J. Physiol. (1969), **200**, *pp.* 763–796
With 4 plates and 13 text-figures
Printed in Great Britain

THE STRUCTURE AND FUNCTION OF A SLOWLY ADAPTING TOUCH CORPUSCLE IN HAIRY SKIN

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(*Received* 21 *August* 1968)

SUMMARY

1. Slowly adapting cutaneous mechanoreceptors, in the cat and primates, have been studied by histological and neurophysiological methods.

2. Each touch corpuscle is a dome-shaped elevation of the epidermis, whose deepest layer contains up to fifty specialized tactile cells.

3. Nerve plates, enclosed by the tactile cell (Merkel cells), are connected to a single myelinated axon in the dense collagenous core of the corpuscle.

4. The corpuscle generated > 1000 impulses/sec when excited by vertical surface pressure. The response was highly localized and showed a low mechanical threshold, the frequency being dependent upon the velocity and amplitude of the displacement. There was a period of rapid adaptation before a sustained response which might continue for > 30 min.

5. A quantitative analysis of the responses to excitation by displacements of differing amplitude, velocity and duration is included.

6. The discharge of touch corpuscle units evoked by a mechanical stimulus was temperature-sensitive, and was enhanced by a fall in skin temperature.

INTRODUCTION

The peripheral mechanisms which underlie the sensory discrimination of cutaneous stimuli have been investigated in three principal ways. Psychophysical techniques established as early as 1882 (Blix, 1884) that sensory spots, which are regions of low threshold to a given kind of stimulus, existed in the skin of man. From any given spot it was possible to elicit a sensation that was perceived as having a particular quality or modality. Four modalities were recognized; touch, cold, warmth and pain; but this simple view of sensory mechanisms has since attracted severe criticism (Teuber, 1960). About the same time a second technique, neurohistology,

was revealing individual, structurally dissimilar, nerve endings in the skin, and von Frey (1895) proposed that different modalities of sensation were served by structurally distinctive nerve end-organs. This is an enduring hypothesis, despite attempts to demolish it on neurohistological grounds (Weddell & Miller, 1962).

A major physiological development occurred when Adrian (1926) and Adrian & Zotterman (1926) recorded electrophysiologically from single active afferent nerve fibres in peripheral nerves. Since then the properties of myelinated afferent nerve endings in hairy skin have been explored many times (Adrian, 1931; Zotterman, 1939; Frankenhaeuser, 1949; Maruhashi, Mizuguchi & Tasaki, 1952; Witt & Hensel, 1959; Hunt & McIntyre, 1960*a*, *b*; Boman & Hensel, 1960) and it is established that cutaneous afferent nerve fibres innervating hairy skin can be separated into categories based on the sensitivity of their terminals to mechanical and thermal stimuli (Iggo, 1968). Even within the limited category of large myelinated axons (6–15 μm) that have receptors with an enhanced mechanical sensitivity, a further subdivision is possible, based on the rate of adaptation of the afferent units to constant mechanical stimulation. This fundamental difference was evident in the first single afferent fibre studies of Adrian and Adrian & Zotterman. In hairy skin Frankenhaeuser (1949) and later Maruhashi *et al.* (1952), Fjällbrant & Iggo (1961), Hunt & McIntyre (1960*a*) reported that a slowly adapting discharge could be evoked from spots in the skin, in contrast to the much larger receptive fields of the rapidly adapting axons. The present work started when it was noticed in the cat that a slowly adapting response, in some cutaneous axons, was evoked by mechanical stimulation of visible, richly vascularized swellings of the epidermal surface between the hairs (Iggo, 1961, 1963*a*). This observation gave rise to the hope that it might be possible to correlate the morphology of a specific cutaneous structure with a particular class of physiological behaviour and so resolve the controversy surrounding the hypothesis that the different modalities of sensation are served in the periphery by structurally distinctive nerve end-organs.

The present paper gives a detailed account of the morphological and physiological properties of these 'touch spots' which provide an unambiguous example of a specific sense organ in hairy skin. Preliminary accounts of these results have been published (Iggo, 1961, 1963*a*; Iggo & Muir, 1962, 1963). There are several confirmatory reports of the distinctive physiological properties of the afferent unit, particularly by Tapper (1965), Werner & Mountcastle (1965), Lindblom & Tapper (1966), and Smith (1968), in the cat, rabbit and monkey. As the results will show, the sense organ can now be identified with the 'hair disk' (Haarscheibe) of Pinkus (1904) (see Pinkus H., 1964, for a historical note) which has been found in

several species including man (Tamponi, 1939; Kawamura, 1954; Straile, 1958, 1960, 1961; Winkelmann, 1959; Siminoff, 1965; Mann & Straile, 1965; Smith, 1968). In the past the afferent unit appears sometimes to have been confused with, or not distinguished from, another less numerous kind of slowly adapting cutaneous mechanoreceptor (Chambers & Iggo, 1967; Iggo, 1968), from which, however, it can now be distinguished on several grounds.

METHODS

Electrophysiology. In most experiments cats were used and in physiological experiments they were anaesthetized with an intravenous injection of chloralose (80 mg/kg) after the induction of anaesthesia with ethylchloride and ether. The peripheral nerve was either the saphenous or the sural, which was exposed in the thigh and prepared for dissection in a pool of paraffin that filled a trough formed by tying the edges of the skin wound to a metal frame. In two experiments one monkey (Vervet, *Cercopithecus aethiops*) and one African baboon (*Papio papio*) anaesthetized with ether followed by Na pentobarbitone were used and skin of the forearm and hand, innervated by the musculocutaneous nerve, was examined. These two experiments were done to establish the existence of touch corpuscles in primates. Details of the dissection and recording method are described by Brown & Iggo (1967).

An important feature of this work was an attempt to establish the relation between the selective sensitivity of morphologically distinctive structures in the skin and the discharge of action potentials in primary afferent nerve fibres. For this reason a careful visual examination of the receptive fields of primary afferent fibres was made using a binocular microscope at magnifications of 10–50 times, combined with exact and detailed mechanical stimulation of the skin while recording electrically from single afferent units. In order to do this the stimulating probe was mounted on a micromanipulator so that it could be positioned to within 10 μm. This exact control of probe position was, in the later experiments, supplemented with exact control of the mechanical displacement of the probe in a vertical axis, using either a piezoelectric transducer or a moving coil transducer. Both these instruments are described by Brown & Iggo (1967). The probe tip was fastened to the skin, when necessary, by a nitrocellulose/polyester resin mixture (commercial nail varnish).

Reserpine-treated animals. Two cats were treated for 4 days with a daily intramuscular injection of 1 mg reserpine (Ciba) prepared according to the method of Leyden, Pomerantz & Bouchard (1956). The animals were anaesthetized on the fifth day and prepared for electrophysiological recording from afferent fibres, as in normal animals. Touch corpuscles were also removed for histological examination from the same or from similarly treated animals.

Light microscopy. In early experiments the cutaneous structures underlying 'touch spots, were examined after the sensitive spot had been found during an electrophysiological experiment on an anaesthetized animal. The spot was marked with Indian ink or the adjacent skin was stained with a small drop of silver nitrate solution. The skin was removed at the end of the experiment and fixed in 10 % formol saline. The small pieces containing the marked area were cut out, sectioned at either 4 or 20 μm and stained by van Gieson's method as modified by Marshall (1946) or by the Holmes silver method (Gatenby & Beams, 1950). In some experiments the skin of the anaesthetized animal was perfused with a methylene-blue solution and fixed for 12 hr in 8 % (w/v) ammonium molybdate solution at 5° C washed and cleared with xylol (Miller, Ralston & Kasahara, 1958). The methylene-blue-stained skin was then mounted on a microscope slide and examined.

Electron microscopy. Several procedures were used. Initially the 'touch spots' were fixed with 1 % osmium tetroxide in veronal acetate buffer. At first the tissues were fixed by intradermal injection of the osmium tetroxide solution, through fine glass micropipettes, but in

later experiments equally good fixation was obtained by removing the skin from anaesthetized cats and immersing it in the osmium tetroxide solution. Perfusion fixation was also employed by injecting 5% glutaraldehyde solution buffered with phosphate at a pressure of 200 mm Hg into the abdominal aortae of anaesthetized cats. This last method gave the best fixation of tissues and most of the electron micrographs in this paper are from animals prepared in this way. Fixation with osmium caused artifacts in these cutaneous nerve endings, notably the development of vacuoles in the nerve ending of the Merkel disk. These swellings were much smaller in the material fixed with glutaraldehyde. After fixation in glutaraldehyde, squares of skin (1 × 1 mm) containing the touch corpuscle were washed in veronal acetate buffer and then osmicated with a 1% solution for 1 hr. Ethanol dehydration was followed by Araldite (CIBA Ltd.) embedding and sectioning on a Porter–Blum microtome equipped with a glass knife. One half micrometre thick sections, mounted on slides, were stained with toluidine blue–pyronin (Ito & Winchester, 1963) for orientation. Sections for the electron microscope were mounted on Athene 483 grids, without a supporting membrane, and were stained with uranyl acetate–lead citrate (Reynolds, 1963) before examination in an AEI EM 6 microscope.

RESULTS

Morphology

The touch corpuscle can be identified by examining the hairy skin of cats with a dissecting microscope. This is easier to do if the hair is removed by shaving or by depilatory agents and the obliquely illuminated epidermal surface is then examined at a magnification of about 20 times. The touch corpuscle appears as a dome-shaped elevation of the epidermis and since the surface of the dome is smoother, it reflects the illuminating light better than the surrounding epidermis (Pl. 1, fig. 1). In the anaesthetized animal, the dome has a reddish tinge due to a rich plexus of capillaries in the underlying dermal core. This feature is lost after fixation, but the fixative accentuates the firmness of the dermis contained within the elevation so that, if the skin is stroked with the side of a dissecting needle to produce a slight traction, the firm core of the dome makes these sense organs more conspicuous because they project from the stretched skin. Each touch corpuscle is 0·1–0·4 mm in diameter. The touch corpuscles frequently overlie the orifice of a large hair follicle (Pl. 1, fig. 1) (tylotrich follicles of Straile) but they are also found away from these follicles.

Light microscopy. The epidermis of the dome is thicker than that covering the surrounding normal dermis; four to five layers of epithelial cell nuclei are present compared with one or two in the adjacent normal skin (Pl. 1, fig. 2). The stratum corneum covering the elevation is thinner than on the surrounding epidermis. On the crest of the dome, a single layer of cells, which differ from the rest of the epidermal cells, lies on the epidermal side of the basement membrane, and have elongated nuclei oriented parallel to the surface, instead of the usual ovoid nuclei in the stratum basalis and stratum spinosum (Pl. 1, fig. 2). These cells have the same shape and location as originally described by Merkel (1875) for the tactile cells

(Tastzellen) in the epidermis of the avian bill. The tactile cells are paler than the other epithelial cells and a particularly pale region is seen deep to the elongated nucleus (Pl. 1, fig. 2). After formol saline fixation and paraffin wax embedding, large clear vacuoles are seen deep to the nuclei of the tactile cells. Similar vacuoles are seen after osmium tetroxide fixation, but as they are rarely observed after glutaraldehyde perfusion they are considered to be artifacts. Where the tactile cells are present the epidermodermal junction is modified, and around the periphery of the elevation there is a further modification where the junction is extensively folded and projects from the base of the epithelium to interdigitate with the dermis (Pl. 1, fig. 2).

