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TWO CLASSES OF SLOWLY ADAPTING MECHANORECEPTOR FIBRES IN REPTILE CUTANEOUS NERVE

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SUMMARY

1. The myelinated fibre spectrum of the plantar nerve of reptile consists of a unimodal distribution corresponding approximately to the delta elevation in mammalian nerve and contains a variety of receptor categories similar to those of mammals except for the obvious absence of structures related to hairs.

2. The various receptor types of reptilian skin do not fall into discrete groups on the basis of conduction velocity.

3. Only a few thermoreceptor fibres were identified but a large proportion of slowly adapting mechanoreceptors responded to rapid temperature transients.

4. Two distinct categories of slowly adapting receptors whose discharge is related to the amplitude of skin displacement have been identified and studied in detail. These two receptors can be distinguished by their patterns of discharge, and display several distinctive features including differences in resting discharge, receptive field size, threshold, response to DC polarization, etc.

5. The mathematical functions describing the response to stimuli of varying magnitude for one receptor type is markedly affected by the sequence of stimulus presentation.

INTRODUCTION

The wide variety of receptor categories in vertebrate skin that would appear to be expected from the morphological specialization of cutaneous nerve endings and the broad fibre spectrum of cutaneous nerves has been demonstrated by the pioneer experiments of Adrian & Zotterman (1926), Zotterman (1939), Witt & Hensel (1959), and Iggo (1959*a*, *b*, 1963*a*, *b*). In the past decade, improved systematic sampling methods have revealed detailed information on the high-threshold mechanoreceptors (Hunt &

McIntyre, 1960*b*; Iggo, 1959*a*, 1966; Burgess & Perl, 1967; Perl, 1968; Burgess, Petit & Warren, 1968; Bessou & Perl, 1969), thermal receptors (Witt & Hensel, 1959; Kenshalo & Gallegos, 1967; Iggo, 1969) and on at least two distinct varieties of slowly adapting, displacement sensitive receptors (Chambers & Iggo, 1967, 1968; Brown & Iggo, 1967; Burgess *et al.* 1968; Iggo & Muir, 1969) in addition to a variety of receptors associated with hairs (Brown & Iggo, 1967; Nilsson, 1969*a*, *b*) and Pacinian corpuscles (Gray & Matthews, 1951; Hunt, 1961; Loewenstein, 1961) in mammalian skin. Particular attention has been directed towards the properties of slowly adapting mechanoreceptors (Tapper, 1965; Werner & Mountcastle, 1965; Mountcastle, Talbot & Kornhuber, 1966; Burgess *et al.* 1968; Siminoff, 1968; Iggo & Muir, 1969) because these receptors presumably provide information required for sensory discrimination of the magnitude of skin displacement, but some of the quantitative features described require re-evaluation in the light of current knowledge suggesting that these receptors do not constitute a homogeneous population (Chambers & Iggo, 1967; Burgess *et al.* 1968; Iggo & Muir, 1969).

The present study was aimed at establishing criteria for classification of varieties of slowly adapting mechanoreceptors and their axons on the basis of conduction velocity, mechanical and thermal sensitivity, discharge pattern, displacement functions and adaptive properties, receptive field organization and response to DC polarization. The results indicate a distinctive fibre spectrum for a reptilian cutaneous nerve and the presence of specialized receptors that had escaped notice in earlier studies of reptilian cutaneous receptor fibres (Siminoff & Kruger, 1968; Siminoff, 1968; Proske, 1969). Comparison with recent studies of mammalian cutaneous mechanoreceptors reveals little indication of differences attributable to evolutionary status except for the appearance of receptors associated with hairs and a separate range of rapidly conducting axons in mammals. Some of these observations have been presented elsewhere in a preliminary abstract (Kenton, Kruger & Woo, 1969).

METHODS

Experiments were performed on alligators and caimans of 0·75–1·25 kg (18–22 in. long) which were anaesthetized with sodium pentobarbitone (Nembutal, 25 mg/kg) administered intraperitoneally and paralysed with an intramuscular injection of gallamine triethiodide (Flaxedil, 4 mg/kg). Artificial respiration was provided by a flow of filtered air from a positive pressure respirator (Medtronic) through a tracheal cannula. The lower extremity was secured to a heavy platform with dental plastic and the femur was clamped to the same platform. Movements of the spinal column were minimized by clamping the dorsal spine approximately one inch above the exposed dorsal roots. Room and animal temperatures showed little fluctuation from an average of 24–26° C.

A 1 in. long incision was made in the tibial region and the plantar nerve exposed and laid on a pair of stimulating electrodes. DC polarization experiments were performed on a number of fibres with polarizing platinum electrodes placed about ¼ in. proximal to the pair of stimulating electrodes.

The dorsal roots and spinal cord were exposed in the lumbosacral region and small filaments in reptile-Ringer solution (7·8 g NaCl, 0·12 g $CaCl_2$, 0·175 g KCl, 0·1 g $NaHCO_3$, 1000 ml. H_2O) were separated by microdissection under 40 × magnification, and placed on a fine platinum recording-hook electrode. During those experiments in which prolonged contact with single fibres was not required, glass micropipette electrodes filled with 3 M-KCl solution were employed for dorsal root recordings in lieu of platinum electrodes. A single-ended emitter follower was used for impedance matching with both platinum and glass electrodes and conventional means were employed in amplifying and displaying neural activity. Signals were continuously monitored on magnetic tape (Ampex SP-300) and oscilloscope records were photographed with a Grass kymograph camera.

Fibre stimulation. Dorsal root filaments were isolated by micro-dissection and placed on the recording electrode after which the entire plantar nerve was electrically stimulated by a rectangular pulse of 0·05 msec duration. If an action potential was observed at the recording site, an attempt was made to locate the receptive field for that fibre. Once the receptive field was identified, the fibre was readily classified as either rapidly adapting (RA, responding only to a mechanical transient) or slowly adapting (SA, discharging continuously during application of a mechanical stimulus).

Conduction velocities (at approximately 25° C) were determined at 3 times threshold intensities. Measurements of conduction distances were made *in situ* at the termination of all experiments by laying a fine thread along the course of the nerve from the recording electrode to the stimulating electrodes. The thread was arranged to follow every portion of the nerve path. The use of a pair of stimulating electrodes (5 mm separation) permitted two independent measurements of each conduction velocity. Conduction velocities determined by these two methods were essentially consistent.

Temperature sensitivity. Temperature sensitivity measurements were performed on all fibres with which sufficiently prolonged electrode contact could be maintained. Upon determination of the mechanical threshold for a particular receptor, a thermistor was placed on the skin surface immediately adjacent to the maximally sensitive area. Radiant heat ($\leqslant$ 50° C) was then applied and the temperature excursion recorded. The skin was allowed to return to room temperature (approximately 25° C) and the receptor was then cooled ($\geqslant$ 3° C) by application of ether or ethyl chloride over the region.

Mechanical displacement. The methods described in the preceding sections were applied to both microdissection and glass micropipette recordings. With its clear superiority in maintaining prolonged contact with individual fibres, the fibre dissection technique was employed exclusively for the recording of extensive stimulus–response studies on slowly adapting fibres.

Receptive fields were determined with a set of calibrated von Frey hairs, ranging from 0·05 to 20 g. The mechanical threshold was determined for the finest von Frey hair that could elicit a response at the region of maximum sensitivity within each receptive field. Skin displacement thresholds, on the other hand, ranged between amplitudes of 2–185 μ, with 25 % of the measurements falling below 10 μ. Receptive field sizes varied widely from approximately 0·25–16 mm^2, depending largely upon position on the limb, with smaller receptive fields near the limb apices (Siminoff & Kruger, 1968).

