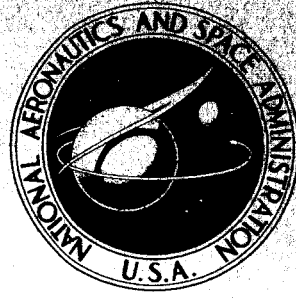


NASA CONTRACTOR REPORT



NASA CR-415

NASA CR-415

FACILITY FORM 802

N66-21094
(ACCESSION NUMBER) (THRU)

109
(PAGES) (CODE)

04
(NASA CR OR TMX OR AD NUMBER) (CATEGORY)

SUMMARY REPORT ON A REVIEW OF BIOLOGICAL MECHANISMS FOR APPLICATION TO INSTRUMENT DESIGN

VOLUME III

edited by J. Healer and M. Messer

GPO PRICE \$ _____

CFSTI PRICE(S) \$ 1.40

Prepared under Contract No. NASw-535 by
ALLIED RESEARCH ASSOCIATES
 Concord, Mass.

Hard copy (HC) _____

Microfiche (MF) 75

for

ff 653 July 65

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for

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

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1. Introduction

This report together with the two preceding Summary Reports¹ summarize the results to date of a review of biological mechanisms for application to instrument design and engineering performed for the National Aeronautics and Space Administration, Biotechnology and Human Research, Office of Advanced Research and Technology under Contracts NASr-16 and NASw-535. Since the material reported in this report and its two predecessors is complimentary and related, this report (both parts) will be called Volume III, in an attempt to tie these three reports together. This report is published in two parts:

ARA 211-F-4
Part I

Summary Report on a Review of Biological
Mechanisms for Application to Instrument
Design - Volume III.

ARA 211-F-4
Part 2

Bibliography on Biosensors - A Sampling of
the World Literature 1960 - 1964 - Volume III

This study is concerned with the investigation (and extension of previous investigations) of the function, structure and operational principles of biosensor mechanisms throughout the animal world, the integrated role of the sensor in a total regulatory control loop, engineering analyses of sensor operation, and the evaluation of this data in terms of present and anticipated instrumentation requirements for a variety of applications. Similarities and differences between these bio-transducers and their physical counterparts were investigated with particular emphasis paid to studying those characteristics of biosensors which are not currently used in instrumentation.

Instrumentation thus conceived may have application in a variety of areas ranging from hydrospace to interplanetary space. The problems and conditions encountered in spaceflight and exploration have created unprecedented instrumentation requirements. Some of these include extraterrestrial life detection, trace contaminant monitoring in a close environment, orbital docking, physiological measurements, communication problems, etc. Many astronaut tasks can be most economically performed only by very careful man-machine intergration. The astronaut's sensory input channels are overloaded making desirable a communication scheme whereby the external sensors are bypassed en route to the central nervous system. Understanding the various sensory systems offers possibilities of using standard sensory channels in different or unorthodox ways.

Some interesting areas of this work are some of the less well understood and less common senses; for example, the electric field sensitivity of certain marine forms which serves as an object locating system and may also have a communication function. There is much to be learned about data processing and pattern recognition by studying this system. The magnetic field sensitivity which is very poorly understood is also of interest. There is evidence to indicate that man, like certain lower forms, is affected by magnetic fields. Very little is known of the basis for or nature of these effects. Space conditions may expose man to magnetic fields significantly different from those to which he is accustomed. Knowledge about the potential effects of these fields can therefore be critical in maintaining man under these conditions and may also provide the basis for developing new methods of interacting with the nervous system.

Improved information handling and data processing techniques are needed for effective management of vast amounts of new data which is now available. Perhaps one of the most interesting and valuable aspects of the study of biosensors will ultimately be their role as information sensors and the data processing capabilities underlying their function in the context of their respective regulatory systems.

The function of man's sensory systems is vital to his performance. Knowledge is still inadequate about the effect (short or long term, immediate or cumulative) of severely altered environmental parameters on these systems and their components. In this sense, more fundamental knowledge about individual sensor mechanisms may enable us to predict response, to protect against adverse effects, and perhaps in some cases, to utilize the response of the biosensor itself as part of a physical sensing or warning system. The lack of gravity in space and its relationship to gravity or acceleration sensors is an area in which additional research is needed. Many adverse effects on a variety of life forms have been attributed to the lack of gravity.

Several of these areas and their application potentials are reviewed in this report. The background analyses for portions of this work, as well as engineering analyses and design concepts based on other sensor mechanisms, are not reiterated here and can be found in two previous reports.

¹ARA-1205

Summary Report on a Review of Biological Mechanisms for Application to Instrument Design, January 1962.

ARA-1026

Bibliography on Biosensors, A Sampling of the World Literature, 1900-1961 (Second Edition).

ARA-T-9211-5
Volume I

Second Summary Report on a Review of Biological Mechanisms for Application to Instrument Design.

ARA-T-9211-5
Volume II

Bibliography of Biosensors, A Sampling of the World Literature 1900 - 1963 (Third Edition) (Revised).

SECTION 2. MECHANORECEPTORS

2.1 Orientation and Equilibration

2.1.1 Introduction

2.1.2 Gravitation and Acceleration

2.1.3 Some Basic Questions

2.1.4 Historical Background and Review of Equilibration

2.1.5 Acceleration Sensors and Equilibrium

A. Vestibular Receptors of Vertebrates

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2.1.6 Discussion

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2.2.2 General Discussion

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2. Mechanoreceptors

The orientation sensation in homo sapiens, and the basic mechanism of mechanoreception in the animal kingdom, are two facets of mechanoreception which are of primary importance to manned spaceflight. The following discussion is the result of exploratory inquiries into both of these areas in order to determine the general state of understanding from a mechanics standpoint, with the ultimate goal of developing useful spaceflight instrumentation.

Information relevant to the exploratory studies was reviewed, certain types of data were sought in each case, and the literature was examined critically from the viewpoint of a specialist in mechanics seeking accurate, specific engineering data. Such a viewpoint would be natural to an instrument designer. The preordained failure of such an undertaking would be evident to a biologist. Experimental observations first had to be separated from the biological conclusions drawn from them, and then restated in terms which have mechanical significance. Upon completion of the sorting process the results were summarized and areas of further investigation needed to provide data of mechanical or engineering significance are discussed.

For a review and analysis of other mechanoreceptors, their mechanisms, and their engineering applications, see the previous reports (Refs. 2-1 and 2-2).

2.1 Orientation and Equilibration

2.1.1 Introduction

The possible effects on an astronaut of the short and long term absence of the gravitational force field continues to be a matter of concern, speculation, and controversy. Relatively little data exists in this regard and even this has been accumulated from short term exposures and on subjects who were restrained during most of their exposure. Concern is directed toward several of the body's systems. Specifically there has been considerable speculation on the effects of weightlessness on the nervous system with regard to sensory response. The Russian literature suggests some alterations in neural function. There were reports of altered electroencephalograms on Tereshkova and Bykovsky, for example, which persisted for several days after the flight. Their four day flight has been the longest to date. There are many factors involved in considering the effect of altering sensory input to the nervous system. Among these are the remarkable adaptation, accommodation, and substitution capacities of the organism which may (or may not) tend to minimize potential difficulties. Of all the sensory modalities it is the input to the mechanical

sensors, in particular, that is most altered by the weightless state. Proprioceptors, muscle spindles, stretch receptors and the labyrinthine receptors are particularly affected. All but the latter show remarkable adaptation after a short learning period. Effects on the labyrinthine receptors, however, are not so readily overcome. The resultant disorientation can be at least partially overcome for task performance by utilization of the visual system but the significance of the altered input to these receptors, and possible changes in their functional state, is still undetermined.

While much attention has been given to these receptors, their response to various types of stimuli, measurement of these responses, and the functional basis for their operation, these sensory mechanisms are, as Vinnikov points out, far from understood (Ref. 2-3).

Until sufficient clinical data are available to determine the ability of an astronaut to adapt to a 0g environment, it appears important to consider the possibility of providing an astronaut with some artificial means of orienting and obtaining other acceleration cues in space in a form which approximates or replaces his capabilities with a receptor system which is accommodated to, and functioning with, the force field on the surface of the earth. In this connection it is necessary to investigate the labyrinthine acceleration (gravity) sensors as the principal receptors responsible for equilibration in man.

In order to determine the more general character of the orientation sense and to examine functional principles common to acceleration sensing mechanisms, this study also included comparison of acceleration sensors from a variety of animal forms.

2.1.2 Gravitation and Acceleration

An object upon the earth is subjected to several types of forces. The major force is a gravitational attraction toward the mass center of the earth. Another is an inertial acceleration force directed radially from the earth's axis of rotation so that the force would be 0 at the terrestrial poles and maximum at the equator. In any event, this force is a minuscule fraction of the gravitational attraction.

Other forces are the gravitational attraction of the sun and the moon. These forces vary continuously in direction (although they are virtually constant in magnitude) depending upon the positions of bodies in space. However, they are

also negligibly small compared to the gravitational field at the surface of the earth resulting from the mass of the earth. That is the major force acting on any earth-bound body, or on any body in orbit near the earth.

2. 1. 3 Some Basic Questions

The earth orbiting process involves an initial stage of high acceleration involving a total of approximately five minutes, after which external forces would disappear and he would be suddenly plunged into the new environment of 0g, in which the earth's gravity would be balanced by inertial acceleration. This raises the fundamental questions to be considered at this point.

1. What information is available to predict how an individual's equilibration apparatus would function after several days or weeks at 0g?
2. Of what importance would be the long time loss of an orientation sense?
3. What compensation can be provided by his other senses, such as vision, to diminish his problem?
4. Is it conceivable that artificial equilibration would be possible and practicable for astronauts?

Whatever the answer to these questions, it seems reasonable to assume that the problem of adjustment to such an environment by an astronaut would be minimized if he were to be provided with a device which could recover for him, his sense of earth surface equilibration (gravitation) by providing the equivalent sensation directed towards some point in space. It may not be necessary to select this point judiciously, it may be arbitrary. Nevertheless, it appears reasonable to consider the possibility of such a substitute device.

2. 1. 4 Historical Background and Review of Equilibration

Spatial orientation is the end result of Central Nervous System processing of the inputs from many individual receptors responsive to several different classes of stimuli. These include photo and proprioceptors, tactile, acoustic, and most important, the stato- or acceleration receptors. In some life forms other sensory modalities also enter into the over-all orientation process, e. g., chemoreceptors in the case of insects and some lower invertebrates, and thermo or infrared sensors in the case of snakes.

Acceleration or equilibrium receptors are the primary sensors involved in equilibration. They respond to all classes of acceleration (including gravity).

The close association of equilibrium with acoustic receptors tended historically to hinder the recognition of the role of the ear in the equilibration process. The ear was so traditionally associated with sound reception that its role in equilibration was long unrecognized and experimentation to establish this function was not reported until the late 1700's. In the light of this, it is quite interesting that, from an evolutionary standpoint, the equilibration function of the ear preceded the acoustic function of this organ. It is believed that the auditory reception function developed in some manner from the equilibrium function. The semicircular canals are phylogenetically related to the lateral line organs which Lee in the 1890's demonstrated to have an equilibration function.

The role of the cerebellum and the vestibular branches of the VIII nerve in the maintenance of equilibrium were recognized long before the vestibular sensors were identified. In 1824, Flourens demonstrated that certain effects produced by cerebellar excitation were duplicated by stimulation of the semicircular canals. Scarpa's experiments in 1769 described the vestibular ganglion and its relation to the cerebellum. This was the start of a series of investigations which led to a definite distinction between vestibular and auditory function.

Flourens is credited with the first systematic work on equilibrium sensing and his outstanding contribution to the recognition and understanding of this sensory process and the mechanism involved is often cited even today. Flourens' work clearly established the similarity between animal response to disruption of the cerebellum, to excitation of the semi-circular canals, and the response to rotation about an axis described by Purkinje (1820). Despite Flourens' work, the belief that the ear's sole function was that of audition was so entrenched, that approximately 30 years passed without particular interest in this area. When this research resumed, its results and their interpretations proved controversial. But the techniques of stimulating and extirpating the canals were perfected into precise and reliable research tools and were used by a number of investigators on a variety of animals. Among these was Goltz, who working with birds, made a distinction between two functional receptors in the inner ear -- the auditory cochlea and a non-auditory equilibration portion. In the 1890's Lee's classical work on equilibrium in fish added further confirmation of the role of the vestibular portion of the ear in equi-

bration. He demonstrated that morphologically the ear and lateral line organs are phylogenetically the same -- both developed from the same ectodermal thickening.

Cyon (late 1800's) was a leading exponent of the doctrine that the semi-circular canals perceive the direction of sound. He believed that the oculomotor centers participated with the central cite for reception of impulses from the canal nerves, in determining the sense of spatial relations. His early experiments consisted of replacing the endolymph with gelatin and then producing pressure changes which he found did not effect equilibrium.

Another group of investigators including Crum-Brown, Brueu, Mach, and Ewald adhered to a hydrodynamic theory of vestibular function. They held that the flow of endolymph deflecting the hairs of the sensory cells of the cristae was responsible for eliciting vestibular sensations. Endolymph motion occurs with velocity change in the pair of canals whose axis is most nearly parallel to the temporary axis of rotation of the body. Endolymph motion, due to inertia, lags behind that of the canal wall thereby creating movement in the opposite direction to that of the rotation. Endolymph flow persists after the cessation of rotation. The flow is in the opposite direction from that at the beginning of rotation and therefore direction of the cupula is also shifted.

Despite objections to this theory raised by a number of investigators, it now appears substantially accurate. The work of Steinhausen and Dohlmans which will be discussed later, and subsequent current work done with precise equipment helped to elucidate the mechanics of this system.

2.1.5 Acceleration Sensing and Equilibrium

Almost every living creature seems to possess the necessary sensing receptors to detect the presence of an acceleration field. An acceleration field can be the result of combinations of motions, both linear and rotary, and the effect of the presence of large masses (gravitational). Within the past 10 years, man has been content to deal with the accelerations that are simply added to or subtracted from the gravitational field of the earth. As space travel became more of a reality, the sensing of the total acceleration field that includes the effects of the other members of the solar system became more of a necessity. The prime navigational scheme of space travel is the sensing of the magnitude and direction

of the acceleration field as a function of time (inertial navigation). The technical excellence that is built into the acceleration sensors (accelerometers) is a direct measure of the ultimate precision of the guidance scheme.

Curiously enough, most living creatures are constructed with a distinct lack of precision to measure the magnitude of an acceleration field. What living creatures do possess however, is a highly sensitive and refined sensing system to detect sudden changes in the existing field and to initiate compensations such as control functions to affect the change. In this regard the sensing and control function can be looked upon as a closed loop control system that is always seeking a null position for offsetting any changes in the acceleration field. In such a system the absolute magnitude of the signal from the sensor or its linearity with the actual applied field is not very important. A null system operates at very high gain so that the output of the sensor will be accurately returned to zero by the appropriate control functions. It should be noted that the living sensors can detect the two qualities of the acceleration field that make it a vector quantity: the magnitude (detected with moderate accuracy) and direction (detected with great accuracy).

One of the primary functions of many animal acceleration sensing schemes is the detection of the local vertical. Indeed, this is also one of the demands which is placed on earth bound inertial sensing systems. (Earth bound in this case would be a voyage between two points on the earth that are quite remote from each other. In this case the verticals at the two locations would be very non-parallel when viewed against a stellar reference). The designer of the inertial platform that performs the guidance functions of an earth bound inertial flight have gifted the platform with the ability to sense the local vertical regardless of the other accelerations that may be present. This is not the case with the living system. The vertical state is only achieved by the complete solution of both a gravity sensor input and a visual input. This, of course, is what makes a living system so inept at space maneuver and why the "coordinated turn" in aircraft can lead human sensors to erroneous conclusions.

As a side light it is interesting to note that when the gravity vertical and the visual vertical are put into conflict in situations where no corrective maneuver is possible, acute anxiety occurs; forcing humans to believe guidance instruments during a coordinated turn, tilted houses that "feel" vertical, etc.

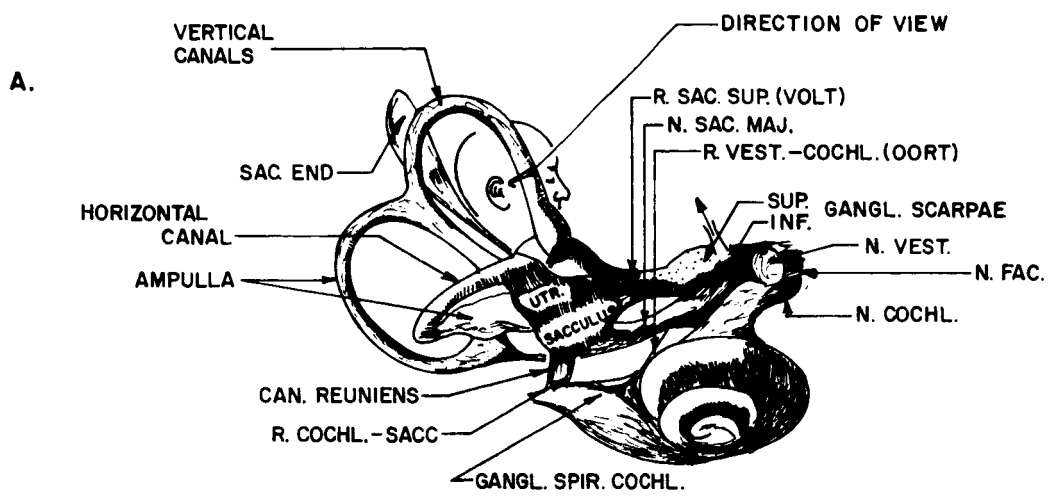
Receptors primarily concerned with gravity, acceleration and equilibrium sensing can be referred to loosely as statoreceptors. This term can include the statocyst receptors found in the invertebrates, and the vertebrate, vestibular or labyrinthine receptors. The vertebrate statoreceptors are of two main types which are roughly analogous to the invertebrate statocysts in function, though there are differences in anatomical detail. In actual use, the sensors all sense the magnitude and direction of the acceleration field, whether the results are used for equilibrium or locomotion.

A. Vestibular Receptors of the Vertebrates

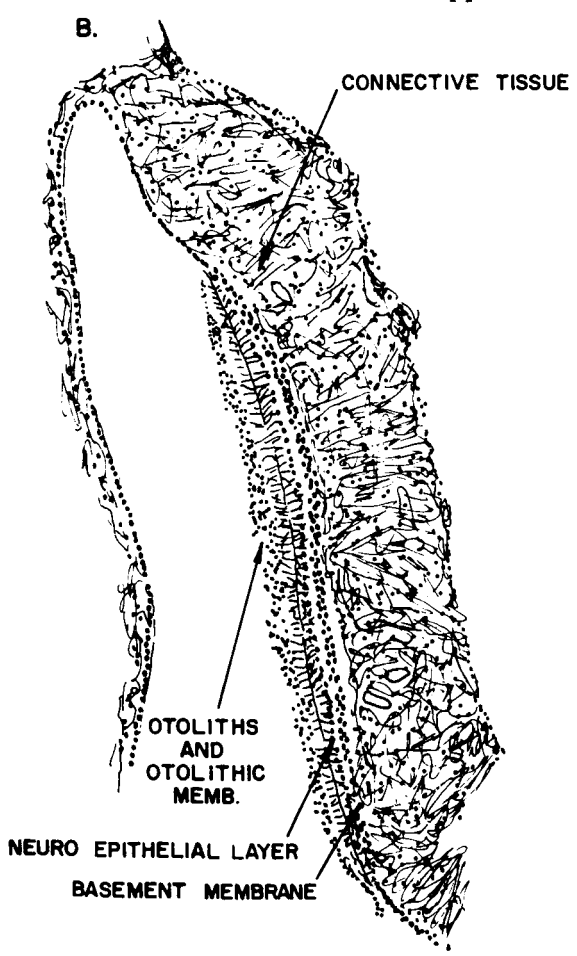
The Ampullary Receptors

In the vertebrates, two different acceleration receptor types have been identified on an anatomical as well as a functional basis (see Fig. 2-1). The receptors of the cristae (ampullary receptors) can be thought of as angular accelerometers responsive to rotational accelerations around all axes in space. The receptors of the maculae which are located in the utricle and saccule function as linear accelerometers responding to accelerations in all directions in space. Gravity is included in this definition. This functional distinction has been demonstrated and is widely accepted. However, work with both experimental animals and man has indicated that this widely accepted functional dichotomy may not be complete (Ref. 2-4 - 2-8).

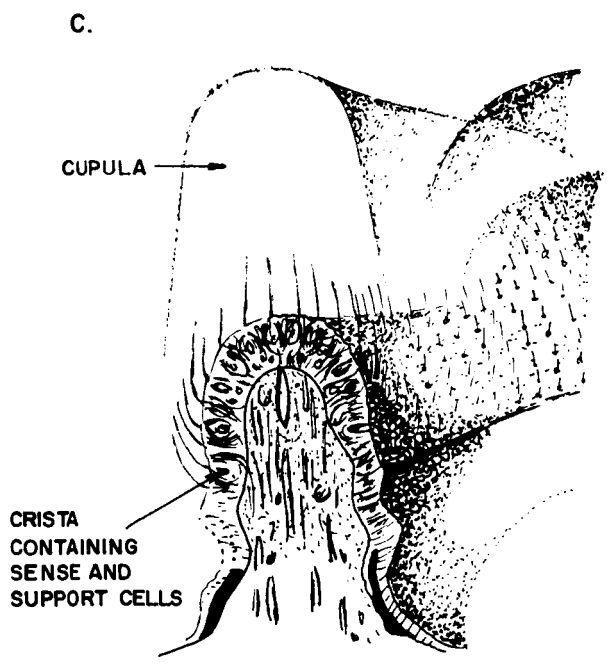
The three thin-walled membranous semi-circular canals which sense angular acceleration lie in three orthogonal planes inside the bony or osseous labyrinth where they are eccentrically suspended by fibrous strands. They are separated from the bony labyrinth by the perilymph and fill approximately one-quarter of this cavity. The canals thus correspond in position to each of the three major planes of the body. They are named according to their orientation - the horizontal (external, lateral) canals, the superior bi-frontal vertical canals, and the posterior or inferior vertical canals. The canals are filled with a fluid, the endolymph, and are all in communication through the utricle. The endolymph is a clear fluid, the density and viscosity of which approximate those of water. At the base of each canal, near its connection with the utricle, is an enlargement (swelling) the ampulla. The ampulla is nearly filled by the cupula, (gelatinous mass) covering and mechanically coupled to the underlying cristae ampullaries. The cristae are composed of two types of sensory cells (Figure 2-2) which differ in shape, innervation and location (position) within the cristae (Ref. 2-9).



A. The innervation and structural relations of human vestibular apparatus and cochlea (from Hardy).



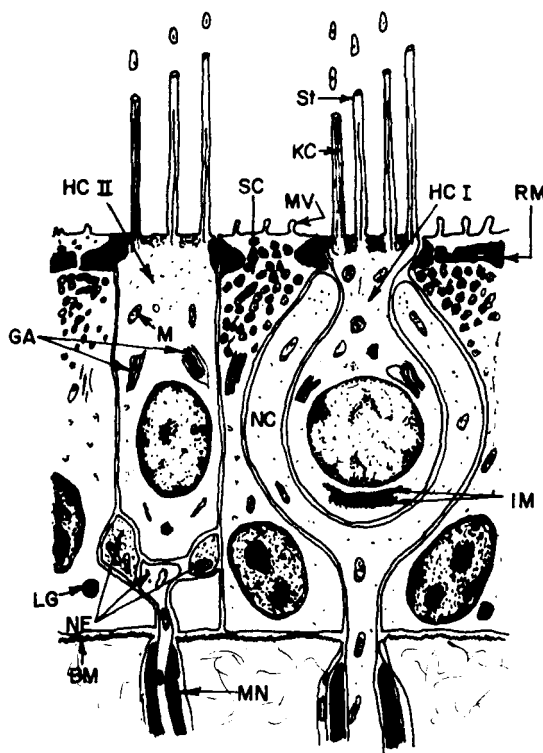
B. Otolith Organ - Drawing of a longitudinal section (low-power) cut through the macula sacculi.



C. Schematic three-dimensional diagram of one-half of an ampullar crista. (From Wersall)

Figure 2-1. Vestibular Receptors of Vertebrates.

