J. Physiol. (1958) 141, 305–322

SOME PROPERTIES OF FROG SKIN MECHANORECEPTORS

By W. T. CATTON

From the Department of Physiology, University of Durham Medical School, King's College, Newcastle upon Tyne 1

(*Received* 29 *November* 1957)

The properties of single sensory units in the skin have been studied in the past using the single-fibre preparation. This has been achieved in the frog either by the recording of antidromic impulses evoked in a severed branch of skin nerve by stimulation of a nearby area of skin innervated by an adjacent nerve branch (Adrian, Cattell & Hoagland, 1931), or by isolation of single afferent fibres in a skin nerve (Maruhashi, Mizuguchi & Tasaki, 1952). An alternative method is to excite individual endings by sharply localized stimulation, and to record from the intact skin nerve. This has the advantages of saving much time in dissection, and of ensuring that measurements, such as velocity of conduction of afferent spikes, are made on the fibre in its normal situation in the nerve trunk, and not exposed to air. Thus using a fine shielded metal tip (diameter 20 μ) both for mechanical and electrical stimulation, it was possible to elicit single unit responses by either means of stimulation. Owing to the simple nature of the method many observations could be made on one preparation. Preliminary accounts of parts of this work have already been presented (Catton, 1957*a*, *b*).

The sensory innervation of frog skin may be briefly described as follows. Myelinated and non-myelinated axons entering the subepidermal layers form a deep and a superficial plexus. From these plexuses arise axons which branch into fine non-myelinated fibres, some ending in the subepidermal layers, some in association with the skin glands and blood vessels and many penetrating and ending freely in the epidermis (Ecker & Wiedersheim, 1904). Only one kind of anatomically differentiated ending has been described, the so-called 'tactile corpuscle' (Merkel, 1880), having a limited distribution. Eberth & Bunge (1893) described 'endzellen', lying close under the epidermis, from which some of the epidermal endings were derived; these do not appear to have been described by subsequent authors. The general picture is one of a closely interwoven network of naked axons, derived by profuse branching of

the myelinated sensory axons, and showing extensive overlapping of areas innervated by single afferent fibres. The dermal endings have been described in more detail using modern techniques (Whitear, 1955).

METHODS

Portions of calf skin of *Rana temporaria*, with attached nerve branch (ramus cutaneus cruralis medius), were mounted in a Perspex chamber. The skin was laid on a silver plate serving as earthed indifferent electrode, and the nerve was laid across two silver wire electrodes connected to the amplifier. The whole preparation was covered with liquid paraffin, and was found to remain responsive for several hours. The chamber was mounted in a mechanical stage on a microscope stand, so that it could be moved in the horizontal plane by small measured amounts. The 20 μ shielded electrode, forming part of the stimulator unit (Fig. 1), was moved only in the vertical plane. The

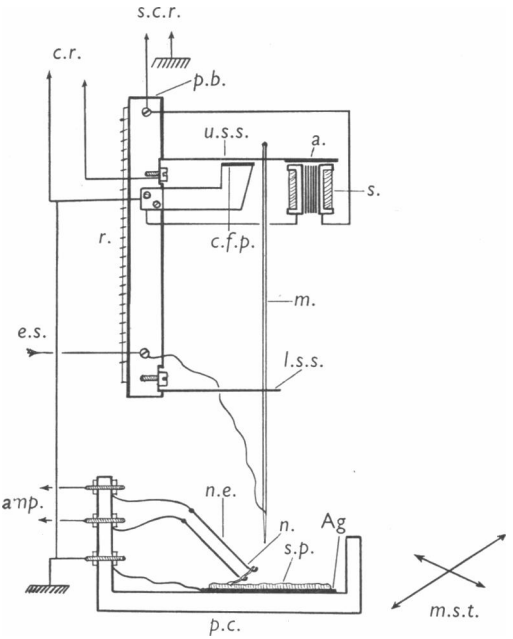

Fig. 1. Diagram of apparatus for skin stimulation. *c.r.*, capacitance recorder; *s.c.r.*, solenoid current supply; *p.b.*, Perspex bar; *u.s.s.*, upper support strip; *a*, armature; *s*, solenoid; *c.f.p.*, capacitor fixed plate; *m.*, micro-electrode; *l.s.s.*, lower support strip; *n.*, nerve; *s.p.*, skin preparation; *Ag*, silver plate; *p.c.*, Perspex chamber; *n.e.*, nerve electrodes; *r.*, rack; *amp.*, leads to amplifier; *e.s.*, lead from stimulator; *m.s.t.*, mechanical stage traverse.

stimulator unit was mounted on the focusing rack, the microscope body being discarded, so that the normal focusing controls were available for setting the initial level of the electrode tip. The unit shown in Fig. 1, using solenoid and armature drive, was the one used in later experiments; it had the advantage that it could be driven by one pulse of a two-pulse electronic stimulator, with the interposition of a single-stage power amplifier to provide the solenoid current. Since the solenoid was some distance away from the pick-up leads, very little artifact due to the current pulse appeared on the oscillograph trace. The rise time of the mechanical pulse was nearly constant at 1·5 msec so that the slope of rise varied directly with amplitude. An earlier

stimulator used pneumatic transmission; the amplitude was nearly constant, but a wide range of slopes could be obtained. With either arrangement the maximum displacement obtainable was about 50 μ, but movements of the order of 5 μ were usually sufficient to evoke responses from single units. The absolute amplitudes of the movements were not recorded, but the movements were monitored by a simple capacitor device attached to one of the electrode support strips. The capacity change was amplified and passed to the second beam of the oscillograph, the nerve responses appearing on the first beam. Electrical pulse stimuli, derived from the second pulse output of the electronic stimulator, were applied to the electrode via a radio-link isolating unit, to minimize the artifact. The latencies of the mechanically evoked responses were measured from the commencement of the mechanical displacement; for the electrically evoked responses, latencies were measured from the electrical artifact. Conduction velocities in main sensory axons were estimated from observed conduction times when stimulation was applied to intradermal nerve branches, and by measuring the length of nerve between these points and the first recording electrode.

RESULTS

Impulse discharges evoked by mechanical stimulation

The discharges evoked by point stimulation could be placed in four main categories: (*a*) large, fast-conducted spikes of amplitude 350–450 μV, conduction velocity 20–30 m/sec; (*b*) medium size and conduction velocity, 200–300 μV and 10–15 m/sec respectively; (*c*) small size and velocity, 100–150 μV and 5–10 m/sec respectively, but still in the myelinated range; (*d*) small, slowly conducted spikes, having the low broad-contour profile characteristic of spikes in non-myelinated fibres, amplitude < 100 μV, velocity 0·1–0·3 m/sec. Further properties were as follows.