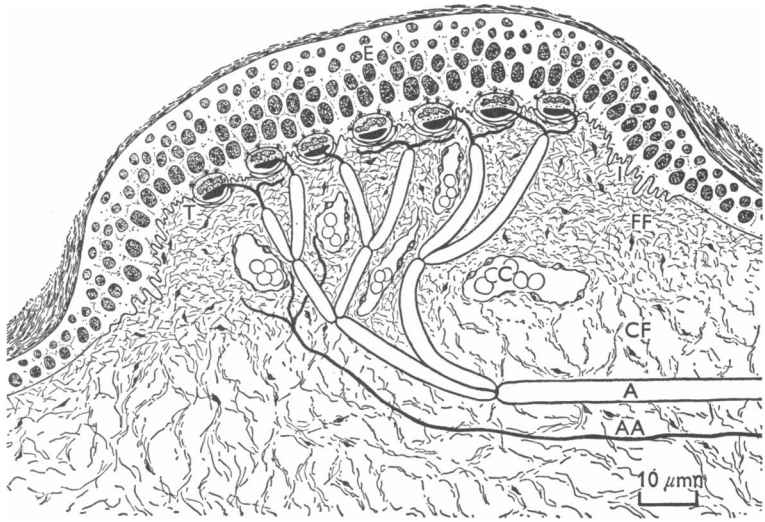
A single large myelinated axon enters the base of the dome; it branches as it approaches the epidermodermal junction, but the branches retain their myelin sheaths until they are less than 10 μm from the junction. Terminal branches then run towards the tactile cells where an expanded nerve plate is associated with each tactile cell. The extent of the myelinated portion is shown by osmium tetroxide fixation and plastic embedding (Pl. 1, fig. 2), and surface examination of a cleared whole mount after methylene-blue staining (Pl. 1, fig. 3) shows the terminal arborizations and nerve plates. Fine leashes of non-myelinated fibres also enter the dome but their destination is uncertain; these are probably the accessory fibres discussed by Boeke (1932).

The dermal core of the dome contains very fine collagen bundles closely woven into a three-dimensional mesh. There is little extracellular tissue fluid space and this composition accounts for the firm consistency of the whole touch corpuscle. The collagen bundles beneath the dome and in the surrounding dermis are thicker but fewer and less closely woven so that they form a coarser mesh with more interstitial spaces. Arterioles and venules are not seen in the core of the touch corpuscle, but a convoluted plexus of capillaries permeates the dermis contained within the touch corpuscle. No adipose tissue cells are present in the dermal core, which has a normal complement of fibroblasts, mast cells and macrophages (Pl. 1, fig. 2).

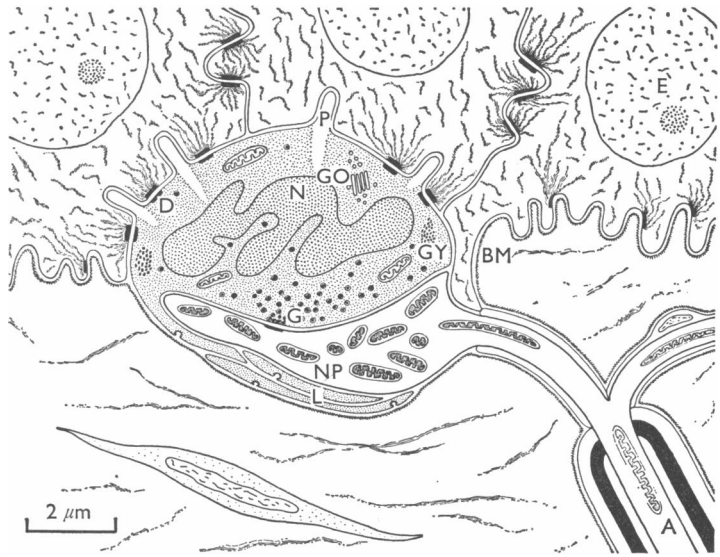
Text-figure 1 is a diagram showing the features of the touch corpuscle which can be demonstrated by the various light microscopic techniques.

Electron microscopy. All the features shown in Text-fig. 1 are confirmed by examining montages prepared from survey electron micrographs. The following account will, therefore, be restricted to the cytology of the tactile cell itself and its relationships with the nerve plate, the other epidermal cells and the underlying dermis. These observations are summarized in Text-fig. 2.

The tactile cell at the base of the epidermis is almost spherical in shape,



Text-fig. 1. A diagram showing the structure of a touch corpuscle as seen in light microscope sections. A, single myelinated axon; AA, non-myelinated axons; E, thickened epidermis of the touch corpuscle; FF and CF, fine and coarse bundles of collagen fibres; I, extensive indentations of the dermis by epidermis at the periphery of the corpuscle; T, tactile cell and its associated nerve plate; C, capillary.



Text-fig. 2. A diagram showing the structure of a tactile cell and its associated nerve plate. A, myelinated axon; BM, basement membrane; D, desmosome; E, epithelial cell nucleus; G, granular vesicles in the tactile cell near a junction with the nerve plate, NP; GO, Golgi apparatus; GY, glycogen; L, lamellae underlying the nerve plate; N, multilobulated nucleus; P, cytoplasmic process from the tactile cell. Iggo & Muir J. Physiol 200 1969 p 768

with its superficial hemisphere being embedded in the epidermis, and its deep half bulging towards the dermis (Pl. 2, fig. 4). A plate-like expansion of the end of the nerve invaginates the tactile cell deep to its nucleus. The single nucleus is multilobulated and extends across the equator of the cell parallel to the skin surface. The complexity of its lobulation and the consequent increase in the area of the nuclear envelope are remarkable features; nucleoli are not as prominent as in the other epidermal cells. The cytoplasm contains a fine meshwork of fibrils which are not compounded into bundles like the tonofibrils of the adjacent epithelial cells. The fibrils in the tactile cell which radiate from the desmosomal plaques on its superficial surface penetrate the cytoplasm as recognizable bundles for only a very short distance before they blend with the cytoplasmic meshwork (Pl. 4, fig. 9). In contrast, the opposed desmosomal plaque, in the adjacent epithelial cell, provides an attachment for tonofibrils which pervade the whole cytoplasm of this cell (Pl. 2, fig. 4). The mitochondria are distributed uniformly throughout the cytoplasm and are curved or twisted cylinders approximately $2 \times 0{\cdot}3\ \mu m$ in size. One or two groups of flattened sacs of smooth-surfaced endoplasmic reticulum forming the Golgi apparatus are seen only on the superficial side of the nucleus (Pl. 2, fig. 4). Clusters of electron-dense particles, with each particle having a compound structure, are found in the cytoplasm, especially near the poles of the elongated nuclei; these are interpreted as aggregations of glycogen (Pl. 3, fig. 6; Pl. 4, fig. 11). Dense bodies containing lipid droplets and limited by a single membrane are identified as secondary lysosomes; they are seen only on the superficial side of the nucleus.

Cytoplasmic organelles in the tactile cell, which are not common features of all cells, are the numerous small spherical granules consisting of a dense homogeneous core surrounded by a membranous envelope. They are concentrated in the cytoplasm between the nucleus and the nerve plate (Pl. 2, fig. 4; Pl. 3, figs. 5–7) and some may extend around the pole of the nucleus to the superficial half of the cytoplasm (Pl. 4, fig. 10). The structure of the granules suggests that they have a catecholamine content, but 4 days after treatment with reserpine, 0·3–0·5 mg/kg daily, no reduction in the number of granules or their contents was detectable. Furthermore, glutaraldehyde fixation does not enhance the density of the granular cores as would be expected if the cores were mainly composed of noradrenaline (Coupland & Hopwood, 1966). Some epidermal cells contain similar granules (Pl. 3, fig. 8) but these cells have a full complement of tonofibrils, and the diameter of the largest of these granules, 120 nm, is appreciably greater than that of the granules in the tactile cell.

The surface of the tactile cell shows considerable specialization; the *superficial half* is attached to the overlying epidermal cells by desmosomes

that are smaller than those between adjacent cells of the stratum spinosum and are scattered all over the superficial surface, including the equatorial region. Rod-like cylindrical cytoplasmic processes from the tactile cell fill corresponding indentations in adjacent epidermal cells (Pl. 2, fig. 4; Pl. 4, figs. 9–11) and are distributed randomly over the superficial half of the tactile cell. These processes are 1·5 μm long and 0·3 μm in diameter, and their plasma membranes are separated from those of the epidermal cell by the usual 15 nm gap. The cytoplasm contained within the process is noticeably pale and devoid of all organelles. If the section passes along the long axis of the process, it can be seen that this pale core extends down into the cytoplasm overlying the nucleus (Pl. 4, fig. 10). These processes do not pass into intercellular clefts, and desmosomes are absent from the part which penetrates the adjacent epidermal cell but are present near the bases of the rods. The *deep half* of the tactile cell embraces the nerve plate by sending thin lamellae around its edge to reach the deep surface of the plate (Pl. 3, fig. 6), which is separated from the dermis by about three or four layers of these thin cytoplasmic lamellae. Few organelles and none of the granules described above are contained in these projecting lamellae, but their plasma membranes show numerous pinocytotic vesicles, especially on their deep surface (Pl. 3, fig. 7). Some of these projections are extensions of the tactile cell, but others may be derived from the last Schwann cell investing the axon. The adjacent epidermal cells send similar projections but these contain tonofibrils, and do not reach beyond the edge of the nerve plate.

The basement membrane (Pl. 2, fig. 4) of the epidermis is an amorphous lamina, about 40 nm thick, which follows the contours of the basal cells and is separated from their plasma membranes by a clear space about 25 nm wide. Fine collagen fibres from the dermis blend with the deep surface of the basement membrane. Since this lamina passes without duplication on to the dermal side of the deepest projection under the nerve plate (Pl. 3, fig. 7) every tactile cell is on the epidermal side of the basement membrane.

The nerve plate is circular or oval, 8–10 μm diameter and 1–3 μm thick. It lies parallel to the skin surface and to the elongated nucleus of the tactile cells. Since very few tangential sections of a tactile cell fail to include the plate it must have almost the same area as the equatorial region of the cell. Its cytoplasm is usually paler than that of the tactile cell and tends to be distorted by vacuolar spaces; these are probably fixation artifacts and they explain the earlier descriptions of clear sacs underlying the nucleus of the tactile cell in both light and electron microscopy (Iggo & Muir, 1963). The numerous mitochondria are longer, 3–4 μm, and more slender, 0·1–0·2 μm, than those of the tactile cell.

The plasma membrane of the nerve plate is separated from that of the

tactile cell by an extracellular space about 15 nm wide, but undulations in both membranes cause considerable variation. However, in discrete regions on the superficial surface of the nerve (Pl. 3, fig. 5) the two membranes run straight and parallel to each other, with an intervening gap of 13 nm. At these contacts, the nerve plate plasma membrane is denser and thicker than elsewhere, while on the cytoplasmic side of the tactile cell plasma membrane there is a diffuse irregular-shaped area of dense material. No more than one such contact region is seen in a single section; their diameter does not exceed 0·5 μm. Although many of these features are similar to those observed at synapses in the central and autonomic nervous systems, the usual small clear synaptic vesicles are absent.

Other cellular elements. The mast cells, fibroblasts and macrophages observed in the dermis show no unusual fine structural features. The capillaries forming a complex plexus have a non-fenestrated endothelium. In osmium-fixed, plastic-embedded specimens, the branching myelinated axon has an internal diameter of 2 μm and the myelin sheath is 1 μm thick. Its short continuations are non-myelinated nerve branches having axonal diameters of 1–2 μm, and each is surrounded by a thin Schwann cell sheath. The basement membrane at the periphery of the dome shows extensive plication; processes of epidermal cells containing tonofibrils extend into the folds, and the fine collagen fibres from the core of the dome are attached to the opposite surface of this basement membrane.

Physiology

Electrical activity was recorded from strands dissected from the saphenous or sural nerves of cats, and a total of 133 single unit preparations were examined. In the absence of an applied stimulus and in skin remote from the operated area there was, with rare exceptions, no discharge from a receptor in the absence of an intentional stimulus. During continuous examination of a single unit for several hours it was unusual to record any background discharge. When present, it was irregular and at a frequency less than 5 impulses/sec. The units in this respect are similar to, if not identical with, the slowly adapting units reported by Tapper (1965), who restricted his study to slowly adapting cutaneous afferent units without any background discharge. They differed, however, from the seventy-two units reported by Werner & Mountcastle (1965); forty-nine of their units carried intermittently recurring impulses 'in the absence of any intentional... stimulation of their receptive fields'.

A characteristic sign of the presence of a touch corpuscle afferent unit in the nerve strand on the recording electrodes in the present work was a brief high-frequency (> 1000 impulses/sec) burst of action potentials when a smooth probe was drawn lightly along the surface of the skin and across

the appropriate touch corpuscle. The area of skin from which this response could be evoked was small and discrete, hence the earlier description of these units as 'touch spots' (Maruhashi *et al.* 1952; Frankenhaeuser, 1949; Hunt & McIntyre, 1960*a*). Visual inspection of the skin, using a binocular microscope, during such a stimulus established that the response could only be elicited from small, reddish, raised spots on the skin surface. When these dome-shaped spots were marked and the skin subsequently examined histologically the touch corpuscles described above were found.