A moving-coil stimulator (3 Ω Goodman vibrator, V 47), equipped with a calibrated strain gauge displacement monitor and driven by a low impedance power amplifier with an excursion range of 1·2 mm (Ling, Model 50), provided the tactile stimuli for these stimulus–response studies. A conical stylus with a flat tip (0·25 mm diameter) was attached and the entire probe assembly was roughly oriented perpendicularly over the appropriate portion of the skin with a heavy ball-joint stage mounted on a rack and pinion. Precise positioning of the probe tip was achieved with a micrometer under microscopic control at 40 × . Calibrated von Frey hairs were used to locate the region of maximum sensitivity within each receptive field. A number of high amplitude initial displacements were performed until the skin (under microscopic observation) returned to the position it had attained between the two previous stimuli. This position was defined as zero displacement with the probe tip just contacting the skin, monitored by noting the position of the probe tip at which a just-noticeable shift was observed in the strain gauge output ($< 3\,\mu$). Except where otherwise specified, the stimulus duration and repetition rate were always 900 msec and 6/min respectively. The maximum mechanical risetime was 2·5 msec at the upper range of probe displacements, which usually did not exceed 700 μ for these receptors.

For each of thirty fibres studied extensively (Table 1), the stimulus–response relationship was determined by applying rectangular mechanical displacements of 900 msec duration to the area of maximum sensitivity within the receptive field. Stimulus intensity was successively increased over the entire dynamic range of the receptor from threshold to maximum response (i.e. that displacement amplitude above which no increase in response could be elicited), with one stimulus application at each amplitude. Upon completion of one such 'ascending' series, stimulus intensity was successively decreased ('descending' series) until threshold displacement was attained. At least three 'ascending' and three 'descending' series were performed for each fibre. The position of the probe tip was constantly observed microscopically to insure that the probe was just touching the skin between stimuli and that the tip was not displaced laterally during application of the stimulus. In the event of either of these irregularities the entire series was discarded.

In addition to these thirty receptors, three type I fibres were studied over only part of the dynamic range (40 to 85 % of maximum displacement), but over a wide range of repetition rates (6/min, 4/min, 3/min, 2/min, 1/min and 40/hr) and with several successive stimulus applications (6 at 40/hr to 15 at 6/min) at each displacement.

Histological analysis. Small blocks of skin outlining the receptive fields of eighty-one fibres were dissected free for histological examination and stained according to a modified Bielschowsky-Gros or Holmes silver methods or with routine haematoxylin and eosin staining. Although a variety of receptors was identified, it was difficult to assign specific morphological patterns to physiological properties in most cases, because either too many endings were visible or staining was unsuccessful in the exact site where a pin was inserted to identify the centre of the receptive field.

Data analysis. Determination of stimulus–response relationships for the extensively studied slowly adapting fibres was accomplished by means of least-squares fitting of the recorded data. Five families of mathematical functions were chosen for the trial fittings for each receptor:

logarithmic $R = a+b\log S,$ (1)

linear $R = a+bS,$ (2)

power $R = aS^b\ (b \neq 1)$ (or: $\log R = a'+b\log S$), (3)

exponential $R = a\exp(bS)$ (or: $\ln R = a'+bS$), (4)

exp (exp) $R = \exp(a\exp(bS))$ (or: $\ln(\ln R) = a'+bS$), (5)

where S is the stimulus, R is the response and a, a', b are the constants to be determined for each fit. For each fibre, the cumulative 'ascending' and 'descending' series data were analysed independently. Any fibre that did not yield consistent results from one 'ascending' or 'descending' series to the next was discarded for detailed analysis.

Correlation coefficients were calculated for each fit and the best fitting curve was determined by the highest valued correlation coefficient.

Computing assistance was obtained from the Health Sciences Computing Facility, UCLA, sponsored by NIH Grant FR-3, and from the Data Processing Laboratory, UCLA Brain Research Institute, sponsored by NIH Grant NB-02501.

RESULTS

Fibre spectrum and conduction velocity. The distribution of axons according to size was determined in a single specimen of the plantar nerve stained with osmium tetroxide in order to visualize myelin sheaths. The cross-sectional area of every fibre (including the myelin sheaths) was measured and diameters assigned on the basis of equal area circular cross-sections, thus enabling reconstruction of a fibre spectrum of all myelinated axons. This sample reveals a single-peaked continuous distribution (Fig. 1*A*) with a large proportion of fibres below 2 μ in diameter and the absence of a distinct peak of large fibres characteristic of the beta range of mammalian nerve. Silver stained preparations revealed the presence of numerous non-myelinated axons but difficulties were encountered in recording from this portion of the spectrum.

Conduction velocities were obtained for 259 fibres in the present study, but a comparison with the fibre size spectrum reveals that the sample is biased by an inadequate representation of smaller diameter fibres; only 13 % conducted at velocities below 10 m/sec at 25° C. In many circumstances, slowly conducting fibres could be identified easily (Fig. 5*A*) and studied at length in dissected multi-fibre fascicles, but a deliberate attempt to isolate such fibres with glass micropipettes was required to enlarge the sample presented in Fig. 1*B*. Both methods (micro-electrodes and single strand dissection) proved difficult for maintaining prolonged observation of smaller fibres, thereby resulting in a distinct sample bias, but, qualitatively, electrical and histological methods show a single peak comparable with the delta elevation of mammalian cutaneous limb nerves (Figs. 1 and 2). The lower range of conduction velocities within this fibre size range in reptilian nerve is presumably largely accounted for by the lower temperature (approximately 25° C) at which these measurements were made.

Types of receptors. Mechanoreceptor categories similar to those found in mammalian skin are found widely represented in the fibre spectrum of reptilian nerve with the notable absence of rapidly conducting hair receptor fibres. Most receptor types fail to display a distinctive range of conduction velocities with the possible exception of those varieties for which the sample is too small to permit adequate comparison. There is a