Type (*a*) *discharge.* These were evoked either by gentle stroking of the outer skin surface, by rapid vertical displacements applied from the inside or outside, or by slower displacements when the point was pressing on the inside surface of the epidermis (Fig. 2i, iii, iv). Stroking of the outer surface evoked these spikes almost exclusively, but they could only be obtained from numerous but discrete limited areas, each about 50 μ square. Sections of skin from such areas were stained by methylene blue and silver methods, but heavy pigmentation made interpretation difficult, and no evidence of specialized endings was found. These large spikes were very rarely discharged more than once per stimulus (Figs. 2iii, iv; 3ii). Under rapid repetitive stimulation they appeared as very brief trains at 200/sec (Fig. 5iii) and more usually followed the stimuli only at frequencies of up to about 3/sec. The maximum following rate was dependent on stimulus strength: thus when a spike failed to follow as the frequency was raised it could be made to follow again by increasing the stimulus strength; when it became fatigued at the new frequency, once again an increase in the stimulus would cause it to follow. A similar phenomenon was described by Keidel (1955) but probably for fibres of types (*b*) or (*c*) below. This threshold-raising effect of repetitive stimulation is illustrated in Fig. 6 for four different type (*b*) responses. The latency of the type (*a*) spikes varied with rate of displacement of the stimulating tip, being as long as 50 msec

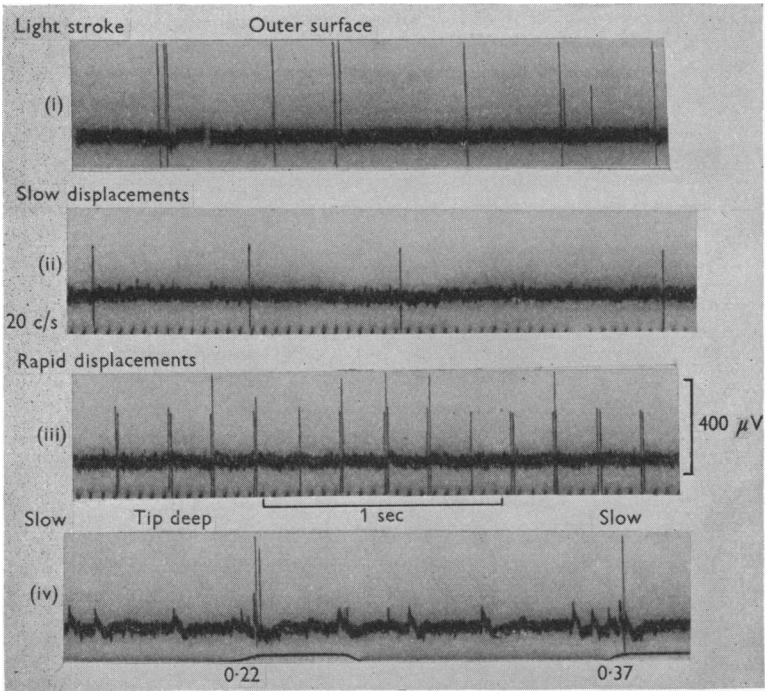

Fig. 2. Sensory ending discharges in skin nerve in response to mechanical stimuli. (i) Type (*a*) discharges evoked by light stroking of outer surface; (ii) Type (*b*) discharges evoked by slow displacements applied to inner surface; (iii) Types (*a*) and (*b*) discharges evoked by rapid displacements at same site as (ii); (iv) Type (*d*) discharges evoked by steady pressure of tip against inside of epidermis, with superimposed slow displacements, signalled by lower trace, evoking type (*a*) discharges. Time marker records (ii) and (iii), 20 c/s.

for very slow, near-threshold displacements, shortening to 5–10 msec for the most rapid.

Type (b) discharge. Spikes in the medium range could be evoked by vertical displacements applied to the inner or outer surfaces, although more readily from the inner. They were obtained generally at lower displacement rates than were needed to produce type (*a*) discharges (Fig. 2ii, iii) and tended to fire repetitively at higher rates (Fig. 2iii). When stimuli were applied from the inside, as the point was progressively sunk deeper the type (*b*) spikes were obtained first, type (*a*) later, and when the point was resting on the inside of the epidermis only the type (*a*) discharge could be evoked (Fig. 2iv). Repetitive discharges of up to 15 spikes at frequencies of 60/sec could be elicited from fresh preparations when large, briefly maintained displacements were used. Under repetitive mechanical stimulation the type (*b*) spikes followed at frequencies of 300/sec for very brief periods (Fig. 5ii), at 100/sec for longer

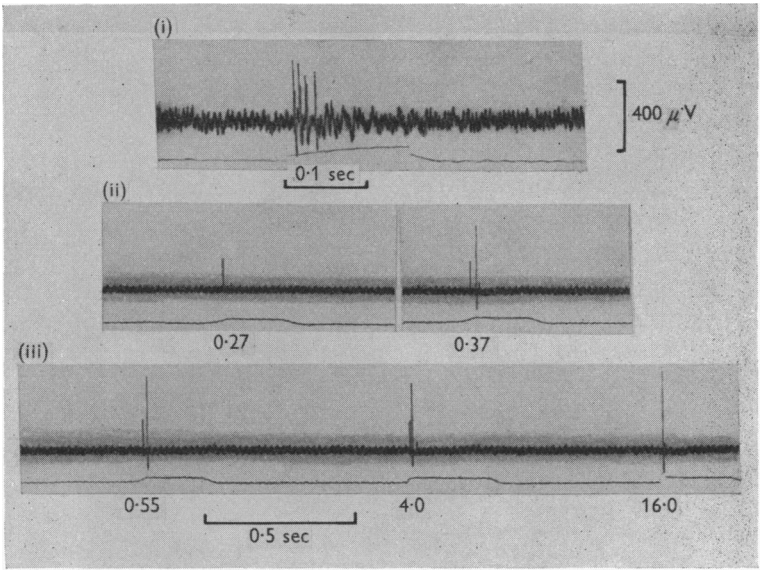

Fig. 3. (i) Train of discharges (upper trace) initiated by a single displacement (lower trace lasting 0·12 sec; note delayed small fibre discharges. (ii, iii) Effect of increasing rate of displacement on latencies of medium and large fibre discharges; rate of displacement shown below record (see text).

