Chapter 2

Peripheral Principles of Organization
Discovered in Skin Organs and Retina.
Fiber Size. Receptive Fields. Receptors
Re-represented in the Brain

1. Introduction. Background of electrophysiological work

The body turns a large sentient surface toward the external world, and this great primitive sense organ has in the course of evolution evolved focalized structures for specific tasks. To these also belong several organs for space analysis, e.g. the "glorified heat spots" of the retina (Sherrington’s term, 1941), reaching to astronomical distances, the vibrissae of certain carnivora—studied by Fitzgerald (1940)—for displacing touch a little further away from the surface than can be done by hairs of ordinary length, or the temperature receptors which in certain snakes have developed into a special kind of eye for the reception of infrared radiation. The impulses from this heat-sensitive structure have recently been studied by Bullock and his collaborators (1952, 1953).

The principle of focalization combined with specialization received great attention in classical psychophysics because of the discovery by Blix of Lund (1882–83, partly translated into German 1884) of the punctate representation of cold, warmth, and pressure. Investigation of touch spots, pain spots, etc. has ever since been a recognized part of skin physiology, just as the Von Frey hairs and algesimeters of different types have been part of the standard equipment in most physiological class rooms. To Von Frey (1895) we owe the notion that the Krause (1860) end-organs are the cold receptors and that the Ruffini (1891–92, 1894) cylinder terminal might be the warmth receptor. Many other end-organs have been identified with specific sensory experiences but it serves no obvious purpose to repeat here what may be found in every textbook dealing with the sensory apparatus of the skin (see also the classical papers by Von Frey, 1894a,b, 1895, 1910). I mention heat and cold because they will be chosen as models in the following discussion of the problem of specificity of skin sensations and of the difficulties in identification. Today the zest for identification of sensory spots with structure is abating. The reasons for this illustrate present trends of development and therefore deserve some comment.

The difficulties of identification began to be noticeable at an early date. At that time "sensation" was often regarded as something simple and different from "perception," which was held to be more of an elaboration of the primary data from sense organs. There may be some foundation for distinctions along such lines in that sensory experiences can be more or less elaborated depending upon the significance for the organism of the information delivered. On the whole, however, the distinction between sensation and perception has lost its validity (cf. Graham, 1951), and by the last chapter of this book, if not before, it should be clear that a sensation is an exceedingly complex affair. For this reason the age-old question of what structure corresponds to what sensation may often be irrelevant, except when raised for highly specialized structures or in a very general fashion.

Bazett and his collaborators (Bazett et al., 1932) tried to determine as completely as possible the number of sensory experiences obtainable from a piece of skin (prepuce) that afterward was sacrificed for histological study. They could not record more than four types of sensation—heat, cold, touch, pain—but the piece contained seven clearly differentiated types of ending. As early as 1905 Ruffini wrote:

De 1891 à aujourd’hui, par l’application des méthodes plus électives au chlorure d’or et au bleu de méthylène, le nombre des formes connues s’est énormément accru, sie bien que ne croyons pas exagérer en disant que la peau, tant en surface qu’en épaisseur, est littéralement remplie d’expansions nerveuses. Et tandis qu’avant cette époque les fonctions étaient beaucoup plus nombreuses que les formes, aujourd’hui, par contre, ces-ci ont pris leur revanche sur les premières [p. 422].

This is one of the many situations in biology in which the extreme rationalist might have had expectations other than those of the empiricist. The former might have referred to Occam’s razor: entia non sunt multiplicanda praeter necessitatem. But the biologist’s attitude
should be humbler. His duty is to admit that he does not know nature well enough to understand its requirements or “necessities.” This is why he experiments. Some of the histological “entities” may be there to facilitate discrimination by providing a greater variability of pattern; some touch receptors may adapt quickly, as those originally described by Adrian and Zotterman (1926b), others very slowly, as those found by Frankenhaeuser (1949), which are unorganized endings in the rabbit’s skin. Some may be there for purposes not necessarily connected with what we call perception (which is a psychological term). Many of these difficulties are clearly of a conceptual nature and do not in the same way taint electrophysiological work.

When the electrophysiologist finds an isolated pacinian corpuscle, which is easy enough in the flexor aspect of tendons (Adrian and Umrath, 1929) and particularly in the mesentery, where they can be seen as small translucent ovals embedded in a still more transparent medium, he can also demonstrate that it is fired by light touch or pull. Gammon and Bronk (1935) found these rapidly adapting organs to be sensitive enough to discharge to the pulsations of the mesenterial vessels (cf. Gernandt and Zotterman, 1946), much as do the slowly adapting pressureceptors in the carotid sinus wall (Bronk and Stella, 1932, 1935; U. S. von Euler, Liljestrand, and Zotterman, 1941).

The pacinian corpuscles are visible to the naked eye, their long axis being 2 mm., and the organ consists of concentric lamellae around a stalk with a terminal expansion, thus admirably suited to perceive localized pressure changes. Their impulses, as elicited by pressure, were first recorded by Adrian and Umrath (1929) from the nerve to the plantar fascia of the cat’s hind foot (for later work on their generator potentials see Chapter 1, sec. 3). From such experiments one may infer that these structures, wherever they may be found, have a similar specificity, as envisaged for the Pacini organ by e.g. Rauber (1867), Von Schumacher (1911), and Sherrington (1900b), the last of whom stated: “The ordinary Pacini, embedded in muscle, is admirably placed for being compressed, especially when, as sometimes, seated in the retiring angle between a septum or aponeurosis and obliquely inserted muscle bundles” (p. 1010). Von Schumacher, who demonstrated that the basal pole of the Pacini organ was vascularized, also pointed out that they were so intimately joined to the mesenterial vessels that they were bound to respond to variations of blood pressure (cf. Sheehan, 1933). A review of the old literature on the pacinian corpuscles and their discovery has been given by Gray and Malcolm (1950).

Some further difficulties in identification might be mentioned. Sensation as a measurable entity is defined psychophysically in c.g.s. units, the precise values of which are difficult to assess with organs hidden within the skin. Sensations as well as impulses in response to touch and pressure arise from skin deformations with unknown distribution of the forces around the organs. Heat and cold have extension and gradients in all three space coordinates. Definition of the sensation in c.g.s. units may therefore prove deceptive. The punctiform mode of stimulation may often be an abstraction. Also, some sensory qualities may not be as fundamental as commonly stated.* I, for one, feel that there is no difference between the modalities of “touch” and “pressure” other than one of quantity (strength). They are not so distinctly different experiences as the two qualities “red” and “green.” Itching or tickling seems to me more genuine as a quality and yet, on reasonably good evidence, electrophysiological (Zotterman, 1939) as well as clinical (cf. Pritchard, 1932; Walshe, 1948), it is held to be a combination of messages from touch and pain organs, possibly only from pain organs feebly stimulated.

Specificity, as defined by electrophysiological means, may have its limitations—it cannot deal with itching—but, when one does define any given peripheral afferent fiber as belonging to a sensory “thermometer,” “tactometer,” etc., the appropriate adequate stimulus has been picked up by the “meter” with one of those particular properties independently of whether specificity resides in form as seen under a microscope or in something else. It is not difficult to find examples of sensitivities to specific agents which are properties of nervous tissues. The papers on chemical stimulation of nerve fibers are legion. Mechanical stimulation is also well known (Tigerstedt 1880). In our laboratory we have devoted considerable attention to the fact that nerve fibers themselves are quite sensitive to temperature changes (Bernhard and Granit, 1946; C. von Euler, 1947; Granit and Lundberg, 1947; Lundberg, 1948). C. von Euler found that small afferent fibers discharge specifically to heat of only a few degrees above normal, while large fibers fire to cooling. These effects are extremely selective and the turning point from heat to cold discharge is around a fiber diameter of 5–6 μ. Small efferents cannot be thermally stimulated (C. von Euler). More recently Dodt (1953) has found that the cold fibers (below 5–6 μ) also respond to cooling but not to heat. Other valuable observations on thermosensitivity of nerve fibers were reported in his paper. Here, * One speaks of “modalities” such as hearing, sight, pain, temperature, and touch, within each of which are distinguished “qualities” such as color, tone, etc.
then, is a kind of specificity, perhaps primitive from the point of view of sense organs but obvious enough to make one realize that very little improvement of this property in either direction would be needed to provide us with two temperature end-organs neither of which need be like a Krause end-organ or a Ruffini terminal cylinder in appearance.

At the opposite extreme there are the glorified heat spots of the retina which perceive light of the order of a few quanta at the absolute threshold (Von Kries and Eyster, 1907; Hecht, Shlaer, and Pirenne, 1942; Bouman and Van der Velden, 1947; Baumgardt, 1950; Pirenne, 1953), and the no less glorified mecanoreceptors in the organ of Corti that are held to respond to vibration of an amplitude of the order of a fraction of the diameter of the hydrogen atom (Von Békésy and Rosenblith, 1951). With these structures specificity is such a unique achievement that they must also be (structurally) unique.

