A Mechanism by Which the Hair Cells of the Inner Ear Transduce Mechanical Energy into a Modulated Train of Action Potentials

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ABSTRACT   Physical models of the hair cells of the inner ear were built and analyzed. These models suggest that a straightforward physical process is capable of modulating the electrical resistance of the hair cell. Strong evidence in the literature indicates that such a change in resistance would modulate an otherwise steady electrical current which flows across the hair cell. This would cause the resting potential of the hair cell to change in a systematic fashion, eventually giving rise to the modulated train of action potentials in the neurons leading from the hair cell to the central nervous system.

INTRODUCTION

The transmission electron microscope has allowed us to peer, with considerable clarity, into the very cells which make up the body. The scanning electron microscope now permits us to view the surfaces of these cells with a similar degree of resolution. We can begin to consider in some detail how these cells are acted upon and in turn, act themselves in performing the specific tasks to which they have evolved. To date, no satisfactory explanation exists as to how the hair cells of the inner ear are capable of transducing mechanical energy or movement into neural signals of considerable fidelity. This paper examines some current physical and physiological concepts of action within the inner ear and an attempt is made to derive an understanding of the events which give rise to transduction.

PHYSIOLOGICAL CONSIDERATIONS

The hair cells of the three types of receptor organs of the inner ear derive their name from the cilia which protrude from the apex of the cell. Fig. 1 shows a scanning electron micrograph of the type of cilia on the hair cells in the gravity receptor organs and semicircular canals of the guinea pig.
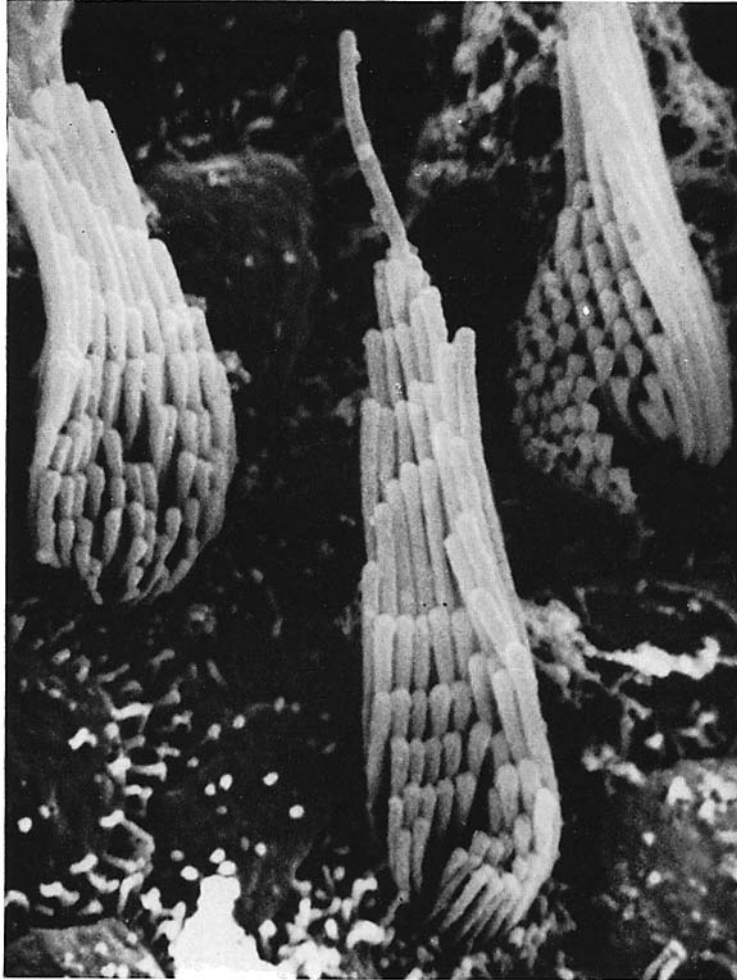
FIGURE 1.   The cilia of the hair cells of a gravity receptor organ of a guinea pig. (Courtesy, H. H. Lindeman, 1973.)

Fig. 2 shows the cilia of the two types of hair cells found in the mammalian cochlea. The cilia of the inner hair cells are relatively large and arranged in a fan shape compared with the smaller hairs of the outer hair cells. These latter can be seen to be arranged in the characteristic "W" pattern. Fig. 3 shows an enlargement of the cilia on an inner hair cell.