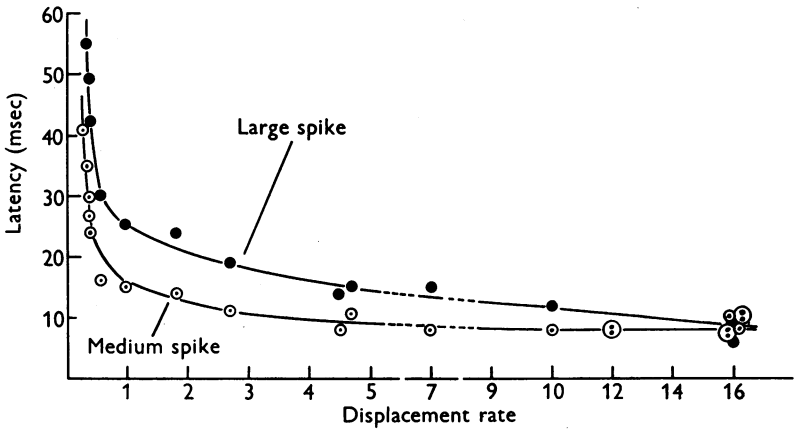

Fig. 4. Latency values for a large (●) and a medium (⊙) spike response plotted against displacement rate (see Fig. 3). The graph has been compressed on the horizontal axis by omission of points at 6 and 8; note altered abscissa scale.

periods (Fig. 5iii) and at 20/sec for several seconds (Fig. 5v, vi). There was a wide variation in the maximum following frequency for different endings. Generally if the following rate of the unfatigued ending was high, then the

steady following rate was also high, but always much less than for the unfatigued state.

Latency values for medium spikes ranged from 40 msec for slow rates of displacement down to 5–10 msec for rapid rates. At all except high rates the latencies were shorter than for type (*a*) spikes, but at high rates the latencies for type (*a*) and type (*b*) became equal (Figs. 3ii, 4). The distribution of type (*b*) spike responses was much more widespread than for type (*a*) and localization of the former was correspondingly more difficult.

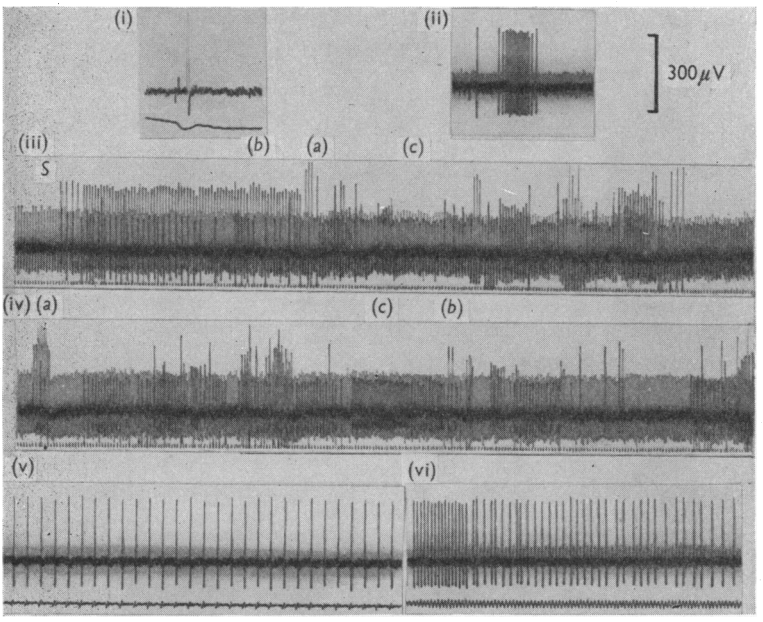

Fig. 5. Impulse discharges in skin nerve evoked by mechanical stimulation. (i) Upper trace, a single type (*a*) spike response, outer surface stimulation; lower trace, mechanical signal; latency 5 msec. (ii) A brief burst of type (*b*) spikes following stimulation at frequency of 300/sec. (iii) Variety of responses obtained by traversing the stimulating tip over the outer surface whilst vibrating at 100/sec; *S*, stimulus artifact, types (*a*), (*b*) and (*c*) discharges labelled. (iv) As for (iii) but vibration frequency 200/sec, showing similar variety of discharges, but only type (*c*) are able to follow for more than a few vibrations. (v) Single type (*b*) spikes following stimuli at a frequency of 20/sec. (vi) As for (v) but frequency 60/sec, showing rapid fatigue. Lower trace, records (iii)–(vi), mechanical signal.

Type (*c*) *discharges*. These had the characteristics of spikes propagated in small myelinated axons. They were most readily evoked by rapid repetitive stimulation and followed at frequencies of 200/sec or more, with less adaptation than was shown for type (*a*) and (*b*) (Fig. 5iv). Their distribution was widespread, as for type (*b*). Spikes in the same range of sizes were produced by various forms of chemical stimulation, by dilute NaCl and HNO_3, as also by ACh.

Type (d) discharges. These had the characteristics of spikes propagated in non-myelinated axons. Fresh preparations showed irregular discharges which persisted in the absence of stimulation for periods of up to 10 min. They could then be readily elicited by pressing the electrode point firmly against the inside of the epidermis (Fig. 2iv). Occasionally a short burst would follow a single displacement stimulus after a long latency (Fig. 3i). Type (*d*) spike responses showed little or no adaptation to maintained stimulation. Their distribution was widespread, and latency values ranged from 40 to 100 msec.

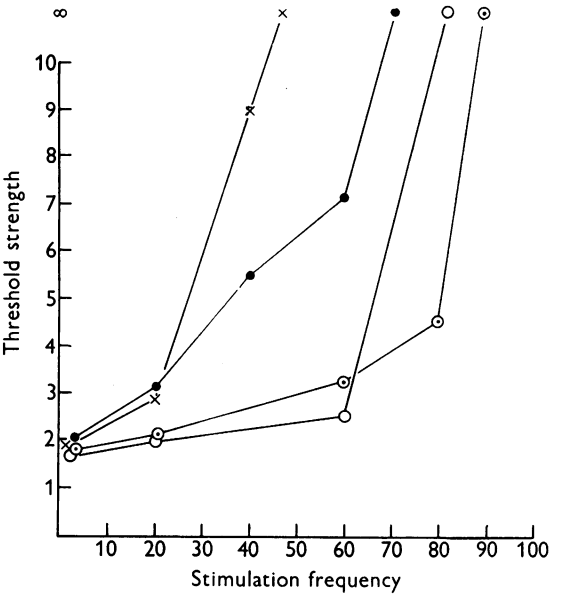

Fig. 6. Variation of threshold with frequency of stimulation for some medium spike responses.