Characteristics of receptive fields. The receptive fields were spot-like when tested with smooth glass probes. Careful exploration of the skin surface using a probe with a small tip (diameter 0·25 mm) established that the mechanical sensitivity was restricted to the raised surface of the touch corpuscle and no obvious variation in sensitivity on different parts of this small (100–400 μm diameter) dome-like surface was evident. When the probe was applied to the immediately adjacent epidermis the threshold displacement for a response was much greater or there was no response. The punctiform character of the receptive fields was further tested by stretching the skin containing a corpuscle; the receptors usually failed to be excited, even when the stretching caused lateral displacement of the corpuscle. Occasionally, if skin was under maintained stretch, an irregular discharge at a low frequency was present. Other kinds of afferent unit may carry a background discharge but these could be distinguished from touch corpuscle units principally because of the irregularity of the discharge of the latter. One kind of sustained discharge arises from a separate class of slowly adapting cutaneous mechanoreceptors which have been called type II by Chambers & Iggo (1967) to distinguish them from the touch corpuscle units; the latter are called type I. Another less common kind of response, synchronous with the arterial pulse, arises in type D hair follicle afferent units (Brown & Iggo, 1967).

Location of touch corpuscles. In a sample of 100 touch corpuscles in the skin of the inner leg and thigh, forty-seven of the sensitive spots were at the mouth of large guard hairs—the tylotrichs of Straile (1960). Forty were remote from guard hairs and thirteen were adjacent to, but not contiguous with, a tylotrich follicle. In the cat, therefore, there does not seem to be any obligatory association between the corpuscles and hairs, as is implied by Pinkus (1927) and reported by Mann & Straile (1965). Even when located at the mouth of a hair follicle, the afferent units were unaffected by movement of the hair along its long axis, by either pulling or pushing it. The effective direction of movement of the hair was that which compressed the surface of the touch corpuscle. The receptors do not, therefore, respond as directionally sensitive indicators of hair movement or position, as would be expected if they corresponded to the slowly adapting

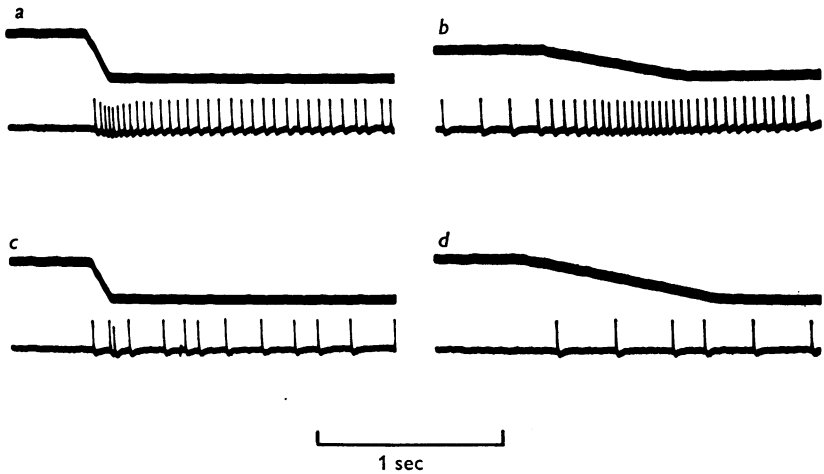
vibrissae receptors of Fitzgerald (1940). They could, of course, be excited by a displacement transmitted to them by overlying hairs if these were pressed down on to skin containing a corpuscle.

Spatial localization. The touch corpuscles have the capacity to provide good spatial localization of a mechanical stimulus, since they are not readily excited by other than a direct vertical indentation. The accuracy of spatial localization will be affected by the size of the receptive fields of individual afferent fibres. Each separate corpuscle has a highly localized sensitivity, but individual afferent fibres may innervate several corpuscles. The mean number of corpuscles supplied by 100 axons dissected from the saphenous nerve was 1·84 per axon. The range was 1–5 and the relative numbers of units were: 1 corpuscle/axon, 37; 2 corpuscles/axon, 42; 3 corpuscles/axon, 10. Only 3 axons supplied more than 3 corpuscles. Whenever an axon innervated 2 or more corpuscles the endings were grouped closely together. The largest group, 5 corpuscles supplied by one axon, were in an area of $2 \times 1{\cdot}5$ cm and the other axons usually supplied corpuscles grouped in smaller areas. No corpuscles were found to be innervated by two or more myelinated axons in normal skin, but a systematic examination of the innervation of all the corpuscles in a given area of skin was not made. The number of touch corpuscles per square cm was estimated in one cat by counting all the visible corpuscles in formalin-fixed skin from the inner side of the leg, and averaged 4·6/cm^2. Since the mean number of corpuscles/axon was 1·8, this gives an average concentration of about 2·5 afferent units per square cm in the skin of the inner leg and thigh innervated by the saphenous nerve.

Simultaneous mechanical stimulation of two corpuscles supplied by a single axon gave the expected result, viz. a discharge of impulses in the afferent fibre determined by the respective intensities and temporal relations of mechanical stimulation at the two corpuscles. The discharge in the main afferent fibre was initiated in one or other corpuscle, as has also been reported by Lindblom & Tapper (1966), and there was no intermingling in the proximal part of the axon of impulses from the two corpuscles. For this reason, although an axon may supply up to five corpuscles, the afferent discharge in the proximal part of the axon probably has its origin in only one corpuscle, except at very low frequencies.

Nature of the effective stimulus. A characteristic feature of the touch corpuscle units was the very high frequency of discharge when the stimulating probe was drawn quickly across the surface of the corpuscle, compared with the lower frequency when the probe was placed directly on the surface of the corpuscle. This difference suggests either that sequential stimulation of transducer elements in the corpuscle or shear deformation of the receptor, rather than compression, is the most effective stimulus.

When the stimulus probe was fastened to the surface of a corpuscle and controlled amplitudes of displacement were applied, the frequency of discharge in both the dynamic and static phases of the response was much less than when the same displacement was applied with the free probe (Text-fig. 3). The tip of the free probe caused a visible indentation of the surface of the corpuscle, whereas when it was fastened to the skin it caused a uniform movement of the whole corpuscle and adjacent epidermis.



Text-fig. 3. The effect on the afferent discharge of fastening the tip of the mechanical probe to the skin with an adhesive. The upper records, *a*, *b*, show the normal response and the lower records, *c*, *d*, the reduced discharge with the probe fastened to the skin. The movement of the probe tip was the same in *a* and *c*, and of the same amplitude but with a lower velocity of indentation in *b* and *d*. Unit 27127-3.

The receptors were not easily excited when the mechanical displacement was applied from the dermal side of the corpuscle. To do this the skin was incised at the side of the corpuscle and a probe was inserted through the slit thus formed and pressed up against the dermis, beneath the corpuscle. The receptors continued to respond in the normal manner when the probe was subsequently applied to the epidermal surface of the corpuscle so that this procedure had damaged neither the axon nor its terminals. This result is in agreement with the insensitivity found to movement of the hairs or stretching of the skin, and indicates good mechanical insulation of the terminals except for displacement of the specialized epidermal surface.

In the sample of 133 afferent units examined, the characteristic localized high sensitivity and slowly adapting discharge were invariably associated with the conspicuous dome-shaped swellings of the epidermis. If an axon supplied several corpuscles, it responded in a similar way to mechanical stimulation of each of them. No axon was found which ended in dissimilar

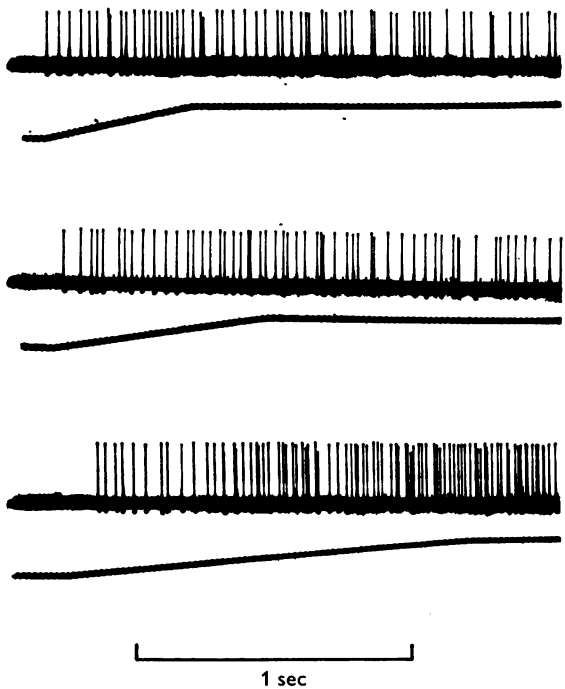
kinds of receptors. That is, if the axon innervated a touch corpuscle it responded with the characteristic slowly adapting response, and no other type of discharge in the fibre could be evoked by mechanical stimulation of receptors elsewhere in the skin. This distinctive and characteristic property of the touch corpuscle unit held even when the afferent fibre supplying the tylotrich follicle (see p. 772) nearest to a touch corpuscle was examined. The axons of the rapidly adapting tylotrich follicle unit and the slowly adapting touch corpuscle unit might innervate receptors associated with the same tylotrich follicle but other branches of the axons also supplied unrelated tylotrich follicles and touch corpuscles. This independent innervation of the two kinds of receptor has also been found in the rabbit (Brown & Iggo, 1967).

Quantitative mechanical stimulation. The touch corpuscle units are normally silent in the absence of an intentionally applied stimulus, and differ in this way from the type II slowly adapting units (Chambers & Iggo, 1967), which often carry a steady background discharge. The mechanical threshold was very low. In a previous report (Iggo, 1963*a*) it was described in terms of the minimal force which evoked a discharge and was less than 1 mg wt. In the present series of experiments the minimal indentation was measured. The tip of the probe was carefully placed, under binocular microscope control, on the surface of the touch corpuscle. An afferent discharge was evoked by displacements of 1–5 μm, but did not persist at these small displacements. This brief discharge was probably a dynamic response. The threshold for a static response was not measured.

The typical response of a touch corpuscle unit to controlled indentation of the skin is shown in Text-fig. 4. The response can be divided into several stages: a discharge at a relatively high frequency while the skin is being indented, called the *dynamic response*; followed, when the indentation is maintained at a constant value, by a discharge the frequency of which declines at first rapidly and then more slowly, the *static response.*

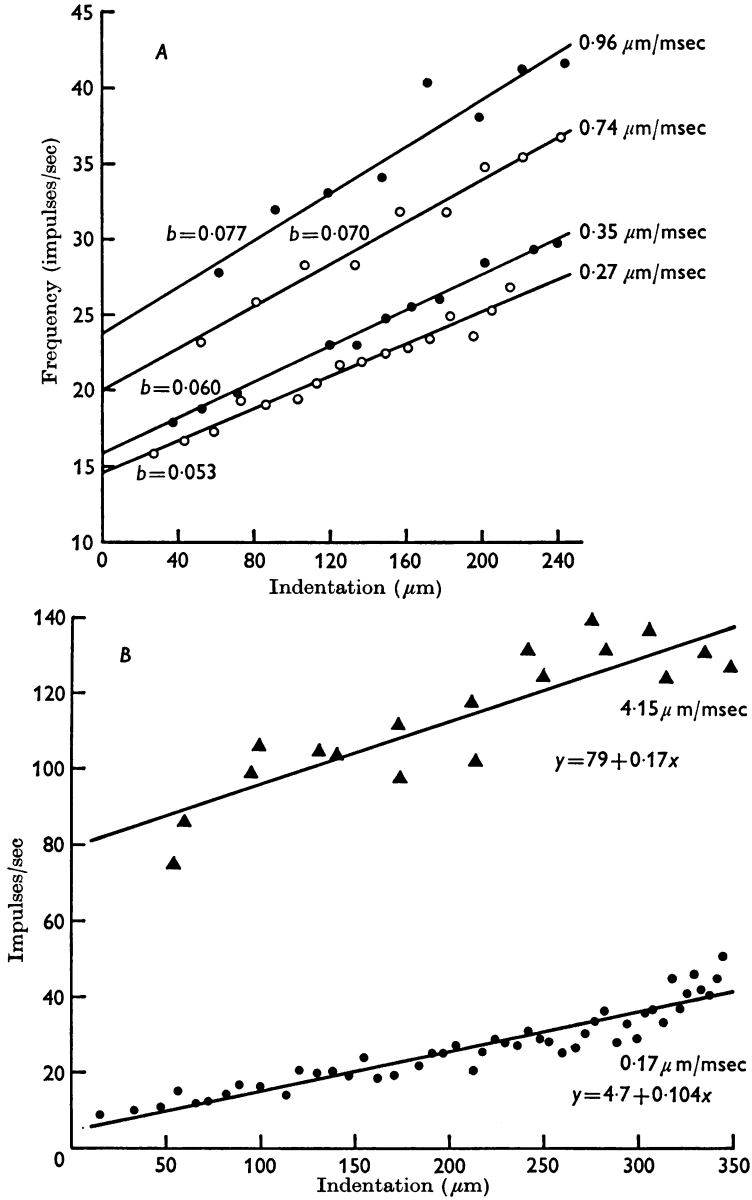
Dynamic response. The discharge in touch corpuscle units has been recorded during carefully controlled indentation of individual corpuscles, at linear velocities ranging from 0·1 to 10 μm/msec, using probes with a tip diameter of 0·25–2 mm. The peak frequency of discharge during indentation of the skin was as high as 1500 impulses/sec. At these very high frequencies, recorded only during rapid indentation, the interspike interval showed a progressive shortening during at least the first half of the indentation at constant velocity. At lower stimulus velocities the frequency of firing was lower and the interspike intervals displayed more variability from one trial to the next. Nevertheless, a characteristic feature of the response was a progressive decrease in interspike intervals except during the later stages of large (> 250 μm) indentations.