Lesser degrees of specificity may well be found in unorganized endings. Weddell and his colleagues (Hagen et al., 1953; Sinclair et al., 1952) recorded the number of touch, pain, cold, and warm spots per unit area in the ear for comparison with similar measurements on forearm and finger tips (right ring finger). There were only minor differences in the number of such spots in the places chosen and the four sensory experiences were everywhere the same. The skin of the ear was found to be well innervated but there were no organized endings such as the organs of Krause, Ruffini, or Meissner (tactile corpuscles). Yet cold, heat, and pressure were perceived. The cartilage did not contain any nervous tissue apart from the fibers accompanying the blood vessels. The finger tip was found to contain both free and organized endings. They write about the latter:

We cannot detect any distinct varieties of the fine arborizing terminal and in the organized group there appears to be an unbroken and graded series of end organs from the simplest to the most complicated, from superficial, loosely encapsulated whorls to the thickly capsulized highly complex dermal corpuscles. If we can rid our minds of the desirability of fitting each observed ending into a rigid classification, we are forced to admit that no such classification can justifiably be made. One type of ending insensibly merges into another, and intermediate forms occur in profusion. Our histological findings, therefore, do but confirm the much neglected statements made by Ruffini,* who noted the existence of intermediate forms and the futility of rigid classification.

*Ruffini (1905).

It might be added that many other histologists (see e.g. Stöhr, 1928) and also psychologists (Nafe, 1942; Morgan, 1951; Jenkins, 1951) have taken similar standpoints.

Fifty years ago Sherrington (1900a) spent twenty pages of his presentation of skin perception on “common sensations” such as tickling, shivering, shuddering, sexual feelings, etc., and one may with some right assume that many of those highly differentiated experiences project back upon minor variations in the peripheral structures which in different ways combine to deliver the cues to the interpreting centers in the brain.

To the electrophysiological approach, as we shall see, the problems appear in different light. Specificity is immediately given by the stimulus of lowest threshold eliciting a discharge in one particular fiber, and identification of the specific end-organ has for its ultimate goal analysis of its physicochemical properties by microtechniques (which so far, however, have not been applied to skin organs). Since the afferent nerves must terminate somehow, it seems only natural that the skin should be “punctuated” by various types of receptors, as was admirably elucidated by a previous generation of workers despite the many difficulties alluded to above. The histology of skin innervation is the natural starting point for electrophysiological research. There are the curious plexus formations looking like skeins and described by the early workers (and by nobody of that period better than by Retzius, 1892) and also the organized endings whenever they can be localized. In more recent times Woollard, by the introduction of his methylene blue intra vitam stain (1935–40), again drew attention to the plexus formations, and since Woollard's death his work has been continued by his former collaborator Weddell (see his summary, 1945). The advantage of this method is that both the fiber and its endings can be traced. It must be admitted that at the moment histology still is far in advance of physiology, and the electron microscope is likely to add a few hundred years to this lead.

It appears from Woollard’s and Weddell’s work (see Fig. 15b) that the cutaneous nerve plexus consists of two layers of dichotomized nerve fibers forming a meshwork from which fibers run as beaded terminals to the epidermis as well as to the hairs. Some of Retzius’ drawings are given as Fig. 15a. The network from any one fiber is interlocked with that of neighboring fibers, a single fiber innervating an area the size of which presumably depends upon the region in which it has been found. Two networks were known also at the time of Von Frey, who wrote (1894b): “What this double innervation
means from the physiological point of view, if the lower network serves pressure and the other possibly pain . . . cannot at the moment be decided” (p. 296). Waterston (1933), confirmed by Woollard (1936–1937), showed that the epithelium with its nerve endings could be sliced away without causing sensations other than touch. Woollard stated that these epidermal endings are rare in man and may be regarded as an accessory organ of touch. The subepidermal nerve net, on good evidence, is held to subserve pain (Woollard, Weddell, and Harpman, 1940). There is definitely branching of one fiber to several end-organs of a single type as well as multiple (overlapping) innervation of hairs. Thus, for instance, the number of hair follicle groups supplied by branches from one fiber was

in the neighbourhood of 300, and a group of hair follicles may contain up to 10 hairs. The terminal ramifications of every main fibre,

when traced, were found to remain independent from those of other fibres, but it was noted that each hair-follicle group was supplied by branches from at least two main nerve-fibres. This also applies to individual hairs . . . so that a single hair may be innervated by as many as 15 terminal ramifications [Weddell, 1945, p 170].

It is interesting to note that Von Frey (1894a) found up to 15 pressure-sensitive points around the hair stalk.

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Fig. 15a. Skin innervation. a1: vertical section through epithelium of soft palate of human foetus showing nerves (n) ending in free beaded terminals. a2: Mouse. Innervation of hair roots from cheek. (Retzius, Biologische Untersuchungen, 4, 1892.)

Fig. 15b. Weddell’s conception of cutaneous innervation, based on the studies described in his article. A: groups of Meissner’s corpuscles subserving the sensation of touch. B: beaded nerve nets subserving pain (probably fast pain). C: Merkel’s discs subserving touch. D: beaded nerve fibers derived from nerve nets subserving pain and associated with blood vessels (probably slow pain). E: nerve terminals around the sheath of a hair subserving touch. F: a pacinian corpuscle subserving pressure. G: a group of Ruffini endings subserving warmth. H, I: groups of Krause’s end-bulbs subserving cold (these lie at somewhat variable depths beneath the skin surface). Note: The organized endings are accompanied in every instance by fine-beaded nerve fibers subserving pain. (Weddell, Brit. Med. Bull., 3, 167. 1945.)
The encapsulated or otherwise organized endings also tend to occur in groups (Meissner, Pacini, and Merkel tactile corpuscles). Multiple innervation is established only with hairs, but several adjacent encapsulated endings of the same type may be innervated individually or by branching from one fiber. Evidence has been obtained in favor of associating the Meissner corpuscles with touch and the Krause end-organs, when they occur, with cold (see the summary by Hensel, 1952). An interesting point is that the well-known innervation of the hairs and encapsulated endings by an accessory fiber, to which so many authors (for references see Woollard, Weddell, and Harpman, 1940) have drawn attention, is ascribed to the nerve nets subserving pain. As has been pointed out by Woollard (1936), Weddell (1945), and Le Gros Clark (1947), this would provide a simple explanation of the observation (Von Frey, 1894a) that any specific stimulus if sufficiently intense will cause pain. While the threshold to pressure (touch) is around 2–3 gr/mm.\(^2\), it is necessary to use 200 gr/mm.\(^2\) to elicit pain from touch spots (Von Frey, 1894a).

From the electrophysiological point of view the problems of skin innervation canalize themselves into four main channels of approach, all of which recur with other sense organs. (1) The study of specific responses to adequate stimuli (touch, pressure, temperature, etc.); the description and analysis of the sensory endings down to the final stage of microscopic identification with microtechniques. (2) The responses should be analyzed from the point of view of principles of organization. One of the leading principles deals with the organization of receptors of the same type into receptive fields. (3) A fundamental problem concerns the significance of fiber size. (4) Finally, the role of the accessory fibers should be elucidated by electrophysiological means.

2. General experiences with skin afferents

In a sufficiently thin branch of a mixed nerve the impulses running in medullated fibers of different size stand out by their differences in spike height. It has been found (cf., for the early work, Erlanger and Gasser, 1937; for later work, Gasser and Grundfest, 1939) that the relative size of the spikes in A-fibers of different diameter is proportional to conduction rate, which in its turn is proportional to fiber diameter (Hursh, 1939a,b; Tasaki, 1953). Rushton (1951) has recently integrated all the observations of Gasser, Erlanger, their co-workers, and others on conduction velocity and fiber diameter in a theoretical interpretation based on internodal length, to which refer-

![Fig. 16. Cross section of part of cat's saphenous nerve, stained by Alzheimer-Woollard method.](image)

conduction velocities, both referable to fiber diameter, have therefore become important landmarks in the identification of specific sensitivities and as such will be continuously referred to in these lectures. Erlanger (1927) was the first to demonstrate that specific sensitivities often were represented in afferent fibers of different size.

In 1934 Gasser gave a summary of older and newer attempts to refer specific sensations from the skin and other receptors of the limbs to different fibers on the basis of (1) compression experiments, which act by pressure and asphyxia (cf. Frankenhaeuser, 1949), and (2) on local anesthesia. At the time he could make out a good case for the view that differentiation by compression first attacked large fibers, while local anesthesia suppressed small fibers before large ones (because of the experiments on electrical identification of fiber size under
such conditions: Gasser and Erlanger, 1929). There were, however, considerable discrepancies between the results of various observers, and we have since had the experiments by Frankenhaeuser (1949), in which it was proved that rapidly and slowly adapting fibers in the rabbit's skin had the same range of conduction velocity, yet the former survived compression a great deal better than the latter. While this does not invalidate the general differentiation by compression in the sense that large fibers suffer before small ones, it is clear that the method never can be very critical. There were already at that time many electrophysiological observations on single fiber preparations from receptors with different specificities, and their number has since increased. A very complete tabulation of available data has been made by Hensel (1952). I shall mention actual figures below, as I proceed with the description of skin afferents. These have supported Gasser's conclusion, reiterated in 1943, "that the fibers belonging to different modalities must be widely distributed throughout the various fiber sizes."

This statement should not be interpreted to mean that there is a complete random distribution of skin sensations over the fiber spectrum. Cold and warmth, as we shall see below, have been found represented only in small fibers, wholly overlapping with pain. Paintal (1953a), in a study of vagus afferents, found the mean conduction rate of fibers from slowly adapting pulmonary stretch receptors to be 36 m/sec., from rapidly adapting ones 25 m/sec., from depressor receptors 33 m/sec., from right atrial types of receptors 20 m/sec., from chemoreceptors 10 m/sec., and from receptors firing on injection of phenyl diguanide 6 m/sec. For other receptors see Hensel's table (1952).