Localized discharges evoked by mechanical stimulation

Localized spike responses to the point stimulus could be obtained both for type (*a*) and type (*b*) spikes, but much more critical adjustment was needed for the latter. In view of the wide area innervated by the numerous branches of one afferent axon and the fact that these areas overlap extensively, as is shown by the original work of Adrian and others, such localized responses are presumed to be elicited by stimulation of one particular terminal branch. This view is supported by various observations. Thus, when the tip, whilst undergoing mechanical movements at a steady frequency was traversed through very small distances in the vicinity of one such isolated response, regular rapid shifts of latency occurred for the identical impulse as picked up in the sensory axon. A position could be found where the latency had a minimum value, all movements from this site causing an increase in latency. A

possible interpretation of this result, related to the terminal branches of a single sensory axon, is as follows. Stimulation at *B* (Fig. 7) would result in a shorter latency of response than stimulation at *A* or *C*, owing to the shorter length of nerve ending underlying *B*. This variability of latency in relation to the precise position of the stimulating tip constitutes one variable factor in mechanical-response–latency measurements, in addition to the well known 'latency-shortening' effect of increased stimulus strength. Conceivably the two might have a common origin, in that increased displacements applied at points such as *A* or *C* (Fig. 7) could cause the site of origin of the impulse to

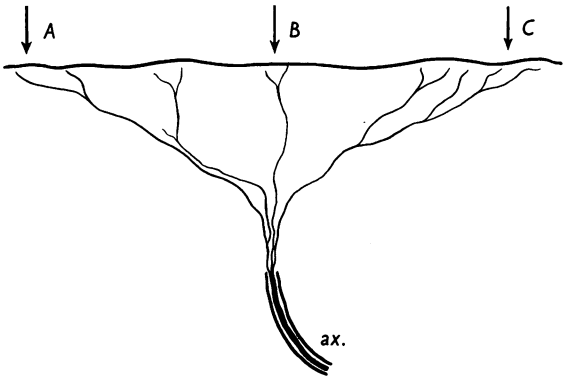

Fig. 7. Schematic terminal fibre distribution of a single myelinated sensory axon (for explanation see text). *ax*, sensory axon.

be shifted to more proximal regions of the terminal arborization. It is not then surprising to find that the frequency–distribution diagram of latency values for mechanical stimulation, from a large number of experiments, shows a wide scatter (Fig. 8). On the same diagram are plotted the results from all electrical stimulation experiments (see below), and it is seen that the distribution of latencies to mechanical and electrical stimulation are generally similar, although discharges in response to electrical stimulation are evoked more commonly than those to mechanical stimulation in the ranges 1–4 and 7–13 msec. The former may represent a proportion of cases where nerve branches were directly stimulated. the latter may include non-mechanoreceptor responses.

Spike discharges evoked by localized electrical stimulation

When an electrical pulse of duration 0·2 msec or longer was applied to the skin via the 20 μ shielded electrode, a pattern of spike discharges of varying latencies was recorded from the cutaneous nerve. It was found that many of these responses, particularly those of longer latency, were rapidly fatigued by such stimulation, and it was necessary to use frequencies not higher than 1 or

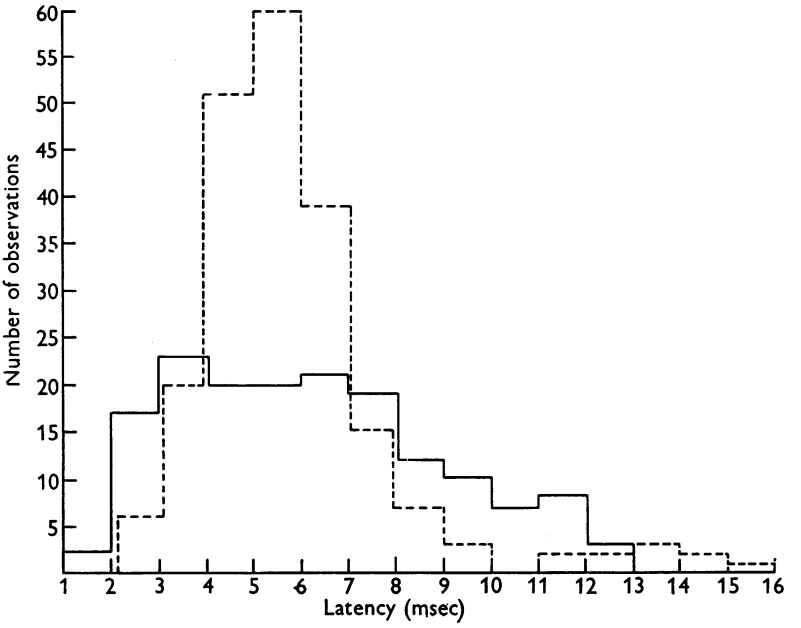

Fig. 8. Latency values for mechanical stimulation (broken line) and electrical stimulation (continuous line) of a large number of sensory ending responses to outside surface stimulation. The values include those of all three types of fast-conducted mechanoreceptor response described.