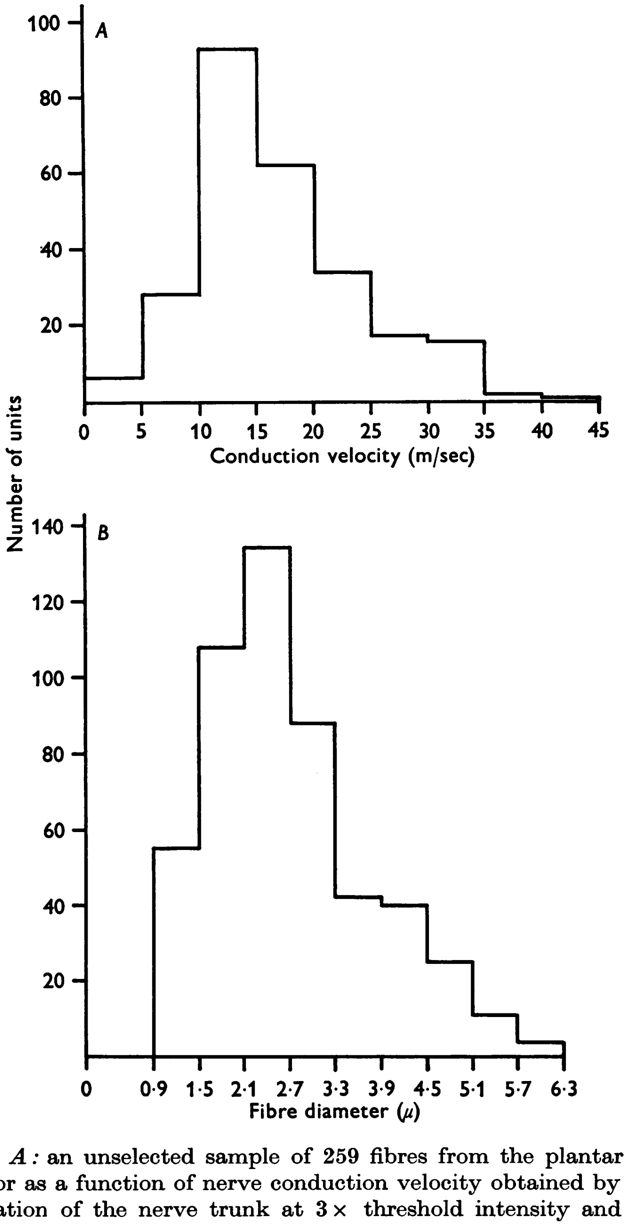


Fig. 1. *A:* an unselected sample of 259 fibres from the plantar nerve of alligator as a function of nerve conduction velocity obtained by electrical stimulation of the nerve trunk at 3 × threshold intensity and recorded with micropipette or platinum hook electrodes at 25° C.

B: distribution of fibre diameters for 507 myelinated axons determined from a myelin stained plantar nerve cross-section.

tendency for rapidly adapting receptor fibres to conduct faster than slowly adapting receptor fibres (Fig. 2), with means of 19·4 and 14·8 m/sec respectively, but fibre size does not constitute a satisfactory basis for separation of receptor types in these reptiles.

Slowly adapting mechanoreceptors. Receptor fibres displaying a sustained discharge whose mean frequency is a direct function of displacement amplitude have been described extensively for mammalian skin (Witt & Hensel, 1959; Hunt & McIntyre, 1960*a*; Iggo, 1963*b*, 1966; Tapper, 1964, 1965; Werner & Mountcastle, 1965; Mountcastle *et al.* 1966; Brown & Iggo, 1967; Burgess *et al.* 1968; Iggo & Muir, 1969) and shown to display a variety of other features that might be employed in delineating distinct receptor categories. A subdivision into two classes in a cat hairy skin has been proposed on the basis of discharge pattern: type I possessing an 'irregular' discharge and type II a highly regular sequence of interspike intervals (Brown & Iggo, 1967; Chambers & Iggo, 1967, 1968; Burgess *et al.* 1968; Iggo & Muir, 1969) The type II discharge pattern is remarkably monotonic and, over the dynamic range, *each* subsequent impulse occurs at a slightly longer delay with a small coefficient of variation during a long discharge train (Werner & Mountcastle, 1965; Burgess *et al.* 1968; Iggo & Muir, 1969); an essentially similar pattern has been observed in forty-four reptilian type II fibres (Fig. 3).

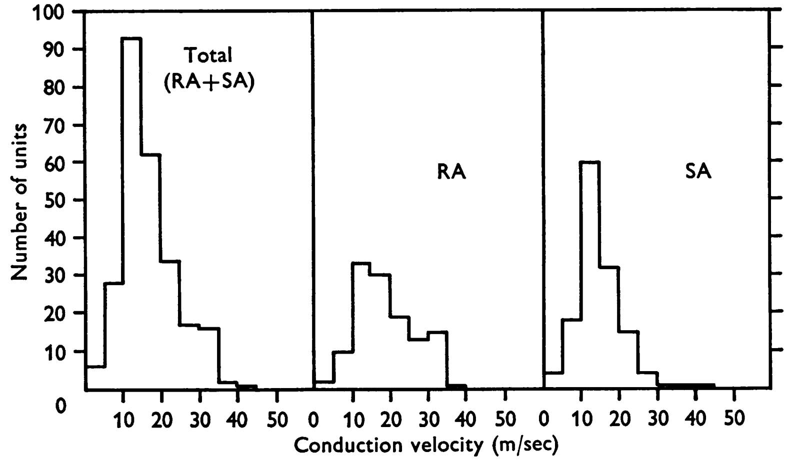


Fig. 2. Left: conduction velocity distribution of 259 plantar nerve fibres studied in these experiments. Mean = 16·7 m/sec.

Centre: conduction velocity distribution of 123 rapidly adapting (RA) fibres of the plantar nerve of alligator. Mean = 19·4 m/sec.

Right: conduction velocity distribution of 136 slowly adapting (SA) fibres of the plantar nerve. Mean = 14·8 m/sec.

The 'irregular' discharge of type I mammalian receptor fibres may be more ambiguous in the reptile because the characteristic clustering of impulses often become less pronounced with large displacements (Fig. 4), although this feature is always easily detected if the 'dynamic range' (see Methods) is studied in some detail. The discharge patterns for three fibres shown in Fig. 4 constitute examples of the range encountered in twenty-seven fibres, classified as 'type I irregular', despite the presence of some periods of highly regular impulse sequences. It might be suggested that there is a continuum of response patterns and that the existence of transitional varieties prevents the application of a rigorous subdivision. Detailed study of other features discussed below should indicate the applicability of this single criterion for subdivision. Variability in the interspike interval histogram, which for the remainder of this account defines type I receptors, is not correlated with variation in the number of impulses in

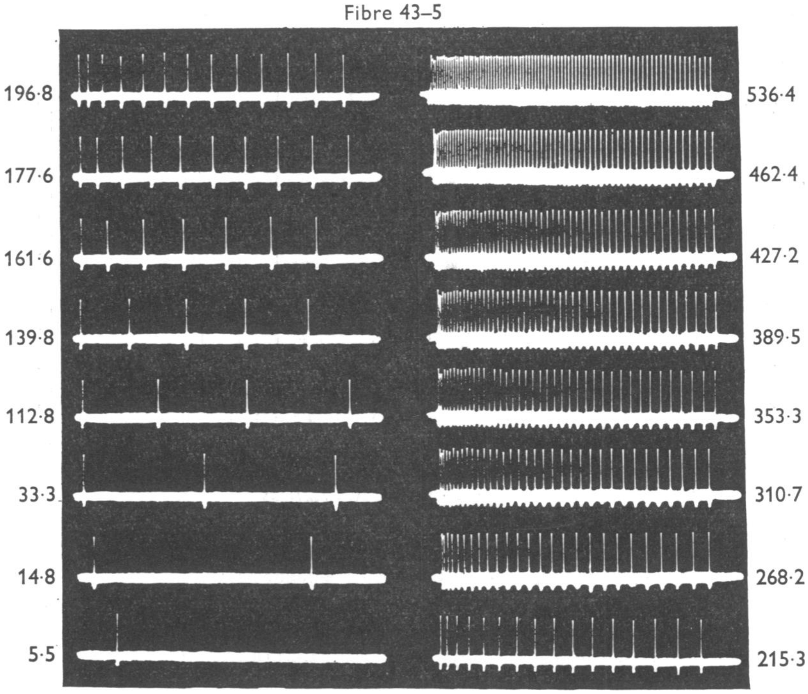


Fig. 3. The discharge pattern of a typical type II ('regular') receptor fibre at varying amplitudes of skin displacement (indicated in microns). At all stimulus intensities the interspike intervals increase monotonically. Stimuli were applied in order of increasing intensity. Stimulus duration = 900 msec; repetition rate = 6/min.

each discharge, which remains remarkably small at each displacement of repeated intensity series.