The hair cells themselves are cylindrical or "vase" shaped with the cilia protruding from the top. The bases of the cells make synaptic contact with both efferent and afferent fibers which lead to the central nervous system. More or less regular arrays of hair cells are interspersed with supporting cells and these arrays make up the sensory epithelium of the sensing organs.

FIGURE 2. The cilia of the inner and outer hair cells of a cat. There are three rows of outer hair cells and one row of inner hair cells. (Courtesy, H. Engström.)

Excellent photographs of these structures may be found in articles by Kimura (1966), Lindeman et al. (1972), Bredberg et al. (1972), and Engström et al. (1972).

Trincker (1962) has shown that the adequate stimulus in the gravity receptor organs is a gliding or shearing motion of the otoliths across the sensory epithelium. Von Békésy (1953) demonstrated that the adequate stimulus
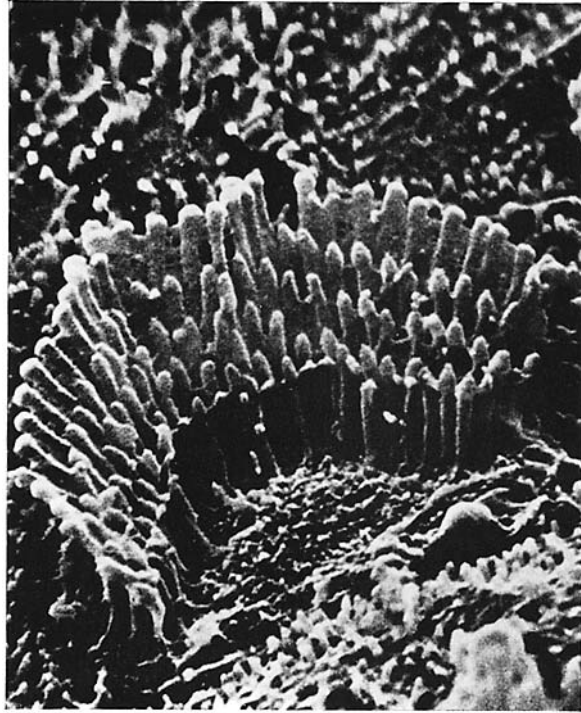
FIGURE 3.   The cilia of an outer hair cell of a guinea pig cochlea, from Wersäll et al. (1970). (Reprinted by copyright permission from *Adv. Oto-Rhino-Laryngol.*, 1973, **20:** 405.)

in the cochlea was a shearing motion of the tectorial membrane relative to the basilar membrane which holds the hair cells. Wever (1971) reviewed many different species and showed that this same shearing mechanism was common to all. It seems likely, in the light of recent studies of the crista-cupula mechanism (Money et al., 1971; Dohlman, 1971; Oman and Young, 1972), that a shearing motion of the cupula over the crista is the effective stimulus of these hair cells also.

The magnitude of the movements which produce adequate stimulation is extremely small. Vilstrup (1951) has shown that when exposed to a force equal to that of gravity, the otoliths move about 15 μm. Studies of basilar membrane movement using the Mössbauer effect show that, at threshold, the motion has an amplitude of the order of 0.01 Å, (Johnstone and Boyle, 1967; Johnstone et al., 1970; Rhode, 1971). To date, no direct measurement of cupular displacement has been reported, but work presently being done in the author's laboratory appears to indicate that it too moves only a very small amount during stimulation.

There is good evidence that the interior of the hair cell has a resting poten-

tial which is negative with respect to the extracellular fluid, (see Johnstone and Sellick, 1972). Smith et al. (1958) have shown that the endolymph, especially in the cochlea of some species, has a positive resting potential with respect to that same extracellular fluid. Thus, under normal circumstances, there is a standing voltage across the hair-bearing surface of a hair cell, with the interior of the cell being negative with respect to the fluid bathing the outer surfaces of the cilia. If these outer surfaces of the cilia are made of semipermeable membranes, then it is reasonable to expect that an electrical current flows through these membranes, along the electrical gradient. In fact, von Békésy (1951) established that movement of the basilar membrane produced changes in a standing current flow. In 1957, Davis suggested that when adequate stimulation of the organs of the inner ear caused the cilia to "bend," somehow this altered the electrical resistance of the hair cell layer. This change in resistance would modulate the standing current observed by von Békésy and account for many of the electrical phenomena seen in association with stimulation of the organs of the inner ear. Kurokawa (1965), Johnstone and Johnstone (1966), and Johnstone et al. (1966) have recorded changes in the effective resistance between the scala media and scala tympani during sound stimulation and indicate that at least part of this occurs in the hair cells of the basilar membrane. It is evident then, that the key to the transduction process lies in events of an electrical nature taking place in and around the hair cells, probably involving the cilia.