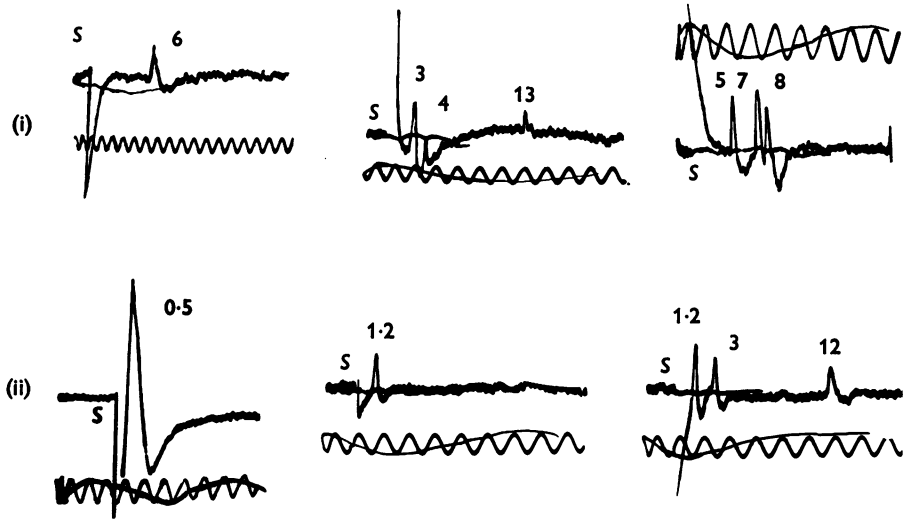

Fig. 9. Afferent impulses in cutaneous nerve in response to local electrical pulse stimulation of outer and inner skin surfaces; single sweep records. (i) responses obtained at three different outside sites; (ii) responses at three different inside sites; in the first an intradermal nerve twig was stimulated. Time marker, first record in line (i), 1000 c/s; remainder 500 c/s; the figures on each record are the latencies in msec; S = stimulus artifact.

2/sec to avoid this. There was no pattern of response characteristic of all sites stimulated, but in general the large spikes showed shorter latencies than the small (Fig. 9) and also had lower threshold values (Fig. 10). Using inside stimulation the earliest spikes (Fig. 9ii, 0·5 and 1·2 msec) were able to follow stimuli at frequencies up to the maximum available (400/sec); it could then often be seen that a small nerve branch in the skin underlay the electrode. These responses were thus attributed to direct stimulation of intradermal myelinated fibres. In this way, by measuring the conduction distance the

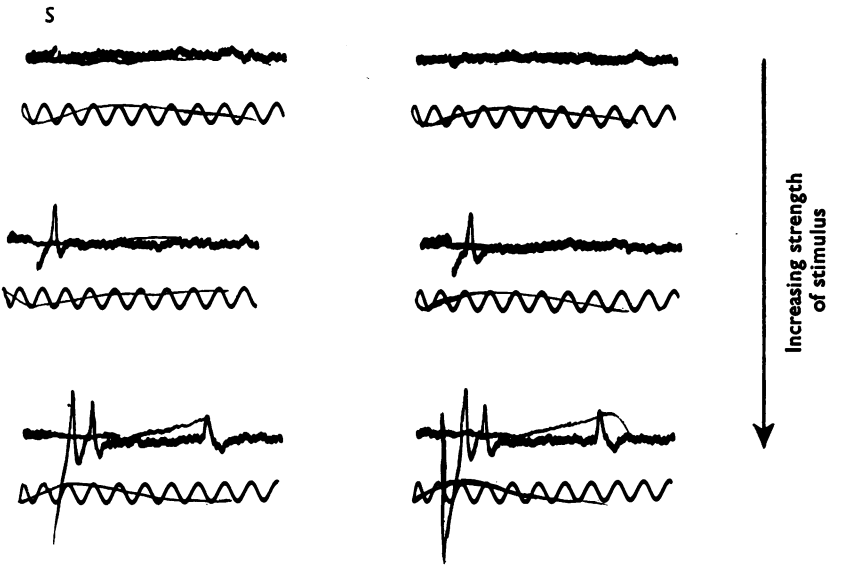

Fig. 10. Responses to electrical pulse stimulation, showing effect of increasing stimulus strength; later spikes have higher thresholds than early ones; *S*, stimulus artifact; time marker, 500 c/s.

conduction velocity in the main axon was calculated for each spike category. The later spikes became fatigued at rates exceeding about 3/sec and greater pulse-widths were needed to elicit them. Typical strength–duration curves for two of these responses are shown in Fig. 11. In order to avoid, as far as possible, the direct stimulation of intradermal nerve branches, electrical stimuli were applied to the outer skin surface in the expectation that in this way the free endings would be selectively stimulated. The results for many observations both for inside and outside stimulation were then plotted as frequency–distribution diagrams (Fig. 12). This revealed that there was a characteristic difference between the patterns of spikes evoked at the two surfaces. Thus inside stimulation elicited a far higher proportion of responses in the shortest latency range (0·5–2·5 msec) than did outside stimulation, where the responses were grouped mainly in the range 2·5–10 msec, with a

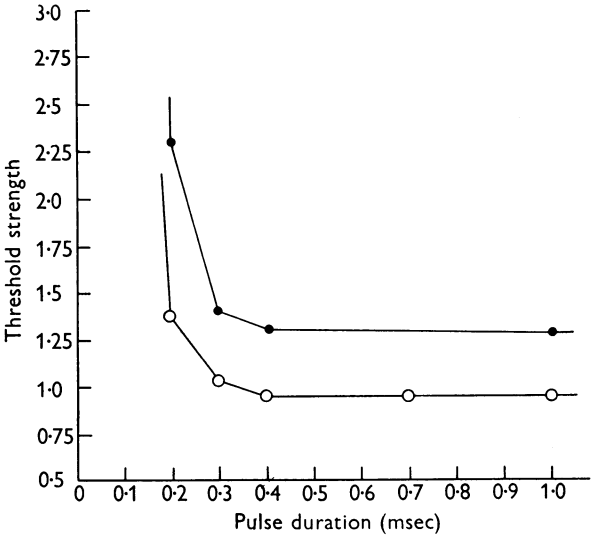

Fig. 11. Strength-duration curves for two sensory endings.

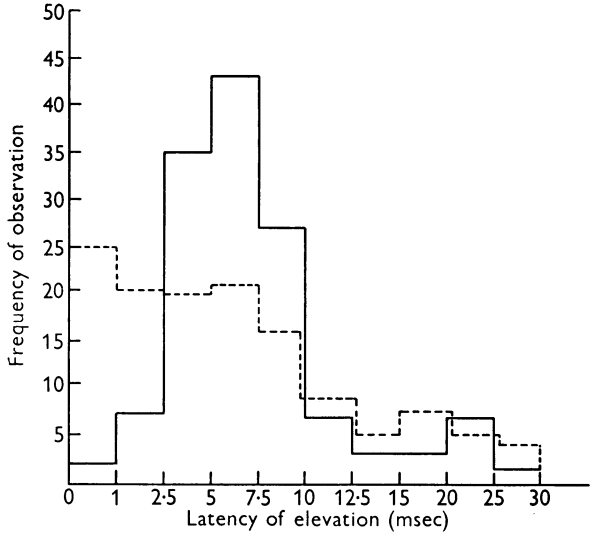

Fig. 12. Frequency distribution of observed latency values for sensory responses to electrical pulse stimulation of outer (continuous line) and inner (broken line) surfaces of skin.