CUPULA MASS



The ultrastructural architecture of the cells and nerve endings of the crista ampullaris (guinea pig). HC I, bottle-shaped hair cell; HC II, cylindrical hair cell; SC, supporting cell; St, stereocilia; KC, kinocilia; N, nucleus; GA, Golgi apparatus; IM, intracellular membrane system; VB, vesicular body; NC, nerve calyx; RM, reticular membrane; M, mitochondrion; NE, nerve endings; BM, basement membrane; MN, myelinated nerve; LG, lipid granule; MV, microvilli. (From Wersall).

Figure 2-2. Sense Cells of Crista.

The receptors described as bottle shaped, tend to be located toward the crest of the cristae while the cylindrical receptor cells occur about the periphery. These receptor cells and their surrounding support cells are firmly attached to their bony foundation. These sense cells are often referred to as hair cells because of the sensory hairs or cilia which project from their surfaces into the mass of the cupula with which they are coupled. Each sensory cell has between 20-100 cilia projecting from its surface. One process on each of these cells has a kinocilium-like structure and is called the kinocilium. It always appears in a particular orientation which is different in the cristae of the horizontal canal than in the vertical canals. The other cilia are stereocilia.

Based on the measurements of dc potential differences (Ref. 2-10 thru 2-12) Trinker assumed that the cilia surfaces bear electrostatic charges with repelling charges of the same sign occurring at a single cilium which can account for the stiffness of a cilia bundle as well as the regular arrangement of cilia within the bundle. After death the cilia clump and stick together within the time period it takes for the electrostatic charges to be lost (Ref. 2-12).

In these receptor cells (as in most animal cells) the cell interior is negative with respect to the outside. The cilia membrane is an extension of the receptor cell membrane. Trinker and Davis (Ref. 2-12) measured a potential difference across the cilia bearing membrane of up to 120 mv. As in other cells, the energy which maintains this difference is furnished by the metabolic process. However, experiments on the perilymph and endolymph demonstrate the similarity of their relationship to the inside and outside of a cell. The perilymph is rich in sodium with little potassium while the endolymph exhibits the reverse of this condition. There can be no potassium battery if the internal and external potassium concentrations are equal and this supports the thesis that there is no ion exchange through the hair-bearing surface of the sensory cells. This would mean that the outer cell and ciliary membrane should behave like an electrostatically charged condenser and this behavior was demonstrated by the presence of microphonics, a-c potentials from the cilia bearing surface of the sensory cells. (Ref. 2-12).

Potassium and calcium ions are known to affect the viscosity of colloids and there have been suggestions that potassium present can affect the mucopolysaccharide cupula consistence and affecting its mechanical properties

(Ref. 2-13 and 2-14). Muccopolysaccharides have been studied (Ref. 2-15) and microphonic-like potentials have been produced in them leading to the suggestion that a film of polysaccharide molecules covering the cilia might be the source of the biological microphonics observed. Several investigators found that vestibular microphonics, like cochlear microphonics as a superposition, synchronized action potentials of collectives of first derivative neurons. The precise role of microphonics in the transduction process, however, has yet to be definitively established.

Angular acceleration produces motion of the endolymph which results in cupular deflection. This deflection is transmitted to the cilia of the sensory cells of the underlying cristae ampullares which project into the cupula mass. Speed of endolymph movement during increased acceleration and the resulting cupula deviations have been measured. Teinhausen (Ref. 2-16 thru 2-18) provided the critical experimental proof that the cupula, when deflected, moves like a swinging door over the cristae. The cupula practically fills the cross section of the ampulla but even when maximally deflected there is very little endolymph leakage. He made these observations by staining the cupula with injections of Chinese ink and thus was able to observe the relationship of endolymph-cupular motion so difficult to observe because of the correspondence of the refractive indices of these two substances. Because of the structural relationships and mechanical properties of the endolymph and cupula which Steinhausen found, he was able to describe the behavior of the coupled endolymph-cupula-system as a damped torsion pendulum. Resistance is provided by the elastic nature of the cupula which exerts an elastic restoring force on the endolymph fluid. This behavior and the viscous forces created by endolymph flow through the narrow space available, provide the damping. The moment of inertia corresponds to the moment of inertia of the continuous fluid within a semicircular canal. The mechanics of cupula displacement according to this model can be described by the second order equation used by Guedry:

$$\frac{d^2x}{dt^2} + 2\zeta\omega_n \frac{dx}{dt} + \omega_n^2 x = a(t)$$

where

- ζ = damping coefficient
- ω_n = frequency
- x = cupula angle
- a = value of angular acceleration

The damping of the system is very high resulting in a periodic oscillation of the cupula.

Dohlman's experiments on codfish further elucidated the mechanics of this system. (Ref. 2-19). He introduced a drop of oil into the semicircular canal and observed its movement and the movement of the cupula in the direction of endolymph flow in response to angular accelerations produced by rotation. He also measured cupula motion by measuring pressure changes with a manometer.

The deflected cupula takes as long as approximately 20-50 sec. to return to its resting position. Dohlman found that the rates of displacement and return of the cupula coincide with the duration of nystagmus during acceleration and the duration of the post-rotational nystagmus.

Electrophysiological measurement can be used to determine cupular response to stimulation. Subjective reaction, behavioral response and many other indirect methods have been employed. A commonly used indicator has been the measurement of patterned eye movements or nystagmus. In an attempt to stabilize an image of a stationary point on the retina when the head is rotated in space, the eyes move slowly in the opposite direction of the rotation without initial delay. When they cannot move further there is a rapid flick back to a central position. Angular velocity of the slow phase can be computed from tracings and is related to cupular position. It is thought that the angular velocity of the slow phase is proportional to the deviation of the cupula.

Rotation of the head in the plane of a canal is the strongest stimulus to the ampullary receptors. They are also stimulated by acceleration about axes oblique to these planes as these too, produce disturbances in the endolymph. When the endolymph in one canal is greatly affected, some may flow into another canal because of their common connection through the utricle but the canals act as shunts and leakage is minimal. Each cupula deflection contains a shearing force component. According to Trinker (Ref. 2-12), corresponding to the degree of cupula deflection (which is proportional to the actual angular acceleration), a sinusoidal function is the characteristic curve of the information input, and represents the 'receptor-adequate' stimulus, the shearing force.

Since the deflected cupula behaves elastically, it returns slowly to a resting position during angular acceleration of constant speed. There is therefore no response to these situations because the endolymph motion no longer lags behind the canal wall movement. The ampullary receptors of all the canals seem to be

more responsive to stimulation (deflection) in one direction than in the opposite direction. (The direction deflection producing strongest reactions in the horizontal canal is the opposite of the direction of greater sensitivity in the vertical canals.) For a time these receptors were thought to be unidirectional but more recent work demonstrated their bi-directional character. However, there is a directional sensitivity and this has been discussed in terms of the location and orientation of the kinocilia in the horizontal versus the vertical canals. In the crista of the horizontal canal the kinocilium faces toward the utricle whereas in the vertical canals it faces away from the utricle. (Ref. 2-20).

Receptors of the Utricle and Sacculae

The other labyrinthine receptors of vertebrates are those found in the vestibular sacs, the utricle and sacculae (Figure 2-1B). These are the otolith containing organs which are very similar to the statocysts found in many invertebrates. If the vertebrate vestibular system is thought of as an inertial guidance system with the ampullary receptors acting as angular accelerometers, the otolith organs with their receptors in the maculae can be thought of as linear accelerometers. While the two receptor organs differ in detail, construction and function, their activities are coordinated in the nervous system to provide a total equilibrium sensation.

Despite the fact that, in vertebrates, different sense organs have developed to measure the two classes of acceleration, it should be noted that the receptor or sensory cells of these two organs are similar structurally and in detailed function. For example, they are all second order neurons. The receptor cells are equipped with cilia or hair-like processes. In the case of the otolith organ these processes project up into the otolith(s) and deformation of these processes initiates the nerve impulse.

These receptors are located in the sac-like utricle and sacculae of the inner ear. The utricle is the larger of the two sacs and the ends of the semi-circular canals open into it. The sacculae is a small pear shaped sac located below and medial to the utricle. Its long axis is nearly vertical. These sacs are filled with endolymph. Inside these sacs are located the maculae which are composed of ciliated sensory cells and support cells. In the utricle, the macula is located on the anterior and medial walls and is approximately horizontal when the head is upright. The macula of the sacculae, with the head upright, is approximately 30° from

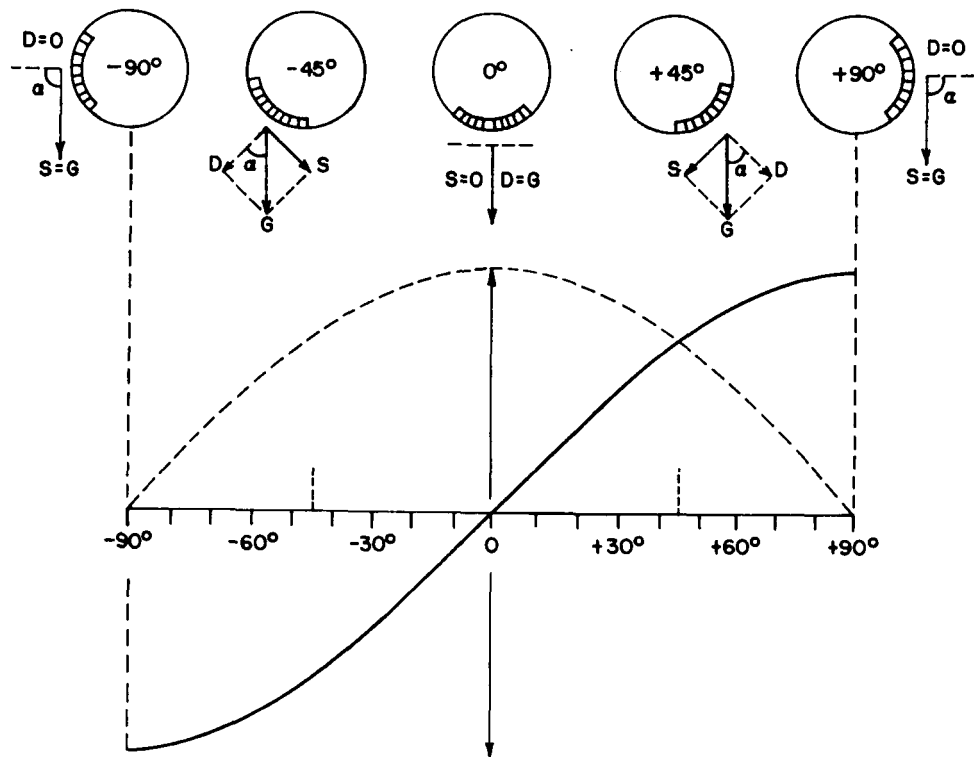
vertical. The maculae are covered by a gelatinous-mucous mass containing the otoliths which are aragonite or calcite concretions of calcium carbonate.

In vertebrates as opposed to some invertebrates, there are a number of these otoliths over each macula. The particles vary in size, composition and number between the different vertebrate families (Ref. 2-3). In the case of mammals, it has been shown that there are particles of several sizes which occur in distinct positions over the macula surface (Ref. 2-21). The receptor cells and their innervation also differ from family to family.

In response to specific linear acceleration or gravity the otoliths, being denser than the surrounding endolymph, obey the law of gravity and move through the endolymph in the direction of the force. Typical densities for vertebrate otoliths are approximately 2.68 - 2.94 and the endolymph density is approximately 1.02 - 1.04 (Ref. 2-12). Since the otolithic membrane moves as a whole, the heavier and lighter portions have to be interrelated. Otolith motion across the macula surface deforms the hair-like processes of the sense cells creating nerve impulses. This motion is limited to about 0.1 mm due to the strands supporting the otolithic membrane. The otolith organs, therefore, act as density difference accelerometers. Considerable controversy has existed as to the mechanism involved in transmitting motion information from the otolithic membrane to the sense cells of the macula. It now appears that Breur's explanation in 1891 was correct. He claimed that pressure or tension applied vertically to the cilia was not adequate stimulus but that only the tangential component of the stimulating force acting on the sensory epithelium activates neural pulses. The opposite view was subsequently taken by a number of investigators.

Measurements made by Trinker (Ref. 2-12) and others of microphonics involved, indicate that only tangential displacements produced bioelectric changes. Thus, the shear force again seems to be the effective stimulus resulting in the familiar sinusoidal function as the characteristic curve representing the information input (see Figure 2-3). There is a bidirectional response with reversal of sign occurring with the direction of shift of the otolithic membrane. The otoliths respond to changes in magnitude as well as direction of specific force. Rate sensitive receptors have also been identified in the periphery of the maculae.

As Vinnikov indicates, there is still much to be learned about these receptor mechanisms. Bizarre responses and illusions have been shown to occur



Stimulation of the macular sensory epithelium by shearing force, and the characteristic curve representing information input. Above: schematic drawings of the utricle, with its macula and statolithic membrane, undergoing tilting in both directions around the horizontal rostro-occipital axis of the head. Forces on the sensory epithelium represented as vector parallelograms. G, gravity; S, shearing force (the component of gravity, acting tangentially on the epithelium); D, pressure (or tension), the component, acting vertically on the macula. In a normal position, $S = 0$; at 90° , $D = 0$. Below: the relationship of shearing force (continuous line) and pressure (broken line) to degree of inclination (abscissa); shearing gives a sine relationship, while pressure gives the cosine. (Ref. 2-12).

Figure 2-3. Stimulation of the Macular Sensory Epithelium by Shearing Force.

when unusual stimulation is provided. The two types of vestibular receptors occur in pairs which behave synergistically. Signals are compared and integrated before transmission to higher centers. Unilateral disturbances created by artificial stimulation or interference results in a variety of unpleasant results indicating vertigo, motion sickness, lowered blood pressure, etc. Compensation does usually occur. Bilateral destruction does not create the violent symptoms of unilateral destruction but there is permanent disorientation in situations of visual deprivation. Denervation of the utricle has resulted in loss of muscle tone.

Another question of considerable interest especially in relation to space flight and exploration has been the nature of adaptation and habitation in both types of vestibular receptors. Prolonged rotation is known to result in a decay of response from the ampullary receptors. Hallpike and Hood (Ref. 2-22) and Lowenstein (Ref. 2-23) found that the receptors show adaptation when the cupula deflection is maintained for prolonged periods of time. Cramer (Ref. 2-24) studied the response of otolith organs of the cat to sustained tilt and concludes that in some cases the static function of these receptors is subordinate to the dynamic functions. He found a vigorous initial response to tilt which decayed considerably within 15-30 seconds and a residual steady-state signal which was weak relative to the initial signal. This area needs considerable additional work as well as a coordination of current work. Experimental techniques often interfere with the experiment and measurements and interpretation of data shows considerable variation.

Of further significance is the recent work of Benson and Bodin (Ref. 2-25) who are concerned with the interaction of linear and angular acceleration on both types of vestibular receptors. They discuss work which demonstrated in experiments with animals and man that the accepted functional dichotomy between the linear and angular acceleration sensors is not complete. In response to a constant linear acceleration vector there were effects produced on the ampullary receptors in animals and in the nystagmic pattern in man. They are examining response (indicated by nystagmus) to a rotating linear acceleration vector and the interaction with angular accelerations. They feel they have evidence which indicates a response of the ampullary receptors to linear acceleration but acknowledge that the macular receptors may be involved. The eye movement measurement method while valuable, is indirect, and it is difficult to actually examine transducer and detailed receptor mechanisms in this way.

B. Statocysts of the Invertebrates

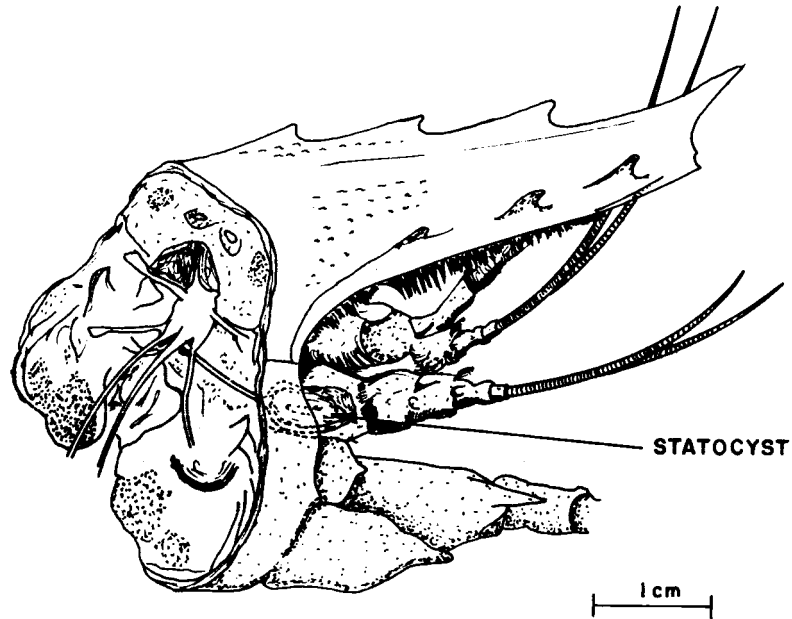
The sense organs of equilibrium statocysts, occur in a variety of invertebrates (see Fig. 2-4). They are considered to be the first sense organs to occur in the phylogeny of the animal kingdom. These organs are similar to the otolith organs in the vertebrates. Basically, the statocyst is a small ectodermal sac found at various locations in the body depending on the invertebrate phylum and individual sub groups within the phyla. The lumen of the statocyst is filled with fluid into which project the processes of sensory cells. The statocyst also contains one or more statoliths which are little stones or calcareous concretions, the specific gravity of which is greater than that of fluid. These particles change position in response to stimuli, deforming the various hairs with which they come in contact creating neural signals.

The statocyst responds to both static and dynamic stimuli in the form of gravity and/or for accelerations. In contrast to the vertebrate macula sensory cells, the hair-like processes of the statocyst receptor cells are composed of non-living cuticle. Furthermore, the sense cells are primary sense cells or neurons with their own afferent axons while those in both the macula and crista are secondary sense cells. Pressure and tension applied to the cuticular cells does not stimulate them but bending is the adequate stimulus. It can be seen that as is the case for all statoreceptors, the shear force component is the 'receptor adequate' stimulus. Stimulation can act in two ways: it can cause a modification of the tonic pulse train emitted by the sensory cells independent of stimulation or it can result in the creation of an independent impulse. The importance of the existence of a tonic pulse train which is independent of statolithic stimulation becomes evident in certain crustacea which lose their otoliths in the moulting process and must then replace them with externally obtained particles. These particles may not always be of the same weight in the statocysts of both sides but compensation occurs for a loss of tonic impulses from one side.

The number of statocysts which occur in an individual is variable. In some cases where these organs are paired, they act antagonistically and in other cases they do not.

Similarities between the basic principles of operation of the crustacean statocyst and vertebrate otolith organs include the facts that the sine law is obeyed in both. The adequate receptor stimulus is the shear force component bending

A



Anterior cephalothoracic region of the lobster *Homarus americanus*. The statocyst is exposed in the basal segment of the right antennule. The nerve seen coursing from brain to the statocyst is the combined statocyst and antennular nerve (From Cohen).

B

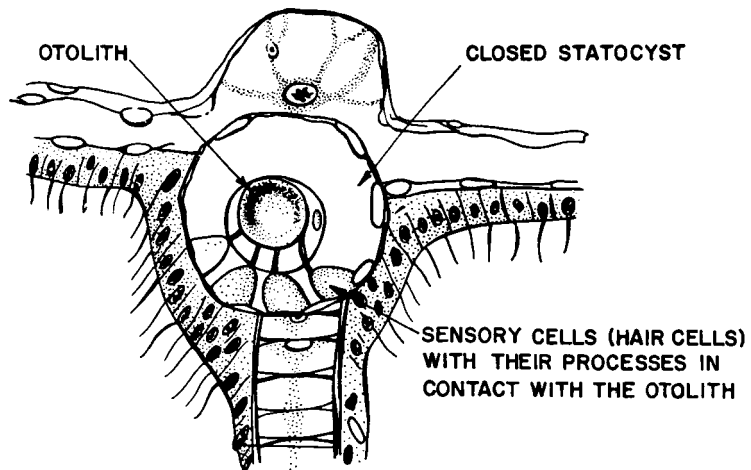


Figure 2-4. Invertebrate Statocyst.

the sensory hair-like process, stimulus and response show a linear relationship, and the sensory epithelium emits an independent tonic pulse train which can be modified by stimuli (Ref. 2-26). Statocysts have been clearly identified in the coelenterates and crustaceans. Rapidly adapting phasic receptors have also been shown to exist. Cohen identified four types of afferent fibres which respond to differing components of the acceleration stimuli (Ref. 2-27 and 2-28).

Statocysts are present in a number of different invertebrates. They are somewhat complex sense organs for the organisms in which they occur. Statocysts are found in the coelenterates where they vary considerably in degree of differentiation, innervation, and structural complexity among the various species and groups of medusae. The simplest type consists of an epidermal pit. This is not a closed structure. Cells in this pit, known as lithocytes or stone cells, contain a statolith. Processes of sensory cells in the statocyst wall are in contact with the lithocytes. Stimulation results when these processes are bent by movement of the lithocyte. Other coelenterates have closed statocysts. In this case the wall is formed of a double layer of flattened epidermal cells with sensory cells and lithocytes occurring in patches. The statocysts of medusae are located between the tentacles where they occur in the hundreds. In some medusae there are many organs which contain both pigment and lens like structures as well as statoliths and sensory cells with hair-like processes. The ctenophores, (a sub-phylum of the coelenterates) have a single statocyst at their aboral end in which is contained a large statolith or morula composed of small round calcareous bodies. This statolith is in direct contact with and supported by elongated hair-like processes, fused cilia, stemming from sensory cells in four distinct areas on the statocyst wall. The statolith is covered by a roof also formed of fused cilia. From the statocyst floor, extending sagittally on each side is a ciliated groove. In the turbellarous, statocysts are lacking in the more advanced forms but do occur in the more primitive ones. The statocyst is generally located near the brain and typically consists of a large cell or nucleated vessicle containing a large vacuole in which a lithocyte is located.

In the nemertine worms only one genus is known to possess a statocyst. Statocysts in this organism consist of one or occasionally two pairs of vessicles located within the brain tissue. These vessicles contain a spherical or dumbbell shaped statolith and non-ciliated epitheium.

Several of the polychaete worms have statocysts which are located in the head or anterior region of the body.

Among the arthropods, the crustaceans are particularly well known for their statocysts. Much present knowledge of the mechanisms and principles of statoreceptor function has come from studies on crustacean statocysts. Number, location, and structural detail of statocysts differ among the members of this group. The small crustacean Mysis, has statocysts located in the tail and last pair of legs. In the crayfish (Cambarus), the lobster, and many other crustaceans, a pair of statocysts are located in the basal segment of the antennae. These statocysts contain sensory cells with hair-like processes among which allocated number of large statoliths (usually sand grains). In some cases the sense cells occur in ridges referred to as sensory cushions. Beneath the sensory cushion are glands which secrete a substance which attaches the statoliths to the hairs.

Many molluscas have statocysts which are generally found near the pedal ganglion although their afferent nerves go to the cerebral ganglion. In this phylum, the Amphineura do not have statocysts.

Among the echinoderms only the sea cucumbers are known to have statocysts. The number occurring in this organism is variable and they do not have ciliated cells but each cell of the statocyst contains its own intracellular statolith which it secretes.

2.1.6 Discussion

An indirect experiment involves relating sensor response to an input not directly applied to the sensor but to a system of which the sensor is a part. This is exemplified by the report of Guedry in which head movements are related to cupula movement. The system may be simplified as shown in Figure 2-5, in which the viscous endolymph moves across and around the cupula deflecting it from the static position.

Guedry related cupula behavior to the well known equation for a damped torsion pendulum. By obtaining solutions to that equation theoretical curves were constructed relating cupula movement to head movement with the viscous endolymph as the coupling agent. However, no measurements were made of endolymph movement and no data were taken on nerve signals. Such information is indirect since it does not relate known inputs to the sensor to measurement of sensor response.