Gasser's (1943) summary of the status of pain is still valid today, eleven years later: barring the objection that the study on animals has to be carried out by observing reflexes or spikes aroused by supposedly painful stimuli (burning, scraping, crushing), it seems perfectly clear that the large majority of pain fibers are to be found among the unmyelinated smallest fibers of all, conducting at rates below 2 m/sec. These give the characteristic massive sensation of burning, lasting pain or "second pain," while a faster group conducting at 15–20 m/sec. or more seems responsible for the initial pain or "first pain" (pin prick) which is experienced too early for the unmyelinated ones to be involved. There is nothing to add to Gasser's clear presentation of this problem, but some papers may be recommended as leading references for a study of the relevant evidence (Ranson and Billingsley, 1916;

Adrian, 1931a; Zotterman, 1933; Heinbecker, Bishop, and O'Leary, 1933; Heinbecker, O'Leary, and Bishop, 1934; Clark, Hughes, and Gasser, 1935; Zotterman, 1936, 1939; Woollard, Weddell, and Harpmann, 1940; Germant and Zotterman, 1946; Maruhashi et al., 1952). The early experiments by Ranson and Billingsley, carried out in the pre-electronic era of research, were particularly interesting. Making use of the fact that in the cat the small fibers enter separately in the lateral portion of the root, they succeeded in cutting them selectively by a small incision into the spinal cord. Reflexes characteristic of pain then disappeared. Unfortunately this arrangement is not found in man. It is only in the trigeminal region that the small fibers can be separated from the rest. Sjöqvist's (1938) operation, the section of the bulbo-spinal tract of the trigeminal nerve, is based on this fact and leads to complete loss of pain in the face, thus vindicating the conclusions of electrophysiology (cf. Zotterman, 1933, 1936).

Tactile fibers seem to be distributed over a particularly large range of the spectrum, the fastest conducting at 90 m/sec. and the slowest at 2–20 m/sec. Considering that tactile fibers arise from such widely different structures as the terminals around the hairs and encapsulated endings such as those of Meissner, Pacini, and Merkel (see e.g. Woollard, 1936; Weddell, 1945), this also should be expected. Localized microrecording would be needed to develop this problem in detail. (For references see Adrian and Zotterman, 1926b; Adrian, 1928, 1932b; Zotterman, 1939; Maruhashi et al., 1952; Hensel, 1952.) Most of the early work following Adrian was carried out on frog skin (Dun and Finley, 1938; Adrian, Cattell, and Hoagland, 1931; Cattell and Hoagland, 1931; Talat, 1933; Hogg, 1935; Echlin and Propper, 1937; Fessard and Segers, 1943).

The ambition of the experimenters was generally directed toward isolating single fibers. However, from the point of view of sensation as well as the understanding of what a simple stimulus really can do, it is of equal interest to follow the events in a thin strand of nerve fibers from a given region in the skin. This was done by Zotterman (1939), from whose work Fig. 17 is taken. It illustrates the frequency distribution of rates of conduction of impulses in response to the stimuli characterized in its legend. The values were sometimes measured directly but were also calculated from the spike height.

Light stroke of the cat's fur (A) activated both slow and fast fibers; very light touch (C and G) activated fibers conducting as slowly as around 2 m/sec., thus overlapping with pain fibers. At least in man Waterston's (1933) results show that light touch is likely to be con-
ducted in very thin fibers. It should be noted that the spikes of the smallest unmyelinated fibers tend to be occluded in multifiber records. Zotterman had good evidence that pain (burning) elicited activity in such fibers. It will further be noticed that responses in the very sma-

![Diagram]

Fig. 17. The frequency distribution of rates of conduction of axon potentials recorded in response to: A, light stroke; B, pulling a few hairs; C, very light touch; D, very light stroke. The three lower diagrams give the distribution of the axon potentials according to spike height: E, needle prick; F, hard stroke; G, very light touch. Diagrams B, C, E, F, and G all come from the same nerve preparation. (Zotterman, J. Physiol., 95, 1. 1939.)

est myelinated (and very likely also unmyelinated) fibers appeared with stimuli as widely different as hard stroke (F) and very light touch. The actual records showed them to be late and usually appearing as an afterdischarge when stimulation was over, even though only a few hairs had been moved. Zotterman associated this discharge with tickling or itching, as he found these sensations to be absent in the face of patients who had undergone Sjöqvist's operation. Tickling would therefore be a combination of touch and pain. The existence of accessory pain fibers to the hairs, alluded to above, may also be adduced in support of his view. Alternatively we may have to assume the existence of double specificity (see below), touch combined with pain, or else interaction between the two in the nerve nets below the epidermis. Inasmuch as interlacing of touch with pain fibers may occur in this network, interaction is quite possible under pressure (Granit, Leksell, and Skoglund, 1944), perhaps even without it (Arvanitaki, 1940). Again we conclude that there is room for investigation of skin receptors and skin afferents with microstimulation. Whatever the causes of the rich fullness of response in Zotterman's experiment, it shows that simple stimuli activate complicated response patterns and emphasizes the necessity of going beyond single fiber analysis in the study of sensation. This was also pointed out by Adrian in his early summary (1928).

So far we have implicitly accepted the idea of single specificities as the basis of interpretation. This is nothing but Mueller's well-known law of "specific energies" in the modern version, namely that end-organ specificity is matched by specificity within a central interpreting structure. Have we any electrophysiological reasons for criticizing this law? Recently Hensel and Zotterman (1951b) were able to locate in the cat's tongue two types of pressure afferents, the large "ordinary" pressure spike conducted in fibers of 12-15μ in diameter and a smaller one in fibers of 8-10μ. The latter is also excited by cooling, but whereas the specific cold receptors (in still smaller fibers) go on discharging permanently to a certain temperature, the cold-sensitive pressure receptors do so only for a few seconds. The effect of direct cooling of the nerve fibers seems excluded by satisfactory controls as well as by the results of Dodt's (1953) later study of thermosensitivity in nerve. The large pressure spike could be excited only by cold sufficient to stimulate its nerve fiber directly. It thus differed from the small pressure spike in being specifically sensitive to pressure alone. The high cold sensitivity of some afferents may well reside in the finest nerve terminals rather than in the end-organ itself.

Recently it has been reported by Bullock and Faulstick (1953) that single afferents from the facial pit organ of the rattlesnake, which is specifically sensitive to infrared radiation, also subserve touch. Zotterman and Hensel did not question Mueller's law. They suggested that the combined cold-pressure receptor has what I have called double
Specificity because of some common basic principle in the function of thermo- and mechanoreceptors. Other alternatives were mentioned above. One might also consider release of excitatory substances in the nerve net (Echlin and Propper, 1937; Feng, 1933; Hogg, 1935) as very convincingly demonstrated by Habgood (1950).

At present, however, double specificities in the sense that two "meters" have relatively low thresholds seem to be exceptions, and the rule is that an afferent is connected to one or several receptors which respond to one particular, so-called adequate, stimulus with greater facility than to any other, i.e. with the lowest threshold. Therefore, relative spike size (conduction velocity) in combination with determination of the adequate stimulus are in actual practice still the two means used for electrophysiological identification.

What role can we ascribe to fiber size from the point of view of central interpretation of the frequency code? Gasser (1943) has pointed out that faster rate of conduction means that impulses in larger fibers can initiate or facilitate effects which impulses in slower fibers then go on to elaborate. He has also drawn attention to the longer duration of the impulse in small fibers. Certain central systems may therefore require spikes of long duration to become activated. Much of Gasser's work (see e.g. in Erlanger and Gasser, 1937) has gone to show that in fibers of different type there are considerable differences in the slow so-called afterpotentials following upon an impulse. It is not known whether these differences play a significant role in the fine terminals at the point of destination of the spike. Gasser himself has chiefly stressed the element of timing. "The more one sees of the exquisite precision with which events take place in the central nervous system the more one is impressed by it. The more the idea of timing grows in meaning content the more it becomes a directive for future exploration. Differential axonal velocities must play their part in the mechanism. Be this their only contribution to integration, it is still a large one" (Gasser, 1946, p. 141).

To this one might add the surmise that fiber size must mean something also in terms of the receiving station in different parts of the brain. Why, for instance, is the number of small fibers so very much greater in the ipsilateral than in the contralateral optic tract (P. O. Bishop, Jeremy, and Lance, 1953, confirmed by myself)? The sense organs, as we shall see, have other projection areas than the well-known specific ones.

3. Specificity illustrated by thermoreceptors.

Re-presentation in centers

Among the skin perceptions the temperature sense is particularly interesting. This is partly because the psychophysical theories (recently reviewed again by Hensel, 1952) have exceeded in number and complexity what the subject could afford in view of the relative ease with which they could be tested by spike recording, partly also because of the analogies with direct thermal stimulation of peripheral nerve. The rule is that cold and warmth receptors are highly specific (Zotterman, 1935, 1936), both effects being transmitted in relatively thin fibers (4-6μ). In the cat's tongue the warmth fibers give larger spikes than the cold fibers, as again confirmed by Dodt and Zotterman (1952a). Thanks to the psychophysical experiments of Hensel (1952), who developed excellent stimulating devices, and the electrophysiological ones of Hensel and Zotterman and Dodt and Zotterman, we are now better informed about temperature receptors than about any other type of skin organ, and for this reason, too, their results deserve to be singled out for a presentation of the problem of specificity as it appears in the light of two well-analyzed skin organs.
These organs, not unexpectedly, turned out to behave like other relatively nonadapting receptors: to sudden stimulation they responded with a discharge characterized by a high-frequency onset, gradually petering out into a low-frequency constant discharge. This is well illustrated by Fig. 18 for temperature drops of 2° starting from three different levels, 44°, 42°, and 38°. Very clearly the drops of 2° of cooling were most effective at 38°. The slow rate of firing goes on indefinitely at sufficiently low temperatures and in this sense every cold receptor behaves like a thermometer capable of delivering information about the actual temperature of its surroundings. Some visual receptors and stretch receptors behave in the same way with respect to their adequate stimuli. With them and most other end-organs (Adrian and Zotterman, 1926a,b), the cold receptors also share the property of responding to the gradient stimulus intensity/time. Quick cooling causes a faster initial discharge than slow cooling. Both these aspects of behavior have been recognized in the psychophysical work of an earlier epoch (see Hensel’s summary, 1952), but the clarity of the electrophysiological analysis makes further comments unnecessary.