Type I ('irregular') receptors usually possess restricted receptive fields (often located in a small portion of a single scale) but some larger or multiple point fields have been observed. In no case has an epidermal protuberance been seen comparable to the dome-like receptors noted by Iggo (1963*a*) in some zones of mammalian skin. Some type II ('regular') receptors responded to stretch of skin lateral to the most sensitive zone (delimited by application of von Frey hairs), but receptive field extent was more closely related to scale size than to receptor category, and no obvious difference could be detected between the type I and type II populations because of the wide range and inexact delimitation of receptive field sizes for type II fibres. The maximally responsive zone may be more restricted for type I receptors, but the present data cannot support this impression on a quantitative basis.

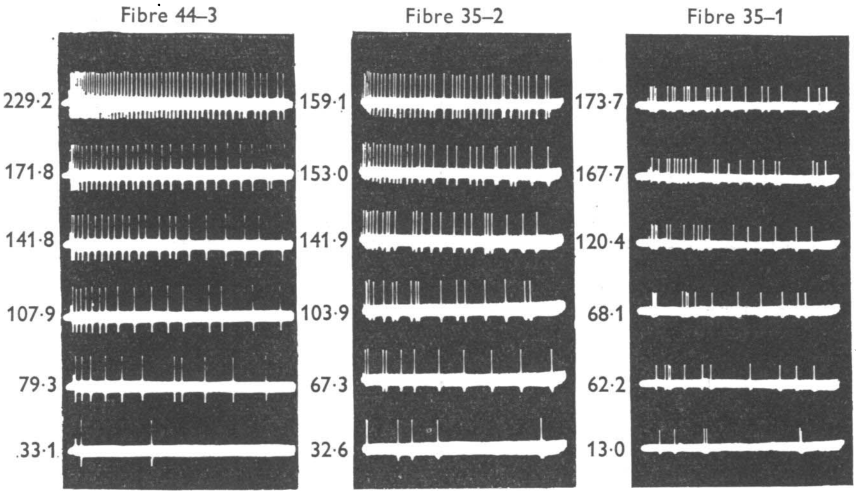


Fig. 4. Examples of three typical slowly adapting, type I ('irregular') receptor fibres of the plantar nerve of alligator at varying amplitudes of skin displacement (indicated in microns). Stimuli in each series were applied in order of increasing intensity. Stimulus duration = 900 msec; repetition rate = 6/min.

Left: a 'slightly irregular' discharge pattern which approaches regularity at high stimulus intensities.

Centre: an 'irregular' pattern exhibiting periods of irregular discharge at all displacement amplitudes.

Right: a' highly irregular' pattern displaying small 'burst' patterns. SA I fibres of this kind are characterized by relatively small numbers of impulse discharges throughout their dynamic range and by greater variability of response at a given skin displacement than less irregular fibres.

Mechanical sensitivity and conduction velocity. The range of thresholds for mechanical displacement determined with graded von Frey hairs showed extensive overlap for all low threshold mechanoreceptors (Fig. 5). Two high threshold 'nociceptor' fibres (Burgess & Perl, 1967) have not been included in this analysis because their thresholds could not be measured with suitable accuracy; these are discussed below. Despite the overlapping range, type I fibres tend to cluster in the low threshold part of the histogram as a sharp peak. This trend would probably be accentuated if the sample were large enough to compare receptors with similar receptive field dimensions. There were no significant correlations between threshold and conduction velocity for slowly adapting mechanoreceptors, but there is a slight tendency for type I receptors to conduct faster

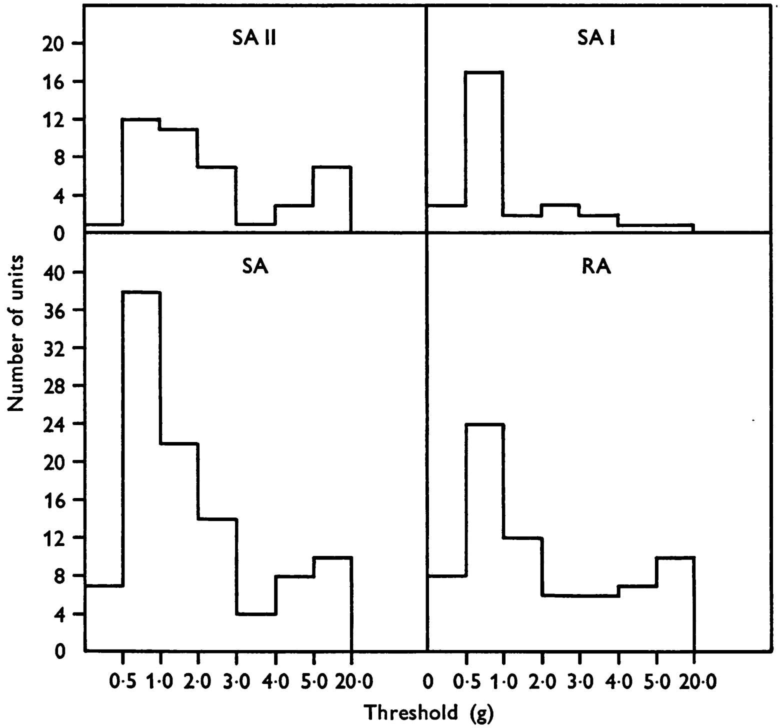


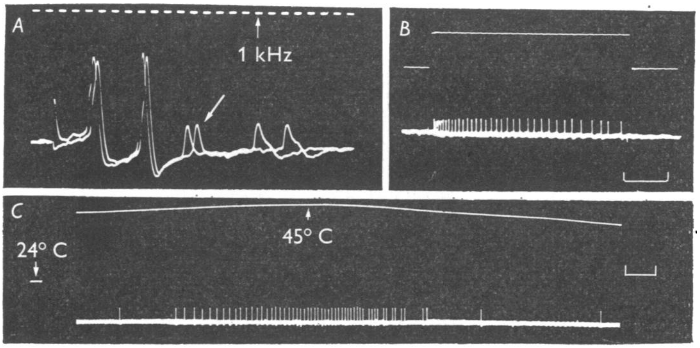
Fig. 5. Mechanoreceptor response thresholds for mechanical stimulation as determined with graded von Frey hairs. The lower histograms show that the range of thresholds for slowly adapting (SA) and rapidly adapting (RA) fibres fall within the same approximate range and distribution. The upper graphs illustrate the threshold distribution of SAI and SAII fibres and indicate that a higher proportion (69 %) of SAI receptors fall in the low threshold range below 1 g than do SAII fibres.

(mean = 15·2 m/sec) than type II (mean = 13·2 m/sec), although the ranges overlap and do not reveal the wider separation reported for mammalian cutaneous nerve (Brown & Iggo, 1967; Burgess *et al.* 1968). It may also be of interest to note that although von Frey hair thresholds are higher than for mammalian skin (Burgess *et al.* 1968), the difference is principally due to the mechanical impedance of the epidermis judging by the similarity of displacement thresholds frequently in the range below 10 μ. There were no significant differences noted in the 'dynamic ranges' (see Methods) of the two varieties of slowly adapting low threshold mechanoreceptors.