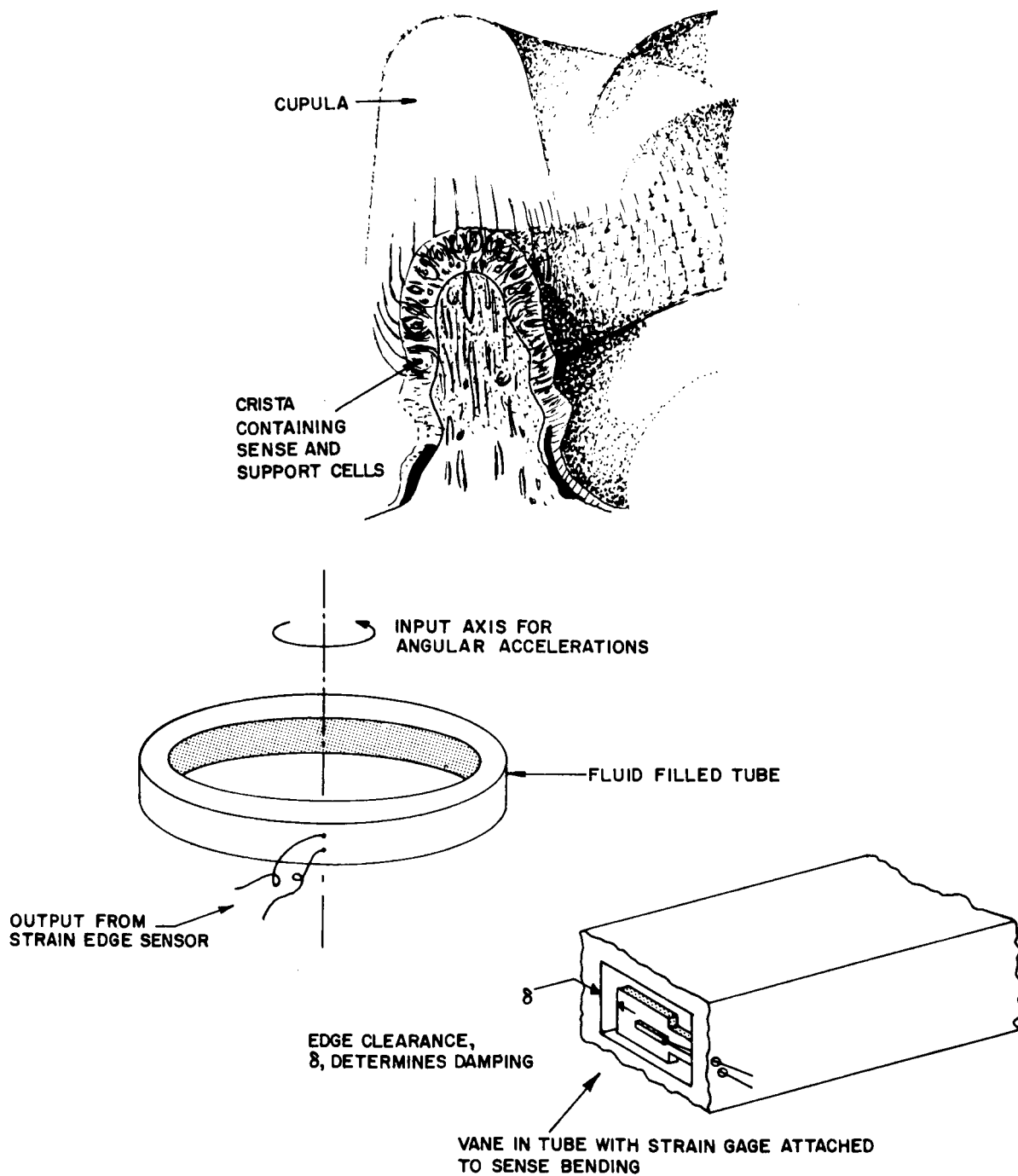


Figure 2-5. Schematic of Cupula Motion and Mechanical Equivalent.

Discussion of Experimental Observations

While the work of Guedry specifies the manner in which accelerations are sensed mechanically, he does not identify the specific mechanism or discuss the manner in which the information is transmitted into and through the nervous system. However, Guedry did point out the important observation that response was mainly to the transient or onset stage of acceleration after which exponential signal decay was observed.

Much of the work discussed in the preceding section is typical of many of the studies conducted on orientation and equilibration. It may be proper to classify them as **symptomatic studies**, or perhaps **behavioral studies**. During the last few decades, however, investigators have begun to examine the specific action of localized regions of the labyrinth with the purpose of identifying the specific function of each element and its relation to the transmission of information through the nervous system. Representative of this approach is the work done by Lowenstein and his colleagues, two examples of which have been selected for discussion.

Lowenstein and Roberts, (Ref. 2-29) developed a surgical technique for isolating the otolith organs of the thornback ray. By subjecting this system to controlled amounts of tilt while recording the electrical impulse discharges initiated at various locations in the organs of the labyrinth, they were able to discriminate between the gravity sensing components and the sound sensing system within the ray labyrinth. The oscillographically recorded traces of the firing patterns indicated that three otolith organs, the utricle, the sacule and the lagena, clearly responded to gravitational stimulus. This sensitivity to gravity in three organs instead of only in the utricle apparently is different from the behavior in a number of bony fish. The tilt studies were performed at rotation rates of the order of a small fraction of a revolution per second. Rotations of 360 degrees were induced with the labyrinth oriented in several different positions relative to the rotation axis. The tilting studies were followed by an examination of the relation of firing rate to frequency of sound input. The frequency ranged from 10 cycles per second to 120 cycles per second. Response to these frequencies was observed in part of the macula sacculi, the macula neglector, and the lacinear of the macula utriculi. They also concluded that the otolith bearing part of the macula utriculi, the posterior portion of the macula sacculi, and the adjoining macula lagenae do not respond to vibration stimuli but contain gravity receptors only. This clear identification of

gravity sensation with functional behavior of the communication system is reflected in the interpretation of behavioral response evident in the work of Guedry.

In connection with these studies of the ray labyrinth, one aspect appears important to consider. The tilt studies were conducted at essentially zero cycles per second whereas sound sensation studies began at 10 cycles per second. It would have been more definitive to extend the tilt studies into and beyond ten cycles per second in order to identify the decay of gravity sensitivity as a function of frequency in the gravity sensitivity organs and the rise of sound sensitivity in the other structures. This spectral distribution of sensitivity could have played an important role in pin-pointing the transition of the centers of gravity sensation to the centers of sound sensation.

The preceding articles relate to the identification of the seat of sensitivity. However, the purpose of this inquiry into the process of equilibration was to determine the possibility of providing an artificial orientation sense. Some means of augmenting gravity senses, or perhaps of bypassing their operation, would appear to be involved in order to achieve that purpose. Lowenstein conducted precisely those experiments on the thornback ray. Applying **electrical currents directly to the sensory endings** in the ray labyrinth and he was able to demonstrate that by this process the same types of firing rates could be initiated as were observed in the labyrinth tilt studies. The impulses were applied to the crista of the horizontal ampula. In man, the crista in each ampula of a semicircular canal is the sensing bed for the deflections applied to the cupola.

It is well known that many factors enter into equilibration. Highly trained athletes and fliers are less prone to distress than the average individual. Furthermore, such augmenting factors as vision play a role in controlling equilibration. Obviously, the problem of providing an artificial orientation sense is much more complex and involves many more considerations than those discussed in this elementary review. Furthermore, if a variation of electrical stimulation of the ray crista were to be attempted in man, it is questionable whether the electrical connections required for this purpose would be tolerable. Undoubtedly some other means of stimulation would be necessary.

As was pointed out by Guedry, the main sensitivities appeared to be to changes in acceleration after which a process of adaptation appears to occur. There, a tentative reply to the first of the basic questions is the indication of the

possibility of adaptation, strictly from the standpoint of orientation sensation. As far as the importance of the long time loss of equilibration, undoubtedly other factors besides direct labyrinth sensation would be important (vision, for one, and probably psychological and conditional factors). In regard to the final question of artificial stimulation a possible hint is revealed by Lowenstein's experiments on the ray.

There can be little doubt that only the most preliminary steps have been made to resolve this general problem. The possibility of creating artificial sensation on a behavioral level may be found to exist in the light of the interesting work being done with external field and radiation effects such as electromagnetic radiation. It appears worthwhile to inquire whether such a technique could function effectively in a manner similar to the artificial electrical stimulation of the ampullar crista of the thornback ray. A description of physical orientation sensing devices based on certain aspects of the biological mechanisms can be found in Ref. 2-2.

2.1 Unification Theory

A mechanoreceptor is a force biosensor. It may meaningfully function alone, as a pressure sensor in a finger, for example, or it may be a component in a sensor system such as receptors of the cristae which respond to labyrinth fluid motion, and provide acceleration information.

Some of the problems of physiological research have stimulated interdisciplinary investigations which now involve physicists, engineers and mathematicians. Perhaps one of the most fruitful areas for this type of team effort is in the realm of mechanoreception. The clear and specific quantitative understanding which an engineer requires to design effectively the instrumentation demanded by modern technology can augment the biologist's appreciation of physiological processes in this field of investigation which is directed at understanding how forces are sensed and how this information is communicated. As will be shown, these biosensors actually have forms familiar to engineers, such as levers and strain gages, for example. This proves an almost natural common ground for this investigation.

2.2.1 Unification Hypothesis

The initial perusal of literature on mechanoreception involved a comparison of the different shapes of mechanoreceptors having different functions (Fig. 2-6). The result of this comparison was the tentative adoption of the hypothesis that all mechanoreception involves basically the same mechanism which may appear in altered size and specific form depending upon bodily function. It is the purpose of this discussion to present the results of explorations to determine how existing evidence supports or contradicts that hypothesis and to define what further data may be required to clarify the issue. A positive result could initiate development of sensitive multipurpose instrumentation.

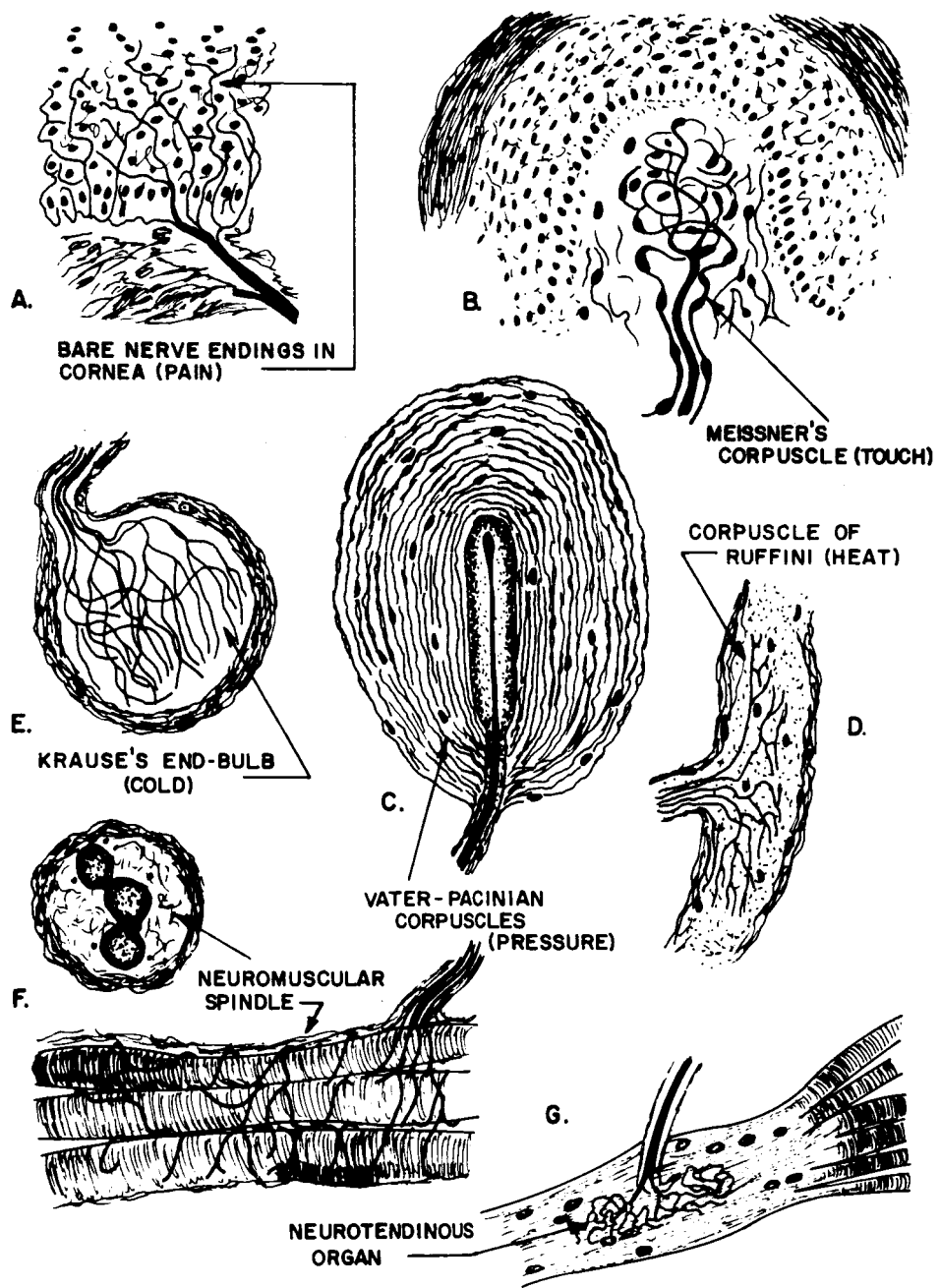
The root of this hypothesis of unified mechanoreception is the fact that the basic mechanism of reception is a small pressure sensitive bulb which is activated by pressure induced directly or through a lever system. It is further hypothesized that the mechanoreceptive elements (including thermal receptors, pressure receptors and force receptors) all utilize this basic type of sensing element.

Consider the action of a hypothetical thermoreceptor with a configuration similar to the type of receptor shown in Fig. 2-6C and with the following characteristics. The coefficient of thermal expansion of the inner material is constant with temperature and that of the outer material varies with temperature as shown in Fig. 2-7. Under conditions where the temperature drops from the normal temperature, the outer material shrinks faster than the inner inducing a pressure rise and thereby activating the receptor mechanism. With the temperature rising above normal the inner material would try to expand faster than the outer and a similar effect would occur.

An additional possibility of pressure induced bulb action would be the operation of a muscle stretch receptor activated by contraction.

2.2.2 General Discussion

Mechanoreceptors usually are associated with detectors of pressure, touch, muscle stretch and equilibration. Biologists do not normally associate the sensation of temperature changes with mechanoreceptors, however, since in the sense that a mechanoreceptor is a force biosensor, this latter discrimination is proper. However, if a mechanoreceptor were to be redefined as a biosensor the fundamental element of which is stimulated by force or deformation, a broader



Diagrams of the various types of nerve endings concerned in cutaneous and deep sensibility.

Figure 2-6. Specific Sense Receptor Morphology.

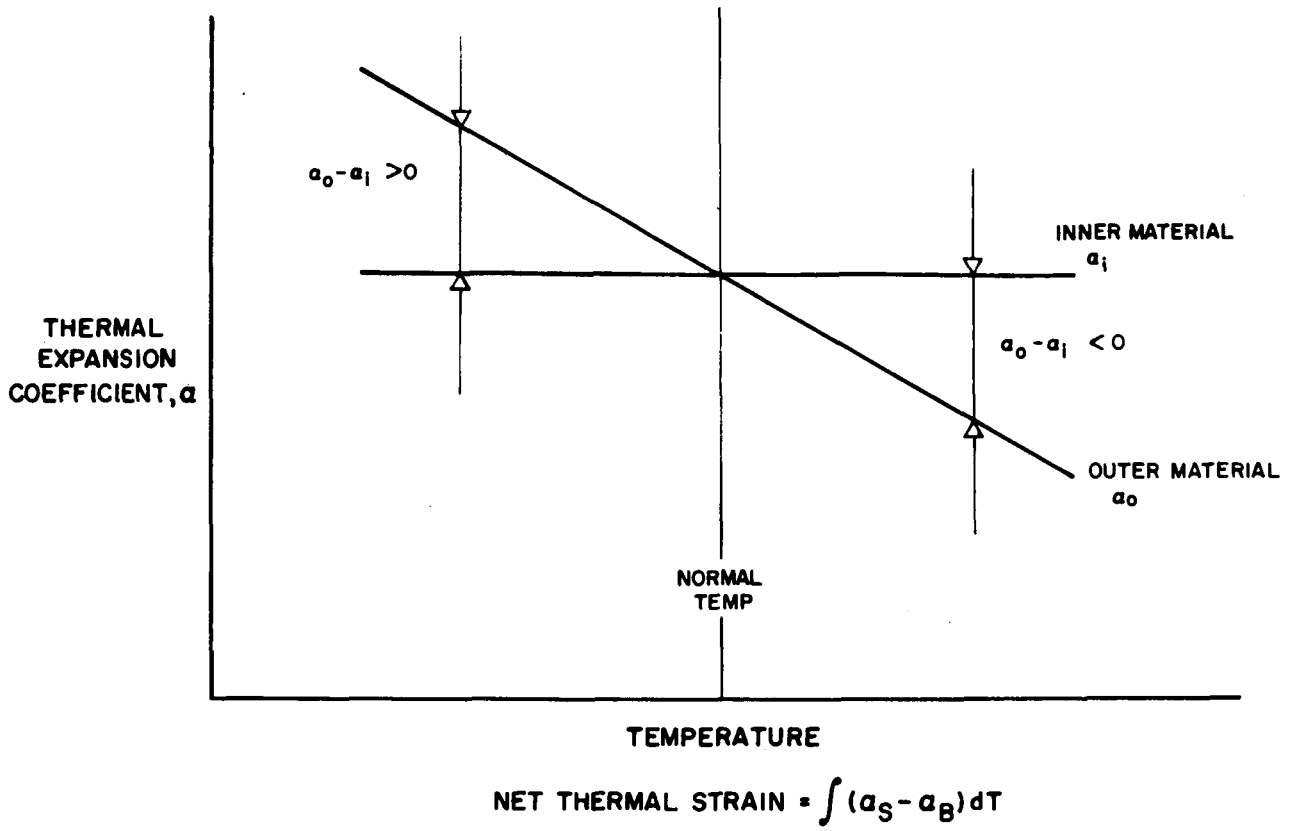


Figure 2-7. Characteristics of a Hypothetical Thermoreceptor.

significance to mechanoreception is possible. In order to include thermoreceptors in this category, it therefore would be necessary to demonstrate how force or deformations act to stimulate the fundamental mechanism. In addition, it is necessary to define what is meant by the fundamental sensing element.

On the basis of the possibility of this new categorization of mechanoreceptors, it is worthwhile re-examining the different types of receptors sketched in Figure 2-6. The ensuing review will deal primarily with pressure receptors. Effort has been devoted to highlighting the general character of data applicable to this question of the hypothesis of unified mechanoreception.

An interesting investigation was conducted by Thurm on mechanoreceptors in the cuticle of the honey bee (Ref. 2-30). He identified the seat of mechanoreception as a small bulb of the order of a micron in diameter which is so encased in surrounding tissue as to respond principally to application of pressure. Uniaxial force appeared to initiate electrical activity of a much lower order of magnitude than that produced by pressure. The transverse motions of the tip of the hair produce deflections at the root which tend to squeeze the body which is presumed to be the fundamental element of mechanoreception (transducer mechanism). The analogy to the cupula movements in the ampulla is obvious. The scale, however, is different by three orders of magnitude.

The pacinian corpuscle is an example of a bulb type mechanoreceptor. Inman has presented an excellent summary of the physiology of this corpuscle. Lowenstein has conducted experiments on the corpuscle in an attempt to locate precisely the seat of mechanoreception. These investigations, which required delicate surgery, involved the continuous removal of the onion-like shells of the corpuscle and the casing of the central core. In this manner it was possible to demonstrate that the main sensing element of the corpuscle is the rod-like core.

The stimulus applied by Lowenstein was a general pressure on a supported core. The precise nature of the mechanical input was not defined. As a result, questions remain. Does the core behave essentially as a strain gage? There is little doubt that the onion structure could transmit longitudinal forces to the core thereby initiating a strain gage type of action. Furthermore, it is not possible to deduce, from Lowenstein's description whether the core functions as a resistor, a capacitor or an inductor.

Hubbard also has examined the action of the pacinian corpuscle. However he studied the complete body in which stimulus was initiated by squeezing between plastic plates. Lowenstein has been investigating the heart of the mechanoreception process and the functional behavior whereby information on the application of a stimulus is communicated to the nervous system. Since the axis of the pacinian corpuscle is in the order of one millimeter long and a small fraction of that length in diameter, the investigation of the body identified by Thurm in the honey bee cuticle may not be possible for many years in the future since that element is only one micron long. Furthermore, the clear identification of the mechanoreceptor function in the pacinian corpuscle requires further experiments of considerable delicacy to identify the precise nature of the mechanical stimulus which triggers the corpuscle sensing element. It is possible to consider the behavior of the core of the pacinian corpuscle analogous to the behavior of the electric strain gage. In this instance the relationship holds true.

The resistance R of an electric strain gage wire of length L , area A and resistivity ρ is:

$$R = \rho L/A \quad (1)$$

by logarithmic differentiation of Equation (1)

$$dR/R = d\rho/\rho + dL/L - 2dA/A \quad (2)$$

In an elastic wire with Poisson's ratio ν , the relation between the linear strain dL/L and the area strain dA/A is:

$$dA/A = -2\nu dL/L \quad (3)$$

Therefore, Equation (2) becomes:

$$dR/R = d\rho/\rho + dL/L (1 + 2\nu)$$

or

$$\frac{dR/R}{dL/L} = \frac{d\rho/\rho}{dL/L} + (1 + 2\nu) \quad (4)$$

The quantity $(dR/R)/(dL/L)$ in Equation (4) is termed the gage factor G . It is usually determined by calibration of the completed gage. Since ν is readily found for the gage material, then the quantity $(d\rho/\rho)/(dL/L)$ may be found from Equation (4). This quantity is the percentage change in material resistivity due to uniaxial applied strain, dL/L , the direct determination of which is a problem in electro-elasticity, a relatively new field of physics in the realm of generalized continuum mechanics.

Another important feature of the preceding strain gage analysis is the precise description of the mode of force application. It is a uniform longitudinal tensile force. Neither Loewenstein nor Hubbard, in their investigations of the pacinian corpuscle, applied such a clearly defined loading to the corpuscle in evaluating the response. The forces were generally vague pressures. They were localized in different fashions and were impossible to define.

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SECTION 3. CHEMORECEPTION

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REFERENCES

3. Chemoreceptors

Previous reports (Ref. 3-1 and 3-2) have dwelled upon the processes involved in external chemoreception specifically those concerned with taste and smell in the higher vertebrates. It is the intention, in this report, to survey the area of internal chemoreception in the higher vertebrate, lesser known chemical senses in the invertebrates, (with particular emphasis on insects), and to explore potential applications of these mechanisms to engineering design.

3.1 Internal Chemoreceptor - Mammalian

Chemical composition and circulation of blood appear to be controlled through the respiratory and cardiovascular centers by means of various chemical and pressure sensitive cells located in two specific areas, the Carotid and Aortic bodies (Fig. 3-1). Extensive investigations have been conducted into the exact role played by these important areas in vertebrates and invertebrates. In vertebrates, both of these bodies are composed of small masses of tissue located in the bifurcation of the common carotid artery on each side and are close to the arch of the aorta.

These chemoreceptors are significant because they are sensitive to O_2 tension as well as CO_2 tension in the blood perfusing them. They provide, reflexly, for the regulation of respiration by monitoring the partial pressure of O_2 . In this way they provide the major chemical control of circulation with a rapidity (reflex) of response lacked by the higher respiratory centers. These receptors act to maintain homeostasis and as such they play an important role in determining changes in the rates of respiration, blood pressure and heart beat which have to be made to counteract internal or external conditions other than normal.

These receptors also serve to increase the rate of blood flow when the oxygen tension (partial pressure) in the blood is inadequate. This occurs for example, at high altitudes or when various poisons that interfere with intracellular oxidative mechanisms are introduced into the body. Corresponding stimulation of breathing and increased blood pressure also excites various pressoreceptors located near these bodies which in some manner act as a protective mechanism, preventing excessive rises in blood pressure by inducing bradycardia. The interrelationship between the chemo- and pressoreceptors of the carotid and aortic bodies is not yet fully understood.