Turning now to assemblies of cold receptors, I think that the existence of an optimum of sensitivity, so clearly shown by Fig. 18, is the most interesting feature in the design of the receptors for cold. In Fig. 19 a number of cold receptors have been analyzed from this point of view. The frequency of the final constant discharge plotted against temperature has optima at different temperatures for different receptors. Sensitivities at the optima are of the order of 2 spikes/sec. for 1° or 20% of the maximum frequency. Considered as organs for responding to disturbances of chemical equilibria set up by temperature changes, the specialization of the receptors upon specific temperature ranges is clearly a more elaborate solution of the problem of specificity than the design of one single organ equally sensitive to the full range needed. There is such an organ in some fish, the Lorenzinian ampullae, which respond to heat by acceleration, to cold by deceleration, of the spontaneous discharge (Sand, 1938). The rattlesnake’s heat-sensitive facial pit also belongs to this type (Bullock et al., 1953). Mammals apparently have greater differentiation. Again, Occam’s razor does not apply. Inasmuch as the end-organs of Krause are responsible for the sensation of cold, these too vary a great deal in appearance, as shown by Belonoschkin (1933) in preparations from the human mamilla, where they are particularly dense and cold sensitivity also is high. When the many differentially cold-sensitive end-organs act together, they actually cover the range from 40° to 20° by an approxi-

![Fig. 19. The steady discharge of different isolated cold afferents in the lingual nerve of the cat as a function of temperature of the tongue. (Hensel and Zotterman, Acta physiol. scand., 23, 291. 1951a.)](image)

Hensel and Zotterman (1951c; Hensel, L. Ström, and Zotterman, 1951), with thermodes on both sides of the cat’s tongue, measured the temperature gradients and spike latencies and could actually localize the depth of the cold receptors with considerable accuracy (to 0.2 mm.). Yet they did not from their histological control (Palmgren silver stain) attempt any further identification than to state that the cold receptors were situated subepithelially partly in the papillas, particularly at their base or just beneath them. However, the tongue is richly supplied with Krause end-organs (Krause, 1860, pp. 112–39; Gairns, 1953).

The warmth receptors (Dodt and Zotterman, 1952a) respond to
heating just as do the cold receptors to cooling, and their range is shown in Fig. 20. There is a similar differentiation among the warmth receptors with respect to their optima, but in the diagram the whole assembly, compared with that of Fig. 19, is shifted to the right. Nevertheless, the overlap is sufficient to make it seem a difficult task for the center to distinguish steady warmth from steady cold in the same skin region without the aid of secondary cues. Actually there are such cues. The cold receptors fire at a steady rate, the warmth receptors in an irregular spluttering fashion and also at considerably lower frequencies than the cold receptors. Fiber size provides an additional cue. Also, when sensory discrimination is concerned, the leading principle, as we shall see, is always one of differentiation by pattern as a cue, and this seems achieved by the statistical sensitivity distributions of the individual receptive units (Figs. 19 and 20).

The degree of specificity of the cold receptors is actually considerable. This is perhaps best illustrated by the well-known sensation of paradoxical cold, discovered independently by Lehmann (1892) and Von Frey (1895, 1910). This is a feeling of cold to stimulation with heat from 45° upward. Dodt and Zotterman (1952b) have succeeded in demonstrating that there is a corresponding discharge of the cold receptors at high temperatures, as illustrated by the secondary rise of the curve for the cold receptor at high temperatures in Fig. 21. The curve for a typical warmth receptor has been inserted for comparision (Dodt and Zotterman, 1952a). Pain fibers will also be stimulated at this temperature (Zotterman, 1939) and, as the sensory threshold for pain in response to heat is around 47–48° (Skouby, 1952), admixture of pain may explain the curiously biting character of the sensation of paradoxical cold (cf. Zotterman, 1953). The behavior of cold and warmth receptors at extreme temperatures have been further elucidated by Dodt (1952b). Cold fibers have also been studied in isolation by Maruhashi, Mizuguchi, and Tasaki (1952). These fibers were from abdominal skin nerves and the plantar nerves (cat) and were found to be between 1.5 and 3μ in diameter, hence the smallest among the myelinated fibers.

A theoretical physicochemical explanation of the high degree of specificity of the temperature receptors is still lacking. The observations on heat and cold sensitivity of nerve fibers (cf. in particular the papers by C. von Euler, 1947; Lundberg, 1948; and Dodt, 1953) suggest an interesting indirect approach by way of analyzing membrane potentials in nerve fibers as influenced by temperature changes.

The observations on temperature receptors have disclosed that they will discharge permanently within the whole range of temperatures to
which the body is likely to be subjected. This seems particularly important in view of their role in thermoregulation, which requires continuous information from receptors. In this task the receptors cooperate with the thermoregulatory center in the hypothalamus known and studied for a number of years in several laboratories. References may be made to summaries by Thauer (1939), Ranson and Magoun (1939), Ranson (1940), Stoll (1943), Grant (1951), Hensel (1952), and Zotterman (1953). Lately a number of fresh experimental contributions have been published by Uvnäs and his collaborators, G. Ström and Folkow (Folkow, Ström, and Uvnäs, 1949a,b; Ström, 1950a–c), who used vasodilatation as an indicator. From our point of view the central issue concerns the existence of thermoreceptors in the brain itself. In agreement with the original observations of Ranson’s school (Magoun et al., 1938; Beaton et al., 1941, and Hemingway et al., 1940), Folkow, Uvnäs, and Ström (see in particular the paper by Ström, 1950a) also find that the anterior hypothalamus is sensitive to local heating with a diathermic needle point, but not to cooling.

Another fresh approach is that of C. von Euler (1950), who noted that heating in this fashion of the hypothalamic region sets up a local slow potential obtainable only within a highly circumscribed region in the anterior hypothalamus. This slow potential is shown in Fig. 22. It correlates well with thermoregulatory reflexes to heat and is the most sensitive index of the effect hitherto found. Hence, this central response is exceedingly specific. Actually, in the best cases, Von Euler obtained a change of potential of 1 mV. per 0.1°. No similar effect to cooling could be found anywhere in the brain. Von Euler suggests that these “heat” potentials serve as generator potentials for the regulatory reflexes panting, sweating, vasodilatation, etc. The hypothalamic local response to heating would therefore mean that the warmth receptors are re-represented in the brain.

These warmth receptors in the hypothalamus are of particular importance because of the relative scarcity of peripheral warmth receptors in relation to cold receptors (cf. König, 1943, 1944). The reflex effects of the latter might easily lead to an overproduction of heat combined with heat stagnation because of contracted skin vessels. The warmth receptors in the brain which respond to blood temperature will prevent this from happening. They are therefore likely to fulfill the role of brakes in a mechanism of self-regulation in the service of homeostasis.

This conclusion that a sense organ might be re-represented in the brain in order to improve certain types of self-regulation in the body seems pregnant with possibilities, particularly for chemoreceptors. Von Euler and Söderberg (1952a,b) followed it up by demonstrating that the respiratory center in the medulla, which is known to respond to the arterial pCO₂ (see e.g. Heymans and Bouckaert, 1939), also sets up a slow change of potential to an increase of CO₂ in the inspired gas. The effect was highly specific for CO₂ and was obtainable only within that region of the brain stem from which Comroe (1943) succeeded in eliciting respiratory responses by injections of a few μl. of buffered carbonate solution. Von Euler and Söderberg found the effect also in a completely denervated respiratory center, and it was associated with the production of a discharge in nerves to respiratory muscles. Thus, these structures had all the attributes of receptors: specific chemosensitivity, generator potential, discharge.
As is well known, Verney (1947) came to the conclusion that within the central area of distribution of the internal branch of the common carotid there were receptors specifically sensitive to osmotic changes. An injection of hypertonic salt solution inhibited diuresis by an effect on the antidiuretic hormone of the posterior lobe of the hypophysis. Andersson (1952, 1953) succeeded in eliciting copious thirst in goats by injecting the paraventricular nuclei with 1.5–2\% NaCl solution in doses of 0.1 cc. C. von Euler (1953), in a preliminary report, has from this general region obtained slow local changes of potential of the order of 1 mV. by injections into the carotids in the manner of Verney. All these observations on receptors in the brain indicate the opening of a new and important field of research in sensory physiology. It would not be surprising if many other blood constituents influenced receptors for hypophyseal control.

