importance in relation to the conduction velocity of medullated and non-medullated fibres.

In Figs. 1 and 4 are represented the fibres isolated in the two sets of experiments. In both there is a noticeable gap between 4.5 and 3 m/sec which is particularly noteworthy because a special attempt was made to fill it. If this gap is genuine it must represent the demarcation between the smallest medullated and largest non-medullated fibres. Therefore assuming that the smallest medullated fibres are 1 μ in diameter (Duncan, 1934) the conduction velocity:fibre diameter ratio at this level is about 4.5 as found by Boyd (1964). In view of the fact that several fibres with conduction velocities between 2.5 and 3 m/sec were isolated (Fig. 1) it seems necessary to extend the upper limit of conduction velocity of non-medullated fibres to 3 m/sec.

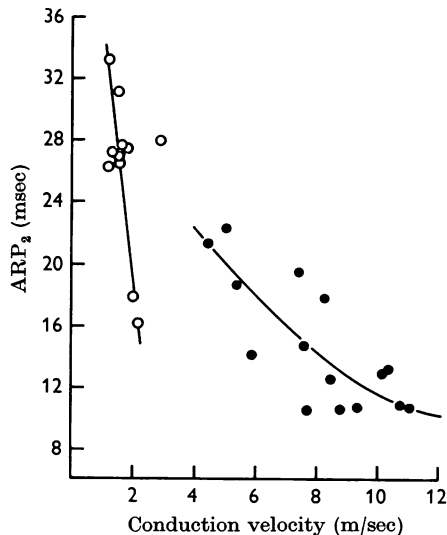


Fig. 4. Relation of ARP_2 to conduction velocity in medullated —●—●— and non-medullated —○—○— fibres.

Effect of temperature on non-medullated fibres. The effect of lowering the temperature on the conduction velocity of aortic and vagal non-medullated fibres is almost identical with that on medullated fibres. Thus in nine aortic non-medullated fibres the mean conduction velocity at 17° C was 21 % of normal. The corresponding value for sixteen aortic medullated fibres examined in the same cats was 22 %. Thus the temperature coefficient for conduction velocity in medullated and non-medullated fibres must be

similar. Further evidence of this was obtained by the determination of the Q_{10} from graphs showing the relation of temperature to conduction velocity. These graphs were similar to those relating to medullated fibres (Paintal, 1965*b*). From such graphs the values for Q_{10} obtained between 37 and 27° C were 1.3, 1.6 and 1.7 in three fibres (average, 1.5); between 28 and 18° C the values were 2.2, 2.2 and 2.0 (average, 2.1). Between 18 and 8° C the mean Q_{10} of six fibres was 3.0 (range, 2.4 to 3.7; s.d. 0.5). The values between 18 and 37° C are similar to those of medullated fibres reported earlier (Paintal, 1965*b*); those between 8 and 18° C are a little less.

The minimum conduction velocity at 3–6° C (i.e. just before block of conduction) averaged 3.7% of normal in five fibres. This yields a conduction velocity of about 3–4 cm/sec.

At about 17° C, the conduction velocity of the second impulse travelling in the relative refractory period of the first impulse averaged 12.6%. This value is almost identical with the value in medullated fibres (see Fig. 4 in Paintal, 1965*b*). Since the conduction velocity of the first impulse is 21% of normal (see above) this means that at 17° C the second impulse will lag behind the first by about 13 msec after travelling over 5 mm length of nerve in a fibre with a conduction velocity of 1 m/sec at 37° C. This concerns the errors that arise in the measurement of ARP (see Methods).

The blocking temperatures (cf. Paintal, 1965*a*) of sixteen non-medullated fibres averaged 4.3° C (range, 1.5–7.1° C; s.e., 0.4° C). The mean blocking temperature of sixteen medullated fibres (with conduction velocities between 20 and 50 m/sec) in the same cats was 6.5° C (range 2.5–8.1° C; s.e. 0.4° C). This value which is in agreement with the mean blocking temperature of vagal medullated fibres reported earlier (Paintal, 1965*a*) is significantly higher than the mean blocking temperature of non-medullated fibres.