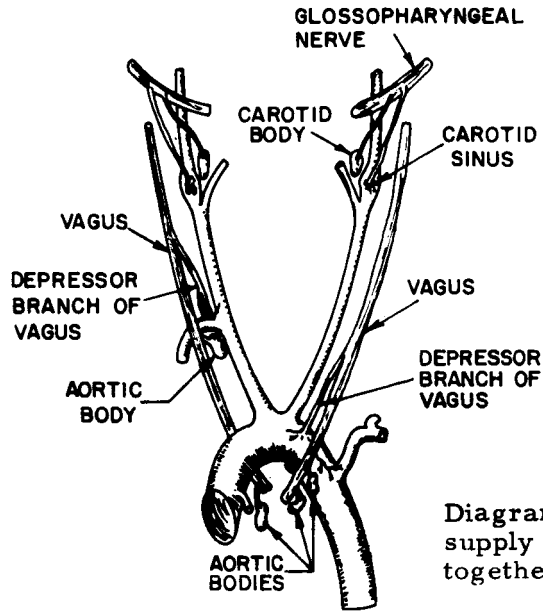


Diagram illustrating position and nerve supply of carotid sinuses and aortic arch, together with carotid and aortic bodies.

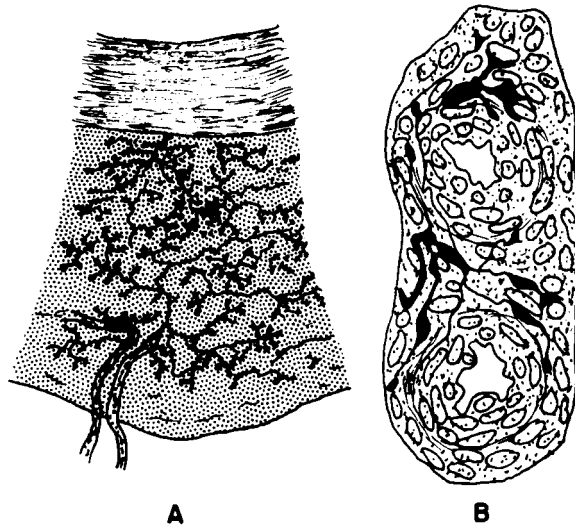


Diagram showing characteristics of afferent endings in (A) carotid sinus and (B) carotid body.

Figure 3-1. Carotid Body Morphology.

In addition to the carotid and aorta chemoreceptors, various chemoreceptors are present in the respiratory centers of the brain itself. Conclusions reached seem to indicate that the carotid and aorta bodies are more sensitive to O₂ and CO₂ while the respiratory center has a lower threshold of response to pH changes.

As blood chemoreceptors both the carotid and aortic bodies receive an abundant blood supply with the main difference being that the aortic body samples the blood soon after it leaves the heart while the carotid bodies sample specifically the blood going to the head. However, both functions appear to be the same.

3.1.1 Carotid Body Morphology

The histological investigations of DeCastro (Ref. 3-3) have shown that the nerve endings in the adventitia of the carotid sinus constitute the anatomical basis for the sinus reflex. In conjunction with the presence of these nerve endings one finds a thickened adventitia, a thinned-out media, and, of course, the increase in calibre which constitutes the bulbus or sinus caroticus. Boyd (Ref. 3-4) points out that the significance of the dilation itself, as an integral part of the receptor mechanism, does not appear to have been given the attention it deserves. The thinning of the media of this segment of the carotid system allows any change in blood pressure to be registered more readily by the nerve endings in the thickened adventitia. The unequal rates of development of the media and the adventitia of the carotid sinus, as compared with adjacent carotid segments, are detectable in the latter part of foetal life and are unmistakable in the full-time foetus. The dilation itself, may or may not be present. In a certain sense, the thinning of the media is primary, and the dilation secondary, either as a direct consequence of the thinning or as the result of a definite growth pattern. It can be shown that the presence of the dilation as a factor modifying the pressure in the commencement of the internal carotid artery can increase the efficiency of the carotid sinus mechanism markedly. This statement is justified by a consideration of the physics of dilation in a vessel subject to hoop-tension. In such a system, neglecting the lengthwise tension, the formula for the excess of internal over external pressure is given as:

$$P = \frac{T}{r} \quad (1)$$

Therefore, an increase in pressure in the narrower portion of such a vessel will cause less change in the tension of the vessel than will occur at a dilation in the vessel.

Any signal which is in response to expansion of a vessel wall will work more effectively at a dilation because the effect of changes in pressure in the general arterial system are magnified at the dilation and consequently, the nerve ending of the afferent nerves which are the receptors in this reflex control system regulating circulation are able to register the changes in pressure more readily than at a narrower part of the vessel. Boyd has shown that:

where p is the pressure, T is the tension and r is the radius of the vessel. From Equation (1) it is easy to show that $P = \frac{T}{r}$

$$\frac{\delta p}{p} = \frac{\delta T}{T} - \frac{\delta r}{r} \quad (2)$$

Now on the elementary theory of elastic substances T is simply proportional to the fractional extension,

i. e. $\delta T \propto \frac{\delta r}{r}$

therefore, $\delta T = k \frac{\delta r}{r}$ (3)

k being a constant of the material.

Then from Eq. (2) by substitution of Eq. (3) for δT ,

$$\frac{\delta p}{p} = \frac{k}{T} \frac{\delta r}{r} - \frac{\delta r}{r} = \frac{\delta r}{r} \left(\frac{k}{T} - 1 \right) \quad (4)$$

From Eq. (1) $T = pr$,

$$\frac{\delta p}{p} = \frac{\delta r}{r} \left(\frac{k}{pr} - 1 \right) \quad (5)$$

i. e. the expansion is given by,

$$\frac{\delta r}{r} = \frac{\frac{\delta p}{p}}{\frac{k}{pr} - 1} \quad (6)$$

If there is to be equilibrium the denominator must be positive, i. e. $k > pr$. If this is not satisfied the tube bursts. Supposing it is satisfied as it must be when the carotid dilation is under consideration, then a larger r means a smaller value of $\left(\frac{k}{pr} - 1 \right)$, therefore a larger value of $\frac{\delta r}{r}$. In other words, the wide part of the tube expands more than does the narrower part. It follows from this statement that an increase in pressure in the narrower portion of the cylinder will cause less change in the tension in the cylinder wall than will occur at a dilation in the cylinder. That is, any adjustment that works in response to expansion (or to diminution) in calibre

will work more effectively at a dilatation as the changes in pressure in the general arterial system are magnified there and, consequently, the nerve-endings of the afferent nerves concerned in the reflex control of the circulation are subjected to a wider range of stimuli. (Ref. 3-4).

Studies of the carotid body have indicated that a prominent feature of the specific cells forming this organ is their granulation, best demonstrated by mitochondrial techniques. DeCastro (Ref. 3-3) described these granules as consisting of two types, true mitochondria and lipoid granules. The latter he believed to be a secretory or pre-secretory product of the cells, which at that time he interpreted as forming an endocrine organ. In a later study, he discovered the sensory nature of the carotid body, but offered no further interpretation of these granules. Hollinshead (Ref. 3-5) has also, however, produced evidence that the majority of the granules are probably not mitochondrial and has suggested that they play some part in the initiation of the carotid body reflexes.

Certain phases of the cytology of the carotid body are controversial. The outstanding features of the cells in the carotid body are their somewhat granular appearance after bichromate fixation, the presence of vacuoles (especially marked in the human carotid body), and the numerous definite granules demonstratable by mitochondrial techniques. The granular appearance of the cytoplasm with trichrome staining is apparently due to those granules which are brought out more clearly by the mitochondrial techniques. After fixation in a fluid such as Carnoy's the cell appears empty and coarsely reticular. The vacuoles of the human carotid body, which so frequently markedly distort the cells, have been variously interpreted as true vacuoles and as artefacts, either intra or extra-cellular. Many of the very much finer vacuoles in the carotid body are intracellular.

The intimate association existing between the individual cells of the carotid body and the circulatory system, on the one hand, and between these same cells and the nervous system on the other hand, would seem to be a necessity for efficient functioning of any structure which is to be influenced by changes in the chemical composition of the blood, and as a result of such change produce reflex action.

Of interest in this connection is the statement of Goormaghtigh and Pannier (Ref. (3-6) concerning the blood supply to chemoreceptors. They have described modified vessels, which they interpret as the arterial segment of arterio-

venous anastomoses, as a characteristic feature of the carotid body and of the chemoreceptor tissue about the heart. They believe the sole blood supply to chemoreceptor tissue is through such arterio-venous anastomoses, and state that the chemoreceptor cells surround the venous segments of these vessels. According to them, this vascular pattern is a distinguishing feature between motor paraganglia and chemoreceptor tissue (which they interpret as sensory paraganglionic tissue).

Hollinshead expresses skepticism on this point. While he found that arterio-venous anastomoses may occur within the carotid body they are by no means characteristic of this tissue.

3.1.2 Chemoreceptor Function

Chemical control of respiration is achieved in two ways:

1. The neurons of the respiratory center are directly responsive to changes in CO_2 pressure, acidity, rate of flow, temperature, and O_2 pressure of the arterial blood which perfuses the medulla oblongata. The CO_2 pressure is by far the most significant of these factors in the regulation of breathing.
2. Chemoreceptors located in the carotid and aortic glomuli are stimulated by a decrease in O_2 pressure, and by an increase in acidity and CO_2 pressure of the arterial blood which richly supplies them. Nerve impulses from the chemoreceptors are conducted to the medulla oblongata over afferent fibers of the ninth and tenth cranial nerves. These impulses reflexly regulate the activity of the respiratory center. A decrease in the O_2 pressure of the arterial blood is the most significant of these chemoreceptor stimuli. The reticulated endings in the aortic and carotid bodies are tonically active at the normal carbon dioxide and oxygen tension of arterial blood. The frequencies of impulse discharge increase with a rise in the carbon dioxide tension in the arterial blood perfusing the aortic body and carotid sinus. This phenomenon also occurs concomitantly with a decrease in oxygen tension. Conversely, if the carbon dioxide tension falls or if the oxygen tension rises, the neural activity falls below the normal to active tonus.

3.1.3 Possible Mode of Operation

Carotid and aorta chemoreceptor response mechanisms are quite complex. Bein (Ref. 3-7) has considered that chemoreceptor cells produce various anaerobic metabolites which are removed by the blood flowing through the surrounding glomus tissue. However, if a small concentration remains it may be sufficient to cause chemoreceptor firing. Thus, by reduction of oxygen pressure of the arterial blood supplying these cells, the rate of formation of these metabolites may outstrip their rate of removal by the flow of blood. Another factor to be considered is that these metabolites may be either basic or acidic and thus are able to partially control the PH of the cells themselves. Winterstein (Ref. 3-8) takes the view that insufficient oxygen supply or excess CO₂ leads to the production of acid substances. Another possibility which has not been previously considered is that in the case of carbon dioxide the enzyme carbonic anhydrase which is necessary to rapidly dissociate formed carbonic acid is somehow inhibited by these metabolites thereby permitting excess acidity to build up. Various chemical changes in conditions which occur at these chemoreceptors serve to either enhance or inhibit the production of acetylcholine (ACh) by their actions on cholinesterase. ACh, of course, has long been speculated as the chemical transmitting agent for conduction and initiation of impulses along axons at synapses. The carotid and aorta cells may well behave similarly to synapses in their function. The fact that certain other substances such as nicotine and lobeline also stimulate these nerve endings may tend to corroborate this theory to some extent. Also, drugs such as atropine, curarine and decamethorium which adversely affect ACh have been found to decrease or even completely abolish the responses.

Winterstein also takes this view in part that insufficient oxygen supply or excess CO₂ leads to the production of acid substances. Another possibility which has not been previously considered is that in the case of carbon dioxide the enzymes carbonic anhydrase which is necessary to rapidly dissociate formed carbonic acid is somehow inhibited by these metabolites thereby permitting excess acidity to build up. Of course the possibility always exists that chemical changes in conditions which occur at these chemoreceptors serve to either enhance or inhibit the production of acetylcholine by their actions on cholinesterase. Acetylcholine, of course, has long been speculated as the chemical transmitting for conduction and initiation of impulses along axons or at synapses. The carotid and aorta cells may well behave similarly to synapses in their functions. The fact that

certain other substances, such as nicotine and lobeline also stimulate these nerve endings may tend to corroborate this theory to some extent (Ref. 3-9). Also, drugs such as atropine, curarine and decamethorium which adversely affect acetylcholine have been found to decrease or abolish the response of chemoreceptors to lack of oxygen (Ref. 3-10). According to Hollinshead and Sawyer (Ref. 3-11) the carotid body contains nonspecific as well as specific, cholinesterase, the former being present in larger amounts than the latter. Using histochemical methods, Koelle arrived at the same conclusion and pointed out that the presence not only of the specific but also of the nonspecific cholinesterase indicates some important function. However, it must be admitted that as yet a release of AcH from the active carotid or aorta bodies has not been definitely proved and the possibility cannot be excluded that the transmitter substance in this case could consist of some unknown choline ester with a general behavior and action similar to those of acetylcholine. This view might coincide with the relatively large amounts of nonspecific cholinesterase which have been found in the carotid body. One question which might be asked at this point concerns itself with the relationship of known pH changes on the general mechanism enhanced response of carotid and aorta chemoreceptors. This is in conformity with the theory of the acid-neurohormonal mechanism of gradation of nerve cell activity as suggested by Sessell, Brassfield, and Hamilton (Ref. 3-12) and Winder (Ref. 3-13) has observed local poisoning of the carotid nerve endings with monoiodoacetic acid. Since monoiodoacetic acid is known to suppress the intermediary or final acid products of glycolysis another possible proof of the relationship of PH to chemoreceptor response can be seen. Finally, Lilhestrand and Zotterman (Ref. 3-14) found that injection of a small dose of ammonia or sodium carbonate led to a sudden temporary disappearance of the action potentials that were initially set up by specific O₂ and CO₂ conditions in the blood stream. The initial increase in pH caused by this latter stimuli has probably been reversed in this case.

In completing this discussion brief mention should be made of the effect of poisons such as various cyanides and sulfides on the respiratory and circulatory system. Both poisons can give strong responses similar to that given by the usual lack of O₂. Apparently these substances inhibit cellular oxidation particularly of glucose and fat by reacting with selective oxidases. As previously indicated, this occurrence would probably change the equilibrium exchange of O₂ and CO₂ between alveolar air, blood and tissue. Dripps and Conroe (Ref. 3-15) divided the drugs that affect the sensibility of the carotid into two groups: those similar

to cyanides and sulfides that produce effects by inhibiting intracellular respiratory enzymes, and those which, like lobeline are synatrotopic and consequently directly affect the transmission of nerve impulses. The action of nerve gas would be similar to the latter in their effect.

It is well known that numerous chemical substances and drugs can stimulate a variety of receptors such as mechanical receptors of the air channels, pulmononary stretch receptors, stretch and pressure receptors located in the walls of the heart and many other areas (Ref. 3-16). These substances have several modes of action, they can directly stimulate the receptors, or sensitize them to their natural stimulus or paralyze them. For example, the initiation of symptoms similar to those caused by lack of alveolar CO₂ (slowing down the rated breathing) following administration of veratridine could result from the continuous stimulation of the slowly adapting pulmonary stretch receptors. The sensitization of these receptors to their natural mechanical stimulus can explain the rapid shallow breathing observed when thrichoroethylene or ether are inhaled; a paralysis of the pulmonary stretch receptors is the mechanism by which high concentrations of anesthetic gases induce certain respiratory reflexes. It remains a possibility that many of these reflexes which are experimentally initiated by foreign chemical substances are actually true chemoreceptors in their initiation of function.

Other areas chemoreceptors have been postulated to occur are thoracic areas, visceral areas, blood vessels, cerebrospinal fluid spaces, and muscles.

3.2 Insect Chemoreception

3.2.1 Introduction

Chemoreception is utilized by the insect kingdom for many purposes. Its importance to organism survival and propagation tends to be often overlooked. Their chemical senses perform the tasks of olfaction, gustation, communication, discrimination, sexual attraction and recognition (in many insects, odors are the only means for bringing the sexes together), species identification, and social cooperation (alarm, distress, departing, food, guidance).

Chemoreception is utilized throughout the animal kingdom, even among the simplest forms. Bonner has established that slime molds (multicellular cell masses) converse with one another by means of a gas "acrasin". This chemical, (emitted by one of a mating pair) is effective up to 1 mm away or over 250 times

the size of the animal, equivalent in man to about 750 feet. This chemical gas "acrasin" influences both the growth direction and acts as an aggregate inhibitor, limiting the density of neighboring colonies.

It is, however, among the insects, that chemoreception complexity is truly phenomenal. In the fire ant (*Solenopsis saevissima*) a chemical acts as a trail substance. This chemical is secreted in minute amounts by Dufour's gland. The substance is distributed by way of an extruded sting in an intermittent fashion. This trail substance not only functions both to activate and to guide foregoing workers in search of food and new nest sites but also constitutes an alarm signal which is emitted by the ants in distress.

The trail and alarm substance are only part of the ants chemical vocabulary. There is evidence for the instance of other secretions that induce gathering and settling of workers, acts of frooming, food exchange, and other operations fundamental to the care of the queen and immature ants.

The alarm scent in ant colonies is produced by various glands located either near the mandibular glands or anal glands. In the ant, *Tapinoma migerrimum*, these scents have been chemically purified and identified as two organic compounds: methylheptenone and propyl-isobutyl-ketone.

The odor trails laid down by various ant species, which serve to indicate food sources, have several interesting characteristics. A number of experiments seem to indicate that the trails are polarized and indicate direction, for if a trail is laid on a turntable which is then rotated 180°, returning ants are disorientated. Experiments delineate the ants ability to "smell direction" have yet to be performed.

Other examples of insect olfaction including a discussion of threshold values may be found in previous summary reports (Ref. 2-1 and 2-2).

3.2.2 Receptor Structure and Unified Theory of Mechanoreception and Chemoreception

In contrast to the internal mucuous membrane covered sense organs of the vertebrates, insect chemoreceptors are located at the body surface. The developmental plan is similar for all sense organs of the insect cuticle as well as for non-sensory hairs, scales, and glands (Ref. 3-17).

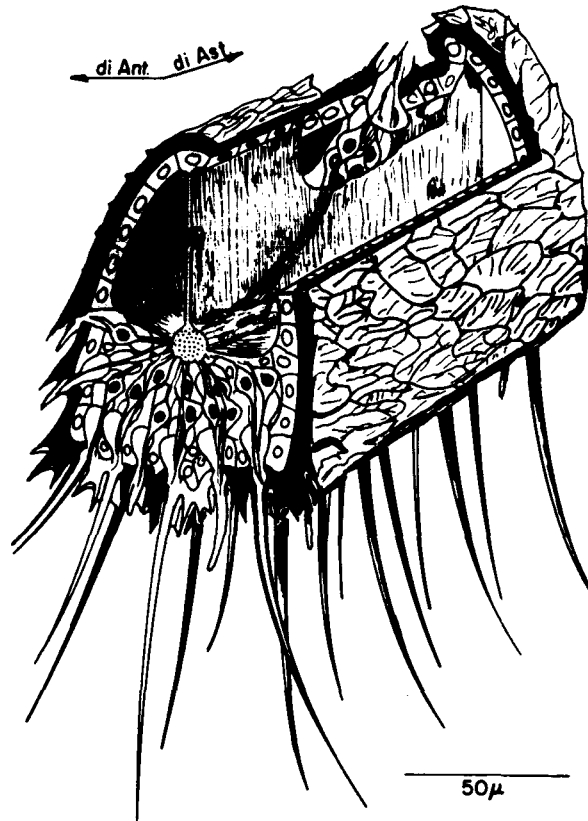
During development of the insect cuticle two daughter epidermal cells differentiate to govern the formation of a specialized area of the body surface which will serve as a contact locus for certain sensory nerve fibers. One of these two cells--the trichogenic cell--builds a hair, a peg, cup or plate-like cuticular piece. The other--the tormogenic cell--builds a ring or socket surrounding this area. Sensory nerve cells such as the formative cells of the specialized part of cuticle are also derived from epidermal cells by differential cell division. Each of these morphologically differentiated pieces of insect cuticle with its formative cells, sensory-nerve cells, and accessory cells, is called a sensillum (Figure 3-2). A single sensillum does not necessarily serve only one sensory modality.

A single sensillum may contain a number of receptors, each of which mediates a different modality (e. g. , a labellar hair, which houses a water receptor, a sugar receptor, a salt receptor, and a mechanoreceptor).

The response of a single labellar hair to more than one modality is due to the multiplicity of their associated neurons.

Previous investigators have reported experiments that indicate non-specific chemo response. Hodgson and Roeder, (Ref. 3-18), concluded that low concentrations of salt sometimes stimulate both L and S fibers (initials designate electrical response; i. e. , L = large spike and S = small spike). Wolbarsh (Ref. 3-19) stated that water stimulates L and S fibers and Hodgson and Roeder (Ref. 3-18) on the basis of the above and some additional work postulated that the primary receptor cell is responsive to chemical, tactile, and thermal stimuli within the normal physiological range and that this is at variance with the usual concept of single specificities of receptor cells. This earlier work can now be re-evaluated in light of the fact that certain hairs contain at least four distinct receptors and the following conclusions can be drawn.

1. Insect chemoreceptor hairs are compound organs which react to a number of parameters containing a number of specific chemoreceptors and usually a mechanoreceptor.
2. Each receptor performs a dual function--- reacting to the stimulus and generating nerve impulses.
3. Each receptor cell reacts with a great deal of specificity to different chemicals.



Three dimensional representation of a portion of a *Bombyx* antennal branch showing short, thin-walled sensilla basiconica and long, thick-walled sensilla trichodea (below) and one sensillum coeloconicum (above) (from Schneider and Kaissling, 1959).

Figure 3-2. Insect Sensillum.

4. There are individual receptors for salt, sugar, water and in many cases a mechanoreceptor.

The mechanics of specific molecular chemoreception have yet to be clearly elucidated. However, several theories have recently been put forth (Ref. 3-20).

In recent years (1962) Beidler has advanced the theory that the ions of the chemical stimulus are physically (loosely) bound to some specific portion of the receptor structure. Beidler based his work on his studies which assumed that the total nervous output of the receptor nerves is directly related to the number of ions or molecules which have reacted with the receptors. He derived the following equations which relate the magnitude of neural output to the concentration of the applied chemical stimuli.

$$\frac{C}{R} = \frac{C}{R_m} + \frac{1}{KR_m} \quad (7)$$

where C = concentration of applied stimulus

R = magnitude of integrated nervous response

R_m = maximum response

K = equilibrium constant.

These conclusions are based on the fact that on the data obtained with sodium salts applied to the above equation, shows that a plot of C/R against R yields a straight line. Similarly, results obtained from microelectrode measurements of the receptor potential of individual taste buds (Kimura and Beidler - Ref. 3-21) from single fiber recordings (Fishman Ref. 3-22) and from the salt receptor cell of the blowfly taste receptor (Evans and Mellon, Ref. 3-23), all produce straight line graphs when the data are plotted as C/R against C.

But, as Duncan (Ref. 3-24) points out, these chemoreceptors are merely typical of many sense organs in the possession of this hyperbolic relationship between the intensity of stimulation and the response. This relationship also holds true for frog muscle spindle (Matthews, Ref. 3-25) and the ommatidium of *Limulus* (Hartline and Graham, Ref. 3-26).

Duncan postulates a unified receptor theory explaining both mechano- and chemoreceptor mechanisms by membrane permeability changes. He hypothesizes that the change in membrane permeability in both mechano- and chemoreceptors

is produced by enzyme activity. The appropriate stimulation of the receptor activates an enzyme reaction whose initial velocity is dependent on the intensity of the stimulus thus producing a change in membrane permeability.

A hyperbolic relationship exists between the application of the stimulus and the generation of the receptor potential in both mechano- and chemoreceptor sense organs. This common relationship can be explained in terms of enzyme activity. Upon examination of the Michaelis-Menten hyperbolic equation of enzyme kinetics,

$$R = \frac{C K R \max}{(C K) + 1} = \frac{C R \max}{C + 1/K} \quad (8)$$

We can then say that the receptor potential (R) is analogous to the initial velocity of an enzyme reaction and the concentration or the chemical stimulus is analogous to the substrate concentration for both mechano- and chemoreceptors.

3.3 Mammalian Olfaction and Liquid Crystals

In the last summary report (Ref. 2-2) considerable attention was given to the various theories of olfaction. This section will concern itself mainly with the updating of previous information and the postulation of a theory of olfaction utilizing the liquid crystalline nature of the phospholipid component of membranes.

3.3.1 Phospholipids and Their Liquid Crystalline Properties

Phospholipids are a class of lipids characterized by the fact that on complete hydrolysis, they yield among other products, inorganic phosphate.