4. Receptive fields. Other organizations of skin receptors

As originally defined by Adrian and his collaborators with reference to skin receptors in the frog (Adrian, Cattell, and Hoagland, 1931; Adrian, 1932), a “receptive field” is the surface innervated by a single afferent fiber. Thus, at least in this animal, the receptive field is not only a physiological or functional unit but also an anatomical constant. The anatomical criterion is not merely a tautological definition. We shall see below that the far more complex receptive fields of the vertebrate eye, though anatomically constant, are variable in size because of the variable amount of interaction of opposite effects within them. Tactile fields, as determined by moving the jet of an air nozzle over the skin, proved to be of exceedingly variable size, from 4 to 100 sq. mm., and overlapped in the manner shown by Fig. 23, from the work of Adrian et al. (1931). Both these principles, overlap and variation in size, also occur with the eye and the ear (see below). The overlap is due to branching of one or several afferents within the same skin field. It is clear and was fully realized by Adrian that all these features are integral factors in a mechanism of discrimination planned for a particular kind of receiver, the central nervous system. In Adrian’s work on receptive fields in the cat’s paw and with cutaneous fields in the guinea pig it appeared also that adjacent receptive fields might be further differentiated in their central projections because their messages were being delivered in fibers of strikingly different size (Adrian, 1931a, 1932b). Tower (1940) measured the receptive fields in the cornea and found them to extend over very large areas varying from 50 to 200 sq. mm. It is perhaps not quite clear whether these receptors subserve pain alone or pain and touch combined, as another instance of double specificity. Most authors (e.g. Von Frey, 1894a, b; Nafe and Wagoner, 1937) hold that the cornea feels only pain (see discussion by Tower, 1940; recent reports on touch in cornea by Jalavisto, Orma and Tawast, 1951). The free terminals in the cornea branch widely, as shown in the recent experiments of Rexed and Rexed (1951, with references). Tower found the receptive fields to be most sensitive in the middle. In the eye this particular property of the fields has taken on interesting fresh aspects (cf. below).

Tasaki and his group (Maruhashi et al., 1952) found the receptive fields for various skin receptors to be punctiform for pressure fibers (1 to 2 sq. mm.); the nociceptive fields in the plantar cushion of the toe pad (cat) were small—up to 3 \( \times \) 3 mm. in area; while those in the hairy regions were about 10 times larger. Most interesting is their finding of special fibers with excessively large receptive fields up to 50 \( \times \) 90 mm. Their afferents responded to light touch, and the nerve fibers had a diameter between 2 and 5\( \mu \). They were abundant in all the skin nerves examined. A special study was made of the receptive fields, of afferents coming from the hair roots. Within their fields, 20 \( \times \) 25 mm. in area, a response could be elicited by bending every
individual hair or even by touching the hair tips. Afferents that seemed to be specifically sensitive to scratch only were also noted.

Summarizing these facts, I conclude that the sentient skin surface which may be regarded as the prototype of all sense organs well illustrates a number of elementary principles in the peripheral organization of the sensory message. The stimuli called touch, pressure, and pain deliver both general and localized messages. The general piece of information is based on very large receptive fields, the localized on smaller receptive fields down to punctiform ones. There is considerable overlap of receptive fields. These principles will recur in other organs, such as the eye and the ear, which are built up as sentient surfaces. There may well be an inverse ratio between the degree of specificity of end-organs and the amount of branching of the sensory nerve.

Discrimination on this basis and general principles concerning the decoding of the frequency code will be discussed in Chapter 8.

Much has been written about aspects of skin innervation which are familiar to most physiologists and neurologists under the headings “protopathic” and “epicritic” sensations (Head, Rivers, and Sherren, 1905; Rivers and Head, 1908). There is, however, little to add to the judicious criticism by Walshe (1948).

Receptors may be joined functionally on the basis of principles other than those concerned with receptive fields. In vision, for instance, the perception of space and distance brings corresponding points in the two retinas into an integration which has been studied a great deal by psychophysical methods but not at all by electrophysiological ones. In the skin the receptive fields of most sense organs from one and the same region contribute to a similarly unique integration of locality. At this stage I shall take but one example of such integrations referring to the skin, chosen because, to the best of my knowledge, this is the only one that has been properly analyzed by electrophysiological means (Hagbarth, 1952). Historically it is a development of Sherrington’s (1906, 1910) notion of the receptive field of a reflex. Sherrington, of course, used the term “receptive field” in a different and wider sense to signify the skin area from which a certain type of reflex response could be elicited. The specific reflex effect is thus an exponent of “local sign.”

It is well known that the easiest ipsilateral reflexes to elicit from any nerve are the flexor reflexes, of which there is both a nociceptive and a postural variety (Sherrington, 1910), the latter generally being neglected in semipopular accounts in which the reflex of ipsilateral flexion is often presented as wholly nociceptive. Submerged below the general flexor activity may also be found extensor contractions (e.g. Sherrington and Sowton, 1910–1911). The concealed extensor reflex, so difficult to elicit and study, was called by Denny-Brown (in Creed et al., 1932) the “residual ipsilateral extension.” Hagbarth (1952) brought clarity into this field by proving that there was a definite functional connection between a muscle and the portion of skin that covers it. Hagbarth’s rule is quite simple: skin and muscle are functionally integrated, so that the muscle is excited by stimuli within its own skin area. Adjacent portions of the skin may be inhibitory. This is true for both flexors and extensors, and so, by his approach, it proved easy to find the formerly elusive ipsilateral extensor reflexes.

The excitatory and inhibitory skin areas for the ankle extensors are shown in Fig. 24a; 24b shows the outcome of a test by pinching the skin over these regions. Testing is carried out monosynaptically (the
technique is described in detail in Chapter 6) and to understand the result depicted in Fig. 24b all that is necessary is to realize that the monosynaptic test volley increases in size during facilitation (upper curve) and decreases during inhibition (lower curve). The same result may be obtained by electromyography and by recording the muscle contraction (myography), but the monosynaptic test, carried out with de-efferented animals, demonstrated that the effects are direct and not secondary to events set up by a reflex loop from the afferents of the recorded muscle or its antagonist.

Thus the skin has established "local signs" for reflex action also, and not only for conscious perception, as, indeed, has been well known practically from the beginning of reflexology.

5. Receptive fields of the vertebrate retina

The principle of discrimination by overlapping fields of different size must indeed be an important one or else it would hardly have reached its pitch of perfection in an organ such as the retina, which is the most complex sensory apparatus in the vertebrates and apparently in many invertebrates. One might have expected, once organs of such minute size as the rods and cones had been developed, that this fineness of grain, just as in the photographic plate, might have had for its sole reason reproduction of detail and as a consequence a 1:1 ratio of sense cells to nerve fibers right up to the center. However, this cannot be the case, because exceedingly slender elongated rods are found in deep-sea fishes (Bayliss, Lythgoe, and Tansley, 1936) in combination with a particularly high ratio of rods to optic nerve fibers. In general, the cones, the organs for visual acuity and daylight vision, tend to be somewhat thicker than the rods, which integrate light over large convergence units with up to hundreds or thousands of receptors per nerve fiber. It is only in the relatively few species with a well-developed fovea centralis that the foveal cones become slender and rodlike in appearance. If we assume that the photochemically sensitive visual purples are located at the surface of the receptors (Granit, Holmberg, and Zewi, 1938; Lythgoe, 1940), it is likely that fineness of grain has for one of its reasons expansion of surface (Bayliss et al., 1936). On the other hand, it cannot be denied that, by analogy to photographic emulsions, reproduction of detail requires discrete units (grain) below a certain minimum size, ultimately determined by the perfection of the optical parts (lens, cornea) as well.

To the old controversy between Helmholtz and Hering is attributed this story (to which in 1922 the late Professor A. Gelb of Frankfurt a/M first drew my attention): Helmholtz, who had stated that if an optician delivered to him as bad a lens as that of the eye he would return it, received from Hering the reply that he might perhaps have kept it after all if he had realized what marvellous compensatory arrangements there were for perfection of the image (contrast in the first instance). Since that time lenses and photographic emulsions have improved but the eye with its faulty optics remains the same, performing better over a range from dusk to brightest sunlight than any instrument designed to imitate it.

The idea that good reproduction also requires fineness of grain is certainly supported by comparative studies of the number of optic nerve fibers in different species. Despite its very much smaller eye, the pigeon, dominated by cones, has much the same number of optic nerve fibers as man. Bruesch and Arey (1942) give 1,010,000 for man, 988,000 for the pigeon, but only 119,000 for a predominantly rod animal such as the cat. Polyak's (1941) figure for man is "800,000 to more than 1,100,000." The optic nerve fibers in the cat are particularly large, the eye not very much smaller than our own. Grain size, in order to mean something in our analogy with photographic emulsions, should, of course, be defined by the size of the receptive field of a single optic nerve fiber.

It is concluded, then, that though the average convergence of receptors on optic nerve fibers is very great, say of the order of 100:1, the retinal surface is nevertheless capable of good discrimination on the same basic principle as is the skin, i.e. by using overlapping receptive fields of different sizes, from very large to very small, the latter likely to be multiplied in cone eyes which have good visual acuity. The presence of an outgrowth of cells from the central nervous system in two layers below the receptors entails further elaboration of the message before it is concentrated into the optic nerve fibers. This makes the retina particularly interesting as a model for what might happen within central projections elsewhere. Thus it seems that restriction of receptive fields to a limited number of pathways transmitting a code of spikes (optic nerve fibers) need not necessarily mean deterioration of the information, provided that the message itself is sufficiently elaborated and that a sufficient number of small fields are included to modulate it. Visual perception, after all, is a dynamic act maintained by a continuous frequency variation and not by a static image on a photographic plate.
Fig. 25. Scheme of the structures of the primate retina as revealed by the method of Golgi. The designation of the layers and the zones: (1) pigment layer, (2, a) outer zone, (2, b) inner zone of the rod and cone layer, (3) outer limiting membrane, (4, a) outer zone, (4, b) inner zone of the outer nuclear layer, (5, a) outer zone, (5, b) middle zone, (5, c) inner zone of the outer plexiform layer, (6) inner nuclear layer with its four zones, (7) inner plexiform layer, (8) layer of the ganglion cells, (9) layer of the optic nerve fibers, (10) inner limiting membrane.