Figure 5 shows the frequency distribution of the blocking temperatures of medullated and non-medullated fibres. These results indicate that at about 3–4° C when more than 90% of the medullated fibres are blocked, about 40% of the non-medullated fibres will still be able to conduct impulses. However, the maximum frequency of impulses which they can conduct at this temperature is of the order of 1–2 impulses/sec. This low frequency can be of importance in the production of certain reflex effects (see Discussion). At 10° C the peak frequency of discharge was 4–13 impulses/sec in five fibres. This is a little lower than the peak frequency in slowly conducting medullated fibres (Paintal, 1965*b*).

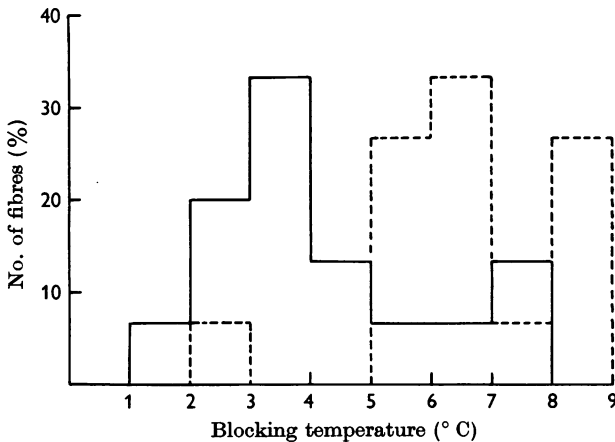


Fig. 5. Frequency distribution of the blocking temperature of medullated (interrupted lines) and non-medullated (continuous lines) fibres. There were sixteen fibres in each group.

DISCUSSION

The present results extend the observations on the temporal characteristics of the nerve impulse reported earlier (Paintal, 1966) into the lowest range of conduction velocities. They are also of interest in connexion with (1) the inverse relation between the time course of the impulse and fibre diameter (or conduction velocity) and (2) the transition from continuous conduction to saltatory conduction.

Regarding the first point, the fact that spike duration, rise time, fall time and ARP_2 of non-medullated fibres bear the same kind of relation to conduction velocity as they do in the case of medullated fibres (Figs. 1–4 and Paintal, 1966) suggests that the underlying mechanisms responsible for this relationship might be the same in the two groups. In both, as the diameter becomes less, the rate of rise and fall of the impulse is reduced. It is possible that the number of active sites on the membrane available for ionic transfer in relation to the total transfer is relatively smaller in the smaller diameter fibres. It is also possible that this may be related to the fact that the volume:area ratio falls with reduction in fibre diameter (D); in fact the ratio (equal to $D/4$) varies linearly with fibre diameter.

If it is assumed that membrane current/cm² is the same in fibres of different diameters then it follows that, because the rise time varies inversely with fibre diameter, the conduction velocity should tend to vary linearly with fibre diameter as observed by Gasser (1950) rather than vary as the square root of fibre diameter. The square root relationship holds if it is assumed that, in addition to other electrical characteristics, the rate

of rise of the impulse is constant in different fibres (Rushton, 1951; Hodgkin, 1954).

Regarding the second point, the noteworthy feature is that the time course of the action potential of the slowest medullated and fastest non-medullated fibres is identical (Figs. 1-3). Of special importance here is the rise time (Fig. 2) and since this is the same it follows that this factor (i.e. rate of rise of the impulse) cannot be responsible for the fact that the conduction velocity of the medullated fibres of about $1\ \mu$ external diameter (4.5 m/sec) is about twice as great as the maximum conduction velocity of non-medullated fibres (2.5 m/sec) with the same diameter of $1\ \mu$ (cf. Gasser, 1950). This increased conduction velocity must be attributed to saltatory conduction. Saltatory conduction must become less and less of an advantage as the length of the internode which varies linearly with fibre diameter (Hursh, 1939; Vizoso & Young, 1948) decreases, till its length becomes so small that it is of little added value. However, probably a more important reason why fibres below $1\ \mu$ are not medullated is the marked increase in rise time that would result with further reduction in diameter. Thus extrapolating the curve for medullated fibres in Fig. 2 to 3 m/sec would lead to a considerable increase in the rise time of the impulse yielding values that would be about $1\frac{1}{2}$ -2 times that of non-medullated fibres of $1\ \mu$ diameter (conduction velocity, 2.5 m/sec). Therefore if the increase in rise time balances the advantages of saltatory conduction, there would be no advantage in having a medullary sheath.