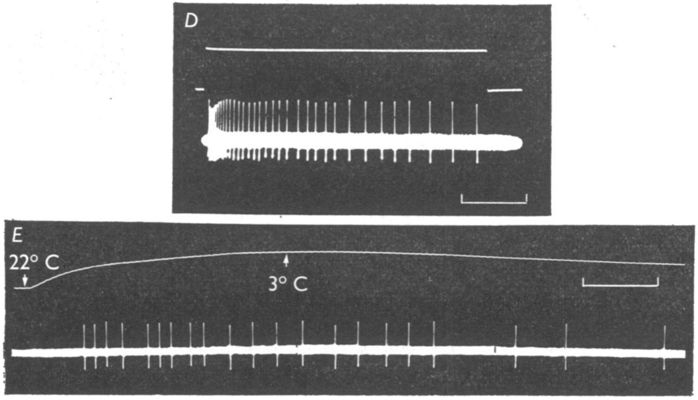
Thermal sensitivity. A surprisingly large number of mechanoreceptors displayed sensitivity to abrupt alterations of cutaneous temperature. This kind of response should be distinguished from thermal alterations of mechanical sensitivity as demonstrated for reptilian vibratory receptors (Proske, 1969) and is essentially similar to the 'spurious thermoreceptor' response described for mammalian slowly adapting mechanoreceptors (Witt & Hensel, 1959; Hunt & McIntyre, 1960; Iggo, 1966, 1969). A large proportion (41 %) of type II fibres displayed thermal sensitivity, the majority of which were responsive to 'cold' stimuli. Spontaneous activity was noted in a substantial number of type II fibres and was initially thought to be a unique feature of these receptors, but this low frequency (less than 6/sec) discharge invariably could be eliminated by a moderate increase in ambient temperature. There were three type II fibres (in the conduction velocity range 10–20 m/sec) responsive to an elevation of temperature but not to cooling. Only 25 % of type I fibres displayed temperature sensitivity, all of which responded maximally to cooling although several (four) fibres also showed a slight increase in discharge frequency with heating, provided the temperature transient was rapid.

Examples of the discharges in two thermosensitive mechanoreceptors are illustrated in Fig. 6. In both examples the response to a temperature change was small compared with the response to mechanical displacement (Fig. 6*B*, *D*) and large temperature transients were required to elicit a response with long delay after stimulus application and alteration of the surface temperature. The delay is presumably related to the deep dermal location of receptors and low thermal conductivity of the epidermis. In any case, the long latency of response suggests that it is not due to direct mechanical effects of applying ether or radiant heat, although slow thermal contraction or expansion could result in epidermal deformation sufficient for eliciting a weak response from low threshold receptors.

The rate of temperature change appeared to be more critical than the temperature increment and excursions of 5–10° C within 3–5 sec were usually required for eliciting any discharge. Repetition of the stimulus after the skin surface temperature returned to the pre-stimulus level was usually less effective, but measurements of deep dermal temperatures would be required to determine whether this is a feature of receptor



Fibre 30–6



Fibre 67–6

Fig. 6. Thermosensitive type I slowly adapting mechanoreceptors.

A: simultaneous recording of a strand containing four nerve fibres responsive to electrical stimulation at two fixed stimulating distances. The use of overlapping traces demonstrates the difference in conduction velocity for each fibre. The third peak (arrow) is the response of a heat sensitive mechanoreceptor fibre illustrated in *B* and *C* (conduction velocity = 6·2 m/sec).

B: the maximal response to skin displacement of this fibre. The upper trace is a strain gauge record of the applied stimulus.

C: response of the same fibre illustrated in *B* to the application of radiant heat. The stimulus is indicated by the output of a surface thermistor placed near the receptor site (upper trace).

D: the maximal response to skin displacement of a type I slowly adapting, cold sensitive fibre.

E: response of the fibre illustrated in *D* to cooling. The upper trace again represents the thermistor record. The time lines in *B*, *C*, *D* and *E* equal 200 msec.

adaptation. The 'burst' discharge pattern characteristic of mammalian thermoreceptors (Iggo, 1966, 1969; Kenshalo & Gallegos, 1967) was never observed. A few observations on true thermoreceptors are discussed below. Thermosensitive mechanoreceptor fibres are distributed throughout the conduction velocity and response threshold range.

TABLE 1. Stimulus–response relationships of reptilian cutaneous mechanoreceptors to mechanical stimulation of the skin

		Ascending series			Descending series		
Fibre type	Fibre number	Function type	Slope (no./μ)	Corr. coeff.	Function type	Slope (no./μ)	Corr. coeff.
SAII	36–6	Power	0·771	0·993	Power	0·774	0·990
SAII	37–1	Exp.	0·00186	0·992	Exp.	0·00174	0·984
SAII	37–6	Exp.	0·00132	0·970	Exp.	0·00148	0·987
SAII	39–1	Exp.	0·00221	0·989	Exp.	0·00213	0·984
SAII	39–3	Power	0·896	0·988	Power	0·830	0·995
SAII	40–2	Power	0·784	0·987	Power	0·768	0·982
SAII	40–7	Exp.	0·00154	0·987	Exp.	0·00150	0·987
SAII	41–2	Exp.	0·00600	0·989	Exp.	0·00710	0·993
SAII	41–3	Power	0·753	0·993	Power	0·735	0·990
SAII	42–4	Exp.	0·00212	0·990	Exp.	0·00206	0·993
SAII	42–5	Exp.	0·00222	0·997	Exp.	0·00218	0·991
SAII	42–7	Exp. exp.	0·00144	0·995	Exp. exp.	0·00129	0·986
SAII	43–7	Power	0·835	0·988	Power	0·812	0·996
SAII	44–2	Exp. exp.	0·00118	0·990	Exp. exp.	0·00126	0·985
SAII	44–5	Power	0·795	0·989	Power	0·810	0·993
SAII	45–1	Power	0·879	0·990	Power	0·854	0·994
SAII	45–4	Power	0·837	0·983	Power	0·839	0·988
SAI	26–1	Linear	0·242	0·992	Exp.	0·0221	0·995
SAI	28–3	Linear	0·211	0·979	Exp.	0·0251	0·974
SAI	35–2	Log.	32·002	0·986	Exp.	0·0105	0·984
SAI	37–3	Linear	0·442	0·992	Exp.	0·0278	0·980
SAI	42–2	Linear	0·463	0·985	Exp.	0·0293	0·994
SAI	43–3	Linear	0·742	0·989	Power	2·647	0·980
SAI	44–3	Power	2·104	0·996	Exp.	0·0120	0·990
SAI	46–5	Linear	0·356	0·988	Exp.	0·0189	0·986
SAI	47–1	Linear	0·240	0·995	Power	1·861	0·986
SAI	48–1	Linear	0·311	0·982	Exp.	0·0149	0·987
SAI	48–2	Linear	0·174	0·989	Exp.	0·0131	0·983
SAI	48–4	Linear	0·365	0·980	Exp.	0·0173	0·993
SAI	49–1	Log.	115·310	0·987	Exp.	0·0472	0·980

Displacement functions. A variety of strategies can be employed in studying the discharge of receptors as a function of stimulus itensity. The principal limiting factor in such studies is usually the limited duration of effective recording. Each fibre was initially studied with a constant regimen. Rectangular mechanical pulses of 900 msec duration were applied at a rate of 6/min and the amplitude of displacement was varied between each stimulus until the entire dynamic range was covered with several 'ascending' and 'descending' series of stimulus intensities. Curve fitting proved to be remarkably unambiguous in almost all instances, even when the sample size was limited and a high mean correlation coefficient of 0·988 was obtained for all fibres studied.