The designation of the nerve cells: (a) rods, (b) cones, (c) horizontal cells, (d, e, f, h) bipolar cells, (i, l) so-called “amacrine cells,” (m, n, o, p, s) ganglion cells, (u) “radial fibers” of Müller.

In this scheme the nervous elements are reduced to their essentials, with, however, the characteristic features of each variety preserved—the location of the bodies, the size, the shape, and the spreading of the dendrites and the axis cylinders—and with the synaptic contacts presented accurately. (Polyak, The retina, University of Chicago Press, Chicago, 1941.)

Fig. 26. The structure of the primate retina reduced to its essentials, including the synopsis of the propagation of the retinal impulses from the photoreceptors to other parts of the retina, to the brain, and from the brain back to the retina (direction indicated by the arrows). The marking of the layers and the zones is the same as in Fig. 11.

Labeling of the cells: (a, b) rods and cones, or the photoreceptors where the nervous impulses are generated by physical “light” (in the scheme only the left group of the photoreceptors is assumed to be stimulated by light); (c) horizontal cells, by means of which the impulses are transmitted to the surrounding rods and cones; (d, e, f, h) centripetal bipolar cells of the mop, brush, flat, and midget varieties, which transmit the impulses from the photoreceptors to the ganglion cells; the bipolars serving as analyzers; (i) centrifugal bipolar cell, a variety of the amacrine cells, which probably receives the impulses from the centripetal bipolars, from the ganglion cells, and also from the brain, by way of the centrifugal or efferent fibers (i) and transmits them back upon the photoreceptors (a, b); (l) an amacrine cell which possibly intercepts a part of the bipolar impulses and spreads them over the surrounding territory; (m, n, o, p, s) ganglion cells which receive impulses from the centripetal bipolars and transmit them to the brain along their axons, called “optic nerve fibers.” (Polyak, The retina, University of Chicago Press, Chicago, 1941.)
Figs. 25 and 26, from Polyak's great work on the primate retina, illustrate the two additional neurones below the receptors, called bipolars, and ganglion cells, as well as the lateral connections, one by the horizontal cells along the feet of the rods and cones, the other by amacrine above the ganglion cells. There are also centrifugal components of which little is known functionally (see Chapter 3, sec. 5).

If the physiological analysis of the messages from the optic nerve with microdissection (Hartline, 1935, 1938a, 1940a,b,c; Thomson, 1953) or microelectrodes (see my summaries, 1947, 1950b; later work by Rushton, 1949, 1953; Barlow, 1953a,b; Kuffler, 1952, 1953) had been able to provide an equivalent interpretation in terms of the circuits and slow potential changes present, it would have been of interest to describe the histology in greater detail with the aid of Cajal's and Polyak's diagrams. As it is, an interpretation has not so far become possible in anything but outlines. And yet, looking back upon what we knew two decades ago, I think that all the painstaking work on single fibers has not been in vain. We do not know enough but we do know a great deal about the workings of the retinal switchboard and can formulate the problems with greater clarity than was formerly the case. It is perhaps true, too, that even if there are simpler structures than the retina available for the study of synaptic excitation and inhibition, the understanding of the principles of central organization and transmission of sensory information is never likely to be very much in advance of our understanding of the principles governing the form and delivery of the retinal messages.

The retina is organized on the general basis of two successive layers of superimposed receptive fields: the receptors converge onto the bipolars, the latter converge onto the ganglion cells, from which our information with microtechniques in terms of spike frequencies is derived. At least in primates and birds there are midget bipolars (h in Figs. 25 and 26) which potentially are capable of delivering a punctate message on a 1:1 basis (from a single cone down to the optic nerve fiber of the ganglion cell), but this message, too, is at the mercy of interaction from adjacent structures, as contemplation of Fig. 25 will show. The overlap of receptive fields is clearly shown by the histological pictures, and functional analysis tells the same story (Hartline, 1938a, 1940a,b). The possibilities for interaction are legion. Functionally true interaction was first demonstrated by Adrian and R. Matthews (1928). The overlapping receptive fields thus collaborate in a more complex fashion than in the skin, for which the inhibitory processes come in at about the level of the spinal cord.

As stated in Chapter 1, sec. 7, Hartline (1938a) first demonstrated that the characteristic discharges to onset and cessation of light (on-discharge, off-discharge) are differentially distributed over the afferents in the optic nerve. There are on-elements (on-fibers), off-elements and on/off elements, the term “element” standing for the single fiber or ganglion cell from which recording takes place. A diagrammatic representation was given in Fig. 14. Some characteristic discharges are shown in original records in Figs. 27 and 28. The fibers discharging at cessation of illumination are inhibited by light (see Chapter 1). In the types of eye so far studied the elements that discharge to both onset and cessation of illumination are in the majority. As far as the large fibers are concerned, the guinea pig's rod eye is an exception. It contains mostly on-elements (Granit, 1942a,b).

![Fig. 27](image)

Fig. 27. Effect of different types of stimulus on the form of the response of a single retinal element of the cat: (1) response to a stimulus of relative energy 6.3 and wave length 6200 A; (2) response to the same wave length at a relative energy of 2.3; (3) response to a stimulus of relative energy 2.5 and wave length 4600 A; (4) response to a wave length of 5,000 A from another experiment. Time marking: 1/50 sec. (Granit, Acta physiol. scand., 5, 219. 1943c.)

In our evaluation of these features of organization of the retinal elements some change has gradually taken place (see Granit, 1950b). Fifteen years ago one used to think of the types of discharge as relatively stable in the sense that the individual afferents had specialized upon the delivery of a certain type of response. This may still be true for certain types of retinæ such as that of the frog and the pigeon (Donner, 1953). In the cat's retina there is, however, an extreme variability of the on/off ratio of the elements (calculated on thresh-
 olds or frequencies) with respect to level of intensity, wave length, and state of adaptation (Granit, 1944; Granit and Tansley, 1948; Gernandt, 1948b). This led to the conclusion that the balance of discharge between onset and cessation of illumination was one of the main exponents of interaction in the retina, as further emphasized by studies with polarizing currents (results summarized by Granit, 1950b). It was actually possible to suppress or emphasize either the on- or the off-discharge to a constant stimulus by maintaining weak polarization across the retina (Granit, 1948). Finally it was shown by Kuffler (1952) with punctiform stimuli and the cat’s eye that within the receptive field of a single afferent some spots gave off-responses, others on-responses, and that mixtures of these in different on/off ratios could be obtained by combining two stimuli from different spots. It is probable, therefore, that most elements are on/off elements merely because this is the most likely state of balance of on- and off-components. On/off discharges are also dominant in the cat’s retina if one tries to evade the large single spikes and uses the massed discharge of small spikes as index (Bohm and Gernandt, 1950). Interaction means plasticity of response, and one of the main variables expressing plasticity is the on/off ratio.

A further step—at least in my own interpretation of retinal organizations—came from our general observation with the cat’s eye that the on- and off-components of the discharge tended to be mutually exclusive (Fig. 29), so that when stimulus intensity was varied, the

Fig. 28. Effect of increasing the intensity of the stimulus on the response of an isolated retinal element of the guinea pig. Relative energy values of stimuli (from above downward): 1 (threshold), 1.3, 1.48, 2.22, 3.91, 9.31. Wave length of stimulus: 5300 A. Time markings: 1/50 sec. (Granit, Acta physiol. scand., 3, 137, 1942a.)

Fig. 29. The large and small spike of Fig. 31, elicited by illumination with wave length 4600 A at the relative intensities indicated beside the records. Period of illumination marked by photocell and amplifier connected to second beam of cathode ray below the one recorded from. The beam also records the 50-period AC of the mains but, at this film speed, so compressed that the duration of 1 sec. has been indicated by separate marks below it. (Granit, J. Neurophysiol., 11, 239, 1948.)

off-discharge often diminished while the on-discharge increased, or vice versa (Granit, 1944). This is well shown also in Fig. 30, from the measurements by Donner and Willmer (1950). Was there perhaps an antagonistic relationship between the two? This problem was first systematically approached by the technique of polarization of the retina by a weak electric current through external electrodes on
either side of the eye bulb. To understand these results it is necessary to realize that although the on/off ratio is variable, it is possible, even in the mammalian retina, to distinguish Hartline's categories of response types when a large enough number of elements are studied under similar conditions, in our case dark-adapted animals and illumination of the whole retina. Thus, some elements are found which act as pure on-elements, others as pure off-elements, though the majority of them respond to both onset and cessation of light.

![Diagram](image)

Fig. 30. A: discharge of an element which changes from the “on” type to the “on/off” type as the intensity of the stimulus is raised. B: discharge of an element which changes from the “on/off” type to the “off” type as the intensity of the stimulus is raised. Ordinates: impulses per sec. Abscissae: time, the duration of the stimulus being 3 sec. (Donner and Willmer, J. Physiol., 111, 160. 1950.)