The frequency of discharge in the dynamic phase was determined by both the *velocity* and the *amplitude* of displacement. The interval between impulses decreased progressively during constant velocity indentation of the skin and the frequency of discharge at a given final indentation depended on the velocity and was higher for rapid indentation. The influence



Text-fig. 4. The response of a touch corpuscle unit to indentation of the skin, using a probe with a tip diameter of 1 mm. The lower trace in each record shows the output of the m-e transducer and registers the vertical movement of the probe. The upper traces show the discharge of impulses in a single touch corpuscle afferent fibre and display the characteristic irregularity of the impulse intervals. Three velocities of indentation are illustrated, in each case reaching the same final value, 250 μm. Unit 1078-1.

of the velocity of indentation can be seen in Text-fig. 5*A*, in which the frequency of discharge has been plotted against indentation and regression lines of the frequency of discharge on the indentation have been calculated and fitted to the responses for individual trials at several velocities. The slopes of the regression lines for different velocities are similar but the intercepts are progressively higher as the velocity of displacement increases. The dynamic response of the touch corpuscle unit can, by this kind of analysis, be separated into two components, one of which is dependent on the velocity of indentation, and has a value given by the

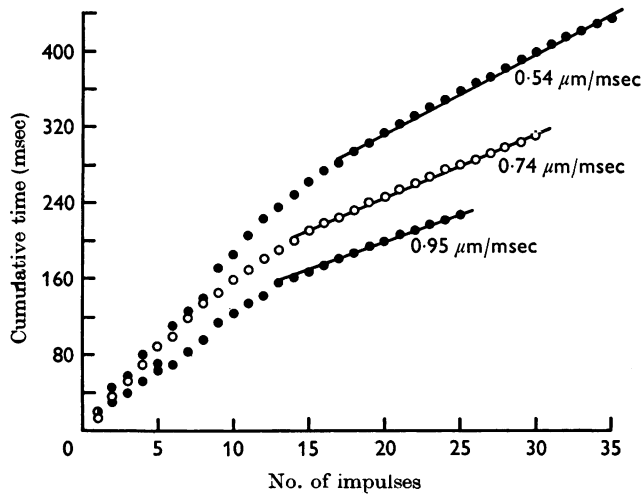


Text-fig. 5. *A*. Dynamic response of a touch corpuscle unit (2747-3) during constant velocity indentation of the skin at the velocities indicated. There is considerable variability in interspike intervals. Linear regression lines have been fitted to each response and the values of the regression coefficients (*b*) are entered on the graph.

B. Dynamic response at two velocities (final displacement 300 μm). Each point is the average of sixteen measurements of the appropriate interval duration from sixteen successive identical stimuli. Unit 30117-2.

intercept, a. The other is dependent on the indentation and has a value given by the regression coefficient, b_{xy}, where x is indentation and y the frequency of discharge.

The results of a similar experiment in which the responses to sixteen identical stimuli at a given velocity have been pooled are illustrated in Text-fig. 5*B*. Pooling the data in this way has reduced the scatter of interspike intervals which is conspicuous in Text-fig. 5*A*. The dynamic response of a touch corpuscle unit to mechanical stimulation thus has both an amplitude and a velocity dependence.



Text-fig. 6. Cumulative interval curves plotted against impulse number for touch corpuscle unit, 2447-1. The curves become approximately linear for the last half of each displacement at each of the constant velocities used. This effect is partly due to the reduction in interspike intervals that occurs in the later part of each response.

An alternative method of analysing the dynamic response of a touch corpuscle unit is to plot the cumulative interval against the number of impulses (Text-fig. 6). It is evident that at certain points in these curves the response becomes approximately linear, at about 50% of the final displacement, as Tapper (1965) has already reported (see his fig. 8), and from which he has drawn the conclusion that the interspike interval during indentation at constant velocity is uniform at each velocity and has a value which depends on the velocity. The present analysis, in which regression lines have been fitted to the data (Text-fig. 5), does not confirm his deductions. A comparison of the two methods of analysing the results suggests that the method of plotting the frequency against displacement is a more sensitive test for the presence of a displacement-

dependent component of the dynamic response than is the cumulative interval plot.

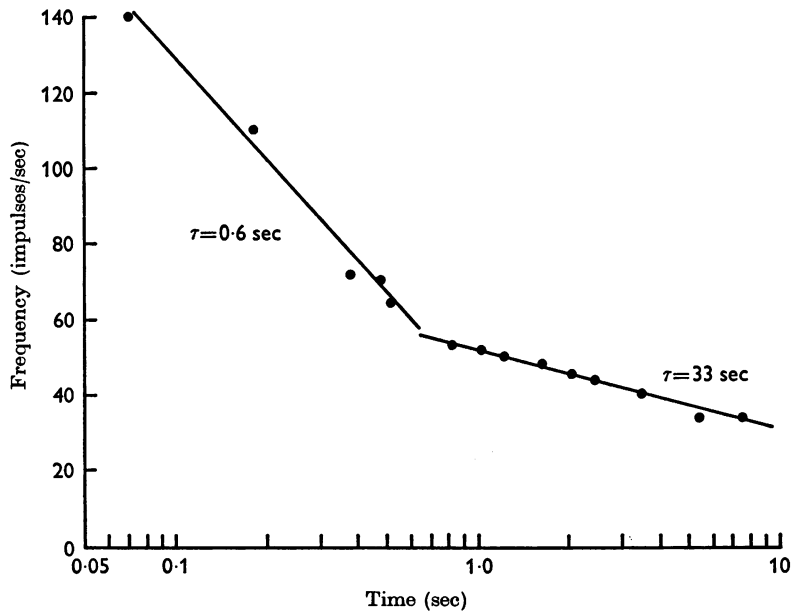
The frequency of discharge and the total number of impulses discharged during displacement to the same final amplitude at each velocity of displacement was related to the velocity, and when plotted on logarithmic co-ordinates a good fit to a straight line was obtained over the range tested (0·1–10 μm/sec) and for indentations up to 350 μm. These results confirm the earlier reports of both Werner & Mountcastle (1965) and Tapper (1965), in which they counted the number of impulses discharged in the dynamic phase.

Static response. The afferent discharge from a touch corpuscle continued for 30 min or longer if the displacement was sufficient. In this respect these receptors are strikingly different from rapidly adapting receptors, such as the Pacinian corpuscle (Loewenstein, 1961) and rapidly adapting hair follicle receptors (Brown & Iggo, 1967), all of which, under rigidly controlled conditions, discharge only during the dynamic phase of the displacement. They are, however, similar to another kind of slowly adapting cutaneous receptor, the type II of Chambers & Iggo (1967).

Immediately after the displacement reached its final value, i.e. at the end of the dynamic response, the discharge frequency began to decline exponentially, sometimes after an initial steep and rapid fall associated with the end of the constant velocity identation. Two time constants were evident in this gradual change in frequency; the first varied from 500 to 600 msec and the second from 10 to 20 sec for different touch corpuscle receptors examined under standard conditions (Text-fig. 7). During the phase of rapid adaptation the interspike interval lengthened progressively and became increasingly irregular. During the first 100–150 msec the frequency was high (155 Hz), the coefficient of variation was relatively low (0·30) and the interspike intervals were normally distributed with only a small degree of skewness (β_1 = 0·03). As the interspike interval became longer during this phase of rapid adaptation it also became more variable but the coefficient of variation remained at 0·30–0·35 (Text-fig. 8 inset).

The phase of rapid adaptation was followed by a phase of slow adaptation, with a very much longer time constant (10–20 sec). This slow adaptation merged into an almost non-adapting phase in which the discharge continued for longer than 10 min. When the stimulus probe was removed the epidermis was usually pitted and part of the slow adaptation may have been due to the slow movement of the skin away from the tip of the probe. The mechanical stimulators used in these experiments were designed to provide a constant controlled indentation of the skin and did not provide a constant force, so that they did not 'follow' the epidermis as it moved away from the tip of the probe. During this phase of slow adaptation the

interspike interval became more variable. In the example shown in Text-fig. 8*A* the standard deviation was proportional to the mean, i.e the variability was larger at lower frequencies of firing and the coefficient of variation ranged from 0·30 to 0·45 in the first 8 sec of indentation. The standard deviation was strongly correlated with the mean during both phases of adaptation (Text-fig. 8, inset) but during longer periods of stimulation, particularly when the frequency had fallen to low values, the coefficient of variation became larger, i.e. the interspike interval became more variable (Text-fig. 8*B*).

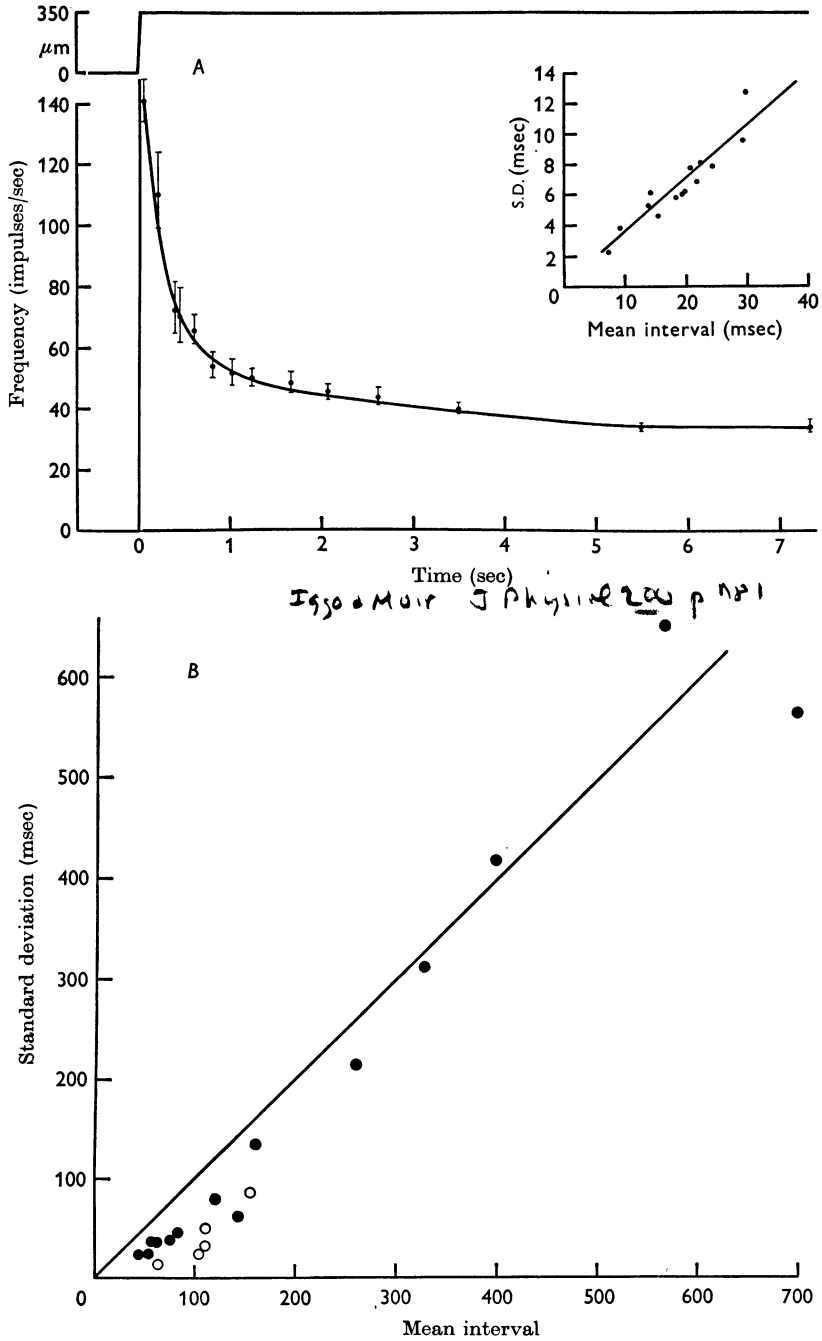


Text-fig. 7. Time course of the discharge of a touch corpuscle unit, plotted on semi-logarithmic co-ordinates, for the first 10 sec of a maintained indentation of the skin. Two time constants are indicated. Unit 3011-2.