Due to the fact that they are the most polar representatives of the class of lipid, they tend to markedly lower surface tension at oil-water interfaces and thus concentrate at all membranes, which represent in a sense, biological interfaces.

It is not surprising therefore to find that phospholipids are an important component of olfactory membranes. This might be of little more than passing interest to an investigation into the mechanism of olfaction except for the recent work by Byrne and Chapmann (Ref. 3-27) who have investigated in detail the liquid crystalline nature of phospholipids. They emphasized that their work showed that the hydrocarbon chains of a phospholipid can be in a liquid condition many degrees

below the melting point of the phospholipid. Thus, it is obvious that there is a specific control on the permeability process of a membrane containing phospholipids, since a unit membrane balances on the borderline of a phase transition sensitive to specific temperatures below which permeabilities are affected.

In view of the fact that phospholipids occur in membranes, it is not unreasonable to hypothesize a theory for olfaction based on the liquid crystalline properties of phospholipids. Phospholipids fall into the class of "cholesteric" liquid crystals. They exhibit a number of peculiar optical properties. The individual molecules are essentially flat with a side chain of methyl (CH_3) group projecting upward from the plane of each molecule, are oriented with their long axis parallel to the plane of layers. (See Figure 3-3).

An optically active cholesteric liquid crystal rotates the plane of polarization through an angle of as much as 18,000 degrees or 50 rotations per millimeter.

Other interesting properties of cholesteric liquid crystals in general are circular dichroism and their optical negativity (light entering perpendicularly to the molecular layer, has a maximum velocity).

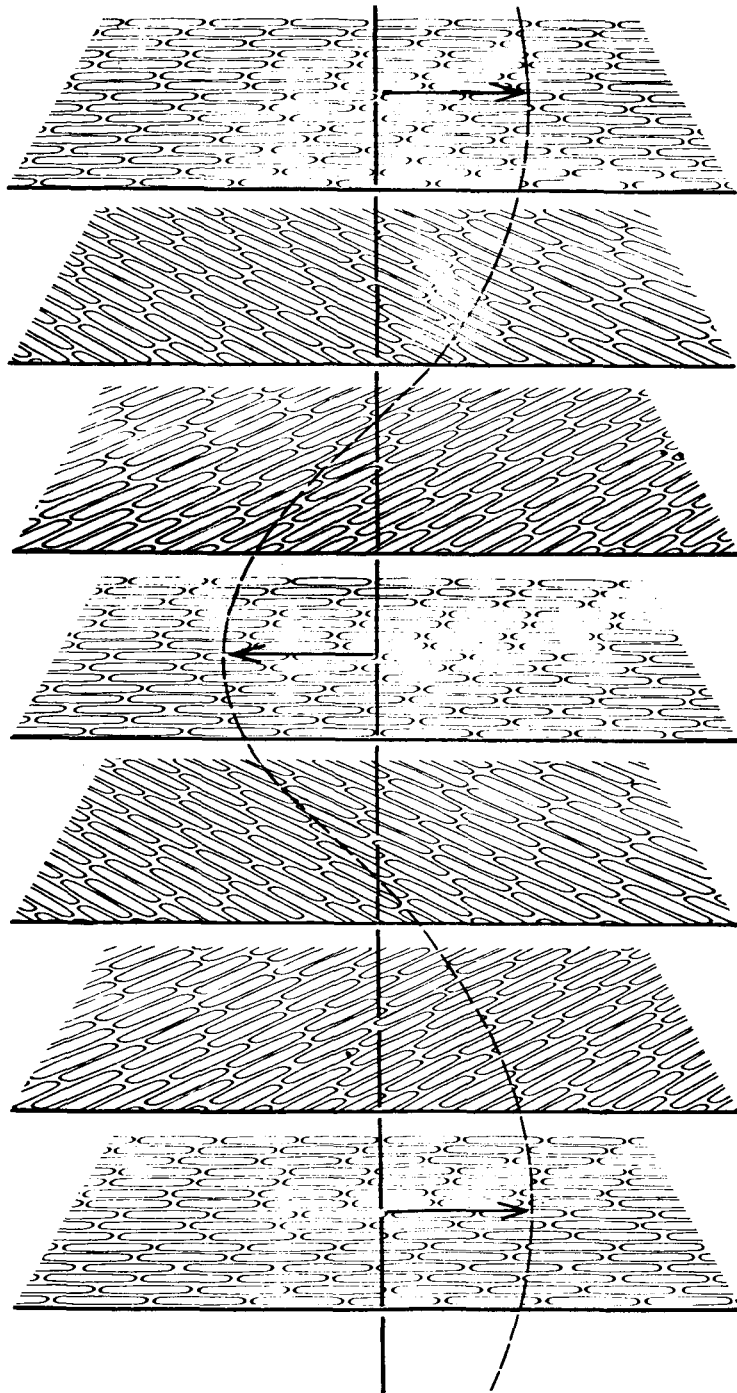
In view of the above brief discussion it can be seen that any small disturbance interfering with the weak forces between the molecules dramatically alters the optical properties of the crystal substance i. e. , reflection, transmission, birefringence, circular dichroism, optical activity and color.

3.3.2 A Theory of Olfaction

A characteristic diagram of the olfactory membrane is shown in Figure 3-4. In the olfactory epithelium the receptor sites for odorant molecules are the hair-like processes of the sense cells which are formed by extensions of the sense cell membrane.

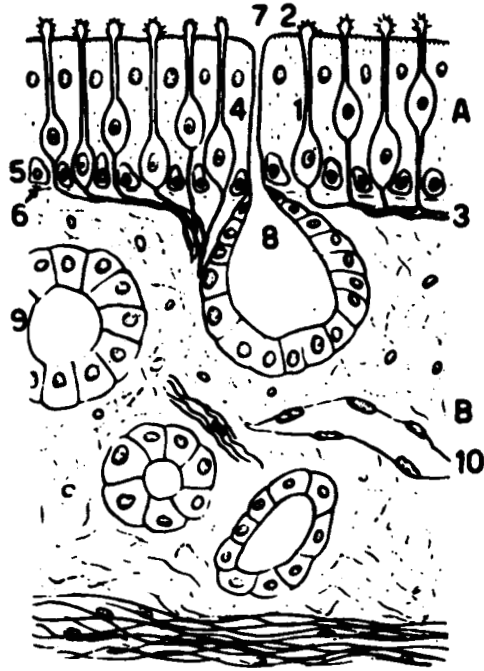
The hair cells are bipolar and oval. The hair processes vary in number from 5-6 in man to 1,000 hairs per cell in the rabbit. The individual hair is 1 to 2 μ in length and 0.1 μ in diameter.

A theory of olfaction utilizing the property responses of the liquid crystalline phospholipids might be proposed as follows.



Cholesteric Liquid Crystals resemble smectic liquid crystals in that the molecules are arranged in layers; within each layer, however, the parallel alignment of molecules is more reminiscent of the nematic phase. The molecular layers are very thin with the long axes of the molecules parallel to the plane of the layers. Because of the peculiar shape of the cholesterol molecules the direction of the long axes of the molecules in each layer is displaced slightly from the corresponding direction in the adjacent layers; the overall displacement traces out a helical path (broken line). Roughly every 300th layer is depicted.

Figure 3-3. Cholesteric Liquid Crystals.



1-2. Bipolar nerve cells; 3. Central extension of olfactory cells, 4. Cylindrical supporting cells; 6. Basal membrane; 7-8. Bowman gland. (From Gerebtzoff)

Figure 3-4. The Olfactory Membrane.

Events Preceding and During Olfaction

1. Adsorption of odorant molecule upon membrane.

(Phospholipid structured receptor membrane of hair process of olfactory cell).

2. Production of heat of adsorption. If one makes the assumption that odorant molecules are initially adsorbed at the olfactory membrane-mucous interface prior to the initiation of olfaction the resultant minute change in temperature can be attributed to the heat of adsorption of the molecule onto the membrane substrate. This heat of adsorption is proportional to the magnitude of the dipole moment of the molecule. Mathematically, the change in surface potential (heat production) that occurs in relation to the strength of the dipole moments created or induced during adsorption, may be stated as follows:

$$\Delta V = \pm 4\pi\Delta (\sigma\epsilon\mu) \quad (8)$$

where ΔV = the change in work function in volts

σ = the total number of sites per cm^2 which may be available to the adsorbate.

θ = the fraction of σ , which is available to the adsorbate.

3. Temperature changes flexing and twisting of Hydrocarbon chain of phospholipid altering permeability processes. Byrne and Chapman have documented the effect of temperature on phospholipids. Working with the infrared spectra of a pure DL- α -dipalmitoylethanol amine, they obtained evidence which points to the flexing, twisting and final melting of the hydrocarbon moiety of the phospholipid with temperature increase.

If, as Luzzati and Husson (Ref. 3-28) have suggested, the membrane (olfactory) exists rather critically on the borderline of a phase transition, sensitive to temperature and below which permeability processes are affected, then

4. Alteration of membrane permeability initiates nerve depolarization
→ sensation of smell. The alteration in the receptor membrane permeability would trigger the depolarization of the afferent nerve fiber which transmits the stimulus to the appropriate centers of the brain. This could be a result of Na^+ and k^+ movement through the membrane.

The theory discussed above pertains to the process of olfaction in general. The well documented specificity of this reception process can also be explained within the confines of this theory.

Phospholipids contain saturated and unsaturated fatty acids. Those with a trans - rather than a cis - grouping present, will have a higher transition temperature for melting of the hydrocarbon chain. These differences in configuration relative to location of phospholipids can provide a variety of receptor sites for odorant molecules of different configurations and compositions in a manner analogous to the "lock and key" theory of olfaction (Ref. 2-2).

3.4 Applications

3.4.1 Introduction

Chemoreceptors are the structures which enable a living organism to monitor its environment (both internal and external).

Some of the ways in which the functional mechanism of chemoreceptors can be applied to develop new concepts of instrumentation, enhance and extend the human senses, and improve the sensitivity of existing instrumentation are illustrated below.

3.4.2 Life Detection

The general approach in exobiology is to seek aqueous, carbonaceous life forms which are biochemically grossly similar to our own. The propulsion systems, now being considered for our space flights impose severe limitations upon the design of a life detection unit. Not only must problems of weight and power requirements be considered; there is also the very real problem of possible contamination of the target planet which must be avoided at all costs.

In this regard, a simple uncomplicated method of measuring ingestion by a monolayer of living substances which would entail little or no weight limitations or contamination problems, would be advantageous.

Numerous organic substances which arise from the products of normal living or cellular activity are surface active and readily concentrate at interfaces to give surface concentrations different from that in bulk; at the same time the surface energy of the solid or liquid is drastically altered. The mechanism by

which the latter occurs is attributed to the dual nature of these compounds wherein groups of varying polarity render certain parts of the molecule lyophilic towards the dispersing medium while other parts are lyophobic. Included in this class are polyethers, polyesters, fatty acids, phospholipids and macromolecules (proteins, enzymes, hormones).

If the surface active molecules are very soluble in the medium reversible adsorption can usually take place at the air-liquid interface with resulting isotherms similar to the well-known Langmuir type for gas-solid interfaces. Surface tension measurements offer a good method of following surface adsorption.

While the majority of surface active substances are quite soluble in the proper medium, monolayers of many insoluble long-chain or complex organic compounds can be put down on liquid surfaces if particular deposition requirements are met.

Allied Research Associates has found that the introduction of living matter into a suitable solvent or substrate will change the properties of the surface in a measurable manner. (i. e. change in surface tension). It is readily seen that a rather highly compressed monomolecular film is most essential for detecting the greatest amount of surface tension change resulting from the smallest amount of protein monolayer hydrolysis that is characteristic of the life-type metabolism taking place at the surface.

Allied Research has already demonstrated the feasibility of the above approach by experimentally reproducing monolayers of a 0.1 percent gliadin solution in increments of 7 micrograms of protein and obtaining a corresponding decrease in surface tension (See Fig. 3-5).

3.4.3 Liquid Crystals

Consideration of the functional mechanism common to both internal and external chemoreceptors, the monolayer theory of olfactory reception, and the membrane principle found in so many biosensors, has led to investigation of the development and applicability of liquid crystals as sensors. While there is evidence to support the hypothesis that liquid crystals exist in living organisms, they have not as yet been isolated or identified as such. Our investigations of the minute organizational structure found in various biosensors tend to support the theory

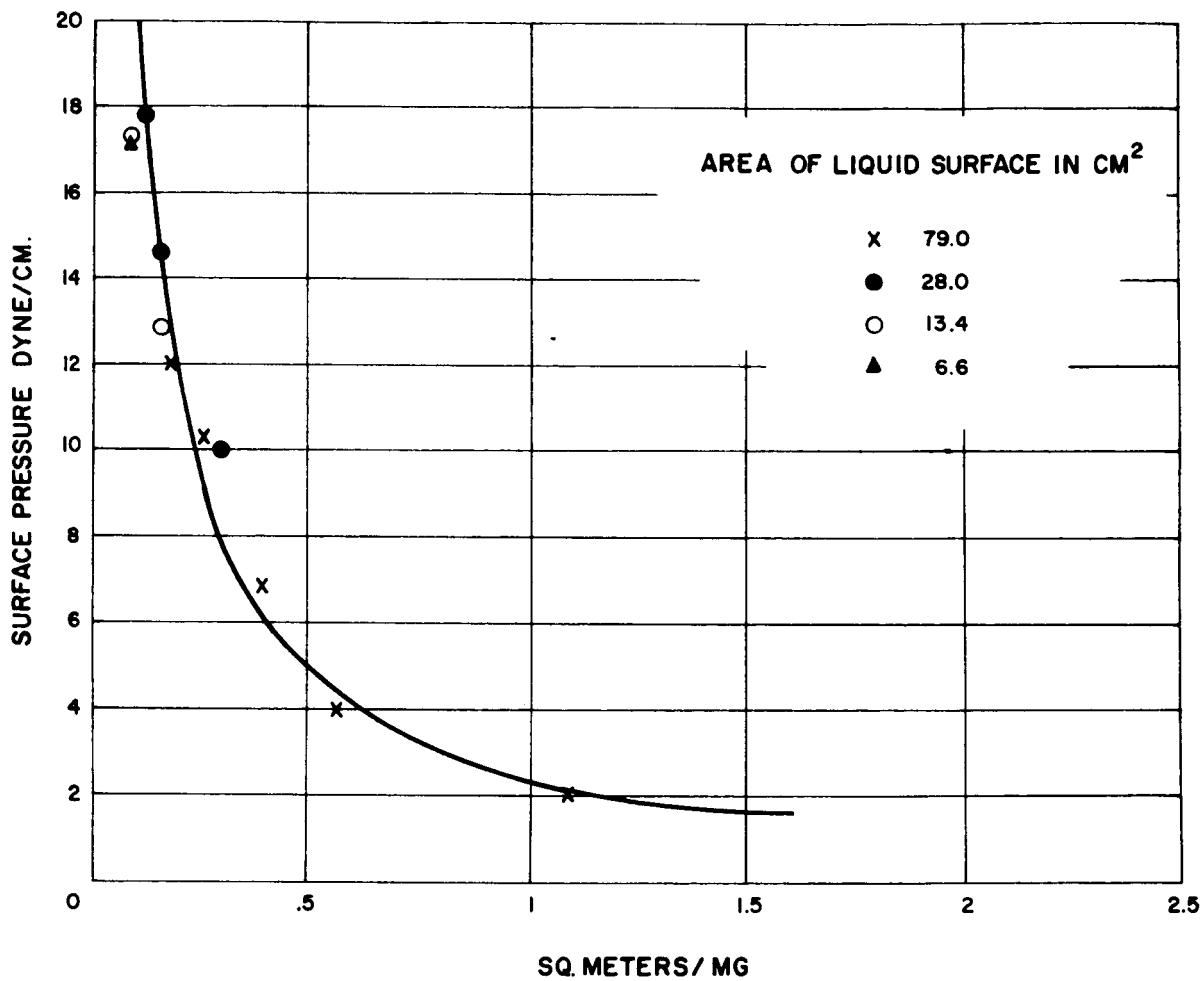


Figure 3-5. Force-Area Curve For Gliadin.

that they may be present. The identification of these crystals would be of considerable value in explaining and understanding organism reaction, sensory and regulatory function.

In view of their several unique characteristics, it seems desirable to exploit the response of liquid crystals to external stress for the purpose of specific sensor design.

Liquid crystals are fairly commonly occurring substances which share some of the properties of both liquids and crystals. Mechanically, these substances resemble liquids with widely varying viscosities while optically they exhibit many of the properties of crystals. Liquid crystals respond to minute fluctuations in chemical environment, temperature, mechanical stress, and electromagnetic radiations, by changing color. They exhibit birefringence or double refraction. Of the three principal classes of liquid crystals, the "Cholesteric" (molecule structure characteristics of a large number of cholesterol-containing compounds) are of particular interest in terms of living organisms because of the natural abundance of cholesterol in all vertebrate animals. Cholesteric liquid crystals exhibit a circular dichroism and are optically negative. They are extremely sensitive to temperature changes.

These liquid crystals seem quite well-suited for use as detectors of traces of chemical vapors. Extremely small amounts of certain chemical vapors can change their basic molecular structure and thereby affect their reflecting properties. The resultant color change can be either reversible, if the crystal serves as a solvent for the vapor, or permanent, if the vapor reacts chemically with the crystal or serves as a catalyst for some other reaction. In the latter cases, only a few parts/million cause an almost immediate color change throughout the liquid crystal substance. Various mixtures of crystal substances can be used to control color response to specific vapors. Several factors tend to suggest a relationship between the olfactory sense of animals and the response of liquid crystals to chemical vapors.

The study of liquid crystals could result in a new class of transducers and possibly multi-purpose transducers. Liquid crystals can be developed which are extremely sensitive to changes in temperature, light, chemical vapors (trace substances), and mechanical stress. As such they are potentially applicable for use in a wide variety of sensing systems.

It is well known that striking optical transformations occur in liquid crystal substances in response to subtle changes in environment. For example, by mixing cholesteric substances in various proportions, any desired temperature-color combination can be obtained. The important point is that at a specific temperature a given material or combination of materials will always exhibit the same color. Moreover, the rate of change from color to color as well as the exact temperature at which specific changes occur are invariable.

3.4.4 Membrane Detector Concept

Based upon familiarity and knowledge of the principles and mechanisms of olfaction and of adsorption phenomena, the concept for a trace gas detection system was developed, and previously reported on. This detection concept consists of membranes or films (monolayers of perhaps multilayers), on which the trace gases of interest will be adsorbed. Films could be developed of optimum and specific adsorbent compositions for particular molecules (adsorbates).

The detection system would consist of various specific monolayers deposited as a film or membrane on an electrode surface. The membrane would be specific (adsorbent) for the particular inorganic or organic molecules to be detected. Changes in surface potential resulting from adsorption of the trace molecule on the membrane surface would be detected by suitable electronic readout apparatus. Signal measurement will involve use of the Kelvin-Zisman electrostatic condenser technique.

Advantages of this detection method include rapid response, extreme specificity, and sensitivity approaching the lowest olfactory threshold found in the biological world (parts/billion-ppb).

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SECTION 4. THERMORECEPTION

4.1 Introduction

4.2 Environmental Temperature Range

4.2.1 Poikilothermous Thermoreceptors

4.2.2 Homiothermous Thermoreceptors

4.3 Possible Receptor Mechanisms

4.4 Conclusion

REFERENCES

4. Thermoreception

4.1 Introduction

Temperature is perhaps the most commonly known ecological factor, the great variation in heat conditions and their general influence are self-evident. Temperature, as an ecological factor, exhibits special characteristics: (1) it is a universal influence, (2) frequently, it is a limiting factor for the growth or distribution of plants and animals, (3) it controls all chemical processes occurring in the body of an organism, and (4) temperature is important directly as a modified of the effects of other ecological agents.

It is not surprising therefore that all living organisms react to and have the means to perceive temperature changes.

4.2 Environmental Temperature Range

In considering the mode of thermal reception, it is important to first investigate the operational range over which individual receptors might have to operate. In the open water of the aquatic environment the temperature cannot drop below the freezing point. This means that the temperature of the water in ponds is never lower than 0°C and in the ocean never lower than about -2.5°C . The maximum temperature in marine environments of any size is probably represented by records of 36°C in the Persian Gulf. In tide pools of the littoral zone and in shallow bodies of fresh water temperatures may be higher. The water in hot springs and geysers may approach 100°C and even higher temperatures occur sporadically in the very special situations presented by volcanic areas.

On land the record for the lowest temperature is held by a locality in the north interior of Siberia where the thermometer was read at -70°C (-93.6°F) in 1947. At the other end of the scale, our temperatures ranging above 60°C (140°F) are recorded in desert areas, where desert soils have been found to rise as high as 84°C when exposed to the noon day sun.

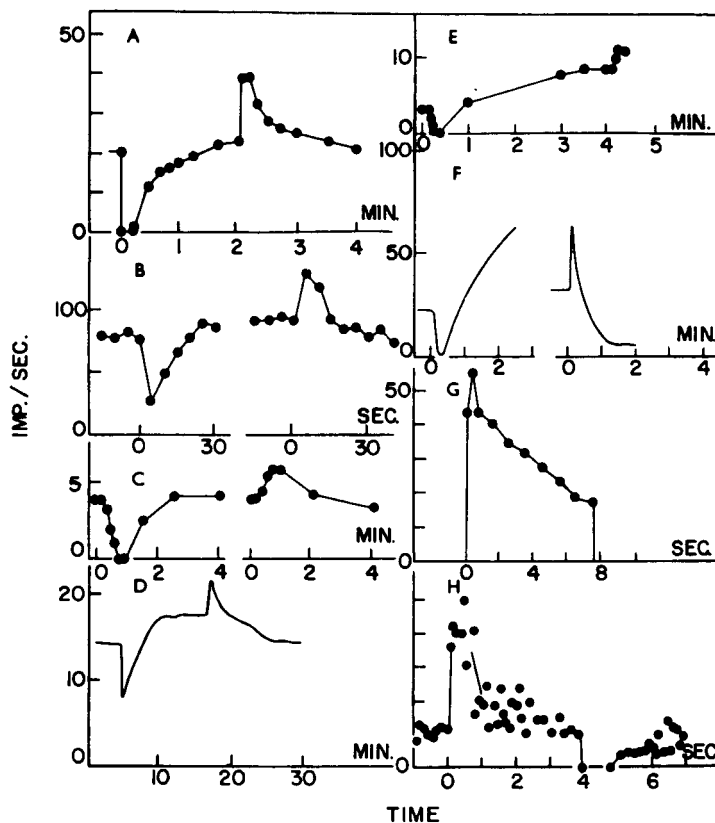
4.2.1 Poikilothermous Thermoreceptors

All animal and plants (except for birds and mammals) are poikilothermous. The tissues of these animals tend to approach the temperature of their immediate surroundings, and to vary with external thermal conditions.

The electrophysiological details of these receptors are not known in any detail. In almost all examples of electrically recorded responses to thermal stimuli, the sensitivity is so low it would seem only to be of use to the animal in a nociceptive context. There are some recordings of thermal responses which are apparently not used in temperature reception by the animal. These "side effects" may, however, be useful to an experimenter in clarifying thermoreceptor mechanisms, where a similarity of the responses to those of known temperature receptors is sufficient, and the preparation is more accessible for experimentation (See Fig. 4-1).

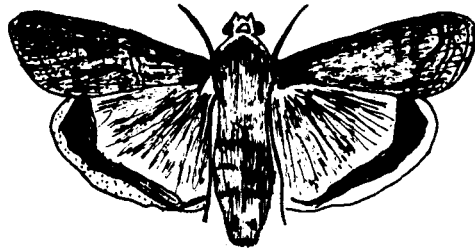
The ampullae of Lorenzini of elasmobranchs (primarily considered an electric field sensor) almost certainly should be considered in this category, for their thermal response is almost identical with that of the cold fibres of the mammalian tongue (Ref. 4-1), and yet the anatomical arrangement of the sense organs and the sensitivity which they show to other modes of stimulation makes the thermal function the least probable (mechanical stimulation Ref. 4-2, 4-3 and 4-4). The thermal sensitivity shown by the ampullae in electrophysiological experiments may therefore indicate not so much a temperature receptor function as the lack of thermal stimulation provided by the environment.