A sample of seventeen extensively studied type II ('regular') fibres

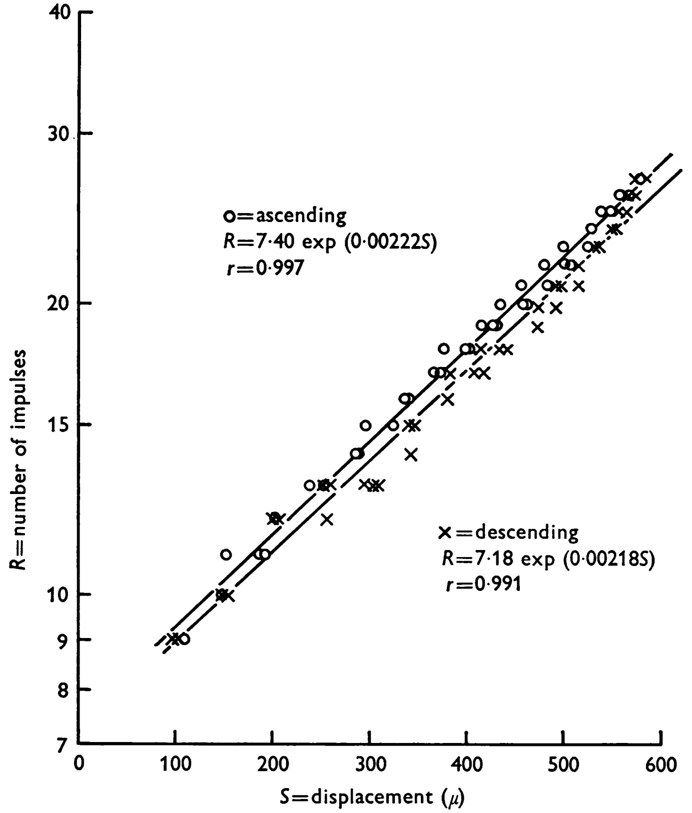


Fig. 7. Fibre 42–5. Semi-logarithmic plot of the stimulus–response relationship for an SA II receptor fibre. Cumulative data from three alternate series of increasing and decreasing skin displacements were analysed separately for the curve fitting process. Fibre response at displacements greater than the upper limit of the dynamic range (585 μ) are not shown since these data were excluded from the least-squares analysis. The slopes of the best-fitting 'ascending' and 'descending' exponential functions fell within each other's standard deviation (0·00222 ± 0·00003 and 0·00218 ± 0·00004 impulses/μ respectively), indicating that these functions are independent of the sequence of stimulus application. Stimulus duration = 900 msec; repetition rate = 6/min; r = correlation coefficient.

displayed either power or exponential functions (Table 1) relating number of impulses to displacement amplitude. 'Ascending' and 'descending' stimulus intensities consistently yielded the same mathematical function with slopes falling well within the narrow standard deviation for any sequence of stimulus change.

The failure to find a *single* family of mathematical functions for all type II fibres in the present experiments is discordant with the power functions for eighteen of twenty-one slowly adapting receptors in the cat (Werner & Mountcastle, 1965) (although there is some uncertainty concerning the receptor type since a highly 'regular' discharge is illustrated by these authors for a typical 'Iggo corpuscle' receptor). The apparent discrepancy between cat and alligator led to the suspicion that different points within the receptive field for each fibre might yield distinctive functions determined by the mechanical linkage, distance from the receptor and elastic properties of the intervening tissue. A detailed spatial analysis performed for three fibres revealed that the slope of the stimulus–response relationship, defined as the experimentally determined constant, *b*, in Eqns. (1)–(5) (Methods), is dependent upon the site of displacement and its distance from the point of maximal sensitivity as might be expected (Mountcastle *et al.* 1966), but the mathematical function describing this relationship did not vary and fairly high correlation coefficients (above 0·970) were maintained for each example. The failure of half of our sample of reptilian type II receptors to display a power function (Fig. 7) may constitute a genuine species difference; experiments in our laboratory of both type I and type II fibres of the cat appear to be consistent with the stimulus–response relationship found by Werner & Mountcastle (1965).

Those fibres listed in Table 1 whose stimulus–response functions are best described by non-power functions are all examples displaying low correlation coefficients for a power function (mean = 0·954 ± 0·014) and high coefficients for the function designated (mean = 0·987 ± 0·006). These findings for reptilian fibres are clearly distinct from our preliminary experience with both type I and II fibres of cat, which display high correlation coefficients for power functions with few exceptions; these latter may be explicable as artifactitious (Werner & Mountcastle, 1965).

The study of type I ('irregular') receptor fibres under the same conditions revealed markedly different behaviour. In a series of thirteen extensively studied fibres of this class, the *sequence* of stimulus presentation proved to be critical in determining the mathematical function fitted to the stimulus–response relationship such that different *functions* described the 'ascending' and 'descending' intensity series for each fibre studied (Table 1). Thus the initial (and subsequent) 'ascending' series generally yielded linear or logarithmic relationships, but each 'descending' series resulted in a different functional relationship, analogous to a time dependent hysteresis loop (Fig. 8). Randomizing the stimulus presentation serves to obfuscate this double-valued response due to the distinctly greater response variability. If it can be assumed that the 6/min repetition rate employed is consistent with stimuli perceived by the animal in natural conditions, the behaviour of type I receptors may provide less consistent information than type II fibres concerning the absolute magnitude of skin deformation. The strong interaction between successive stimuli suggested the need for a more extensive study of repetition rate for both varieties of slowly adapting receptors. For this purpose, a larger number of responses was recorded for each of several displacement amplitudes at different repetition rates, maintaining a constant stimulus duration. At the con-

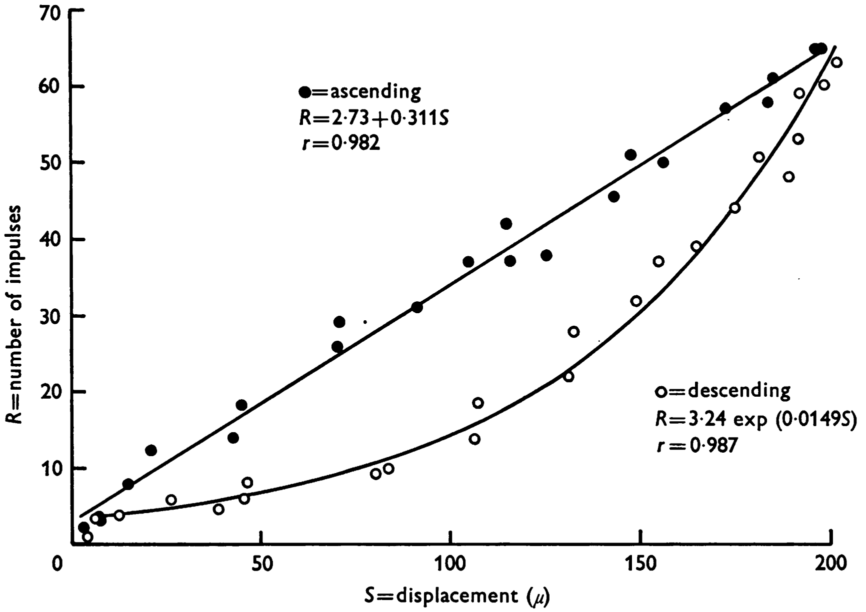


Fig. 8. Stimulus–response relationship for an SAI fibre. Cumulative data from three alternate series of increasing and decreasing skin displacements were analysed separately for the curve fitting process. Stimulus–response data collected at displacement amplitude beyond the dynamic range are not shown. In contrast to type II fibres (Fig. 7), whose stimulus–response relationships were independent of the sequence of stimulus application, type I 'ascending' and 'descending' relationships were described by different families of mathematical functions. For the data illustrated (Fibre 48–1), least-squares analysis yields a linear 'ascending' and an exponential 'descending' functional relationship. Stimulus duration = 900 msec; repetition rate = 6/min; r = correlation coefficient.

stant repetition rate of 6/min employed throughout these experiments, type I fibres displayed greater response variance to a constant stimulus intensity than type II fibres, although the latter exhibited a slight decline in discharge frequency to reach a 'steady state' after the second or third stimulus presentation. For type II fibres, stimulus repetition rates from 6 to 21/min yielded the same functional relationship irrespective of the sequence of stimulus intensities; the net effect of rate variation was to alter only the slope.