Legend to figs. 8*A* and 8*B*.

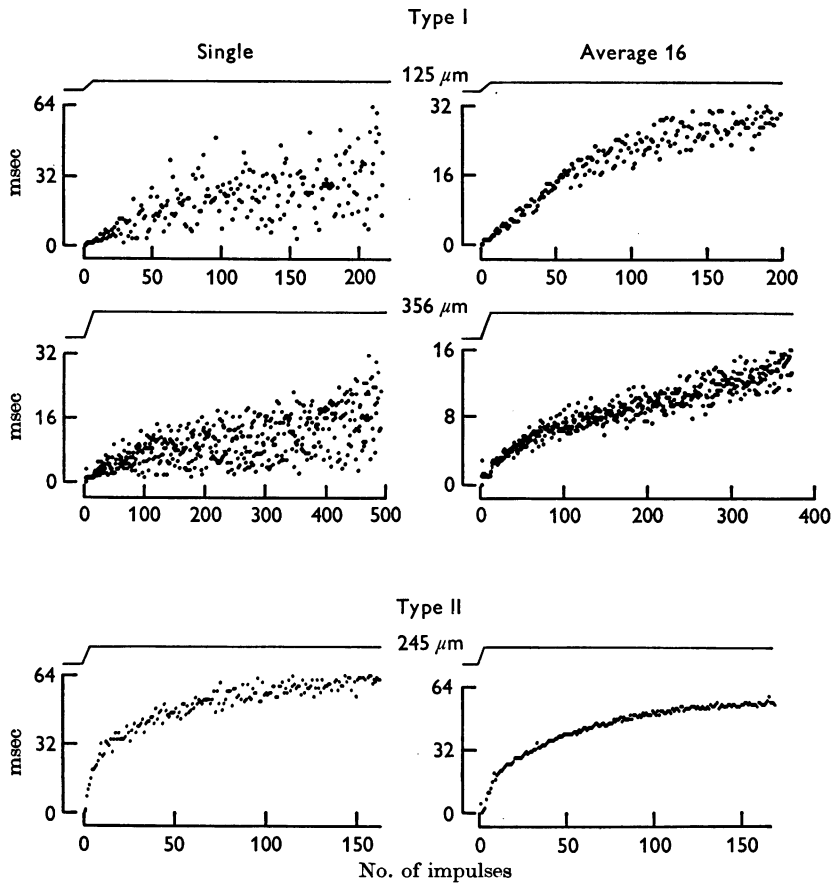
Text-fig. 8. *A*. Time course of the discharge of a touch corpuscle in response to indentation of the skin (350 μm) shown in the top curve. The curve has been calculated by pooling the results of sixteen identical stimuli. In the graph each point plotted is the mean for a short collection period and the standard error for each point is indicated by the vertical bar. The inset diagram shows the relation between the mean and standard deviation for each set of values. The coefficient of variation anged from 0·3 to 0·35. Unit 3011-2.

B. The relation between the standard deviation and the mean of the interspike intervals for the adapted discharge of touch corpuscle units in the cat ●–● and baboon ○–○. The coefficient of variation is less than 1 at the shorter mean interspike intervals but is close to 1 for the longer intervals.



Figs. 8*A* and 8*B*. For legend see opposite page.

The relatively large coefficient of variation (0·3–0·45) of the response of touch corpuscle units during the first 8 sec of maintained stimulation indicates a considerable variability of interspike intervals during individual stimuli. This variability is illustrated in Text-fig. 9, which also includes the response of a type II unit for comparison. When sixteen successive stimuli were delivered at intervals of 30–90 sec and the successive



Text-fig. 9. Variability of interspike interval. In each record the interspike interval is represented on the ordinate and the sequential interval number on the abscissa. The records were obtained using a Biomac computer in the dwell histogram mode. The upper two pairs of records are from a touch corpuscle (type I) unit at two different identations (125 and 350 μm) and the lowest pair of records is from a type II mechanoreceptor (245 μm). The records in the left column show the responses for a single mechanical stimulus, wave form indicated at the top of each record. The corresponding right-hand records are the averaged responses of sixteen stimuli at the same intensity. Averaging reduces the variability of the response, but the type I units, even after averaging, are still more variable than a single type II response.

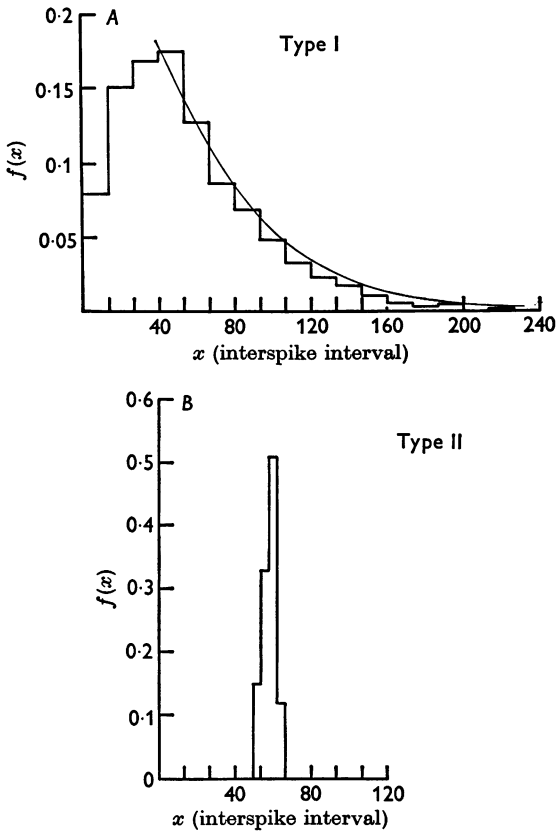
intervals summed (i.e. all first intervals, all second intervals,...n intervals) and each averaged, the variability was considerably reduced but was still relatively large when compared with a single type II response. It was, of course, considerably more than for the averaged type II response. In addition to this individual variability there was also an evident trend in the lengths of the intervals for the type I unit, the slow adaptation referred to above.

Interspike interval histograms for the discharge recorded several minutes after the adaptation described in the previous paragraph show a very strongly skewed distribution (Text-fig. 10) and coefficient of variation of 0·5 to greater than 1·0. A coefficient of variation of 1·0 would be expected for an exponential distribution of events which, for a renewal process (Cox, 1962), would be a process in which the times of occurrence of impulses were independent of each other if each was drawn from a population with a uniform probability and statistically random distribution. To test this hypothesis, probability density functions (p.d.f.) were calculated and tested against the hypothesis that the distributions were exponential. For such distribution the p.d.f., $f(x) = \rho e^{-\rho x}$ where ρ is the rate parameter and x the interspike interval. This p.d.f. uniquely defines a renewal process with an exponential distribution in which the lengths of intervals between events are statistically independent (on the assumption that the process is a stochastic point process: Cox & Lewis, 1966; Perkel, Gerstein & Moore, 1967). The mean and standard deviations are equal for such a theoretical distribution and are equal to $1/\rho$. This method of analysis has been used to assess randomness in the discharge of miniature end-plate potentials (Fatt & Katz, 1952) and spike trains (Biscoe & Taylor, 1963). An example of the adapted discharge is given in Text-fig. 10*A*. A good fit to the exponential distribution is obtained when the curve is calculated for the distribution of time intervals longer than 45 msec. The whole sample, however, showed a poorer fit, due to the relatively small number of intervals shorter than 45 msec. A similar analysis for another touch corpuscle, for which 1983 intervals were measured, showed the same effect with a progressively increasing absence of intervals less than 50 msec. These results are thus consistent with the hypothesis that the distribution of events is exponential for intervals longer than 45–50 msec and, therefore, that the impulses at intervals longer than this arise at random times, but that there is an interaction at shorter intervals.

A few of the touch corpuscle units had a resting discharge in the absence of an applied stimulus. The mean frequency of such a discharge was always low, less than 5 Hz. The interspike interval was characteristically irregular and, like the fully adapted response, had an exponential distribution. This is in striking contrast to the resting discharge from the type II slowly

adapting cutaneous mechanoreceptors (Chambers & Iggo, 1967), in which the interspike intervals are normally distributed (Text-fig. 10*B*) and the coefficient of variation is small (less than 0·1) at the same low frequency of discharge.

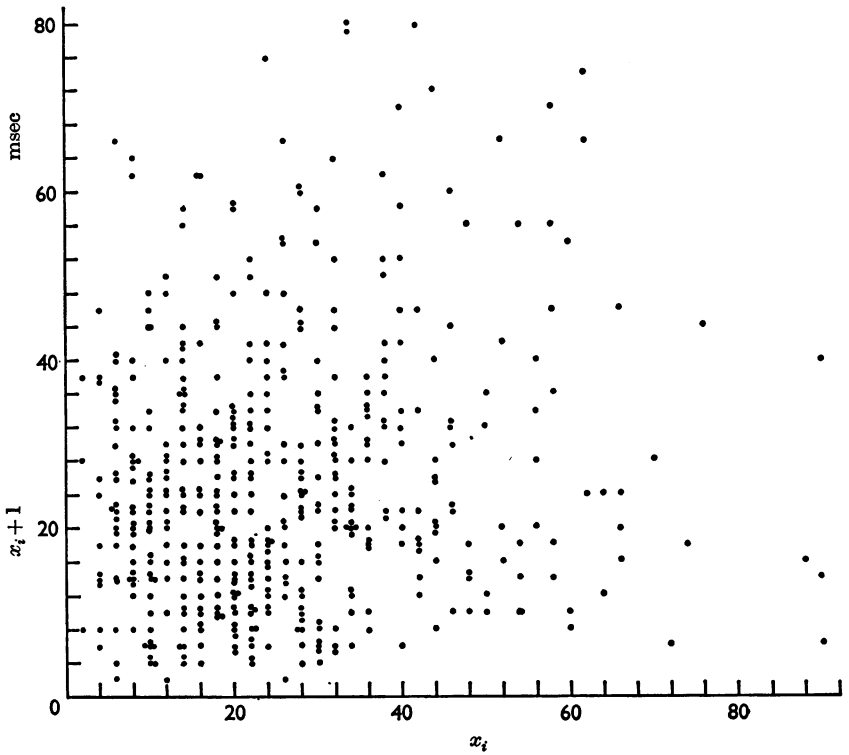
Independence of intervals. The occurrence of long and short intervals in the adapted discharge of a touch corpuscle raises the question whether there is any correlation between the lengths of successive intervals in a



Text-fig. 10. *A*. Frequency distribution curve of interspike intervals for the adapted discharge of a touch corpuscle unit (28–1) for 1460 successive interspike intervals (isi), expressed as a probability density function. The theoretical density function has been calculated $f(x) = \rho e^{-\rho x}$ and is entered as a continuous curve, using as ρ the reciprocal of the mean frequency, 63 msec, obtained after excluding the intervals shorter than 26 msec. n = 1440. Mean isi = 57·0 ± 36·3. Frequency = 17·4 Hz. Coefficient of variation = 0·63.