PHYSICAL CONSIDERATIONS

Consider the action of two parallel plates, separated by a layer of fluid, when one of those plates is made to undergo a shearing motion with respect to the other. Each plate retains a boundary layer of the fluid which stays with the plate. Since one of the distinguishing characteristics of a fluid is that it offers very little resistance to shear, the shearing motion will be distributed evenly throughout the fluid between the plates. If the fluid is thought of as being divided into very thin laminae, each lamina would have the same velocity with respect to the next lamina as all the other pairs of laminae. Thus, the velocity of a point in the fluid relative to one of the plates is a linear function of the distance of that point from the plate. If the fluid is thought of as resembling a deck of cards, then the motion of the fluid will be similar to pushing the top card of the deck, causing all the lower cards to slide evenly, giving the edges of the deck a slanted or tilted appearance. This relationship is true so long as the relative velocity of the plates is not so high as to cause the fluid motion to become turbulent.

Another property of fluids is that when a solid object moves through a fluid the drag on the object exerted by the fluid is proportional to the velocity of the object relative to the fluid. The tectorial membrane, otoliths, and

cupula all slide with respect to the sensory epithelium to produce stimulation of the sensory nerves. Thus the fluid which lies between these moving parts must also exhibit shear in the manner described above. The longest cilia will experience the largest bending *moment*, either because they actually touch the moving part (tectorial membrane, otolith, cupula), or because they are simply the longest hairs. The length is important from two points of view; first, because the fluid farthest from the hair cell has the greatest velocity and thus produces the highest drag, and second, the moment of that drag is proportional to the length of the hair. The total bending moment is thus proportional to the square of the length of the cilium. Hence the angle through which the longest of the hairs will be bent is larger than the angle through which the next shorter hairs will be bent, and so on. The fact the hairs stand close together will distort the flow pattern somewhat, but it is still correct to say that the longer hairs will be bent more than the shorter ones.

The question arises as to whether the cilia will bend in the manner of a rigid pole, hinged at the bottom or alternatively, like a flexible rod. Transmission electron micrographs of the long sections of cilia, (such as Wersäll and Lundquist, 1966) show how the base of the cilia is quite tapered with the filaments of the main body of the hair compressing together to form a core and rootlet. This tapered section is much more likely to bend when a shearing force is applied to the cilia than is the whole cilium itself. Furthermore, it is well known that if an electric charge is distributed over the surface of a flexible cylinder, the cylinder will become rigid. Since the inside of the cilium is at an electric potential quite different from the endolymph, one can expect that the cilia move like rigid poles which are hinged at their bases.

A set of models was constructed of the hair-bearing surfaces of different types of hair cells and the cilia which these surfaces support. The reticular layer was made from small plates of ½-inch "phenolic" board, a material having high strength and great resistance to splitting. A series of holes was drilled through the board in the pattern of the cilia and nails were then inserted into the holes such that they fitted snuggly and protruded through the opposite side approximately ¾ inch. Flexible plastic tubing, whose inside diameter matched the diameter of the nails, was used to represent the cilia. Pieces of tubing, about 6 inches in length each, were fitted over the protruding ends of the nails and trimmed with scissors to resemble the cilia seen in the scanning electron micrographs.