If a particular node is stimulated with a brief pulse, then only after the impulse in it has reached a critical amplitude (say over 20% of spike height) can it depolarize the next node sufficiently to yield an impulse there. In other words, the speed of depolarization of a node must depend on the rate of rise of the impulse at the previous node. This factor which has been taken into account in the prediction of conduction velocity of the squid axon (Hodgkin & Huxley, 1952; Huxley, 1959) has not received sufficient attention because it was believed that the rate of rise of the impulse is the same in all medullated fibres of different diameters (cf. Tasaki's personal communication in Rushton, 1951). Consequently, the conduction velocity of medullated nerve fibres has been computed largely in terms of the cable constants of the nerve (Rushton, 1951; Huxley & Stampfli, 1949; Hodgkin, 1964). As shown in the previous paper (Paintal, 1966) and in this one (Fig. 2), the rate of rise of the impulse varies inversely with fibre diameter. This probably plays an important part in determining the speed of conduction and in determining the relationship of fibre diameter to conduction velocity.

There is apparently very little difference between ARP and ARP₂ (see Fig. 23 in Hodgkin, 1938). The ARP₂ has been determined in the present

investigation since it was not possible to determine the ARP of the slowest fibres accurately enough owing, as pointed out in Methods, to the considerable lag of the second impulse in the cooled section of the nerve. This lag accounts for the appreciable difference between ARP and ARP_2 of the slower fibres (especially in fibres with conduction velocities of about 10 m/sec) observed in the previous paper, a difference that was absent in the five faster conducting fibres with conduction velocities greater than 30 m/sec (Fig. 8*A* in Paintal, 1965*b*). This error in the measurement of the ARP, if present to a significant degree, would lead to an underestimate of the ARP. It must have been insignificant in the case of the main measurement (i.e. Fig. 8*C* in Paintal, 1965*b*) since the value of ARP of the slow fibres at 16° C in that paper is close to the value recorded at 17° C in the present paper (Fig. 4). Anyway this experience indicates that it is safer to measure ARP_2 than ARP using the present methods since for practical purposes there is no difference between the two as shown by observations on the crab axon (Hodgkin, 1938) or in the medullated fibres with conduction velocities greater than 30 m/sec (Paintal, 1965*b*).

The results indicate that the blocking temperatures of non-medullated fibres is significantly lower than that of medullated fibres, which as shown previously (Paintal, 1965*a*) are all blocked within the same range of temperature regardless of fibre diameter. The difference between non-medullated and medullated fibres might therefore represent a difference arising out of continuous and saltatory conduction in them respectively.

The fact that at about 3–4° C, when the large majority of medullated fibres are blocked, about 40 % of the non-medullated fibres can still conduct about 1–2 impulses/sec is of importance in certain reflex studies where nerves (e.g. vagus) are cooled locally to block reflexes selectively. In the case of those non-medullated sensory fibres which are normally active, this ability to conduct 1–2 impulses/sec will not be of much importance because when the frequency of discharge exceeds the maximum transmissible frequency (Paintal, 1965*b*) either total block results, or the emerging frequency is greatly reduced below the maximum transmissible frequency (Paintal, 1965*b*). However, if the fibres are normally silent, then a sudden stimulus will result in the transmission of at least one large volley in the large numbers of non-medullated fibres usually present.

At 10° C the peak frequency of discharge in non-medullated fibres is 4–13 impulses/sec. Therefore unlike the sensory medullated fibres, the degree of block of the normal discharge in non-medullated ones is not likely to be profound since the usual frequency of discharge in them is low.