In contrast to this simple behaviour, varying the repetition rate potently affects the intensity *function* for type I fibres over a wide range of repetition rates. A systematic exploration designed to determine the interval required between stimuli for sequence independence in the more variable type I discharge proved difficult because of the unexpectedly slow recovery of these receptors. For the mid-range of stimulus intensities, distinct and consistent reductions in discharge rate were observed for successive stimulus applications at rates up to 40 *per hour*. Thus for these reptilian type I fibres, interstimulus intervals exceeding 1·5 min are required in order to avoid significant interaction between successive stimuli; a requirement that can rarely be met in obtaining numerically adequate data for studying intensity functions. The remarkably slow recovery of type I receptors clearly distinguishes them from type II receptors and accounts, at least in part, for the response dependence upon the sequence of stimulus presentation. This feature of receptor 'adaptation' provides a far more precise criterion for distinguishing receptor categories than might be expected from the discharge adaptation observed during a constant stimulus and is presumably related to the location of receptors and the mechanical properties of interposed cutaneous tissue elements.

The character of discharge for each type of slowly adapting receptor may be an inherent property of its axon. Application of DC polarizing current to the nerve bundle evokes different characteristic responses from SA I and SA II fibres. SA II fibres consistently exhibit a regular discharge for longer time intervals than SA I fibres. This effect is also evident when the receptor is disconnected by severing the plantar nerve distal to stimulating and recording sites and thus suggests an adaptive axonal specialization similar to that demonstrated for crustacean sensory fibres (Nakajima & Onodera, 1969). For all type II ('regular') fibres examined in this manner, the maximum instantaneous frequency of response to DC stimulation was consistently higher, by at least a factor of two, than the maximum response frequency during mechanical stimulation. The maximum discharge frequencies of the type I fibres, on the other hand, were almost equal during both mechanical and DC stimulus conditions and generally displayed brief periods of spike clustering. However, maximum discharge frequency to DC stimulation was observed to be greater in type I than in type II.

Other cutaneous receptors. In the course of sampling cutaneous nerve fibres for the purpose of classification, several incidental observations were made that are worthy of brief mention. Rapidly adapting receptors were particularly numerous and were distributed throughout the conduction velocity range of myelinated axons. The majority of these fibres responded with one or two impulses to each mechanical transient and were capable of following vibratory frequencies in the range 200–400/sec. A few fibres extended into a higher frequency range and may constitute a distinct class similar to the vibratory receptors described in snake by Proske (1969). Histological examination of silver stained sections of the receptive field for nineteen rapidly adapting receptors essentially proved unsuccessful, but in two cases dermal Pacinian corpuscles were detected. Further analysis should reveal whether the Pacinian receptor constitutes a functionally distinct class in reptilian skin.

Two high threshold mechanoreceptors were isolated with micropipettes for a sufficient time to enable characterization. The conduction velocity for both fibres was below 5 m/sec and these fibres were best excited by firm pinching of the skin with fine forceps or by exerting pressure with a sharp pin. One fibre responded to a strong heat stimulus before recording contact was lost. Numerous fibres in the lowest conduction velocity range proved inexcitable during the short period in which they could be studied and it is possible that these belong to a distinct class of high threshold fibres similar in sensitivity and discharge pattern to the 'nociceptors' described in mammalian skin (Zotterman, 1939; Iggo, 1959*a*; Burgess & Perl, 1967; Perl, 1968; Bessou & Perl, 1969).

Four fibres that were mechanically inexcitable proved sensitive to thermal stimuli but none could be studied long enough for detailed analysis. One rapidly conducting fibre in this group was exquisitely sensitive to small increments in temperature and maintained a prolonged high frequency irregular discharge (mean = 77·8/sec) if the skin temperature remained elevated. Fibres responding to a decrease in temperature ('cold' receptors) could not be studied carefully. None of the thermal receptors responded with 'burst' discharges of the type reported for mammalian thermoreceptors (Kenshalo & Gallegos, 1967; Iggo, 1966, 1969).

DISCUSSION

The fibre spectrum of the reptilian cutaneous nerve studied in these experiments is markedly different than that reported for mammalian cutaneous limb nerves (Hunt & McIntyre, 1960*b*; Burgess & Perl, 1967;

Burgess *et al.* 1968) despite the remarkable similarity of the mechanoreceptor types seen in both vertebrate classes. The fibre size spectrum and conduction velocity histogram (Fig. 1) both display a unimodal distribution which appears to correspond approximately to the delta range of mammalian nerve. The small differences in the range of conduction velocities between the delta fibre group of mammals and the total reptilian spectrum are presumably the result of the lower temperature (approximately 25° C) of the reptilian measurements. The principal acquisition associated with evolutionary specialization in mammalian skin noted to date is the appearance of a distinct group of rapidly conducting fibres giving rise to a bimodal distribution of myelinated axons due to the presence of beta fibres. These fast fibres are principally associated with several varieties of hair receptors (Brown & Iggo, 1967) but other varieties of specialized mechanoreceptors, especially in glabrous skin, are also represented in the beta group of cutaneous nerve. It should be of interest to determine whether some reptiles possessing specialized epidermal derivatives develop a distinct large fibre component.

Aside from the lack of end-organs associated with hairs, the mechanoreceptor population of reptilian skin appears remarkably similar to that of mammals. Mechanoreceptor types whose physiological properties do not differ significantly in reptile and mammal, and which appear in the large fibre (beta) range of the mammalian distribution (Brown & Iggo, 1967; Burgess *et al.* 1968), are found within the total delta fibre spectrum of reptile cutaneous nerve. A particularly disappointing aspect of this study has been the apparent paucity of true thermoreceptor fibres innervating the skin of a poikilothermic animal. Perhaps the 'spurious' thermal sensitivity (Fig. 6) of numerous slowly adapting mechanoreceptors (Iggo, 1969) subserves the feeble thermoregulatory behaviour of reptiles, but it is possible that thermoreceptors in the non-myelinated fibre range, comparable to those of mammals (Iggo, 1959*b*) will be uncovered by further study.