Poikilothermous organisms are usually considered unable to regulate their temperatures. This view is based on the observation that during periods of inactivity the body temperature coincides closely with that of the ambient air, rather than remaining continuously high (Ref. 4-5). Recently however, (Ref. 4-6) Adams and Heath found that while this phenomenon occurs in *Celerio lineata* the sphinx moth; during periods of activity the thoracic temperature rises to a consistent level, independent of the ambient temperature, preceding activity, and remains there for the duration of the activity period. These high thoracic temperatures are apparently maintained by a bipartite negative feed-back system reminiscent of that in mammals. On the basis of their results they believe that their results establish that *Celerio lineata* is not only capable of raising the thoracic temperature to consistent levels prior to flight, but that it is also competent to maintain this temperature throughout its activity period. The maintenance of body temperature within a prescribed range under conditions of varying thermal loads constitutes temperature regulation. This regulation may be accomplished by any combination of behavioural and metabolic adjustments. In *Celerio*, the mechanism may be compared with a model, such as a bimetallic thermostat, (Fig. 4-2). The 'on'



A. Ampullae of Lorenzini, Raja, single fibre, $+0.5^{\circ}$ then -0.5° . B. Lateral line organs, Zenopus, multifibre, $+6^{\circ}$ then -6° . C. Muscle stretch receptor, Raja, single fibre, $+10^{\circ}$ then -10° . D. Stretch receptor, Astacus, single neuron, $+5.7^{\circ}$ then -5.7° . E. Lateral line organ, Raja, single fibre, $+10^{\circ}$ then -10° . F. Abdominal ganglion, Astacus, many neurons, $+13^{\circ}$ and -6° . G. Motor nerve from leg, Maia, single fibre, low calcium, -8° only. H. Facial pit receptor, Crotalus, single fibre, $+0.025^{\circ}$ then -0.025° .

Figure 4-1. Impulse Frequencies In Various Temperature-Sensitive Preparations.



Temperature Regulation Analagous to Bimetallic Thermostat.

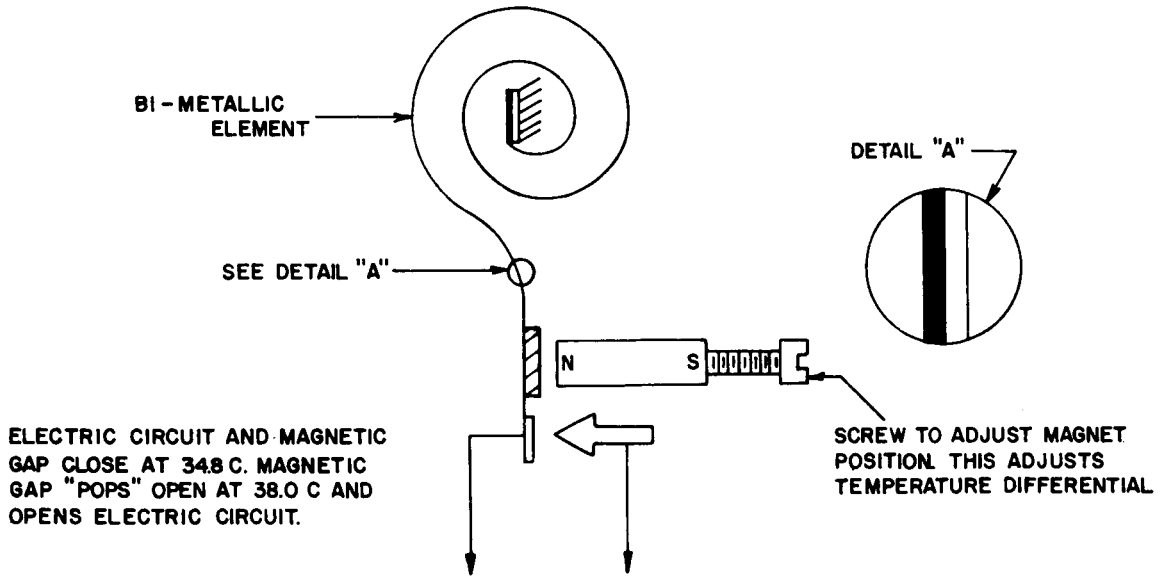


Figure 4-2. Mode of Temperature Regulation of Sphinx Moth.

response, initiation of heating by shivering, occurs at 34.8°C, and the 'off' response, the maximum voluntary tolerance or the cessation of shivering, at 38°C. At either end of the temperature range, the thermostat acts as a feed-back mechanism. Oscillation of body temperature between these limits results in homeostatic temperature regulation. This scheme differs from that in mammals, where the temperature fluctuates about a single core-level.

The ability to begin and cease activity abruptly results in economy of energy; this compensates in part for the small size and unfavorable radiating-surface volume ratio of the moth. Therefore, energy utilization in this moth may be as efficient as in those endothermic vertebrates known to undergo frequent torpor, such as humming birds. Recognition of the similarity in thermal biology of endothermic insects and small birds and mammals affords an opportunity for further investigation of energy conservation and the related problems of hypothermia and hibernation in exceedingly small warm-blooded animals.

Recently the first example of an insect (*Melanophila acuminata*) possessing distinct sense organs for detecting infrared radiation has been reported.

This insect has previously (Ref. 4-8) been reported as being attracted over long distances to a variety of burning materials such as wood, oil, mill refuse, smelter products and trash in refuse dumps. Other species of *Melanophila* are known to have similar habits. Evans (Ref. 4-7) found that all six species of the North American sub-genus *Melanophia* are attracted to fires and all possess a sensory pit contiguous with lateral margins of both coxial cavities of the mesothoracic legs.

To determine their sensitivity to infrared radiation, Evans stimulated a specimen with radiation from a tungsten lamp passing through a camera shutter and a series of lenses and infrared transmitting filters. He obtained responses at shutter speeds of 1/2 - 1/300 sec. in the wavelength region of 0.8 - 2.7 μ , and also responses were obtained from brief exposures to radiation ranging as high as 6.0 μ in a spectrophotometer.

A related species, *Melanophila drummondi* Kirby, which does not possess the mesothoracic sensory pit did not respond to wave-lengths of 1.25 μ or greater. Both species, however, responded when the antennae were stimulated

with very intense radiation passing through a Kodak 87-C filter which starts transmitting at about 0.8μ . These reactions did not take place when wave-lengths greater than 1.25μ were used and it is likely that temperature receptors which are present on the antennae of *Melanophila acuminata* and which can detect a difference as small as 2°C in air temperature were responsible for these reactions.

The above work is of special interest in so far as this is the first example known of an insect possessing distinct sense organs for detecting infrared radiation.

It would seem that the next logical step would be an investigation into the electrophysiological details of these receptors as there is a noticeable lack of this type of data concerning invertebrate receptors. The only receptor of this type that has been thoroughly investigated has been the facial pit receptors of the *Crotalidae*. A comparison of the mode of operation between the two infrared receptors, one present in an invertebrate and one in a vertebrate, should answer many pertinent questions in this area of physiology.

4.2.2 Homiothermous Thermoreceptors

Homiothermous organisms - birds and mammals - are those who maintain their own constant internal temperature and whose tissues are insulated from the heat or cold of the outside world. The thermal range that they can tolerate is generally much greater than that of other animals and plants. Limits exist, of course, beyond which these animals cannot maintain their temperature control, but by allowing a regulated amount of evaporation to take place from their bodies they can keep their own temperatures down to normal values under the highest environment temperatures ordinarily encountered. Thermoreceptors play an indispensable role for the maintenance of life for these organisms, and have been intensively studied over the years. Various types of thermoreceptors have been classified and investigated, but the dual questions as to the mode of operation and the nature of the thermal stimuli have not been definitively answered. Recent work, however, by Iggo (Ref. 4-10) does much to clarify the situation. He reported that thermoreceptors in the skin of the cat, rat and dog had properties similar to the thermoreceptors found in the tongue. The afferent fibres, however, had low conduction velocities characteristic of non-myelinated axons. The receptors fell into two categories: those excited by a rise and those excited by a fall in cutaneous

temperature, above or below the neutral temperature of the skin. At certain temperatures each of the fibres was firing steadily and when tested would continue to respond at a nearly constant rate of discharge for 30 minutes or longer. (See Figure 4-3). The very low conduction velocities of all the afferent fibres, less than 1.5 m/sec, was difficult to fit with results based on psycho-physical and nerve-block techniques in man, which indicated that most of the afferent fibres mediating cutaneous thermal sensations had conduction velocities faster than 4 m/sec, although Landau and Bishop (Ref. 4-11) have more recently brought forward evidence that in man, too, some thermal sensations can be mediated by non-myelinated fibres in peripheral nerves.

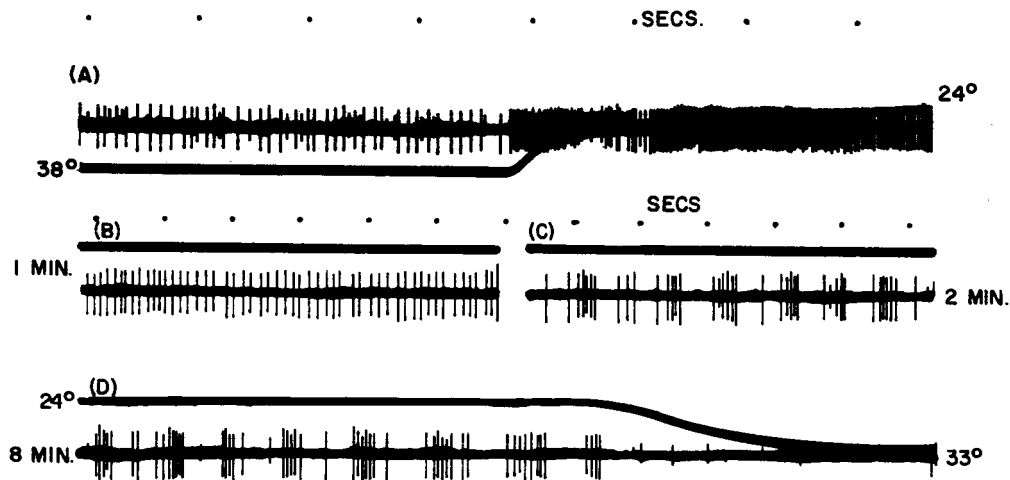
None of the receptors could be excited by innocuous mechanical stimulation such as moving hairs, stroking or pressing on the skin. Some units were excited by pressing a small probe firmly on the skin using a force (5g m weight) about 2,000 times the threshold of the most sensitive cutaneous mechanoreceptors. The thermal and mechanical receptive fields were coincident so it is likely that the mechanical stimulus was acting on the temperature sensitive elements.

The sizes of the receptive fields, the thermal sensitivity and persistence of discharge at constant temperature taken together with size of the afferent fibres suggest that if, as seems likely, man and monkey have similar cutaneous receptors, then the receptors described here have a crucial role in thermal sensation. They are probably the cutaneous cold receptors, specifically signalling thermal conditions in the skin and thus the environment.

4.3 Possible Receptor Mechanisms

Various modes of receptor mechanisms have been proposed. These range from Marcus' (Ref. 4-12) suggestion that the mechanism of reception of certain flask-like insect antennal receptors is due to an increase in gas pressure in a closed vessel due to the initial temperature rise to the theory of Williams (Ref. 4-13) that the sensitivity of the ampullae of Lorenzini might be due to differential coefficients of expansion of the enclosed jelly, the ampulla itself and the surrounding connective tissue.

At this point it is convenient to point out that while in sense organs in general, there is summation of currents resulting from relatively large potentials, the limiting factor being the resistance, which is altered as the active region changes



The discharge of impulses in a cold receptor in response to lowering the temperature of the skin. In record A. the upper trace shows the impulses in the fibre and the lower trace shows the temperature of the skin. The water flowing through the thermode was switched to 24°C. As the cutaneous temperature was falling there was an acceleration of the discharge which was maximal (peak 120/sec) before the skin had reached the new steady temperature. B, 1 min. after the change, the skin temperature was still falling very slowly and the discharge was still regular. C, 2 min. after the change the temperature was steady and the grouped discharge had made its appearance. D, 8 min. later the grouped discharge was still present and disappeared when the temperature was raised. The time marks are at 1-sec intervals.

Figure 4-3 Cold Receptor Response.

in area; this is not the situation in thermoreceptors. As Murray (Ref. 4-14) points out, in the case of thermoreceptors, the temperature change affects the whole area, but only to a slight extent. Summation of potentials due to a doubling up of the terminal branches is not feasible since a temperature difference of 1° is only 0.25 mv. The temperature change must be producing change of current (or resistance). If the above conclusion is generalized, it would lead to a concept of "generator currents". This would be the end result of the stimulus (or transmitter substance, if present) acting through resistance changes. The intensity of the "generator current" would depend upon the initial stimulus strength, and could summate at the stem axon. During the course of experimentation the actual signal detected is the generator potential (the graded potential signifying the actual current passage through the nerve membrane).

The sensitivity of a temperature receptor presupposes summation between effects in parallel branches. Utilizing the concept of "generator currents" it becomes necessary to investigate the changes in effective permeability (i. e. physical permeability minus active transport). This in effect would give a specific absolute change in current; the sensitivity of the receptor proportional to the magnitude of the resting current. Therefore the combination of a highly permeable ending, and a balancing high "pump" would give rise to a resting discharge. This resting discharge will be modulated by the temperature stimulus and the magnitude of the effect due to temperature change will increase with the rate of activity of the sodium ions.

4.4 Conclusion

The above discussion concerned itself with noting some of the latest work in the area of thermal reception and tried to point out that the complete understanding of temperature receptor function hinges upon the clarification of the events occurring during the initiation of impulses in excitable tissues. It does not seem necessary to postulate any special accessory function to explain the behavior of temperature receptors in general.

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5. PHOTORECEPTION

5.1 Introduction

5.2 Invertebrate Photoreception

5.2.1 Insect Electroretinograms

5.2.2 Biological Amplification

5.2.3 Analagous S-potentials

REFERENCES

5. Photoreception

5.1 Introduction

Photoreception is the perception of visible radiation by an organism. In comparison with the size of objects in an organisms environment, wavelength of visible light are small indeed. Therefore, since each of these objects, reflect, scatter, and absorb light in a unique manner, it is obvious that a device which would receive, correlate, and act upon this knowledge would provide invaluable environmental information. This device (a photoreceptor) is exploited by nearly all animal forms to a remarkable degree.

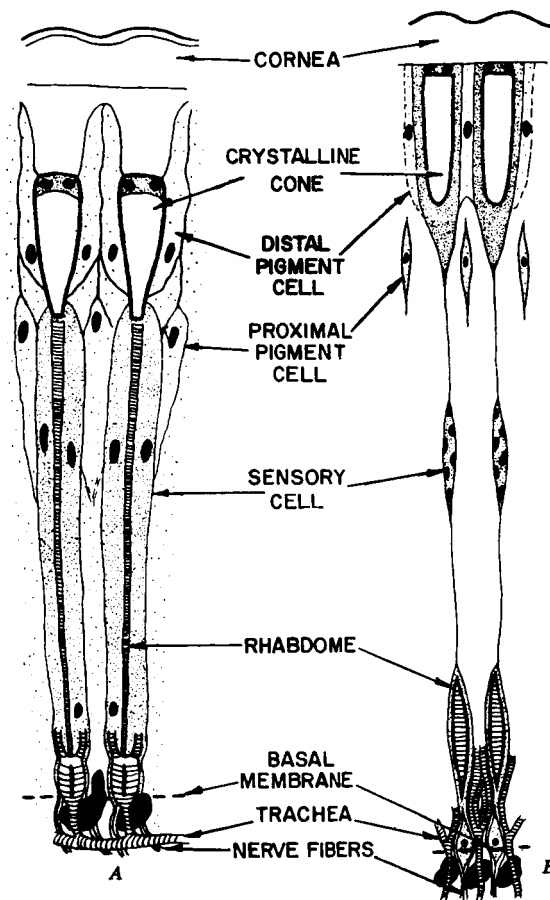
In the vertebrates the act of photoreception is one of immense complexity; not only encompassing the transduction by the battery of photoreceptors of the original stimulus into a electrochemical signal; but also transmission of information "bits" by the optic nerve fibers to the brain where it is further processed, stored, and in specific instances relayed to the appropriate effector organ. This act is only slightly less complex among the invertebrates. The objective of research into photoreception is to understand the detailed operation of the individual sub-units and integrate this relationship into the whole system.

A logical and systematic way to begin such an investigation, is to survey the animal kingdom and to look at in detail the different photoreceptor mechanisms.

5.2 Invertebrate Photoreception

Photoreceptors in the invertebrates exhibit a high degree of structural regularity (See Fig. 5-1). Photoreceptors in general, exhibit (resulting from their compact paracrystalline structure) marked birefringence; and due to the orientation of the photoreceptors, those found in the lower animal phyla (notably in echinoderms and some pelecypod mollusks) lack any accessory structures and is not associated with other sense cells to form a specific organ. The first sign of any specialization is found among the flagellates where definite organelles called stigmata, consisting of ball-like masses of opaque red or black pigment are found.

The initial reaction in any photoreceptor is absorption of photons - the quanta of radiant energy - by a pigment. The photosensitive pigments extracted from invertebrate and vertebrate eyes appear consistent in having their effective



Ommatidia from apposition (A) and superposition (B) eyes of insects. The receptor process occurs in the portion of the sense cell surrounding the rhabdome.

Figure 5-1. Insect Photoreceptor Morphology.

maximum of absorption between 400 and 700 mu - well within the spectrum visible to man.

According to Dartnall (Ref. 5-1) the study of the visual pigments of the invertebrates is in an early stage. Although only seven species of invertebrate have been examined to date, the visual pigments found have had maximum ranging from 440 to 520 mu thus indicating that all the pigments are based on vitamine A₁.

5.2.1 Insect Electroretinograms

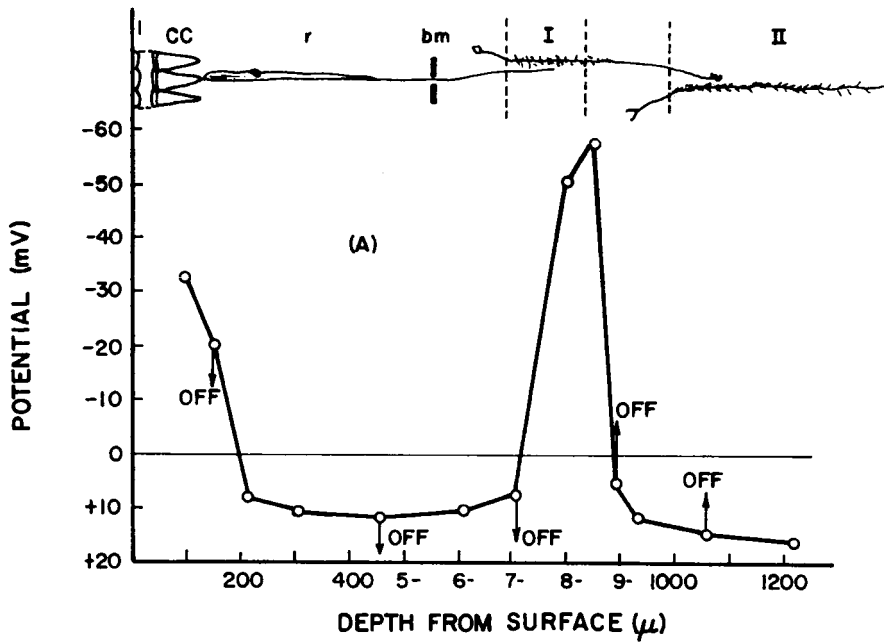
By far the most provocative work done in the past year in the area of invertebrate photoreception is that of Burt and Catton (Ref. 5-2) in determining the potential profile of the insect compound eye and optic lobe.

The insect eye and optic lobe together can be considered functionally equivalent to the vertebrate retina. Due to depth and lack of anatomical inversion, as compared with the vertebrate eye, they present a unique preparation for the study of "potential" distribution.

The nature of the insect electroretinogram (ERG) has long been a subject of controversy, however on the basis of various experimentation, it is possible to make certain conclusions concerning the nature of the ERG and of the fundamental neuronal pathways involved in the visual process. The insect electroretinogram records the potential changes present in the insect photoreceptor under varying visual stimuli. A typical insect visual receptor is diagrammatically shown in Figure 5-1. Immediately following this area (shown in the above mentioned figure) there are found three major regions of neural synapses.

A characteristic profile of D. C. potential for the eye and optic lobe of the locust is obtained by the insertion of a glass microcapillary electrode, whose resistance was 1-5 MΩ, through a hole in the cornea, for a distance of 1200 μ. A normal profile is shown in Figure 5-2. This profile shows the following characteristics.

- a. a zone of negativity near the cornea;
- b. a positive zone, corresponding in depth to the region of the retinula cells and rhabdomes;
- c. a well defined peak of negativity of a depth corresponding to the first synaptic region (first optic ganglion);



Normal profile of d. c. potential recorded along the axis of the light-adapted eye and optic lobe of a locust with above (b) a schematic section showing the structures encountered along the line of penetration. The arrows on the profile indicate the direction of the transient change of potential when the light was briefly extinguished. bm, basement membrane; cc, crystalline cone; l, cuticular lens; r, retinula cell (photoreceptor). I and II, first and second synaptic regions.

Figure 5-2. Normal D. C. Potential Profile of an Insect.

d. a return to a positive level about the same as that in (b).

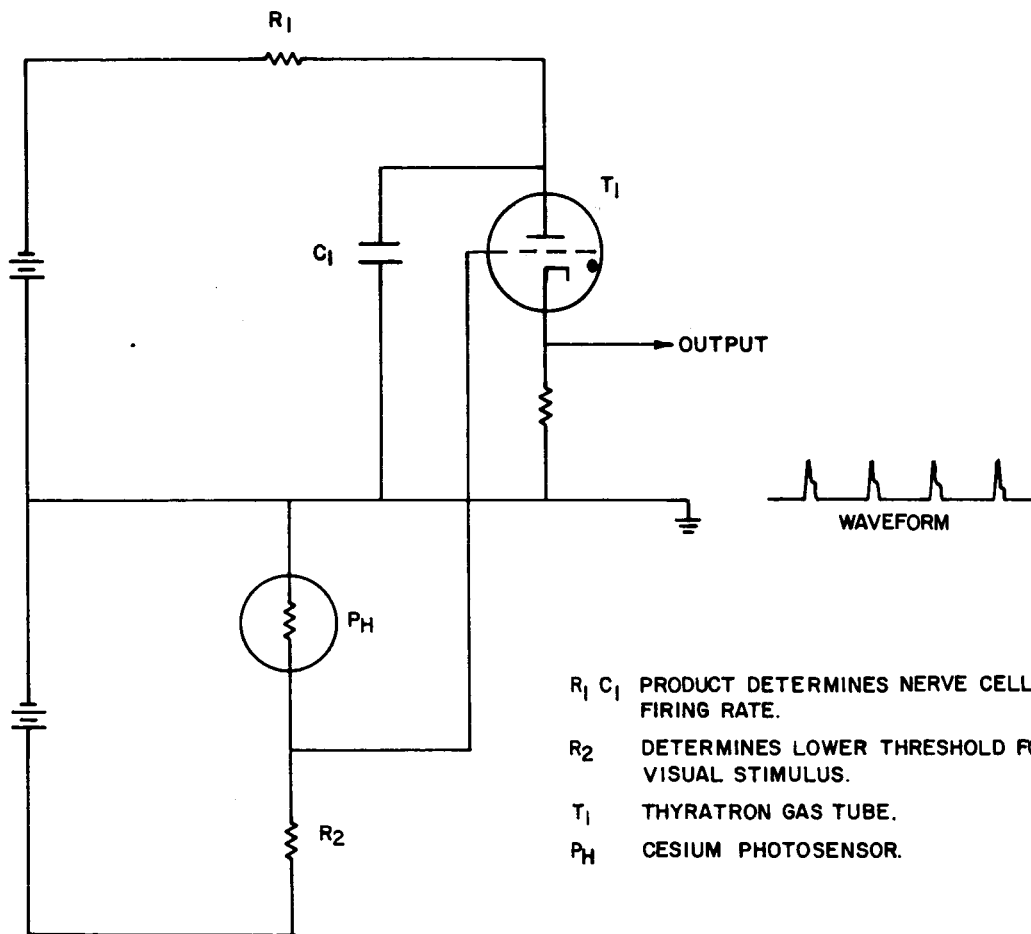
5.2.2 Biological Amplification

The significance of a large steady potential difference of about 70 mv (which exists in both light and darkness) between the photoreceptor zone and the first synaptic region of the optic lobe, is that the photoreceptor cells are exposed to a steady positive bias. D. C. biasing of sense organs is not an unknown phenomena. It is exhibited by (1) the endolymphatic potential of the mammalian cochlea, (2) the difference of potential across the pigment epithelium of the retina and (3) in insects a standing potential across the cuticle in the vicinity of sensory hairs on the labellum (Ref. 5-3). The functional significance of the polarization potential of the cochlea has been discussed in terms of a "carbon microphone" or "biological amplifier" theory (Ref. 5-4). According to this theory the primary effect of the sound stimulus is to cause a fall in resistance of the hair cells or their processes, so that current flows into the cells, the ensuing depolarization then initiating the impulse discharge. The e. m. f. which drives this current would be the sum of the membrane e. m. f. of each cell plus the polarizing (endolymphatic) potential of a 80 mv. This results in an increased sensitivity due to a much larger depolarizing current flow than would be expected from the initial stimulus, as would be the case in an unbiased receptor.