I am much indebted to Professor B. Katz, F.R.S. for valuable discussion and suggestions.

REFERENCES

- AGOSTONI, E., CHINNOCK, J. E., DALY, M. DE BURGH & MURRAY, J. G. (1957). Functional and histological studies of the vagus nerve and its branches to the heart, lungs and abdominal viscera in the cat. *J. Physiol.* **135**, 182–205.
- BOYD, I. A. (1964). The relation between conduction velocity and diameter for the three groups of efferent fibres in nerves to mammalian skeletal muscle. *J. Physiol.* **175**, 33–35P.
- BOYD, I. A. (1965). Differences in the diameter and conduction velocity of motor and fusimotor fibres in nerves to different muscles in the hind limb of the cat. In *Studies in Physiology*, ed. CURTIS, D. R. & McINTYRE, A. K., pp. 7–12. Berlin: Springer-Verlag.
- DAVSON, H. (1964). *A Textbook of General Physiology*, 3rd edn., p. 174. London: Churchill.
- DEVANANDAN, M. S. (1964). A study of the myelinated nerve fibres of the aortic nerve of cats. *J. Physiol.* **171**, 361–367.
- DUNCAN, D. (1934). A relation between axon diameter and myelination determined by measurement of myelinated spinal root fibres. *J. comp. Neurol.* **60**, 437–462.
- GASSER, H. S. (1950). Unmyelinated fibres originating in dorsal root ganglia. *J. gen. Physiol.* **33**, 651–690.
- GRUNDFEST, H. (1941). Bioelectric potentials. *A. Rev. Physiol.* **2**, 213–242.
- GRUNDFEST, H. & GASSER, H. S. (1938). Properties of mammalian nerve fibers of slowest conduction. *Am. J. Physiol.* **123**, 307–318.
- HODGKIN, A. L. (1938). The subthreshold potentials in a crustacean nerve fibre. *Proc. R. Soc. B* **126**, 87–121.
- HODGKIN, A. L. (1954). A note on conduction velocity. *J. Physiol.* **125**, 221–224.
- HODGKIN, A. L. (1964). *The Conduction of the Nervous Impulse*, pp. 52–53. Liverpool: University Press.
- HODGKIN, A. L. & HUXLEY, A. F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.* **117**, 500–544.
- HURSH, J. B. (1939). Conduction velocity and diameter of nerve fibers. *Am. J. Physiol.* **127**, 131–139.
- HUXLEY, A. F. (1959). Physical and chemical aspects of nerve impulse conduction. *Ann. N.Y. Acad. Sci.* **81**, 221–246.
- HUXLEY, A. F. & STAMFFLI, R. (1949). Evidence for saltatory conduction in peripheral myelinated nerve fibres. *J. Physiol.* **108**, 315–339.
- PAINTAL, A. S. (1965*a*). Block of conduction in mammalian myelinated nerve fibres by low temperatures. *J. Physiol.* **180**, 1–19.
- PAINTAL, A. S. (1965*b*). Effects of temperature on conduction in single vagal and saphenous myelinated nerve fibres of the cat. *J. Physiol.* **180**, 20–49.
- PAINTAL, A. S. (1966). The influence of diameter of medullated nerve fibres of cats on the rising and falling phases of the spike and its recovery. *J. Physiol.* **184**, 791–811.
- PAINTAL, A. S. & RILEY, R. L. (1966). Responses of aortic chemoreceptors. *J. appl. Physiol.* **21**, 543–548.
- RUSHTON, W. A. H. (1951). A theory of the effects of fibre size in medullated nerve. *J. Physiol.* **115**, 101–122.
- STAMFFLI, R. (1954). Saltatory conduction in nerve. *Physiol. Rev.* **34**, 101–112.
- TASAKI, I. (1955). New measurements of the capacity and the resistance of the myelin sheath and the nodal membrane of the isolated frog nerve fiber. *Am. J. Physiol.* **181**, 639–650.
- VIZOSO, A. D. & YOUNG, J. Z. (1948). Internode length and fibre diameter in developing and regenerating nerves. *J. Anat.* **82**, 110–134.