Fig. 4 is a photograph of the model which represents an outer hair cell of the mammalian cochlea. As can be seen, when a force similar in effect to viscous drag is applied to the cilia, directed from the shortest to the longest, the rows of hairs spread open. That is to say, each row moves relative to the
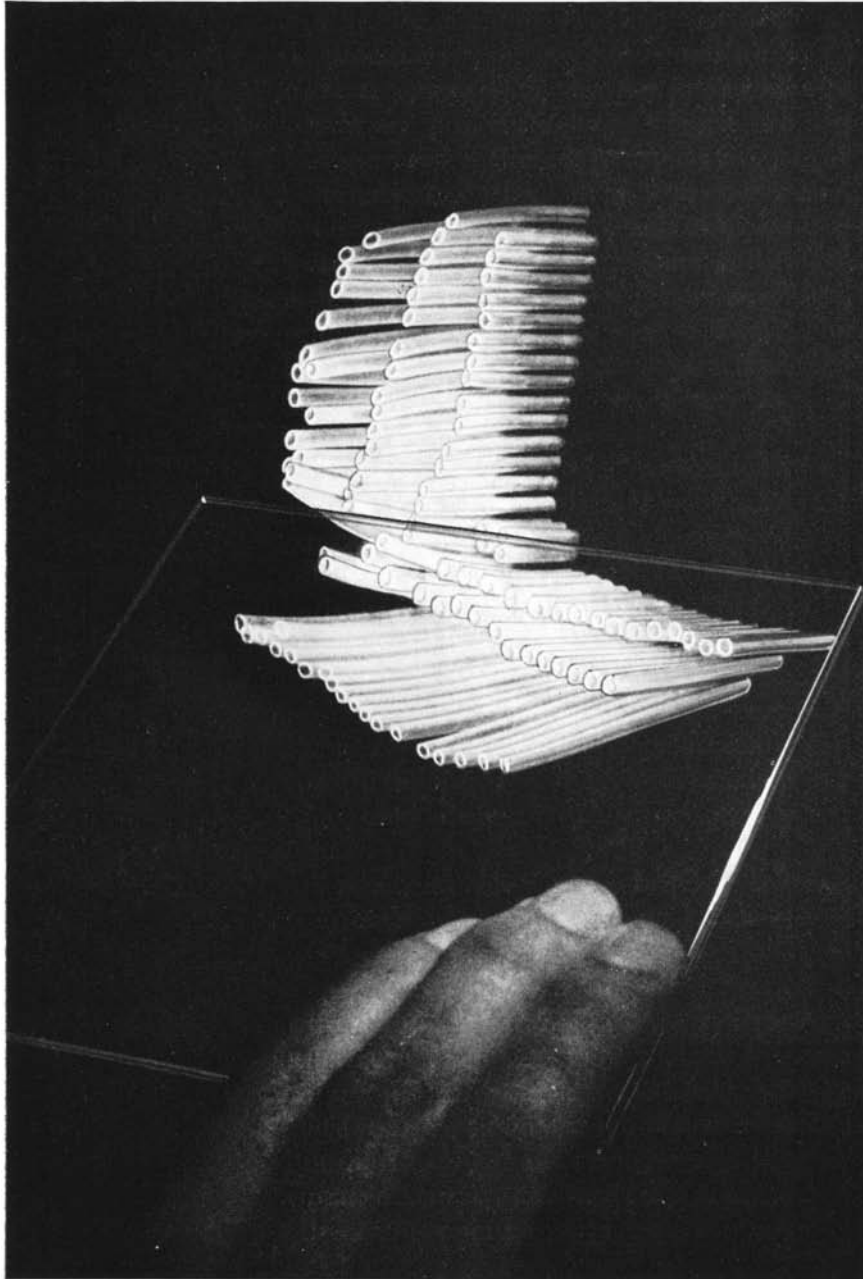
FIGURE 4. Model of the cochlear cilia showing the results of a shear force directed from right to left. Notice how each successive row of hairs spreads away from the other rows.
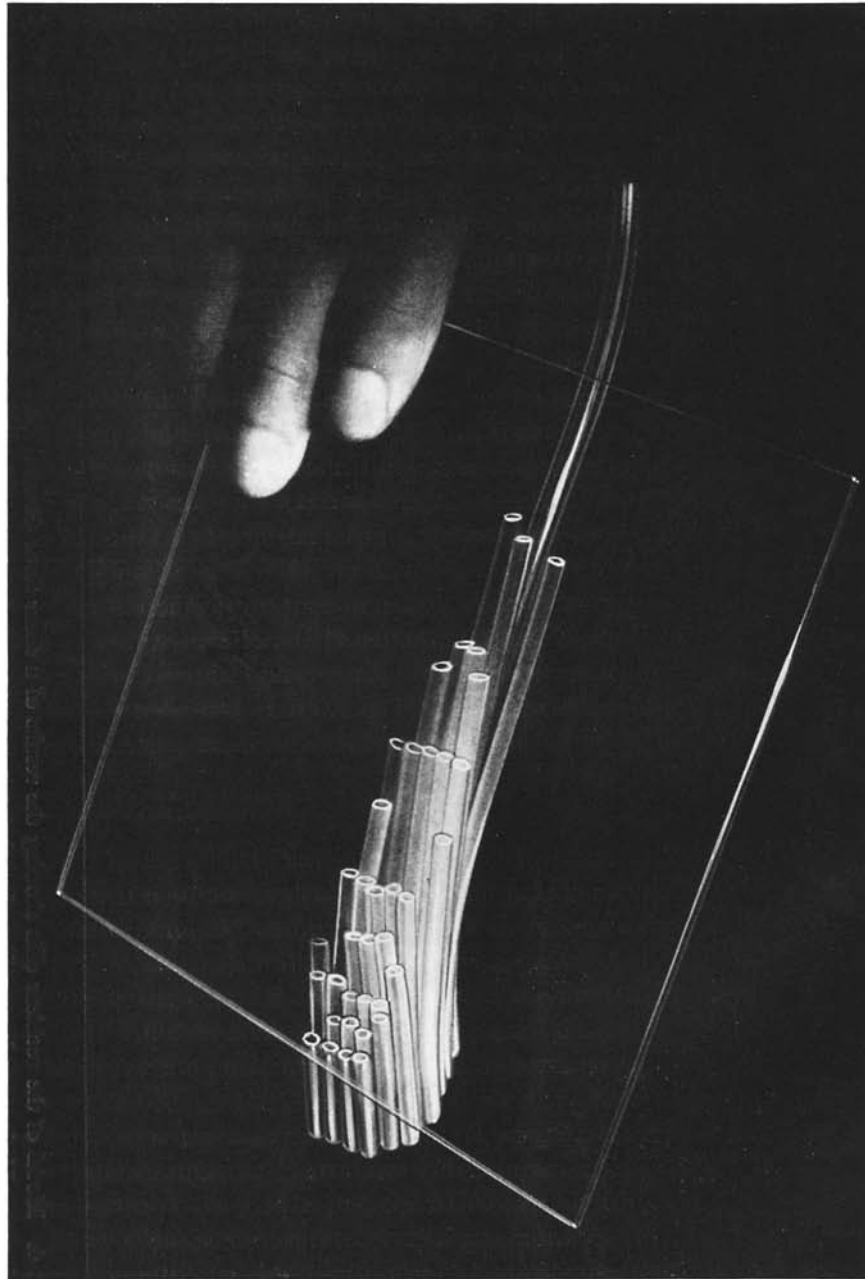
FIGURE 5.   Model of the cilia from a gravity receptor organ. The shear shown in the photo is in the direction known to be excitatory to this type of cell.