peak from 5 to 7·5 msec. This peak would include the peak of latency values for mechanical stimulation in all experiments (Fig. 8) and the mean latency value of 5·1 msec given by Gray & Malcolm (1951) for mechanical stimulation of the dorsal skin–nerve preparation. This seems to suggest that the majority of the spikes produced by outside electrical stimulation were derived from mechanoreceptors, although it would be expected that thermal and chemo-

receptor endings would be excited by the same stimulation. A further possible deduction from Fig. 12 is that the conduction time in the free nerve endings is of the order of at least four times greater than in the peripheral axon. (Latency of spike produced by stimulation of ending = 5 msec; that produced by stimulation of intradermal myelinated axon = 0·5–1·0 msec; difference = 4·0–4·5 msec; ratio of conduction times ending: main axon = 4:1–9:1). Since the length of the naked endings cannot exceed 1 or 2 mm the conduction velocity would then be very low, e.g. for 1 mm length of ending and conduction time of 4 msec it would be 0·25 m/sec; for 2 mm 0·125 m/sec. These values are in the range expected for small non-myelinated axons, and indeed fall in the range (0·1–0·3 m/sec) estimated for the pain fibres, which are non-myelinated throughout their course.

Receptor delay

This term is understood to denote the time interval between the commencement of the mechanical stimulus and the instant of discharge of the first impulse at the mechanoreceptor ending. The technique employed seemed to permit the measurement of this delay by the following procedure. A single spike was evoked by a mechanical stimulus and its latency (threshold value) was noted. An electrical pulse was then applied without moving the electrode and an attempt was made to identify a spike of identical characteristics, which could therefore be regarded as being propagated in the same axon and hence derived from the same ending, or at least from another ending of the same axon. It was assumed that the electrical stimulus initiated an impulse with negligible delay. Evidence of identity of the spikes evoked by the two modes of stimulation was sought as follows. The spikes were regarded as being propagated in the same axon if they obeyed the conditions: (i) they should have identical amplitudes and (ii) identical duration; and (iii) when the two spikes were evoked on the same time base and made to approach each other, the second spike should be abolished within the refractory period due to the first (1–3 msec). Of many responses tested only a small proportion were found to fulfil all these conditions; often it was not possible to elicit a response to an electrical stimulus at a site which gave a mechanical response, and vice versa. In cases where identity was certain, the latency to the electrical stimulus was in general shorter than to the mechanical stimulus, although in some cases the electrical latency was longer. The time differences observed covered a fairly wide range. Out of 70 cases the values of receptor delay (mechanical latency minus electrical latency) ranged from 0·5 to 4·5 msec, 55 being in the range 1–3 msec and 46 of these in the range 1·5–3 msec. No distinction could be made between receptor delays for types (*a*), (*b*) and (*c*) responses, all giving values falling within the full range. A reasonable deduction would be that the receptor delay at these endings is similar for all fast-conducted mechanical

responses and has a value close to 2 msec. The value would in any case be expected to be small and of this order, since the plots for all results of electrical and mechanical stimulation (Fig. 8) show no evidence of a large relative displacement in time. Further evidence for a change in excitability of the endings at a time interval of about 2 msec was afforded by the experiments reported in the next section.

Lowering of threshold to electrical stimulation by a preceding subliminal mechanical stimulus

Subliminal mechanical stimuli were applied at a site from which both electrical and mechanical stimuli evoked a response. With electrical and mechanical pulses widely separated in time, the electrical stimulus was set just below threshold. When now the time interval was shortened, the electrical response appeared at an interval of about 2 msec following the beginning of the mechanical pulse, and disappeared again at a time interval of about 6 msec. Thus, following a mechanical stimulus, after a delay of about 2 msec, the excitability of the ending rises and remains above normal for a further period of about 4 msec. The effect was of a marginal nature and it was not possible to plot the time course of the change in excitability with the apparatus available. The converse effect, lowering of the threshold to a mechanical stimulus by a preceding subliminal electrical pulse, was obtained only with inside siting of the electrode, using outward-flowing current for the conditioning pulse. These excitability changes following a pulse stimulus may possibly be presumed to indicate the time course of a membrane depolarization ('generator potential') at the sensory endings.

DISCUSSION

Since we do not know what sensations the frog experiences from stimulation of its skin, we work by analogy with such comparable data as are accepted from human and mammalian experiments. The behaviour of the intact frog confirms that it is sensitive to mechanical stimuli applied to its skin and its responses are in general similar to those evoked in mammals by comparable types of stimulus. In mammals it is accepted that tactile sensations are mediated in large sensory axons, pain sensations in small myelinated and in non-myelinated axons. The sensory discharges are further characterized by differences in rate of adaptation to maintained stimulation.

The following sensory functions may be tentatively assigned to the four categories of mechanoreceptor described:

Type (*a*), fast-conducted, fast-adapting discharges from touch receptors probably sited mainly in the epidermis. They appear to correspond to the type A_1 endings of Fessard & Segers (1943), to the tactile endings of Maruhashi *et al.* (1952) and to the touch endings studied by Loewenstein (1956), all on frog skin.

Type (*b*), slower conduction and slower adaptation than for type (*a*); probably sited mainly in the subepidermal layers. They seem to correspond to the type A_2 endings (slowly-adapting touch receptors) of Fessard & Segers, and to the 'stretch' endings studied by Loewenstein. The effective mechanical deformation which initiates an impulse is in all cases probably a stretching of the naked fibre termination. Thus, whether we call type (*b*) spikes slowly adapting touch, pressure or stretch responses depends essentially on the mode of application of the mechanical stimulus. In the present experiments the skin was not grossly stretched, but the type (*b*) spikes have the same characteristics as those evoked by stretch in Loewenstein's experiments. The microanatomy of the subepidermal endings has been described by Whitear (1955).

Type (*c*) spikes show yet slower conduction and slower adaptation than type (*b*). Since they are particularly readily evoked by rapid repetitive stimulation, they seem well fitted to subserve the role of vibration-receptors, if vibration sense is to be regarded as a separate modality. It has been shown that the minimum movement required to evoke a sensation of vibration at the finger tip in man is about $0{\cdot}02\,\mu$ at 400 c/s (Wilska, 1954). There is the possibility that the type (*c*) discharges may originate primarily from chemo- or thermo-receptors stimulated anomalously in this way, since they fall in the same range of spike size and it is known that the converse effect is possible, i.e. that mechano-receptor responses can be evoked by thermal stimulation (Hensel & Zotterman, 1951; Dodt, 1955).