The principal result of these studies is the demonstration of two physiologically distinct types of slowly adapting mechanoreceptors capable of transmitting information concerning the magnitude of cutaneous deformation, similar in many respects to the receptors described for mammalian skin (Chambers & Iggo, 1967; Burgess *et al.* 1968; Iggo & Muir, 1969). In both reptiles and mammals the difference between the 'irregular' discharge pattern associated with type I receptors and the strictly 'regular' sequence of monotonically increasing interspike intervals characteristic of type II receptors might have been ignored if not for several striking correlates. In mammals it is now evident that type I receptor fibres are associated with distinct epidermal protuberances containing a specialized receptor complex rediscovered by Iggo (1963*a*) and described in excellent detail (Iggo & Muir, 1969); the Iggo-Pinkus 'dome' receptor. Comparable structural specialization has not yet been identified in reptile skin, but this may be due to technical difficulties and the absence of distinct surface landmarks. Although these receptors are distributed in hairy skin of mammals and many may be associated with 'hair disks' (Mann & Straile, 1965), the existence of a reptilian receptor with several similar physiological properties suggests that these structures are probably homologous, and have evolved in the absence of hairs. As in mammals, reptilian type I ('irregular') receptor fibres were less subject to lateral stretch than type II (Chambers & Iggo, 1967), although there were no correlations between receptor type and receptive field size or threshold and only a suggestive separation of conduction velocity ranges compared with the clear separation reported for the cat and rabbit (Brown & Iggo, 1967; Burgess *et al.* 1968). 'Spurious' thermal sensitivity (Iggo, 1969) was noted for both type I and II receptors and some quantitative differences may prove meaningful with more intensive analysis. Differences in sensitivity and discharge pattern following application of DC current pulses, even after cutting the nerve distally, suggest that some differences in adaptive properties may be inherent in the parent axon rather than in the end-organ. Evidence for separate spinal pathways for these two types of first-order slowly adapting receptor fibres in the cat (Petit & Burgess, 1968) would further justify their separation on functional grounds, although this finding may be questioned (Brown, 1968).

The striking differences in displacement functions and adaptive properties for type I and II fibres in reptilian nerve, particularly the double-valued stimulus–response relationships found exclusively in the type I receptors, provide still another firm basis for physiological separation of two receptor categories. Many type II fibres display power functions as reported by Werner & Mountcastle (1965) for a very extensively documented example of a 'regular' fibre in the cat, believed to be associated with an Iggo-Pinkus 'dome-like' receptor. Their study of twenty-one slowly adapting fibres in mammals revealed only three fibres which were not fitted by power functions. The decision that non-power function behaviour was anomalous was based upon the belief that the skin in which these three receptors were embedded lay directly over the tibia thereby enhancing the force applied to these receptors by the probe tip, especially for large skin displacements. None of the fibres in the present experiments that failed to display power functions (Table 1) were located directly over bone, thus suggesting that stimulus–response relations other than power functions for reptilian receptors are probably not related to receptor or cutaneous mechanical properties. Although the 'dome' receptors almost invariably display an 'irregular' discharge pattern (Iggo, 1966; Burgess *et al.* 1968; Iggo & Muir, 1969), a small number of 'regular' (type II) units associated with elevated structures indistinguishable from type I 'domes' may be present in the cat (Burgess *et al.* 1968). Thus the receptor discharge illustrated by Werner & Mountcastle (1965, p. 366) is presumably an atypical example of an Iggo-Pinkus 'dome' receptor discharge. Studies on the cat in progress in our laboratory reveal little variation from power function behaviour by both slowly adapting receptor types in mammalian skin. The observation that different mathematical functions describe stimulus–response relationships for individual reptilian fibres of each type is securely established by the high correlation coefficients (Table 1) for each function. Although highly consistent mathematical functions are displayed by type II receptor fibres with stimulus repetition at 10 sec (irrespective of the order of stimuli of different magnitude and of receptive field position), the unexpectedly long recovery time of nearly 90 sec over certain portions of the receptor's dynamic range for some type I fibres of reptile skin imposes severe limitations on the quantitative study of these receptors in the time generally feasible for study of a single fibre. The data collected for uniform repetition at 10 sec intervals clearly indicate a distinctly different kind of functional relationship for incremental and decremental stimulus intensities *only* for the 'irregular' type I mechanoreceptors and suggest that longer recovery periods are required for obtaining a consistent response to a constant stimulus. Employing the extremely slow repetition rates consistent with complete recovery for type I fibres, however, severely limits the scope of extensive studies, since under natural conditions, stimulation of these receptors usually occurs at rates for which interactions between successive stimuli presumably occur. The existence of stimulus interactions with high repetition rates over extended time intervals is undoubtedly relevant to an investigation of the information handling capabilities of the animal.

The different recovery rates for type I and II slowly adapting receptors further emphasizes the validity of recognizing the separation proposed for the homologous receptors of mammalian skin (Chambers & Iggo, 1967; Burgess *et al.* 1968; Iggo & Muir, 1969) and raises several unsolved problems. The elastic modulus and natural frequency of the tissue interposed between the skin surface and receptor site presumably play a more important role than end-organ adaptation in accounting for slow recovery. The slow mechanical return of the compressed skin can be seen easily with a binocular microscope following vertical displacements exceeding 100 μ. Nevertheless, it is puzzling that the two receptor types are differentially affected by the mechanical impedance of the tissue unless the depth and distribution of the receptors vary significantly. Histological analysis of the receptive fields for sixty-two slowly adapting fibres unfortunately failed to solve this problem due to technical difficulties in silver impregnation of a suitable proportion of the receptors, but it is likely that this problem will be amenable to study in the near future. The overlapping range of thresholds for type I and II fibres suggests that factors other than the depth of receptors may be involved.

The present results (Table 1) indicate that a single mathematical relationship cannot be employed to infer reptilian receptor discrimination of different amplitudes of skin displacement, although Werner & Mountcastle (1965) have shown that a good power function fit to their pooled stimulus–response data (normalized to percentiles of maximum skin displacement and maximum response for each receptor) can be achieved for a class of mammalian cutaneous receptors. The variety of mathematical functional relationships necessary to describe the responses of both types of mechanoreceptors listed in Table 1 precludes such a generalization for reptilian fibres. It would be of particular interest to understand the sensory role of distinct receptor types capable of transmitting information by means of different stimulus–response relationships.

Numerous criteria which can be employed to distinguish slowly adapting mechanoreceptors provide suitable means for separation of the two varieties described in mammals and reptiles: (1) association with elevated structures on the skin (Iggo-Pinkus 'domes') for type I in mammals only (Iggo, 1966; Burgess *et al.* 1968; Iggo & Muir, 1969); (2) regularity (monotonic increase) of interspike interval during adapted discharge for type II throughout the entire dynamic range of receptor sensitivity in reptile and mammal, although some type I fibres approach this condition at high discharge rates (Fig. 4); (3) higher probability for resting (spontaneous) discharge in reptile and mammal for type II (Iggo & Muir, 1969); (4) generally higher maximum instantaneous frequency of discharge of type I receptor fibres in both reptile and mammal (Iggo & Muir, 1969), although appreciable overlap of range exists between type I and type II populations in reptile (Figs. 3, 4); (5) greater sensitivity of type II to lateral stretch of the skin in both reptile and mammal (Iggo & Muir, 1969); (6) generally lower von Frey hair threshold for type I in reptile and mammal (Burgess *et al.* 1968), although considerable overlap exists between type I and type II in reptile (Fig. 5); (7) higher mean conduction velocity for type I than for type II in both mammal and reptile with a more pronounced difference in mammal (Burgess *et al.* 1968); (8) longer time intervals of regular discharge upon application of DC polarizing current for type II than for type I in reptile; (9) interaction between successive stimuli giving rise to a double-valued stimulus–response relationship found only in type I fibres in reptile (Fig. 8) for stimuli presented at 10 sec intervals; (10) distinctly slower recovery of type I fibres to repetitive stimuli in reptile, although this effect is less apparent in mammal; and (11) a dorsal column pathway for conveying first-order type II receptor fibres in mammal (Petit & Burgess, 1968), whereas the type I Iggo-Pinkus 'dome' receptor fibres, which have also been noted in the dorsal columns (Brown, 1968), cannot be antidromically activated from the dorsal column, and may project upon this pathway only after synaptic linkage.

Further study of the quantitative relations for both slowly adapting receptor types at different central nervous system sites should help clarify the role of these receptors in the determination of stimulus magnitude.

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