To sudden polarization with the electric current the isolated elements respond either with excitation or inhibition at the threshold. Reversal of the current reverses the response. The polarizing electrodes in such experiments are in the temporal and nasal cavities, the micro-electrode on the inside opposite the nasal electrode. Also, by this technique of measuring the threshold effects of polarizing currents, the antagonism between the on- and off-components of an element came to light in that the pure on-elements tended to discharge to the cathode, the pure off-elements to the anode (Gernandt and Granit, 1947). The same result may also be stated differently: the on-elements tended to be inhibited by the anode, the off-elements by the cathode. A third way of stating this generalization is that light and the cathode tended to act in the same way: the on-elements, excited by light, were excited by the cathode, the off-elements, inhibited by light and discharging at cessation of illumination, were inhibited by the cathode. The mixed on/off elements were of either type, cathodal or anodal, as defined by the excitatory effect. This antagonism between “on” and “off” is not due to a shift in the leading-off point relative to the distribution of the polarizing current. In Fig. 31 the same microelectrode is picking up from two fibers. These adjacent on/off elements are clearly of opposite polarity. The illustration of the mutually antagonistic behavior of the two elements in Fig. 29 with respect to light at different intensities is from the same experiment with the same spikes. Perhaps the simplest way in which to demonstrate that the on- and the off-components are mutually exclusive is to shorten step by step the duration of stimulation (Granit, 1951). The discharges are long-lasting events compared with the flash, and so the on- and the off-discharge will sooner or later collide. In this situation “on” and “off” do not add their effect upon the ganglion cell, but the one that has the shorter latency or is otherwise stronger impresses its frequency upon the cell, and the effect of the other one is inhibited. The same effect is very marked in an on/off flicker response to intermittent light at frequencies of stimulation for which the two components clash (Enroth, 1952). This antagonism of the on- and off-components is of considerable interest in color reception (Granit, 1949).
The receptive fields of the retina, to which we now are prepared to
turn our attention, thus contain two antagonistic systems, the one
discharging to onset, the other to cessation of illumination. Whatever
notions one entertains about the origin of on- and off-discharges, it is
clear from what has been said that inasmuch as these two discharge-
provoking systems converge upon the same ganglion cell, they cannot
both activate it at the same moment. The one inhibits the other. Thus
the two systems have confluence points somewhere in the retinal
switchboard above the level of the ganglion cells. When the on-path
is active it places the off-path to the same ganglion cell under inhibition
and, vice versa, during the activity of the off-path there is blockage
of the on-path at some confluence point.

As stated above, the off-discharges are inhibited by illumination.
It is possible, of course, to regard this inhibition as but one aspect of
the antagonism of on- and off-components just described. I hesitate
to subscribe to this identification. A very essential feature of pure
off-elements is that they in silence, as it were, pile up excitation during
illumination (see also Hartline, 1938a, 1940b, c), afterward to release
it in the form of a vigorous discharge the moment the light is turned
off. For some time (Granit, 1933, 1947, 1950b, 1952b) I have held
the view that the off-discharge is a release from inhibition produced
by a positive potential change, which upon its return swings to
the negative side and excites at “off.” I find this view supported by Parry’s
(1947) results (see Chapter 1, sec. 6). The total balance of evidence
(see e.g. Granit, 1952b) seems to me to support the idea of a primary
mechanism for the production of off-discharges as well as a primary
excitatory mechanism for the production of on-discharges. However,
since these primary mechanisms themselves are antagonistic, the whole
point of this organization would be missed if at the ganglionic level
on- and off-discharges were mixed indiscriminately. The synaptic
arrangements in the retinal switchboard must be organized to preserve
the on/off distinction, and this is done by the mechanism of synaptic
antagonism leading to the inhibition. It will be shown in Chapter 5
that complex electrical feedback mechanisms operate in the retina,
suggesting a definite reason for the arrangement of receptors in combi-
nation with synaptic layers. It will be some time before these facts
are fully understood.

It seems to me that Kuffler’s recent work (1952, 1953) shows
that the mutual exclusiveness of “on” and “off” within the receptive
field of the ganglion cell is organized in such a delicate fashion (see
below) that it is easier to understand it in terms of synaptic arrange-
ments similar to those responsible for the organization of reciprocal
reflex effects in the spinal cord. This also appears to be Kuffler’s view
(1952). Admitting that these problems of retinal inhibition are ex-
ceedingly difficult to penetrate, at the moment I would, nevertheless,
think it the simplest explanation of all the available facts to assume
that primary “on” and “off” mechanisms are taken care of secondarily
by a retinal organization of reciprocal innervation in secondary neu-
rones.

Fig. 32. Chart of the receptive field of a single optic nerve fiber of the frog.
Each line encloses a retinal region within which the exploring spot light (relative
size shown above, left)—of an intensity the log. of which is given on the line—
produced a response from the fiber. On each line the indicated intensity was the
threshold; the set of curves constitutes a contour map of the distribution of
the retinal sensitivity to light with reference to this particular fiber. (Hartline, J. Opt.
Soc. Amer., 30, 259. 1940.)

The size of the receptive field was found by Adrian and Matthews
(1927a, b, 1928) to be of the order of 1 mm. in diameter in the eye of the
Conger eel. The result was based on discharges from the whole
nerve. By exploring the frog’s retina with a minute light spot, 0.55
mm. in diameter, Hartline (1940a, c) studied the receptive field from
which the single spike could be elicited. He arrived at much the same
figure. Hartline’s chart is shown in Fig. 32. The receptive field is
very sensitive in the middle, less so toward its edge. The curve of Fig.
33, from Thomson’s work, confirms Hartline’s result and is recorded
from the rabbit with the spike seen in the record, isolated by a micro-
 electrode stuck into the optic nerve itself. Barlow (1953a, b), with
the microelectrode technique used as in our laboratory on the inside
of the opened bulb (frog), added the significant observation that around the on/off elements the roughly circular receptive field was surrounded by a ring of inhibition. When this ring was illuminated separately, a discharge to light elicited from the middle of the receptive field was inhibited, even though the ring illuminated by itself failed to give a discharge and thus seemed to be outside the zone projected onto the single fiber. If we assume the receptive field to be the sum total of converging receptors and bipolars, this means that the surrounding inhibition may have been carried by internuncial neurones for lateral spread (amacrines, as originally suggested by Graham and Granit, 1931). At any rate, an organized inhibition of the type found by Barlow is very difficult to understand on any other basis than that it is organized by the neural network, probably to constitute a basis for simultaneous contrast. This was Hartline’s (1940a) view also, based on the fact that within a receptive field there was inhibitory summation as well as excitatory summation. At the background of this is Sherrington’s experience that reflex excitation and inhibition in the spinal cord have the same properties but with opposite algebraic sign.

Barlow’s experiment raises the question of what to define as a receptive field. In the absence of proofs to the contrary the discharge pattern of an element may be assumed to be affected by events so far away from it that it may seem worth while, for the time being, to preserve the distinction between element and receptive field, concepts which otherwise would be indistinguishable. Thus, for instance, Gallego (1953) has recently demonstrated in the cat’s retina a quite specific widespread plexiform layer which may well serve to integrate vast areas into a diffuse discharge in the dark. Kuffler (1952) in the same animal actually has found receptive fields up to 4 mm. across in the dark but is worried by spread of light, which is known to be considerable. He therefore always uses some background illumination and then obtains values of the order found by other workers on other animals. However, when scatter is wholly excluded, as by Wirth and Zetterström’s (1954) method of studying the electroretinogram elicited by light passing through blackened Perspex cones applied directly onto the retina (see Chapter 5, sec. 1), 4–5 mm. of diameter is also necessary to obtain all the features of the normal high-intensity type of electroretinogram. The question of what to include in a receptive field therefore embodies a real experimental problem and not dialectics. I shall return to it below in connection with the question of receptive fields as a function of state of adaptation.

Hartline (personal communication) found both large and small receptive fields in the frog’s eye, apart from proving that the field increased as much as double its size when stimulus intensities 100–1000 times the threshold were used. These are still modest intensities for an eye. Within the receptive field, as stated, there is summation of excitatory effects in on-elements and summation of inhibitory effects in off-elements (Hartline, 1940a).

An interesting feature of Kuffler’s (1952, 1953) recent study of the receptive fields in the cat’s eye is the preservation of an intact eye by inserting the electrode through a small opening in the sclera. By using two small light spots he was able to demonstrate in a particularly elegant way the above-mentioned antagonism between the on- and off-components of an element that I had seen when using the simple expedient of making on- and off-discharges clash by shortening the time of exposure (Granit, 1951; Enroth, 1952, with flicker). Kuffler’s most important new findings concern the minute organization that is characteristic of the receptive fields. Thus, in Fig. 34 it is seen that the center of the field gives on-effects only, in an intermediate zone...
on/off discharges are obtained, and the surroundings produce pure
off-discharges. There were other fields designed in an opposite fashion:
the center producing off-discharges, the periphery on-discharges. Since
the center, in agreement with all previous work, is the most sensitive
part of the field, its characteristics will be emphasized by properly
choosing stimulus strength and background illumination. All these

factors, including area of stimulus and position, were studied one by
one and found to be capable of altering the type of discharge from the
field. By these experiments Kuffler also considerably deepened our
understanding of why the on/off ratio of the cat’s eye is so variable,
and we always have found it to be. It is very likely that rod-cone antag-
onism in an eye with a large number of rods complicates this issue.