B. Frequency distribution for the adapted discharge of a type II slowly adapting mechanoreceptor plotted on the same abscissa scale as *A* but on a reduced ordinate scale. n = 1088. Mean isi = 60·38 ± 2·82. Frequency 16·5 Hz. Coefficient of variation = 0·05.

train of spikes. On a superficial examination there was an indication that short intervals were followed by long intervals. This suggestion has been tested by preparing joint interval distributions for pairs of intervals and an example is plotted in Text-fig. 11. The only indication of any interaction is in the absence of short intervals followed by short intervals. The distribution otherwise has the appearance expected (Perkel *et al.* 1967) for



Text-fig. 11. Joint interval distribution for touch corpuscle unit 28–1 plotted for 250 pairs of successive impulses (x_i, x_i+1). The general scatter of the points indicates a lack of any correlation between the lengths of adjacent intervals, except for the absence of intervals less than 5 msec.

an independence of intervals. The sparsity of short intervals would, in any event, be expected from the interval distribution histogram (Text-fig. 8) which displays a relatively small number of intervals less than 45 msec for this particular unit. Serial correlation coefficients were calculated for lag 1 and were very small ($r < 0{\cdot}01$).

Touch corpuscles in primates. The physiological experiments on the monkey and baboon confirmed the existence of touch corpuscles in these species. The general properties of the units were the same as described for

the cat. The touch corpuscles were less readily seen in the skin of the arm of the primates, at least partly because of the pigmentation of the epithelium which obscured the blood vessels in the dermal core of the corpuscle. The coefficients of variation for the adapted discharge of one unit at several intensities of stimulation were calculated and are entered on Text-fig. 8*B*. The interspike intervals for this unit were slightly less variable than for the cat although more variable than type II units in primates. Histological examination of skin also confirmed the general features of the corpuscle as described for the cat.

These results thus establish the touch corpuscle mechanoreceptors (type I slowly adapting units) as distinctive and recognizable afferent units in primates. Type II slowly adapting units are also present and correspond to the 'touch field' units described earlier (Iggo, 1963*b*) and had a characteristic regular discharge of impulses compared with the irregular discharge of the touch corpuscle units.

Reserpine-treated animals. The presence of osmiophilic granules in the tactile cells raised the question whether these structures contained catecholamines. Cats were treated with reserpine for 4 days. This period of treatment was sufficient to abolish transmission to the nictitating membrane, tested by stimulating the cervical sympathetic nerve in anaesthetized animals.

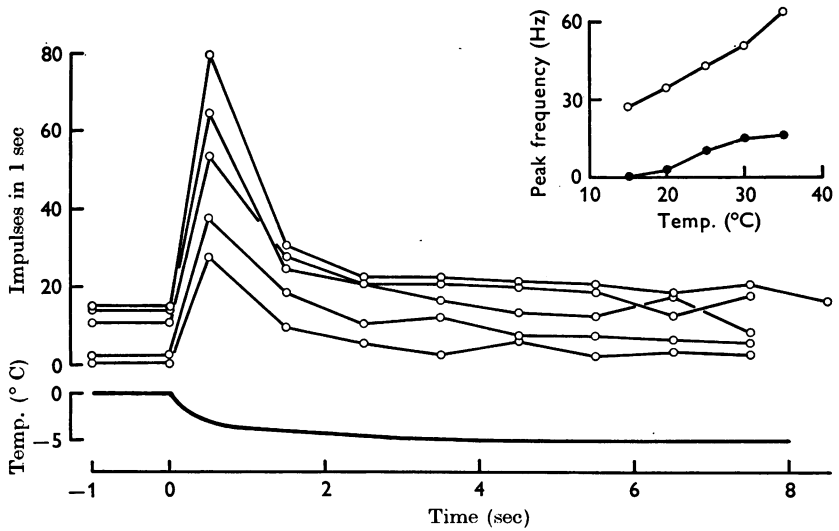
The touch corpuscles were unaffected by this treatment and single units examined in two cats were not demonstrably different from normal receptors. The dynamic and static responses were tested by repeated mechanical stimulation for at least 30 min and there was no indication of any progressive failure of the units.

Ultramicroscopical examination of the receptors also failed to reveal any change in the tactile cells and in particular the osmiophilic granules were still present in apparently normal numbers. The pharmacological properties of touch corpuscles have been examined recently by Smith & Creech (1967), who failed to affect the receptors except by nicotine. Earlier work by Fjällbrant & Iggo (1961) had shown that histamine, 5-HT and acetylcholine all have an initial excitant and later depressant action on slowly adapting receptors, and in several experiments these results were confirmed as applying to the touch corpuscles.

Thermal sensitivity. The touch corpuscle units can be excited by a fall in temperature of the skin, and any background discharge is temporarily depressed when the skin temperature rises. The thermal sensitivity of touch corpuscles was assessed by placing a metal thermode on the skin and adjusting its pressure to produce a continuous adapted discharge of impulses in the afferent fibre. In these circumstances a fall in temperature of the thermode, and therefore of the skin, evoked a marked increase in the

rate of discharge of impulses which depended on the initial temperature (Text-fig. 12). The peak frequency of discharge in the unit illustrated bore a monotonic relation to the initial temperature (Text-fig. 12). The response is thus similar to cold receptors (Iggo, 1969) and the touch corpuscle units could be confused with them, if a systematic analysis was not made.

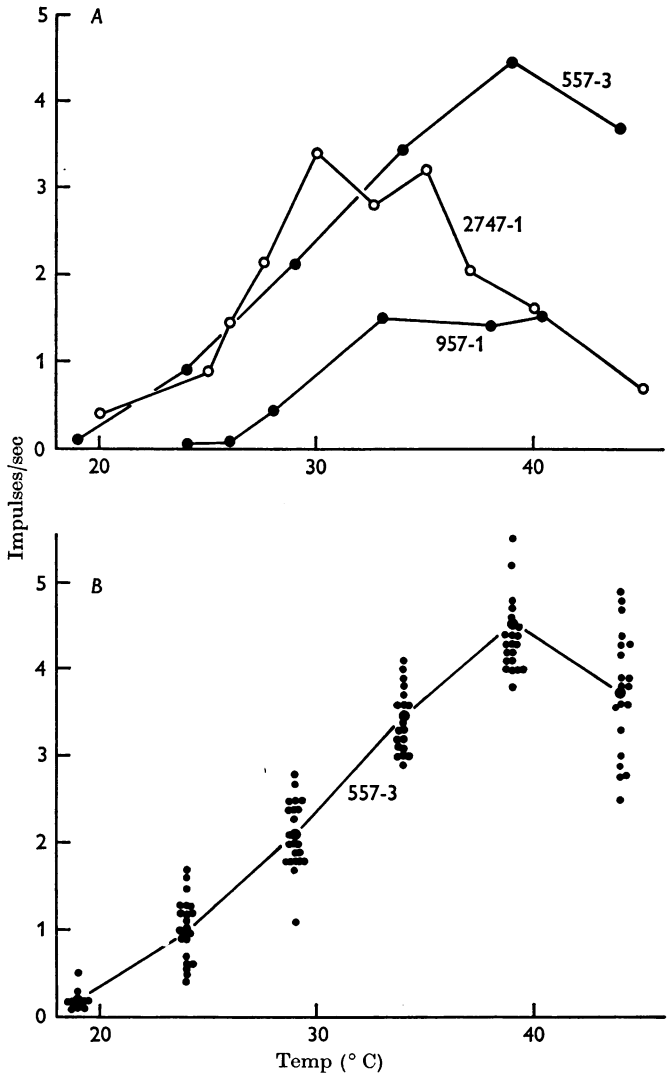
The adapted discharge of touch corpuscles was also temperature-dependent, and in four units was measured over intervals of several hours.



Text-fig. 12. The dynamic response of a touch corpuscle unit (5101-1) to thermal stimuli. The frequency of discharge, evoked by the constant mechanical stimulation of a thermode pressed on the skin and modulated by temperature, is plotted against time. At zero time the thermode temperature was lowered as indicated at the right hand side of the lowest full line. In each case there was an enhancement of the discharge which lasted less than 2 sec. The dynamic, ○—○, and static, ●—●, sensitivity curves of this unit are plotted in the inset diagram. At 12° C the unit was silent but could be excited mechanically by increasing the pressure of the thermode on the skin. The initial temperatures for the five curves, from above down, were 35°, 30°, 25°, 20° and 15° C. Iggo & Muir J. Physiol 200 p 787

The results in Text-fig. 13*A* show the average frequency of discharge over a range of temperatures from 18 to 45° C, for three of these units. In all cases the adapted discharge was at a frequency less than 20/sec and the peak frequency occurred between 30 and 40° C. The average frequency values were obtained by pooling at least ten samples, each collected for 10 sec intervals, after the skin had been held at a constant temperature for at least 3 min. There was a wide variability in the individual average values for the separate 10 sec collection periods (Text-fig. 13*B*), which was greatest at a skin temperature of 42° C. In another touch corpuscle unit the

response was adversely affected when the skin was maintained at 45° C for several minutes and the normal response to mechanical stimulation was absent after returning the skin to a temperature below 40° C. A similar response to thermal stimuli is also found for the type II slowly



Text-fig. 13. Static temperature sensitivity curves for three touch corpuscle units. Each point in *A* is the average frequency, measured 3 min after the temperature had become steady, obtained during at least ten consecutive 10 sec sampling periods. The variability of the adapted discharge is shown in *B*, in which the values for each of the 10 sec sampling periods for the unit are plotted, together with the average frequency at each given temperature.

adapting mechanoreceptors and it is probable that the temperature sensitive mechanoreceptors described by Witt & Hensel (1959) and Hunt & McIntyre (1960*a*) are in this category or at least include both types I and II.

DISCUSSION

The receptors described and analysed in this paper have a distinctive, indeed unique, morphology and an equally distinctive physiological behaviour. Many of the functional characteristics may be dependent on the structure of the corpuscle. Its superficial epidermal location would increase its sensitivity, while the attachment of the surrounding epidermis to the dense collagenous core of the dermis at the circumference of the corpuscle insulates its epidermal covering and could explain the localized sensitivity. The location of the tactile cells, supported on the dense fine collagen of the dermis, with processes penetrating the more turgid overlying cells of the epidermis, may account for the sensitivity of the corpuscle to shearing deformations due to stroking or pressure. The tactile cell presumably corresponds to the Merkel cell originally described in the avian bill (Merkel, 1875) and subsequently identified in the basal layer of mammalian epidermis (Pinkus, 1904; Miller *et al.* 1958). The fine structure of the Merkel cell and its nerve plate was described by Cauna (1962), Munger (1965) and Smith (1968), whose results are confirmed and extended by the present findings.

When the highly characteristic physiological properties of the touch corpuscles were first correlated with the dome-like structures in the skin (Iggo, 1961, 1963*a*) they were described as 'new specific sensory structures' in hairy skin. It is now clear that the receptor was described as early as 1904 by F. Pinkus, who called it the 'Haarscheibe' (hair disk) because it occurred in hairy skin and, in his experience, in association with hair follicles. The results presented in this paper clearly establish that there is no obligatory association of the corpuscles with hair follicles and that they function independently of the hairs. For these reasons the appellation Haarscheibe has not been adopted.

On either or both of these morphological and physiological grounds the touch corpuscles can be distinguished from all other cutaneous receptors and the touch corpuscle (type I slowly adapting mechanoreceptor) now joins the Pacinian corpuscle as a rigorously tested, specialized cutaneous receptor. These two kinds of mechanoreceptor are as yet the only cutaneous afferent units for which this more or less complete and detailed analysis has been carried out. Furthermore, the special physiological properties of the touch corpuscle are not only associated with the specialized morphology of the receptor but actually depend on it. Re-innervation of

denervated receptors leads to a return of the characteristic properties to the afferent unit only when the typical appearance of the normal receptor cell layer in van Gieson stained histological sections has returned (Brown & Iggo, 1963).