An analogous circuit to explain photoreception is seen in Figure 5-3. The circuit shown in Figure 5-3 is one possible equivalent circuit for a photoreceptor and its included nerve cell. The response of the circuit is analogous to the photoreceptor response in that the thyatron, T_1 , does not fire until the grid bias reaches a certain critical value determined by the light flux on the photosensor. After firing does commence, the circuit continues to fire at its own characteristic frequency until the light is dropped below the critical value at which time tube firing ceases.

It is not unreasonable to apply the above hypothesis to the insect eye as the following statements can easily be justified.

1. Although the polarizing potential is opposite that in the cochlea; the orientation of the receptor cells is itself opposite in the two cases.



- $R_1 C_1$ PRODUCT DETERMINES NERVE CELL FIRING RATE.
- R_2 DETERMINES LOWER THRESHOLD FOR VISUAL STIMULUS.
- T_1 THYRATRON GAS TUBE.
- P_H CESIUM PHOTOSENSOR.

Figure 5-3. Electrical Equivalent of Photoreceptor Unit.

2. The polarizing potential originating in the photoreceptor area is reduplicated in the second and third synaptic regions.
3. In both cases the sensory axon emerges on the negative side of the polarizing potential and the partial membrane depolarization produced in this way would be expected to set the threshold of the receptor fibre close to the level of impulse firing.
4. There has been experimental evidence (Ref. 5-5) that suggest that the retinula cell spikes originate in the post-retinal fibre where it passes through the basement membrane, a region where current flow would be particularly concentrated.

Experimental evidence has also been found to support the theory that there is a fall in resistance accompanying exposure to light. This is especially true in arthropod eyes. Tomita (Ref. 5-6) found a sudden decrease of resistance in photoreceptor cells of *Limulus* at the onset of illumination while Burkhart and Autrum (Ref. 5-7) recording intracellularly from single retinula cells of the eye of *Calliphora*, that a marked fall of resistance occurred during exposure to light.

The microelectrode was inserted into a retinal cell, and maximum depolarization was produced by a light stimulus of high intensity. Under these circumstances spikes originating from neurons in the optic lobe were now detected by the microelectrode; and they concluded that a marked decrease of membrane resistance must have occurred for these spikes to be detected from within the cell. They further observed that, even when the membrane potential of the impaled cell had fallen to near zero, the characteristic negative wave response to light was still obtained. Since there was no reversal of sign this wave could not have originated from adjacent cells with normal membrane potentials. They concluded that the e. r. g. response did not originate in the retinula cell bodies, but from some external structure, for which they proposed the rhabdomere.

The fall in membrane resistance of the photoreceptor cell due to light stimulation does not prove that there is a "biological amplifier" action in the presence of a polarizing potential. A fall in membrane resistance, in the absence of an external source of e. m. f. would give rise to a current flow.

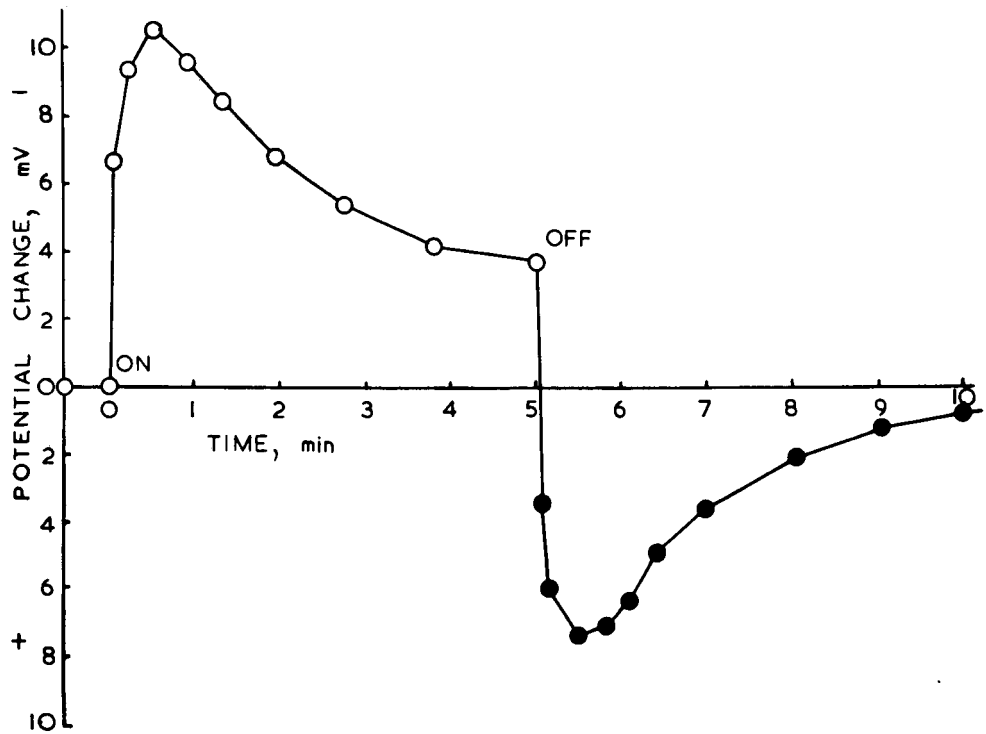
A significant response would be to show that removal of the polarizing potential modified the responses of the eye.

5.2.3 Analagous S-potentials

As a corollary to the above work experimental evidence has been found (Ref. 5-8) showing the potential changes in the eye and optic lobe during light and dark adaptation. The sequence of potential variations from dark adaptation back to dark adaptation seems to typify a system having two stable states, one in complete dark adaptation and another in complete light adaptation, (See Fig. 5-4). At the level of intensity used the final potential level was in each case transiently overshoot.

Burt et al, further concluded that the initial rapid transient and the later slow phase have separate origins, on the basis of the following evidence. When the illumination is increased in a series of steps the early transient increases more rapidly than does the final amplitude of the slow phase, and obey a logarithmic law with respect to increments of intensity. When records are made at different depths in eye and optic lobe the early transient reverses sharply in sign at the level of the first synaptic region, coincident with a strong negative peak in the axial potential profile. The slow phase does not reverse sign, but is simply attenuated. When the optic lobe is crushed, or subjected to procedures producing anoxia, the early transient is eliminated, leaving a slowly rising potential which reaches the same final value as in the normal eye.

The large wave-like potential changes are in some respects similar to the "S-potentials" of the fish retina as described by Svaetichin (Ref. 5-9). These potentials showed sharp increases at light on remained steady during illumination, and fell sharply at light off. Their amplitude was proportional to log (intensity). They were shown to originate outside the rods and cones and to have a diffuse distribution in the retina. The S-potential was however, of positive sign, such as to hyperpolarize surrounding cells and inhibit their discharge. Rushton (Ref. 5-10) has suggested that the function of these potentials is to adjust the sensitivity of the retinal elements so as to provide optimum conditions of contrast. He has further pointed out that in investigations of the Weber-Fechner law, where a luminous background is used to raise the threshold to a superposed test flash, the sensitivity change is too great and too rapid to be explained on the basis of photochemical changes, but could well be accounted for by a rapid switch of potential such as is afforded by the S-potential.



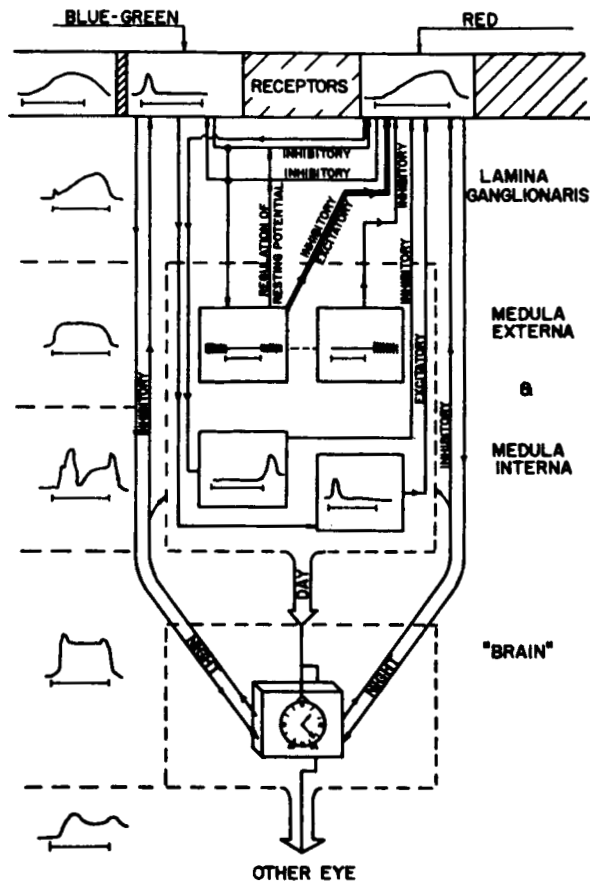
Variation of potential in retinula cell zone of locust eye during light-adaptation (open circles) and dark-adaptation (solid circles). The baseline in this figure is the steady potential associated with full dark-adaptation.

Figure 5-4. Light Adaptation of D. C. Potential Profile of An Insect.

As a final note of interest, the work of Swihart (Ref. 5-11) is worth looking into. Swihart investigated the nature of the electroretinogram of a tropical butterfly and found that this organism is programmed within its sensory ganglia in a manner comparable to that found within the motor ganglia, and that the release of these programmed patterns is affected in an identical manner (See Fig. 5-5). The visual processes in the tropical butterfly (*Heliconium erato*) are apparently highly developed to:

1. Provide accurate information concerning color, intensity, and movement. The "on" excitatory nervous component is associated with the activity of the fast, blue-green receptor, and the "off" inhibitory response is associated with the slow, red-sensitive receptor.
2. Provide information specifically relevant to the requirements of the organisms behavior patterns.
3. Maintain the primary receptor tonicity at a level optimal for the existing conditions.

The intricate programming ability of the insect brain hold the key to technical advances of a "science fiction" quality. However, it is equally apparent that the key is actually a detailed understanding of the neural excitation and conduction, and this awaits further developments in the field of micro-instrumentation.



Graphic presentation of basic waveforms and hypothetical neuronal pathways. Waveforms in left-hand column represent the effect of adding the indicated nervous tissues to the basic photoresponse. Thus, receptors alone yield only slow response. Lamina gangularis modifies this response into 'slow-fast' type waveform, etc. Extensive brain activity suppresses peripheral activity and produces 'night-type' response. Many neuronal pathways have been postulated. Four squares in the optic ganglia represent various nervous components. The two upper squares (showing single-fibre responses) represent the spontaneously active neurons and the 'post-off' effect. The precise location of this latter component is not known. The two lower squares (presenting smooth waveforms) represent the "B" wave nervous component and the 'off' effect. The brain is presumed to be the site of the biological clock mechanism.

Figure 5-5. Basic Waveforms and Hypothetical Neuronal Pathways of Biological Clock Mechanism of a Butterfly.

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SECTION 6. ELECTRO-RECEPTORS AND MAGNETIC FIELD SENSORS

6.1 Electro -Receptors

6.1.1 Introduction

6.1.2 History of Electro-Reception

6.1.3 Morphological Data on Electric Organs

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6. Electro-Receptors and Magnetic Field Sensors

6.1 Electro-receptors

6.1.1 Introduction

The essential elements of the sense organs are the receptor cells which respond to physical and chemical disturbance and transmit information about it to the central nervous system. A mere 'sensitivity' can only be termed a 'sense' if it forms part of a closed causal sequence. Sensitivity to a certain type of stimulus, even if leading to motor activity, does not constitute a sense unless appropriate stimuli arise in the normal environment.

6.1.2 History of Electro-Reception

Fish were the first organisms postulated to possess an electric sense. Descriptions of their properties are found in Aristotle, Plato, Plutarch and Galen. The school of Galen used electric organ extracts for various purposes, some of which are still in fashion in primitive populations to whom the animal is available. Electro-shock was known to Scribonius Largus, physician to Emperor Claudius, who applied electric fishes directly to the heads of patients suffering from persistent headaches. The first speculation as to their origin came from Wagner (Ref. 6-1) who in a rather obscure passage at the end of a paper on the anatomy of Torpedo, speculates whether certain structures known as Savi's vesicles conduct the excitation from the electric organ to the central parts, and hence contribute to the feeding instinct. On the other hand, Thornton (Ref. 6-2) sought to attribute the ability of blind deep-sea fish to catch their prey to the existence of an electric sense. He showed that moving fish would generate electric currents by induction in the earth's magnetic field, and that these might be detected by a predator equipped with electric receptors. The first irrefutable experimental evidence that fish possess an active electric sense was provided by Lissman (Ref. 6-3) who found a continuously varying electric discharge in *Gymnarchus niloticus* and proposed that this fish could locate obstacles by the distortion caused to the electric field around its body. This hypothesis has now been fully confirmed.

The experiments of Lissmann and Machin, using *Gymnarchus niloticus*, were designed specifically to establish that the fish could detect objects by the distortion which they caused to its own electric field in the water. The fish was

contained in a large aquarium into which could be lowered the test objects which were to be distinguished. Each test object comprised a porous pot, the central cavity of which could be filled with various solutions, or could contain water and one of a number of glass rods. Near the pot was suspended a small piece of minnow; a 'positive' reaction involved taking this food, and a 'negative' reaction was recorded if the fish ignored the food for three minutes. The fish was trained to give a positive reaction to the porous pot containing a certain solution, and to react negatively to a different solution. After any mistake, the fish was punished by dipping a copper fork into the water nearby; it appeared that the electric currents produced in the water by impurities in the wire were sufficiently discouraging. After training, two pots which were to be distinguished were presented repeatedly in random order, and the reactions of the fish noted. The test objects used can be divided into two classes: (a) pots filled with air, distilled water or paraffin wax, or having a close-fitting glass rod in their cavity; (b) pots filled with aquarium water, KCl solution of the same electrical conductivity as aquarium water, or acetic acid solution of the same conductivity as aquarium water. This fish could always distinguish between any object of class (a) and any object of class (b). It could not distinguish between objects in the same class. If it were trained to give a positive response to an object in, for example, class (a), it would then respond positively to all the other objects in class (a) without further training.

The distorting effect of a cylindrical object on the electric field can be calculated approximately. A quantitative measure of this effect is given by $a^2 \left(\frac{\sigma_0 - \sigma}{\sigma_0 + \sigma} \right)$, where a is the radius of the cylinder and σ and σ_0 are the conductivities of the cylinder and its surroundings respectively. This quantity has been called 'imprimence', a word coined to avoid the subjective implications of such terms as 'electrical perceptibility' or 'visibility'. Two test objects can now be made with different internal construction, but with the same value of imprimence. Thus a porous pot filled with a 75 percent solution of aquarium water, and a pot containing a glass rod of 9 mm. diameter in aquarium water, have the same imprimence. To both these test objects the fish gave a positive response. It reacted negatively to 40 percent aquarium water and to a 15 mm. glass rod, again objects of the same imprimence.

To summarize: the fish can distinguish between externally identical objects which cause a different degree of distortion of the electric field in the water, but cannot distinguish between objects of different internal construction which distort the field similarly. The conclusion that the fish has a true electrical sense,

involving a mapping of the distribution of electric field due to its own emissions, is inescapable. For such an electrical sense to operate, there must be a large number of receptors distributed over the body of the fish, with the aid of which the field distribution can be mapped.

The next section of this report will concern itself with a discussion of the known morphological data on electric organs.

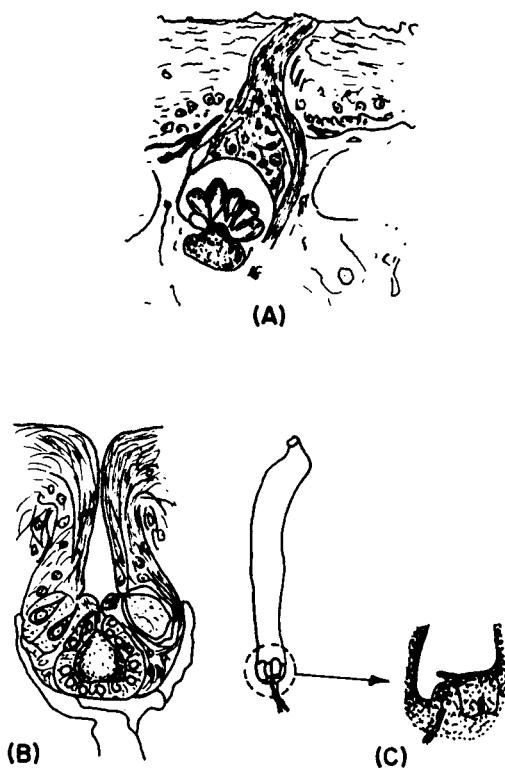
6.1.3 Morphological Data on Electric Organs

Lissman has considered in detail what structures could serve as receptors, and suggests for this role certain cutaneous sense organs, connected to the surface by jelly-filled pores. Such structures have been described in mormyrids ('mormyromasts'), Torpedo ('Savi's vesicles'), catfish ('pit organs'), elasmobranchs ('ampullae of Lorenzini') and Gymnarchus (See Fig. 6-1).

In *Gymnotus* the electric organ is made up of four pairs of roughly cylindrical structures. Longitudinally, the laminae of electric tissue are divided into small quadrangular compartments by thin collagen sheets placed perpendicularly to the thicker longitudinal septa. Each of these compartments encloses one electroplate. Both faces of the electroplate are limited by papillary formations; the papillae of the anterior face are larger than those of the posterior face. An electroplate is made up of a common mass of cytoplasm enveloped by a delicate membrane, the electrolemma; the nuclei are preferentially disposed at the interior of the papillae. Only the posterior face of the electroplate is innervated. The remainder of the compartment is filled by a gelatinous substance, stained metachromatically by thiazine and oxazine dyes; metachromasia can be prevented by the action of hyaluronidase, from which we can imply the presence of acid mucopolysaccharides.

The orderly piled disposition of the electroplates of *Gymnotus* is only seen at the caudal regions. At the medial third they are placed at different levels.

Electrophysiological studies on single electroplaques on a number of electric fishes (Ref. 6-4) have uncovered much new information contribution to knowledge of electrogenic mechanisms. One major functional difference characterizes electroplaques of marine and fresh water electric fishes. Those of the marine forms, teleost as well as elasmobranch are electrically inexcitable. In those of all the fresh water fishes studied thus far, one or both major surfaces are electri-



Cutaneous sense organs, thought to be electric receptors. (a) In a gymnotid; (b) 'Mormyromast'; (c) Ampulla of Lorenzini.

Figure 6-1. Possible Electro-Receptors in Various Fishes.

cally excitable, the electroplaques comprising the electric organs of certain fresh and salt water fishes, differ electrophysiologically not only between different species, also among different electroplaques in the same animal and even in different parts of the same cell. In some cases these differences are partly accounted for by factors of morphology, as for example, by differences in sites and densities of innervation. Others are probably base of factors residing in differences at the molecular level. It seems likely that new information might be gained from a comparative study of different electroplaques employing electron microscopic and histochemical techniques, guided by electrophysiological data on the same systems. These studies have yet to be carried out in detail.

6.1.4 Electrophysiology of Marine Electric Fishes

There are certain forms and features which seem to be common to all electric organs. The chief resistance to current flow occurs in the surface membranes of the electroplaques. The specific conductance of the extracellular fluid is high in contrast to the surface membranes which generally have very low specific conductances. Presumably this arises because the membranes have specific structural properties giving them low ionic permeabilities so that the internal environment of the electroplaques, for example, can be maintained with the characteristic ionic concentrations. Eccles (Ref. 6-5) suggests that the folding and the canaliculi are designed in order to compensate for the low specific conductances of the interfaces between the intracellular spaces by providing a large increase of the surface membrane. On the innervated side there are foldings underneath the nerve, while from the non-innervated side there are canaliculi extending into the substance of the plaques. These canaliculi provide potentially a large increase in the non-innervated surface membrane of the electroplaques, so it remains to be shown whether this increased surface can be effectively used for the flow of current from the interior to the exterior of the electroplaque. A rough calculation may be based on the assumption that the surface of the canaliculi has the same electrical properties as that of giant nerve fibers and of nerve cells. Canaliculi 500°A in diameter would have a space-constant of about $30\ \mu$, so there would be very little voltage drop as currents flow along canaliculi many microns in length, which means that they are very effective in conducting current from the interior of the electroplaque. On the innervated surface of the electroplaque, the folding also causes an increase in the effective area of the surface membrane because the transmitter diffuses quite rapidly for short distances ($1\ \mu$ in $1\ \text{m sec}$), therefore,

the whole folded innervated surface would be rapidly exposed to transmitter action and become highly permeable to all ions. Therefore, it is obvious that the canaliculi and the folds are excellent physiological devices to deliver large currents across membranes which have low specific conductances.

A. Eel vs Elasmobranch

It was established only about a decade ago by Brazilian (Ref. 6-6) and French (Ref. 6-7) workers that while the eel electric organ possesses two excitable systems, one direct-excitabile by directly applied electric currents and an indirect which responds to neural stimuli; the elasmobranch electric organs respond only by way of stimulation of their nerves.

It was in the work of Grundfest (Ref. 6-8) where he applied both direct and indirect stimulation to eel electroplaques and intracellularly recorded and analyzed the data that the full significance and the broad theoretical implications of these differences between the direct and indirect excitabilities of electric organs became apparent. His analysis led to the suggestion that the transmissional and conductile electrical activities are generated by fundamentally different kinds of membranes. One, associated with receptor and synaptic activity, responds only to neural or chemical stimuli and is electrically unexcitable. The second responds to any adequately large depolarizing electrical stimuli including the depolarizing postsynaptic potential evoked in the electrically inexcitable membrane by a neural volley. As far as known, all fresh water electric fish have organs that are electrically excitable, although an electrically unexcitable, synaptic component is present in each electroplaque. This striking difference between marine and fresh water fish no doubt has evolutionary implications.

B. Bioelectrogenesis

The chemical basis for the generation of bioelectric currents is an immensely complex area; but the work of Nachmansohn (Ref. 6-9) leads to the following conclusions.

1. The conducting membrane is endowed with the unique and specific ability to use the ionic concentration gradients existing between the interior of living cells and their outer environment, for generating bioelectric currents which propagate impulses. A rapid transitory change of Na conductance permits the flow of ions. Thus, a specific mechanism present in conducting membranes must be postulated for the process.

2. The strong initial heat coinciding with electrical activity, the high energy of activation, and the high temperature coefficient show that the electrical activity requires a chemical reaction. Since the Na conductance change is the specific event responsible for electrical activity, the chemical reaction must be linked to this specific process.

The following facts are evidence that the action of acetylcholine is essential for the **rapid transitory** change of conductance:

3. The enzymes forming and hydrolyzing acetylcholine, acetylcholinesterase and choline acetylase occur in all conducting tissues, in all types of fibers, they are not present in non-conducting tissue such as liver and kidney. This fact suggests a specific role of the acetylcholine system in conducting tissue.

4. If the action of acetylcholine increases Na conductance, its rapid return to the initial value should be made possible by the rapid removal of acetylcholine by acetylcholinesterase. The high speed of the enzyme activity satisfies this crucial prerequisite. The enzyme is one of the fastest acting enzymes known, the turnover time being around 40-50 μ sec.

5. The concentration of acetylcholinesterase is very high in all conducting fibers. The average activities, referred to gram tissue (fresh weight), are about 0.01-0.03 gm ester split per hour in fibers and 0.1-0.3g in brain or ganglia. The enzyme is, however, not evenly distributed, but localized in the region of the conducting membrane. Per gram active material, the concentration must be extremely high, permitting the inactivation of significant amounts of acetylcholine per m sec.