other rows, while the position of each hair within a row remains virtually unchanged. Conversely, if the force is applied from the opposite direction, the rows of hairs will move closer together.

The characteristic W pattern of the rows of cilia on the outer hair cells, as seen in Fig. 4, ensures that a force originating within a wide range of angles will produce this same effect. In fact it can be seen that such a force could emmanate from an angle within an arc of more than 90° and still cause at least one set of hairs to spread open. Von Békésy (1953) has shown that the tectorial membrane of the guinea pig can move in directions which are at right angles to each other, all the while adequately stimulating the hair cells below.

Fig. 5 shows a model of the cilia from the macula of the guinea pig. The clear tube which is longer and thicker than the others represents a kinocilium, such as can be seen in Fig. 1. On the hair cells of the crista ampullaris, the kinocilium is usually seen to be much longer. Once again it is evident that a force gradient causes the rows of hairs to spread open. Similarily, if the force is from the opposite direction, the spaces between rows will close even more than in the resting condition. In Fig. 6 it can be seen that a force from the side will have no net effect on the relative spacing between the rows of hairs. This is in accord with the findings of Melvill Jones and Milsum (1969), who demonstrated that when an otolith was moved at right angles to the direction of maximum stimulation of a given sensory cell, then no stimulation of that cell was produced.

The outer layer or wall of the cilia is known to be continuous with the membrane which makes up the cell wall of the hair cell (Wersäll and Lund-quist, 1966). It is reasonable to assume then, that the cilia are semipermeable as is the cell wall, and that current can flow down the electrochemical gradient which exists between the inside and the outside of the hair cell. There is some evidence to show that this current consists, at least in part, of potassium ions flowing from the endolymph into the cell along an electrical gradient, (Johnstone and Sellick, 1972). It is also possible that this current leaves the cell via an active pump located in the cell wall opposite the reticular lamina (Katsuki et al., 1966).