The structure of the touch corpuscle, in addition to the regular organization visible in the light microscope, has several interesting features when examined electron-microscopically. First, the terminal expansion of the afferent nerve is completely or nearly completely enclosed in other cellular elements and does not end freely as a 'naked' nerve-ending. The expanded disk-like nerve terminal has a large accumulation of mitochondria, which suggests a high level of metabolic activity in contrast to the Pacinian corpuscle. This presumed high level of metabolic activity would be expected for slowly adapting receptors, which can sustain continued high levels of activity and therefore require to maintain ionic equilibria in conditions of a continuous high level membrane activity.

The structural relationship of the nerve ending and the associated 'tactile cell' exhibits special characteristics: there are occasional closely apposed regions of neural and tactile cell membrane, close to which there are concentrations of dense osmiophilic granules in the cytoplasm of the tactile cell. On structural grounds these regions do not correspond to the tight junctions seen, for example, in other epidermal tissue (Loewenstein, 1966). They may serve a necessary function in transduction. The granules, which are most abundant between the nucleus of the tactile cell and the subjacent expanded nerve terminal, raise the question whether they play some part in the transduction process, perhaps as chemical transmitters. No evidence has been found to refute or support this hypothesis. Reserpine treatment failed to modify the behaviour of the receptors and no chemicals other than histamine, 5-HT, ACh (Fjällbrant & Iggo, 1961) and nicotine (Smith & Creech, 1967) have been found to exert any excitant action.

The touch corpuscles are innervated by myelinated axons and a detailed account of the conduction velocities of the axons of the afferent units reported in this paper is given by Brown & Iggo (1967). The sample of 113 was 22·6% of the total population examined. The mean conduction velocity was 57·2 m/sec in the cat, corresponding to axons with a diameter of 9·5 μm. The touch corpuscle units could not, on the basis of axon diameter, be distinguished from either type II slowly adapting units or type G hair follicle units, although they were slower than type T follicle units and so their distinctive functional properties are not allied to a particular band of axonal diameters in the cat. In the rabbit the touch corpuscle (type I) units had axons that conducted at significantly higher velocities than all other categories of afferent unit supplied by the saphenous nerve.

Now that the touch corpuscle units are established as possessing very distinctive morphological and physiological features it is of interest that they can be clearly distinguished experimentally from the other main classes of cutaneous mechanoreceptors. These are the rapidly adapting Pacinian corpuscle and hair follicle receptors both of which respond only during actual displacement. The hair follicle receptors respond as velocity detectors (Brown & Iggo, 1967) whereas the Pacinian corpuscles probably are more significant, within specified frequency limits, as vibration detectors (Talbot, Darian-Smith, Kornhuber & Mountcastle, 1968). The touch corpuscles are more likely to be confused functionally with the type II slowly adapting mechanoreceptors but can be distinguished from them on several grounds (Chambers & Iggo, 1967), which include (1) greater probability of a resting discharge in type II, (2) insensitivity of type I to stretching the skin, (3) higher frequency of discharge in type I, and (4) a normal distribution of impulse intervals during the adapted discharge in type II compared with an exponential distribution in type I. In a detailed statistical analysis of slowly adapting cutaneous receptors in cats and monkeys, Werner & Mountcastle (1965) established a logarithmic relation between the stimulus (indentation of the skin) and the frequency of discharge in the afferent fibre. A close scrutiny of their published results suggests, on the basis of the criteria given above, that their units included examples of both types I (touch corpuscles) and II. The analysis of the 'early steady state' used by Werner & Mountcastle (1965, pp. 365–368), established a very exact linear relationship between the mean and the standard deviation of the frequency of discharge with a small coefficient of variation. These results are not characteristic of the touch corpuscle units (type I units) of the cat that we have described. Instead they resemble the discharge of type II units in both the cat and the monkey. The coefficient of variation in their Figure 5 is 0·14, which is much lower than in type I units ($> 0{\cdot}3$, Text-figs. 8 and 9) and more comparable with type II units in which coefficients of variation are usually less than 0·2 (M. R. Chambers & A. Iggo, unpublished). The regular discharge seen in their Figs. 3 and 4 is also typical of the type II units. The individual variability of discharge in the touch corpuscle units is well illustrated in Text-fig. 9 and the reduction obtained by pooling consecutive interspike intervals is also evident. Despite this averaging process (sixteen stimulus responses were superimposed) the type I units are still more variable than a single response of a type II unit. The general validity of Werner and Mountcastle's results is not affected, in particular, that the stimulus–response relationship is logarithmic for the touch corpuscle units.

A characteristic feature of the adapted discharge of the touch corpuscle units is an exponential distribution of impulses, which would be predicted

if the impulses were generated at sites that were independent of each other. The anatomical organization of the receptor, with each nerve-end disk, or expanded ending, enclosed and separately supplied by a single branch of the stem axon (or perhaps two or three disks in tandem on a branch) and axonal myelination to within a few micrometres of the enclosed nerve ending is consistent with the idea of separate generators; each expanded ending operating as a generator. A contrasting situation is provided by the crayfish stretch receptor (Eyzaguirre & Kuffler, 1955), in which there is a single site of initiation of the conducted action potentials (Edwards & Ottoson, 1958) and a very regular interspike interval. Other analogous situations are the primary spindle receptors (Buller, Nicholls & Ström, 1953) and probably the type II slowly adapting cutaneous mechanoreceptor (Chambers & Iggo, 1967), for which the interspike intervals during an adapted discharge (10 sec or longer after the stimulus indentation was applied) are normally distributed. In the touch corpuscle units there is greater deficiency of impulses at intervals less than 45 msec than would be predicted for an exponential distribution (Text-fig. 10). This may be due to an interaction within the corpuscle. An impulse travelling from its site of initiation, if this is a receptor cell, and propagating orthodromically towards the spinal cord would be expected to invade other terminal branches of the afferent fibre and these impulses would travel antidromically back to other receptor cells within the touch corpuscle. They would either collide with orthodromic impulses or reach the receptor cells and 'reset' the discharge, as is found in the muscle stretch receptors (Matthews, 1933). This type of interaction may account for the relatively sparse occurrence of the shortest intervals. The emergence of an exponential distribution of interspike intervals can be followed as the frequency of discharge declines during adaptation. Immediately after a stimulus has been delivered, that is, during the phase of rapid adaptation (100–150 msec after indentation has reached its final value) the discharge is at high frequency, 155/sec, has a low coefficient of variation (0·30) and is normally distributed about the mean. In this phase of the response it is similar to the adapted discharge of the type II slowly adapting units (Text-fig. 10) although much more variable. As the frequency of firing decreases during maintained displacement of the touch corpuscle, the coefficient of variation of the interspike intervals increases and increasing skewness of the intervals also becomes evident until eventually the exponential distribution emerges. It is well known that the discharge of impulses in afferent fibres is less regular at low frequencies but even in the same range of frequencies below 5/sec the type I units are very much less regular than type II so that some additional property, such as the existence of multiple generators in type I, is likely to account for the difference.

Our gratitude is due to Dr Nora Campbell, who drew the diagrams shown as Text-figs. 1 and 2, and to R. McDougall for his skilled technical assistance with various aspects of this study. We are grateful to the Wellcome Trust and Royal Society for providing experimental facilities, and to Margaret Chambers for permission to use unpublished data for Text-fig. 10*B*.

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EXPLANATION OF PLATES

PLATE 1

Fig. 1. Surface view of the skin of the thigh from an adult cat after removing the hair with a depilatory agent. A touch corpuscle and its relation to a guard hair is seen. × 72.

Fig. 2. Glutaraldehyde fixation, Araldite embedding and toluidine-blue staining. Five tactile cells (T) are present in the deepest layer of the epidermis; the inset shows the relative pallor of the tactile cells and that the stratum basalis extends down to the basement membrane between the tactile cells. A myelinated nerve (N) is shown next to a part of the capillary plexus. The fine collagen of the dermis contains fibroblasts (F), and, at the periphery of the dome, it is indented (I) by epidermal cell projections. × 800, inset × 1,250.

Fig. 3. Intravital methylene-blue staining, cleared whole mount. This touch corpuscle contains about forty stained nerve plates, which are seen through the cleared epidermis. Short lengths of the terminal axons are also evident. × 200.

PLATE 2

Fig. 4. EM, glutaraldehyde fixation. One tactile cell, with its multilobulated nucleus (NN), Golgi apparatus (GO) and nerve plate (N), is shown. The deepest layer of the epidermis is separated from the dermis by the basement membrane (BM). Layers of cytoplasmic projections form lamellae (L) beneath the nerve plate. The superficial part of the tactile cell is attached to other epidermal cells by desmosomes (D). × 8,500.

PLATE 3

Fig. 5. EM, glutaraldehyde fixation. A specialized contact zone between a nerve plate (N) and a tactile cell (C) containing numerous granules (G) is shown. The apposed plasma membranes run straight and parallel to each other and the nerve membrane is thickened. × 57,000.

Fig. 6. EM, osmium fixation. A thin flat projection from the tactile cell (L) encloses the nerve plate (N). Aggregations of glycogen (GY) are seen near the pole of the tactile cell nucleus. × 16,000.

Fig. 7. EM, osmium fixation. A considerable area of the surface of the pale nerve plate is in direct contact with the basement membrane (BM). The lamellae beneath the nerve plate possess pinocytotic vesicles (P). × 23,000.

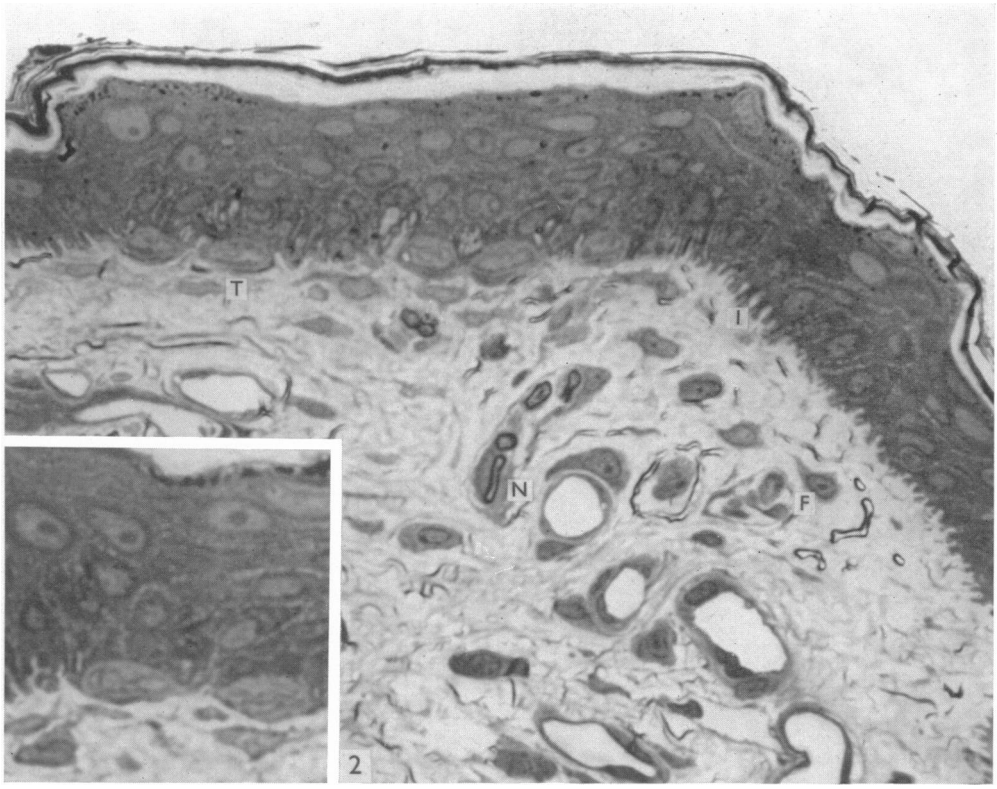
Fig. 8. EM, glutaraldehyde fixation. The superficial part of a tactile cell is on the left of the field. In the epidermis, there is a pale cell containing spherical dense granules; tonofibrils (T) are present in its cytoplasm and its granules are larger than those of the tactile cell. × 11,000.

PLATE 4

Fig. 9. EM, glutaraldehyde fixation. Two processes (P) containing clear tactile cell cytoplasm penetrate the adjacent epidermal cells. Desmosomes between epidermal cells (D_1) and between the tactile cell and an epidermal cell (D_2) are present. × 25,600.