Type (*d*) discharges clearly represent slowly-conducted pain.

A comparison of the properties of types (*a*) (*b*) and (*d*) discharges with the categories A_1, A_2 and 'pain' described by Fessard & Segers is given in Table 1. Clearly with the present method the spike amplitudes are about ten times greater, the spike duration of the larger fibres much shorter, and the conduction velocity of the non-myelinated fibres much lower. These results are much more in accord with the usual properties of frog nerve fibres and may reflect a more nearly normal preparation.

Electro-physiological investigations of the sensory responses of mammalian skin have indicated that in a general way it is possible to correlate specific modes of sensation with characteristic discharges in corresponding types of afferent fibre, grouped according to diameter (and hence according to spike amplitude and conduction velocity). Such findings have not been widely accepted by many anatomists who have closely studied the morphology of mammalian cutaneous sensory endings, and little correlation appears to exist at present between the physiological and anatomical schools of investigation. Thus modern anatomical studies (e.g. Weddell, Palmer & Pallie, 1955) have led to the conclusion that all nerve fibres entering mammalian skin terminate in arborizations of fine ($<1\,\mu$) naked exoplasmic filaments which probably

end freely. This is identical with the picture in frog skin. So far has the anatomical school deviated from acceptance of the doctrine of 'specific nerve energies', that Sinclair (1955) has stated the view that cutaneous sensation is mediated by a spatially and temporally dispersed pattern of impulses leaving the skin. The physical characteristics of this pattern are to be the determining factors in the experience of sensory quality, with the conclusion that there are no histological grounds on which to erect theories of cutaneous sensibility based on the existence of four primary modalities, touch, warmth, cold and pain,

TABLE 1. Summary of characteristics of frog skin mechanoreceptors

	Fast-adapting touch		Slow-adapting touch or stretch			
	A_1*	Type (*a*)†	A^2*	Type (*b*)†	'Pain'*	Type (*d*)†
Spike size (μV)	30–50	350–450	10–20	200–300	1–5	100
Spike duration (msec)	2·3	1	3·5	1	7–18	5–15
Adaptation rate	Quasi-instantaneous	Instantaneous	'a few seconds'	0·5 sec	'Several minutes'	Of the order of minutes
Conduction velocity (m/sec)	18–20	20	11–14	10–15	'A few m/sec'	0·1–0·3
Minimum displacement rate to elicit	High	High	Moderate	Moderate	—	—
Rate of following repetitive stimulation	Above 75/sec	300/sec unfatigued 5/sec fatigued	Below 50/sec	300/sec unfatigued 20/sec fatigued	—	—

* Responses described by Fessard & Segers (1943); † Responses described in present work.

operating within the 'law of specific nerve energies'. Further, that there is no evidence for the existence of specific nerve endings subserving these modalities. Certainly recent work (e.g. Lele & Weddell, 1956) has shown that the cornea, possessing only free nerve endings, subserves touch and temperature, as well as pain sensation. In general, then, the ability of a system of free nerve endings to originate impulse discharges in sensory axons related to specific modalities of sensation, although difficult to explain in the context of our present knowledge of the mode of origin of the sensory impulse, is a fairly well substantiated process. On the other hand, views such as those expressed above must be regarded as extreme, in that they leave no role for the highly specialized encapsulated endings dispersed so widely in mammalian skin.

As regards the present work it has been shown that at least four types of mechanoreceptor are found in frog skin, having characteristic properties. The question of choice of terminology has arisen in designating the recorded impulses. Thus in earlier work it was customary to use the terms 'fast' and 'slow' to designate the large tactile spikes and the very small and broad contour spikes of pain receptors respectively. Since spike size and conduction velocity in myelinated fibres are closely proportionate quantities, in general either term may be used for descriptive purposes in a constant experimental situation.

But what is generally observed in the first instance is spike size, and the estimate of conduction velocity could only be approximate with the method used. Thus the responses were classified according to size and such estimates of conduction velocity as could be made showed that there was a general proportionality between spike size and velocity.

The variation reported here of latency with rate of mechanical displacement covers a wider range than has been recorded previously. This may be due to the wide range over which the rate of displacement could be varied in these experiments. We may briefly speculate on the factors which may contribute to the latency-shortening effect of increased rates of displacement. The following sources of delay must be considered: (*a*) a short delay, due to the transmission time of the wave of mechanical displacement through the tissues; (*b*) the time taken for the 'generator potential' at the ending to reach the critical amplitude for the firing of an impulse; and (*c*) variable delay due to excitation occurring progressively at points nearer the main axons as the stimulus strength rises. Of these (*a*) is not known, but is likely to be small and constant; (*b*) is also not known but is likely to be of the order of 1 msec or so (cf. results of Gray & Sato (1953) on Pacinian corpuscle of cat's mesentery), and variable over a short range; (*c*) seems most likely to contribute most of the variation observed, but can only do so within the limits of the conduction time along the naked sensory fibre termination, which is of the order of 4 msec. The sum of all these delays (perhaps 10 msec) thus falls far short of the longest latencies (40 msec or more) measured experimentally, and no explanation for these long latencies is immediately evident.

The method used for measurement of receptor delay is based on the three assumptions: (*x*) that an electrical stimulus initiates an impulse at the ending with negligible delay, (*y*) that the mechanical stimulus evokes an impulse discharged in the same axon, and (*z*) that each type of stimulus initiates the discharge at the same region of the extended sensory termination. Of these, (*z*) is possibly the least justifiable. It seems likely that, as described above, the point of excitation to a considerable extent determines the value of latency measured, according to the length of naked fibre termination which must be traversed before the impulse reaches the beginning of the main axon. Since the conduction time in these naked terminations is long compared to that in the main axon, marked errors in latency estimation will be associated with shifting of the effective point of excitation either along the length of one termination, or from the tip of one to the tip of another of shorter length. Taking into account these uncertainties which perhaps account for the wide range in estimated receptor delays (1–10 msec), it is surprising to find that nearly 80% of values measured fall in the range of 1–3 msec. This range includes the values from 1·5 to 3 msec obtained for receptor delay at the Pacinian corpuscle (Gray & Malcolm, 1950; Gray & Sato, 1953).