To illustrate the fundamental antagonism between the on- and the
off-components within a single receptive field I am reproducing as
Fig. 35 an experiment from Kuffler’s work. One of the exploring spots

\( (A), 0.2 \text{ mm. in diameter, was placed near the tip of the recording }
\text{electrode in the center of the receptive field and proved to give a high }
\text{frequency on-discharge to light. The other spot (B) was placed within }
\text{that part of the field which gave off-discharges only. Each vertical }
\text{row of records shows first A and then B by itself as control, then the }

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig35}
\caption{Cat retina. Interaction of two separate light spots. Single ganglion
\text{cell discharge during background illumination of 20 m.c. Spot A, 0.1 mm. in}
\text{radius, was placed in center of receptive field at tip of recording electrode.}
\text{Spot B, 0.2 mm. in radius, was 0.6 mm. away in surroundings. Flashed sepa-
\text{rately, they set up “on” (A) and “off” (B) responses. With a simultaneous flash,}
\text{A + B in col. I, “off” response is suppressed and at same time number of “on”}
\text{discharges in A + B is slightly reduced as compared with A. In col. II intensity}
\text{of spot A was reduced, while spot B was increased (note flash strength indica-
\text{tion on second beam). As a consequence B suppressed “on” discharge of A. In col. III,}
\text{both spots were “strong.” When flashed together (A + B) they reduced each}
\text{other’s discharges. Flash duration was 0.33 sec.; potentials were 0.3 mV. (Kuf-
\text{fier, J. Neurophysiol., 16, 37. 1953.)}}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig34}
\caption{Cat retina. Distribution of discharge patterns within receptive field
of ganglion cell (located at tip of electrode). Exploring spot was 0.2 mm. in
diameter, about 100 times threshold at center of field. Background illumination
approximately 25 m.c. In central region (crosses) “on” discharges were found,
while in diagonally hatched part only “off” discharges occurred (circles). In
intermediary zone (horizontally hatched) discharges were “on/off.” Note that
change in conditions of illumination (background, etc.) altered discharge pattern
distribution. (Kuffler, J. Neurophysiol., 16, 37. 1953.)}
\end{figure}

\text{effect of making them clash (A + B). In the first vertical row when}
\text{A is strong B is suppressed by collision with A. In the second row A is}
\text{weakened and B increased in strength. When they clash, A is sup-
\text{pressed. In the third row both A and B are strong and both have lost in}
\text{effectiveness by the collision. Enroth’s (1952) flicker studies with}
\text{single elements gave similar results, though not in terms of receptive}
\text{fields.}

\text{This antagonism of the on- and off-system in the retina seems to me}
of fundamental importance for another reason: it is maintained over such a broad range of phenomena. First of all, the on-discharge is excited by light and stops in the dark, while the off-discharge is inhibited by light and excited by darkness (Fig. 14). Second, the two seem to be closely associated with opposite slow potentials in the retina. Finally, they are mutually exclusive when they clash on the ganglion cell. One might say, too, that all these results are a belated vindication of the essential truth of Hering’s contention that there are two fundamental processes of opposite character in the retina, even though he could never have foreseen in what way his idea would come true. His notions were derived from the phenomena of contrast, for which no doubt the antagonism described is of fundamental importance, though a great deal of painstaking work will go into showing just how.

In many visual phenomena light adaptation and illumination of the background tend to have an equivalent effect (see e.g. Lythgoe and Tansley’s work on perceived flicker, 1929; Craik and Vernon’s demonstration that the summation area shrinks in light adaptation, 1941). It is therefore of considerable interest that Kuffler (1952) has found that as the background illumination increases, the receptive fields shrink. This effect was noted with all types of fields. The smallest receptive fields reported by Kuffler, explored with light spots 0.1–0.2 mm. in diameter, were themselves not larger than 0.5 mm. in diameter, yet they responded with on/off discharges. This suggests that the high flicker frequency noted in light-adapted animals with strong stimuli (Dodt, 1951a; Dodt and Enroth, 1953; Dodt and Wirth, 1953) and consequent light adaptation is a flicker with a small receptive field. Since the pigeon’s eye under such conditions runs up to fusion frequencies of around 140 flashes per second (Dodt and Wirth, 1953), its cone-retina is probably characterized by particularly small receptive fields, as suggested by Dodt and Wirth on the basis of the pigeon’s large number of optic nerve fibers, nearly 10 times greater than in the cat (Bruesch and Arey, 1942).

Kuffler (private communication) in work with Barlow has recently found that at the threshold (heavy background activity) the receptive fields in the dark-adapted cat’s eye tend to be uniform, i.e. give over its whole area the response which is characteristic of the center during light adaptation. At the same time area summation occurs over the whole field, while in light this happens only over the small central or surrounding areas respectively. This again suggests a physiological role for Gallego’s widespread plexiform layer, mentioned above.

6. Limitations of the technique of single fiber analysis

It remains to discuss what limitations should be imposed upon the interpretation of all these experiments with single fibers or single ganglion cells in the retina from the point of view of the technique itself. The experimenter, inasmuch as he wants to perform long-lasting analyses, tends to go in for large spikes which are delivered by large ganglion cells (Rushton, 1949, 1953). These in the cat are likely to have large receptive fields (Cajal, summary, 1933; Polyak, 1941). In my early work on color reception I did not follow this line of procedure alone but often measured the threshold of the spike most sensitive to a given narrow spectral region and was not too particular about isolation. Some of these spikes were just as likely to come from optic nerve fibers as from ganglion cells because, as pointed out at the time (Granit, 1941a), when microillumination was used (Granit and Svætichin, 1939), there was often a considerable distance between the spike and the microilluminated spot. Donner (1953) too, in his recent work on color reception in pigeons, measures the discharge from isolated small spikes. Gernandt (1949) studied the spikes more closely and found two kinds in the cat’s eye which since have been clearly differentiated by Kuffler (1952) in the same eye and by Barlow (1953a,b) in the frog eye, the one coming from optic nerve fibers, the other from ganglion cells. This difference would be of little significance for analyses in terms of spike frequencies had it not become customary to go in for rather large spikes in order not to lose them in long-lasting experiments.

Receptive fields have not been systematically studied with small spikes but it is well known that these, too, give on/off discharges (Bohm and Gernandt, 1950, with the cat’s eye; Donner, 1953, with the pigeon’s eye; Barlow, 1953a,b, with the frog’s eye). Also, some of the fields studied by Kuffler, as we have seen, were quite small, yet gave on/off discharges. One further line of evidence suggests that the difference between large and small spikes should not be exaggerated: provided stimulus strength is high enough, the large spike in the cat’s eye can be made to follow flicker up to the highest frequencies known for the human eye under similar conditions (70–80 flashes per second), as proved by Dodt and Enroth (1953). The rod eye of the guinea pig cannot follow equally fast rates of intermittency (Dodt and Wirth, 1953). Thus, the large spikes are capable of perfect dis-
discrimination of the flashes in flicker. We shall return to flicker in connection with the general problem of discrimination. Again, the assumption that the small spikes do not possess off-discharges is not only contrary to first-hand experience but also very unlikely when one considers that the off-discharge is the only retinal phenomenon capable of furnishing a peripheral cue for successive contrast which reaches its climax in color vision.

While it is highly desirable to have more work carried out with small spikes, I cannot share the surmise of Rushton (1953) that the small spikes may have very different response patterns. Even in the fovea of primates the private 1:1 path over the midget bipolar has other connections which make it potentially subject to influences from adjacent paths. It may well act in isolation in one context and together with adjacent receptors in another. Animals without fovea see well enough to make it a problem how they can do it. Also, it seems very unlikely that the principles discovered by the work on relatively large spikes would suddenly have been sacrificed at the very late stage of phylogenetic development (primates among mammals, birds) when a fovea occurs. To enumerate these principles briefly, they are: (1) the existence of two systems antagonistic throughout—the on- and the off-systems; (2) an organization similar to the one in the sentient skin and consisting of overlapping receptive fields of very different sizes; (3) a minute organization of these fields, which serves to emphasize the properties of the center of the field, either “on” or “off,” at the expense of the periphery; (4) means of expansion or contraction of the receptive field with variations in state of adaptation.

In the absence of studies of the fovea we can, for the time being, well disregard it and be content with the fact that the retina is a good organ for discrimination, even in animals without a fovea. If we fail to make sense of its properties as known at the moment, we are not likely to succeed very much better when the foveal records become available (see Chapter 8, dealing with discrimination).

Chapter 3

Spontaneous Activity in Sense Organs and Its Functional Significance.

The Principle of Centrifugal Control

1. Introduction. The peripheral mechanism

The ideas we entertain today about spontaneous activity in sense organs are entirely a product of the electronic era of sensory research which made it possible to observe the impulse. This does not mean that these problems are wholly without a history in psychophysical research. Do we have spontaneous sensations? To be sure, most sense organs are held to possess in the normal state an absolute zero-point of no sensation, but of old the eye has been regarded as an exception, since something is always perceived, even under closed lids in the dark. This to Helmholtz (1867) was the Eigenglüt produced by internal excitation and to Hering (1925) the autogenetic gray (das Eigengrau). These great opponents also disagreed about the sensation of “black.” With Helmholtz’s acceptance of Young’s color theory went the notion that white is the sum of all colors and black the absence of sensation, while to Hering “absence of sensation” was something that one saw with one’s back, and deep black, as perceived, was just as positive a sensation as white, besides being obtainable only by contrast against white. According to Hering’s theory black and white were the opposite poles of his two antagonistic processes, assimilation and dissimulation; and the autogenetic gray, just as any other gray, was some intermediate point.

If the calculations of Bruesch and Arey (1942) to the effect that 38% of all the sensory input in man is delivered through his one million optic nerve fibers are correct, there need not be much spontaneous activity in these fibers to produce a sensation of gray. We are exceptionally visual animals.

With the advent of electronics into the study of sense organs spon-