Fig. 10. EM, glutaraldehyde fixation. The pale core of cytoplasm from a process extends as far as the nucleus (NN) of the tactile cell. A few granules (G) are present in the cytoplasm of the superficial half of the tactile cell. × 23,000.

Fig. 11. EM, glutaraldehyde fixation. Three tactile cell processes penetrate the same epidermal cell. Abundant glycogen (GY) is seen near the pole of the tactile cell nucleus. × 13,000.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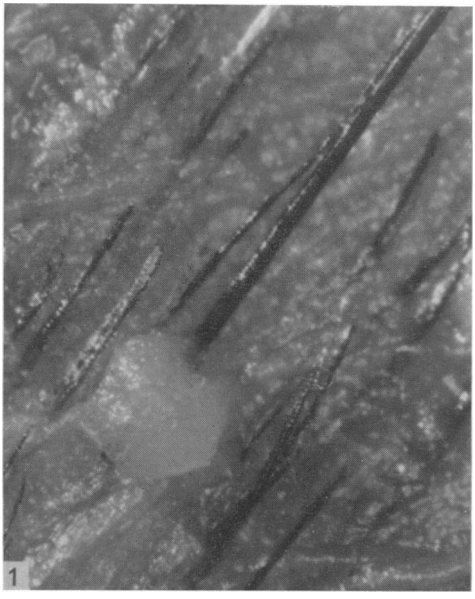
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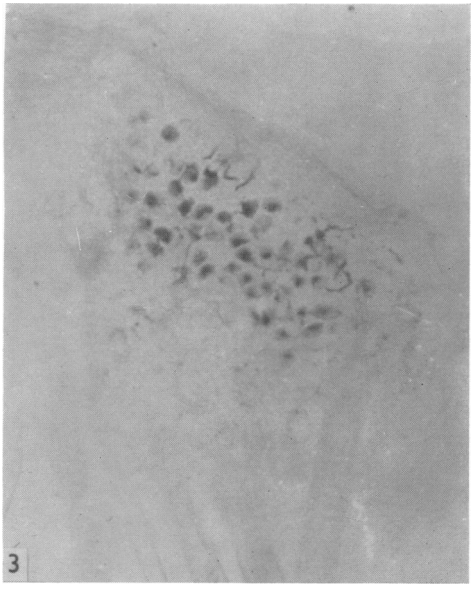
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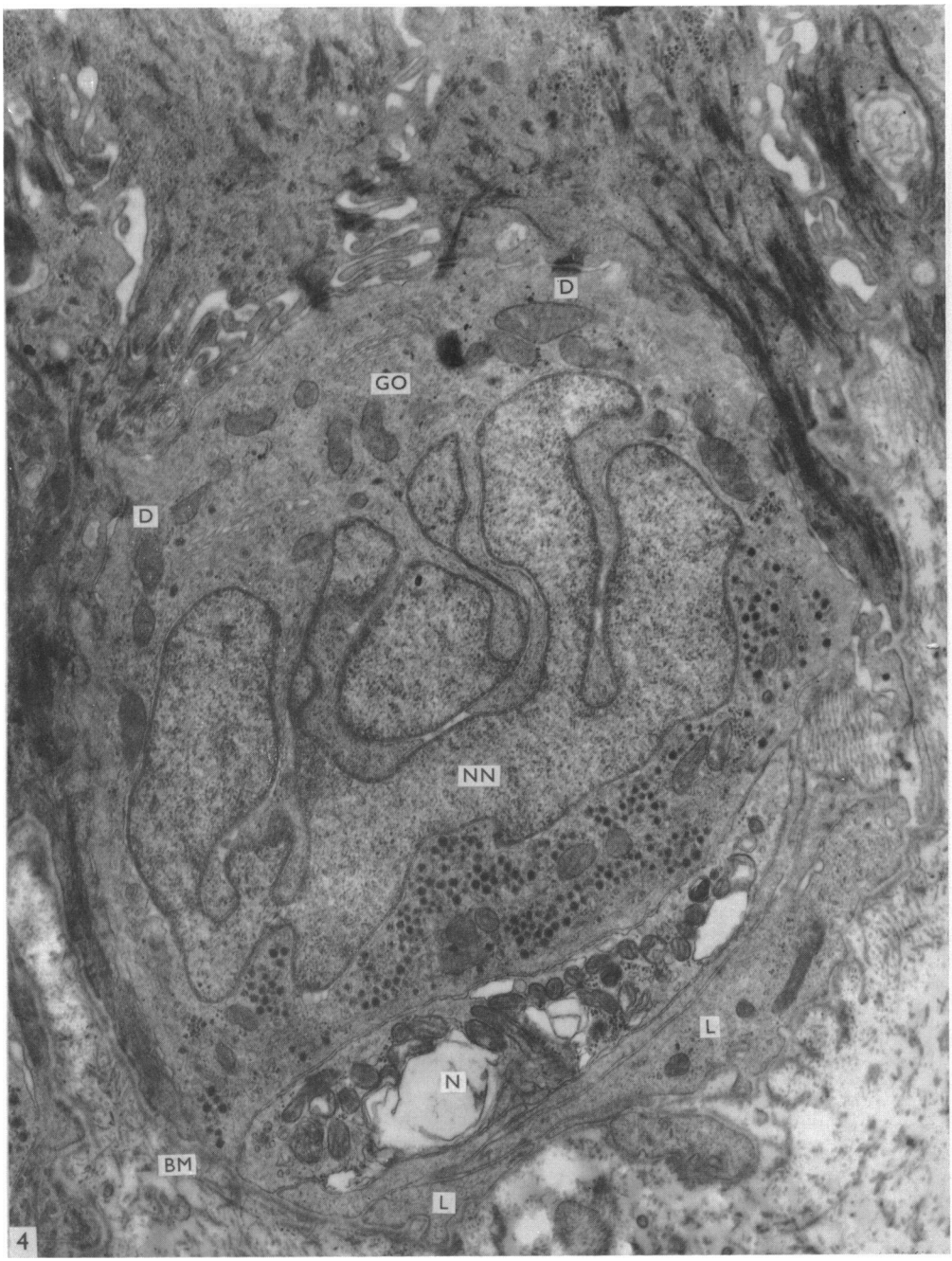

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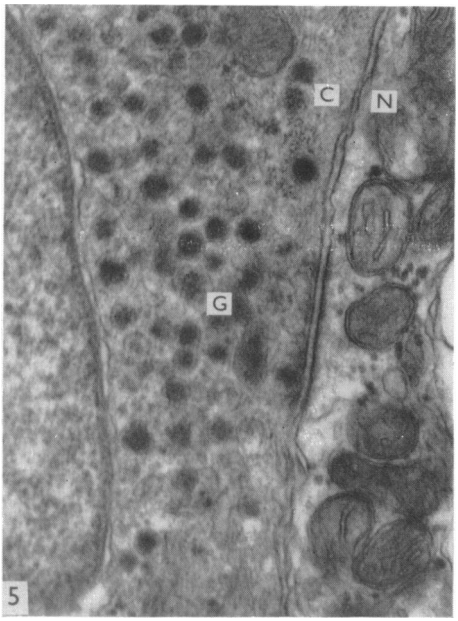
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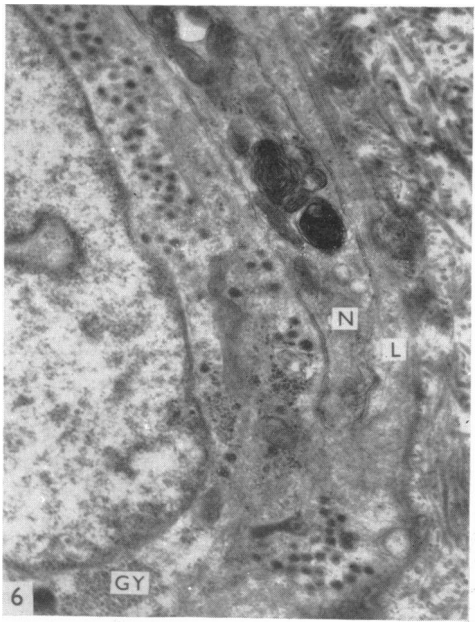
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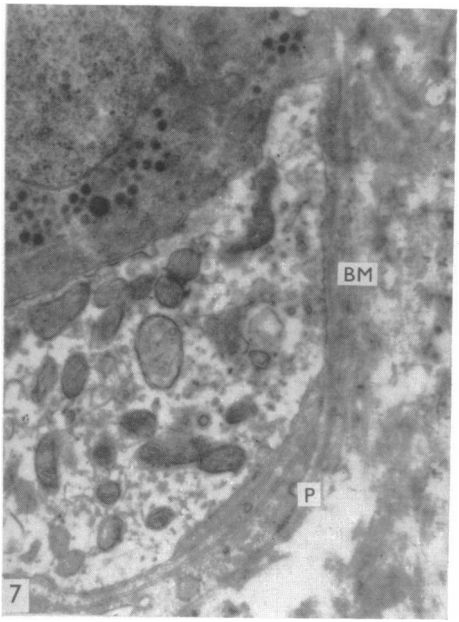
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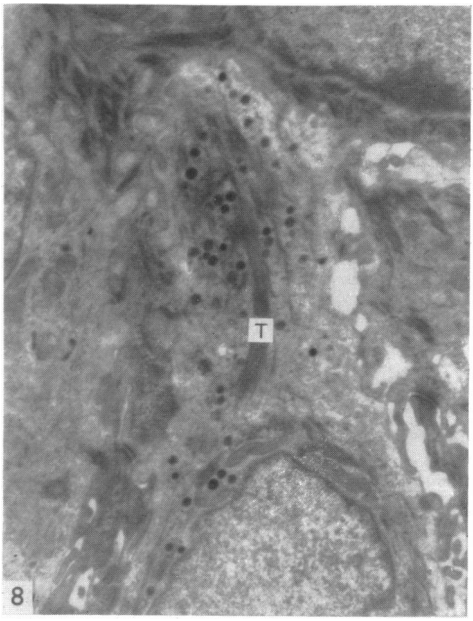
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D_2
D_1
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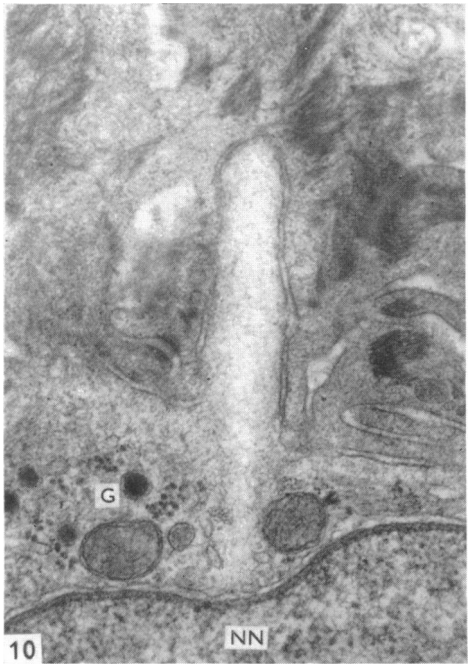
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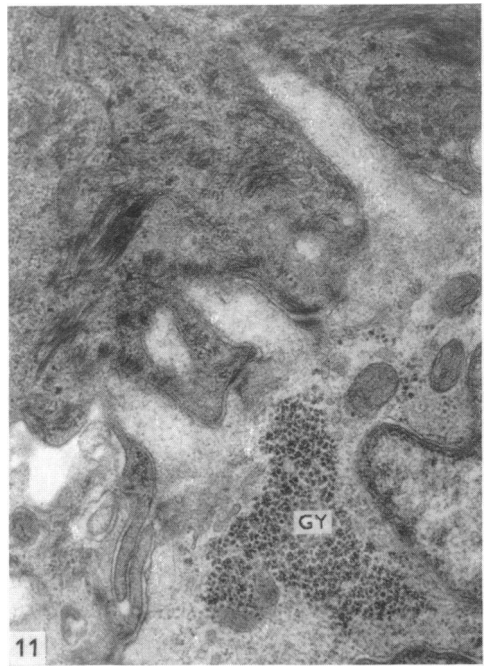
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