It is difficult to account for the finding that the responses to electrical pulse stimuli fatigue much more readily than do those to mechanical stimuli. Thus for mechanical stimulation many of the smaller responses (type *c*) follow at frequencies of 200/sec or more; yet none of the electrical responses which could be excluded as direct nerve responses were capable of following at frequencies higher than about 3/sec. Used in this sense, fatigue might be regarded as an index of rate of adaptation or accommodation, being measured in terms of rise of the threshold value. Thus electrical stimulation seems to bring about a very marked accommodation, or alternatively is effective at a region where accommodation is more rapid than for mechanical stimulation.

There still remains the problem of differentiation of sensory function among a population of sensory endings presenting apparently homogeneous morphological characters. Loewenstein (1956) has suggested a possible basis for such functional differentiation in the case of frog skin. He found that the application of constant stretch to a skin preparation altered the characteristics of the normally fast-adapting touch receptors so that they behaved in the same way as the more slowly adapting 'stretch' receptors. According to Loewenstein the fast-adapting endings are in a state of relaxation, with their membranes partially folded, whereas the 'stretch' endings are normally extended, with no folding of their membranes. The application of constant stretch causes unfolding of the membranes of the fast-adapting receptors; in this 'biased' condition they now become slow-adapting. A similar suggestion has been made for the specialized stretch receptor cells of certain Crustacea (Eyzaguirre & Kuffler, 1955). For the slow-adapting RM_1 receptor less slippage is possible between the dendrite terminals and surrounding tissue than for the RM_2 type (fast-adapting), so that the RM_1 type could be under some degree of tension before application of the mechanical stimulus.

SUMMARY

1. A method is described for applying to frog skin sharply localized mechanical or electrical stimuli, separately or in combination. Single sensory unit discharges could be recorded by the method.

2. By mechanical stimulation four types of spike responses could be recorded from the cutaneous nerve; the characteristics and probable functional correlations of these responses are described.

3. Electrical pulse stimulation evoked patterns of spike responses of a wide range of latency values; stimulation of the inner surface produced a much higher proportion of short-latency responses than was found for outside stimulation. It could be inferred from the results of electrical stimulation that conduction of the sensory impulse in the fine naked axon terminations was much slower than in the main myelinated axon, and an approximate value for

conduction velocity in these endings would be 0·25 m/sec. The responses to electrical stimulation generally fatigued at much lower frequencies than did those to mechanical stimulation of the same area.

4. Receptor delay for these endings was estimated by making independent measurements of the spike responses of the same ending to electrical and to mechanical stimuli. Most values fell in the range 1·5–3 msec.

5. Following a subliminal mechanical stimulus the excitability of the endings begins to be enhanced at a time of 1·5–3 msec after the application of such a stimulus. The excitability remains above normal for a further period of 3–6 msec. This may represent the approximate time course of the 'generator potential'.

REFERENCES

ADRIAN, E. D., CATTELL, M. K. & HOAGLAND, H. (1931). Sensory discharges in single cutaneous nerve fibres. *J. Physiol.* **72**, 377–391.

CATTON, W. T. (1957*a*). Micro-electrode stimulation of frog skin. *J. Physiol.* **136**, 33*P*.

CATTON, W. T. (1957*b*). Responses of frog skin to local mechanical stimulation. *J. Physiol.* **137**, 81–82*P*.

DODT, E. (1955). Aktivierung markhaltiger und markloser Schmerzfasern bei Temperaturreizen. *Pflüg. Arch. ges. Physiol.* **260**, 225–238.

EBERTH, C. J. & BUNGE, R. (1893). Die Endingungen der Nerven in der Haut des Frosches. *Anat. Hefte*, Bd. 2.

ECKER, A. & WIEDERSHEIM, R. (1904). *Anatomie des Frosches.* 3 Abt. Braunschweig: Viewig.

EYZAGUIRRE, C. & KUFFLER, S. W. (1955). Processes of excitation in the dendrites and soma of single isolated sensory nerve cells of the lobster and crayfish. *J. gen. Physiol.* **39**, 87–119.

FESSARD, A. & SEGERS, M. (1943). Quelques caractères différentiels des récepteurs cutanés. *C.R. Soc. Biol., Paris*, **137**, 212–213.

GRAY, J. A. B. & MALCOLM, J. L. (1950). The initiation of nerve impulses by mesenteric Pacinian corpuscles. *Proc. Roy. Soc.* B, **137**, 96–114.

GRAY, J. A. B. & MALCOLM, J. L. (1951). The excitation of touch receptors in frog's skin. *J. Physiol.* **115**, 1–15.

GRAY, J. A. B. & SATO, M. (1953). Properties of the receptor potential in Pacinian corpuscles. *J. Physiol.* **122**, 610–636.

HENSEL, H. & ZOTTERMAN, Y. (1951). The response of mechanoreceptors to thermal stimulation. *J. Physiol.* **115**, 16–24.

KEIDEL, W. D. (1955). Aktionspotentiale des N. dorsocutaneus bei nieder-frequenter Vibration der Froschrückenhaut. *Pflüg. Arch. ges. Physiol.* **260**, 416–436.

LELE, P. P. & WEDDELL, G. (1956). The relationship between neurohistology and corneal sensibility. *Brain*, **79**, 119–54.

LOEWENSTEIN, W. R. (1956). Excitation and changes in adaptation by stretch of mechanoreceptors. *J. Physiol.* **133**, 588–602.

MARUHASHI, J., MIZUGUCHI, K. & TASAKI, I. (1952). Action currents in single fibres elicited by stimulation of the skin of the toad and the cat. *J. Physiol.* **117**, 129–151.

MERKEL, F. (1880). *Über die Endigungen der sensiblen Nerven in der Haut der Wirbelthiere.* Rostock: H. Schmidt.

SINCLAIR, D. C. (1955). Cutaneous sensation and the doctrine of specific energy. *Brain*, **78**, 584–614.

WEDDELL, G., PALMER, E. & PALLIE, W. (1955). Nerve endings in mammalian skin. *Biol. Rev.* **30**, 159–195.

WHITEAR, M. (1955). Dermal nerve endings in *Rana* and *Bufo*. *Quart. J. micr. Sci.* **96**, 343–349.

WILSKA, A. (1954). On the vibrational sensitivity in different regions of the body surface. *Acta physiol. scand.* **31**, 285–289.