6. The electric organs of Electrophorus and Torpedo, the most powerful bioelectric generators created by nature and a tissue highly specialized in its function, are capable of hydrolyzing 2-4 g of acetylcholine/gm fresh tissue, in spite of the fact that this tissue contains 93 percent water and only 2 percent protein. The activity per gram active material must be several orders of magnitude higher.

These features are physiologically significant and prerequisites for attributing to the acetylcholine system the specific property of conducting membranes, namely to change Na conductance and to generate electricity. The following direct evidence has been obtained:

7. It is impossible to separate electrical and acetylcholinesterase activity. With potent and specific reversible inhibitors, electrical activity of axons is reversibly

blocked, with irreversible inhibitors, irreversibly. About 20 percent of the initial enzyme activity is required for unimpaired conduction. The interdependence of enzyme activity and function has been demonstrated with a variety of procedures and under a variety of conditions. It has been tested on all types of conducting fibers. The interdependence of electrical and enzyme activity has been demonstrated on intact axons.

8. Electrical activity, irreversibly blocked by an organophosphate, can be restored by a specific chemical reaction, namely by the reaction of the enzyme by benzoyl pyridine oxime methiodide, a compound displacing the phosphoryl group specifically from acetylcholinesterase.

9. According to theory, electrical activity is produced by the action of acetylcholine on the acetylcholine receptor protein. This receptor protein has been shown to react specifically with local anesthetics, known to block electrical activity. The stronger the binding of local anesthetics to the protein in solution, the stronger is the effect on electrical activity in the intact cell. The competitive nature between the action of local anesthetics and that of acetylcholine has been demonstrated on the intact cell.

The evidence for the essentiality of the acetylcholine receptor protein for generating bioelectricity thus supplements the essentiality of acetylcholinesterase.

10. The failure of acetylcholine and curare to act on axons has been considered to be a strong evidence against a possible role in conduction. However, it has been unequivocally shown that this failure must be attributed to the existence of structural barriers preventing lipid insoluble quaternary nitrogen derivatives to enter the axon. (a) After a long exposure to very high concentration of prostigmine (0.01 M) and acetylcholine (0.1M), the compounds are not found in the axoplasm, in contrast to tertiary nitrogen derivations which do enter. (b) Recently, rapid and reversible block of electrical activity has been obtained with curare at the Ranvier nodes of myelinated fibers where the barriers are more previous and on squid giant axons after preliminary treatment with cobra venom which apparently reduces the barriers.

11. In the sequence of energy transformations acetylcholine hydrolysis precedes that of ATP. It is capable of a depolarizing (electrogenic) action thereby excluding a role in recovery. Other compounds have a depolarizing action but none of them satisfies the prerequisites to have the physiological function attributed to acetylcholine.

It has thus been shown that the ester has the properties required for the specific operative substance in the elementary process of nerve activity in the sense attributed by Meyerhof to ATP in the elementary process of muscular activity.

6.1.5 Applications

The inevitable end to any information gathering process in the interpretation of the data. The gathering of the data can indeed be a challenging process as, for example, the electro-receptors of "Gymnarchus". But, in the end, the data analysis is the final process that produces the reason and action out of a seemingly chaotic mass of information.

The mental process in mammals used to interpret the mass of electrical data delivered from neurosensing receptors relies on a comparative process. The conclusion is reached by reviewing a mass of chaotic electrical signals and comparing these signals to some form of stored pattern of information. The comparison process operates at different levels; initially there may be a gross overall comparison to detect any difference whatsoever and then painstaking step by step scanning to find differences at very microscopic levels. Both of these methods can be brought into play sequentially as, for example, the photographic techniques used during World War II in the evaluation of aerial photographs of anti-aircraft installations. Here, the microscopic comparison of two photographs of the same area a few days apart would often fail to detect the change of a gun position, all too important to offensive action. In this case hundreds of comparisons would have to be made between small areas of two almost identical photographs. However, a scheme was devised whereby the first day photograph was taken on color film with a red filter over the camera lens. The second day photograph was taken through a green filter. These photographs were viewed in a stereoscope so that the images were fused. In this way, areas of "sameness" appeared almost dark purple, a blending of red and green. Areas on the second day photograph that were different from the first stood out in bright red. This primary comparative sorting process is comparable to the "Gymnarchus" surveying the pattern of his self generated electric field in the immediate area around his lair in an effort to detect small changes on a familiar background. Once an unfamiliar object is detected, the photo-reconnaissance reader would move to more detailed maps for microscopic examination, and analogously the electric field detecting fish would move closer to the object for more detailed observations.

At very low signal levels the *Gymnarchus* is operating well within the noise level of its electric field detection system. In fact, it is proposed that a scanning system is put into operation that raises the signal-to-noise ratio to unity when small signals are being sought after. The purpose of the scan process is to provide enough information that useable signals may be extracted from the background noise. The scheme by which the fish may extract information from signal noise might be compared to the scheme was used by the MIT Lincoln Laboratories for the radar reflection experiment on the planet Venus.

In this experiment, the distance was great enough that angular uncertainties as far as the antenna patterns was concerned were critical. Additionally, the signal attenuation was such that a successful production of an echo was not immediately obvious. For each experimental trial a record was made over a broad enough time interval to be certain that the return signal was contained in the record. Each of the single records appeared to be a record of simply white noise. However, when many records were added together on a common time base by a computing machine, the white noise remained at a constant amplitude because of the statistical cancellation of elements of the noise signal from record to record. At the location of the echo, there would be an ordered signal that would accumulate as many records as were analyzed. Finally, a strong signal would appear at the time location of the echo pulse.

It might be proposed that this type of statistical sorting is different than the comparison scheme whereby the incoming signal is compared to an old, stored signal pattern. In the case of noisy signals the first "burst" of data could be the initial input into a blank memory storage, all subsequent burst being added in on top of the preceding one. In this scheme, the position of a signal would begin to emerge from the background noise as the results of the addition of many scans of receptor information are accumulated.

6.2 Magnetic Field Sensors

In certain living systems there is little room for doubt that some sort of magnetic field sensing takes place. Unlike a gravitational field that acts upon all objects, stationary magnetic fields act upon only a few substances or elementary electrical particles. Detection of the presence of a magnetic field in all probability makes use of one of the possible interaction phenomena although any exact mechanism of performance remains a mystery.

In Figure 6-2a the magnetic fields that are generated by a bar magnet and by the earth are depicted. In these diagrams the lines represent lines of magnetic induction. The greatest density of the lines (lines per unit area) is reached right at the poles, the lowest density at great distances from the poles. This density is expressed in webers/meter² or more commonly, in gauss*. It should be noted that the magnetic field of the earth is best represented by a bar magnet of about 1/10 the earth's diameter located at the center of the earth. This gives rise to the field shown in Figure 6-2a with the approximate angles of intersection with the surface on the earth as shown. This means that at various latitudes the magnetic induction line has a unique angle with the local surface of the earth. This angle is called the magnetic declination and is one of the surface properties of the earth's magnetic field. In short, the magnetic field at any point on the surface of the earth is a vector quantity possessing both magnitude and direction.

The methods of detection of the presence (and subsequently the properties) of a magnetic field number very few and center around two basic principles: the magnetic moment imposed on a secondary magnetic field brought into a primary magnetic field (the simple magnetic compass needle, for example) or the force developed on a charged particle that is given a velocity in a magnetic field (deflection of charged, moving, nuclear particles for example). Other magnetic interactions are outgrowths of these two interactions in as far as is known. It is certainly not dismissed that there may be complex nuclear interactions that are just beginning to be disclosed by modern nuclear physics that may lead to new, novel magnetic-particle interactions, but at the level of physiological electrophenomena these interactions would not be likely to occur.

Figure 6-2b shows a brief summary of the primary magnetic interactions that totally or in part could be operative in the magnetic sensing of normal systems. The scheme of a sensor being composed of a piece of pre-magnetized solid state magnetic material, although perhaps possible, is not as physiologically appealing as the concept of a pulsed, current element shown in Figure 6-3a. The electric organ in *Gymnarchus* is an unusually developed electric generator capable of generating trains of pulses 1 m sec in width at a repetition rate of 300 cycles per second. It could be reasoned that the same elements could be brought into employment to produce current pulses in a "conductive membrane" structure as

* 10,000 gauss = webers/meter²

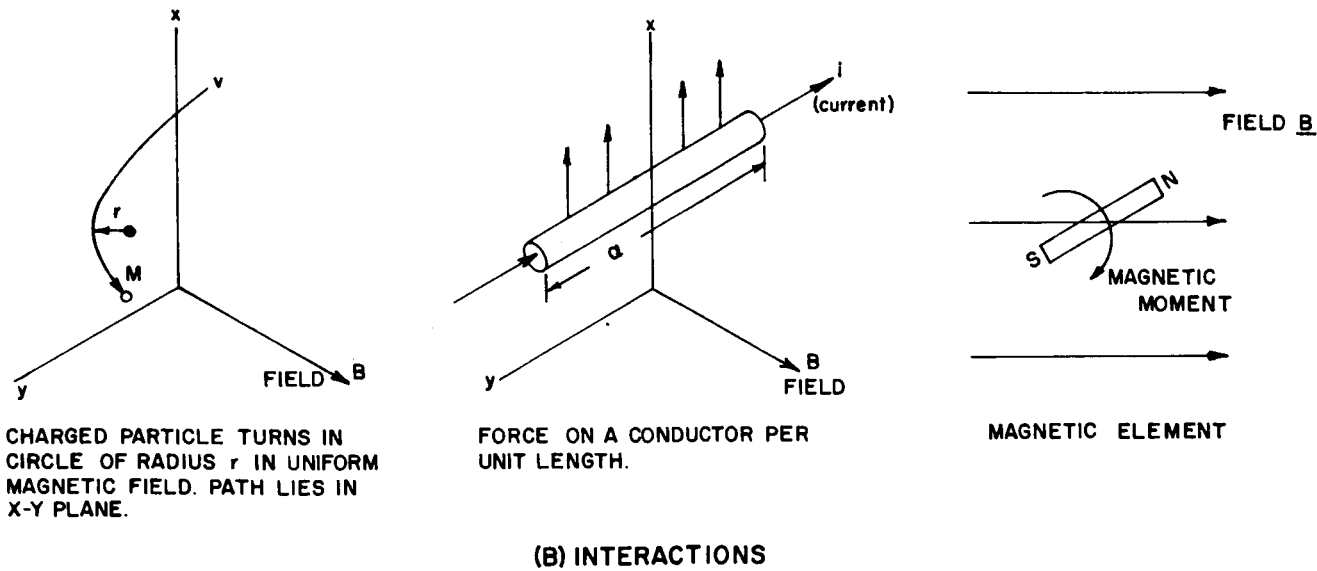
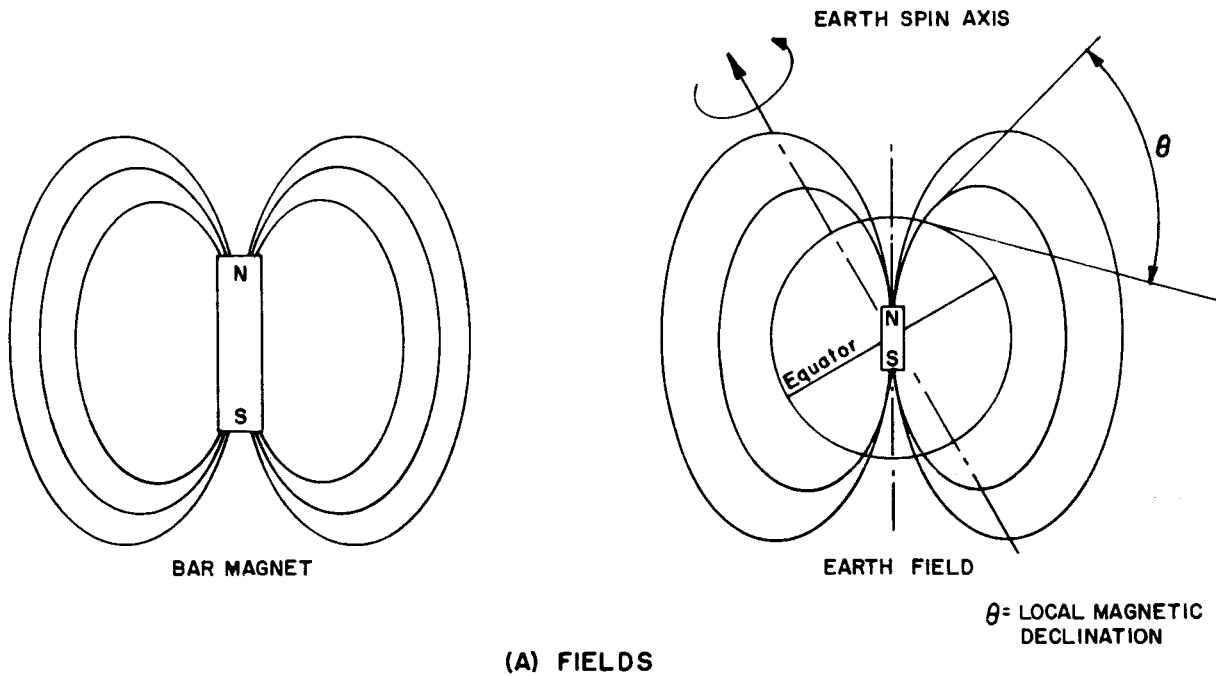
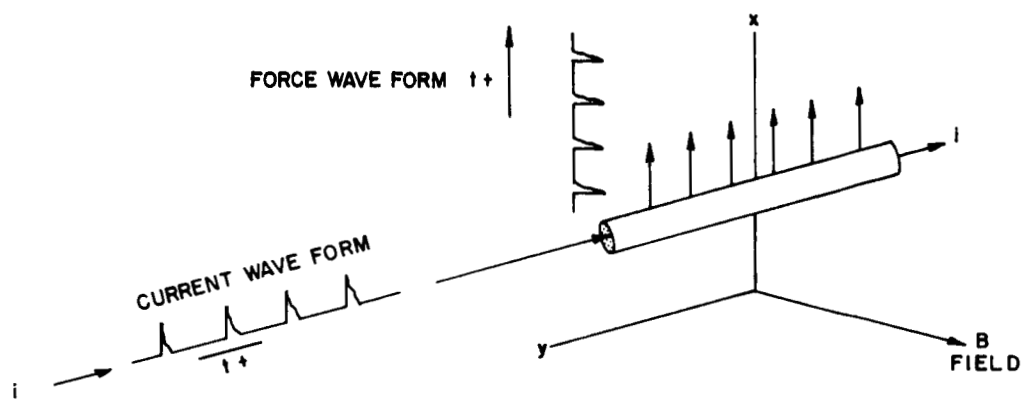
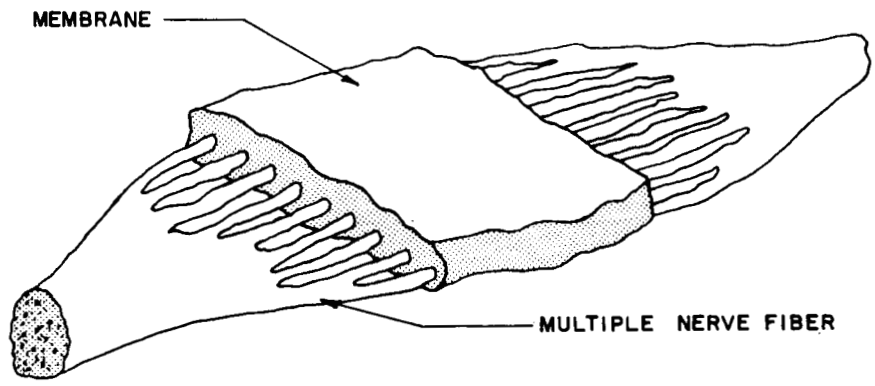


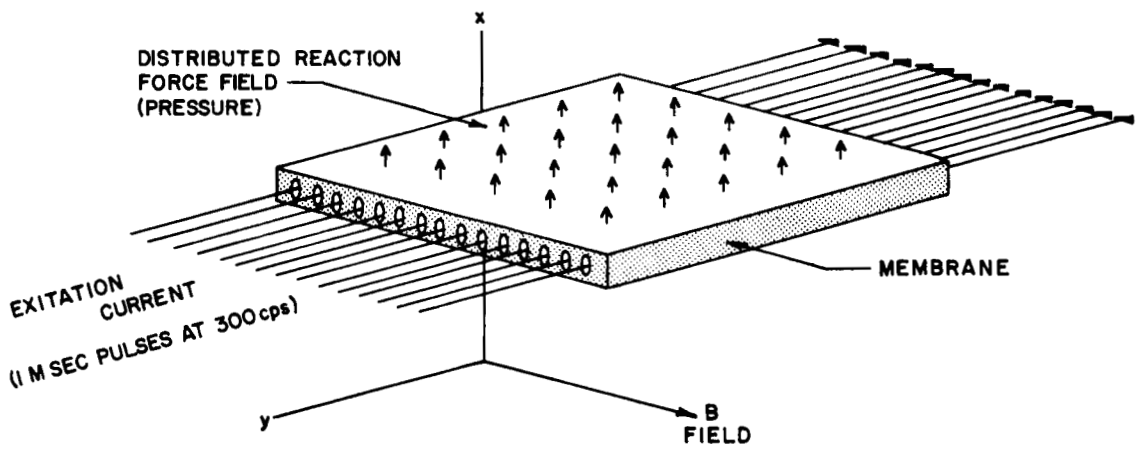
Figure 6-2. Elements of Magnetic Fields.



A. PULSED CIRCUIT ELEMENT



B. CONDUCTIVE MEMBRANE



C.

Figure 6-3. Proposed Gravitational Field Sensor.

as shown in Figure 6-3b. If the "conductive membrane" carrying current pulses were exposed to a magnetic field, then pressure would be developed that could be sensed by a mechanoreceptor of the appropriate physiological design. Indeed, if the architecture of such an electromechanical system was carried to the level of perfection found in the higher forms of transduction schemes (the human cochlea, for example) the detection of the earth's magnetic field would be feasible. Consider the following calculation.

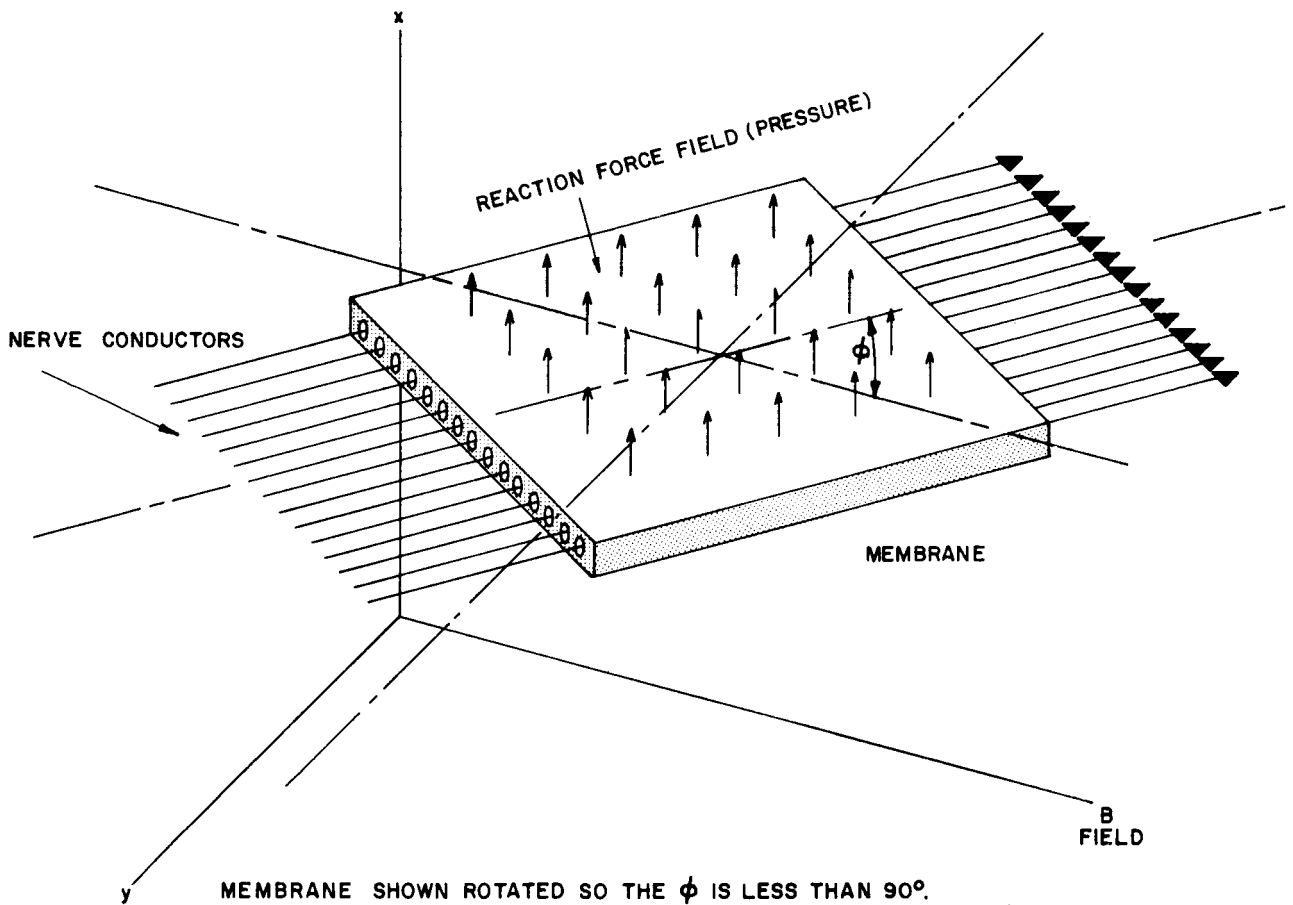
1. In the rudimentary sensor outlined in Figure 6-3b, a small current in the form of pulses as a result of nerve firing is made to flow in the nerve fibers covering the pressure sensing membrane. When the membrane is aligned with the field as shown in Figure 6-3c, a pressure is developed during the "on" period of the pulses of current in the nerve fibers. There remains the task of selecting a reasonable value for the magnitude of current flowing in the nerve fibers. It is well known that some of the more energetic electric cells can develop currents as high as one ampere at 600 volts. Currents this high are completely unreasonable for sensing schemes, of course. A reasonable value for nerve current carrying capacity are in the range of 100×10^{-9} amperes as quoted by Eccles (Ref. 6-10).

2. The simple relation:

$$F = iBl; \frac{F}{l} = iB \text{ (force per unit length)} \quad (1)$$

gives the force on a conductor of length l carrying the current i in a magnetic field of intensity B . For Cambridge, Massachusetts, Sears (Ref. 6-11) quotes a value for the earth's magnetic field of 5.8×10^{-5} webers/meter². Equation (1) and the data above yields 3.3×10^{-14} pounds/in for the force applied to a one inch length of nerve fibre. Since the basilar membrane contains up to 16,000 nerve fibers per inch of length (Ref. 6-12) it seems reasonable to postulate that there might be 4,000 nerve fibers side by side covering a pressure sensitive membrane. The total pressure resulting, then, on a one inch square membrane would be 1.3×10^{-10} pounds/in². This compares favorably to the auditory pressure threshold for the human basilar membrane which is 1.4×10^{-10} psi (Ref. 6-13). This indicates that sensing fields as feeble as the earth's magnetic field is within the capacity of the known architecture of electric and mechanoreceptors.

It is interesting to speculate how such a proposed system might be used. Referring to Figure 6-4 it can be seen that as the position of the membrane is



MEMBRANE SHOWN ROTATED SO THE ϕ IS LESS THAN 90° .
 AT 0° , REACTION FORCE IS ZERO. REACTION FORCE VARIES AS $\sin \phi$.

Figure 6-4. Membrane Sensor - Magnetic Field Interactions.

varied so that ϕ goes from 0° to 90° , the pressure on the membrane varies since the force on the conductor decreases as the sine of ϕ . If the current pulses in the nerve fibers were 1 m sec wide at a repetition rate of 300 cps (a typical nerve discharge frequency) then the pressure pulses would be "felt" or "heard" at the same frequency as the electric nerve pulses. The creature possessing such an organ could seek angular orientation by simply "nulling out" or seeking the position of zero sound. This mechanism would endow the creature with a direction sensing mechanism dependent only on the earth's magnetic field.

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