AN HYPOTHESIS

It is proposed that a standing current flows through the membranes of the cilia which lie between the endolymph and the intracellular fluid. These ciliary membranes act as a simple passive resistance to the current. The total resistance offered by a given cell is thus a function of the total surface area of membrane across which this current can flow.

From electron micrographs of the cilia of the inner ear it can be seen that each hair is very close to, if not actually touching, its nearest neighbors. The
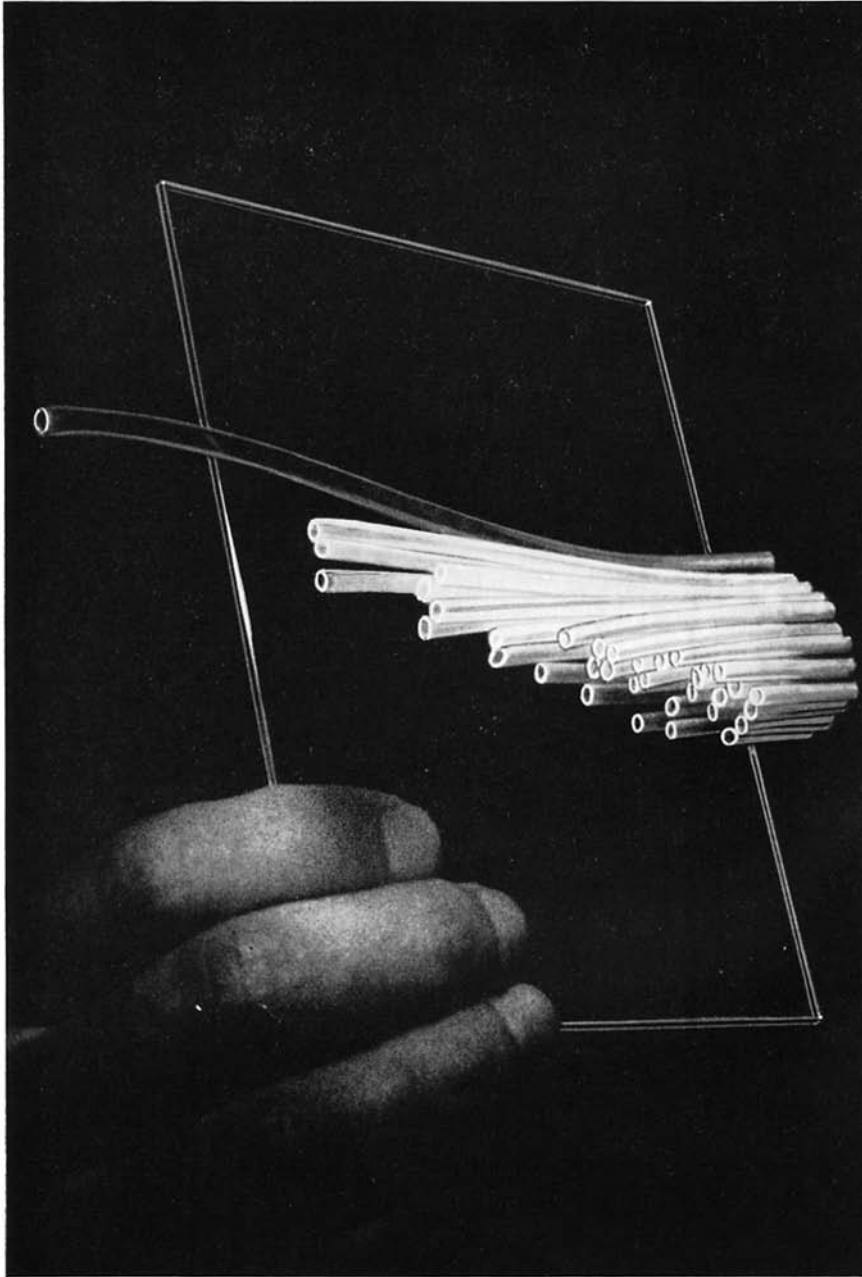
FIGURE 6.   The effects of shear from the side of the hair bundle. The net change in spacing between the hairs remains unchanged.

channels between adjacent cilia are very fine indeed and would offer quite a high resistance to the movement of ions, especially hydrated cations. In histologically fixed specimens, where shrinkage is known to occur, one typically sees the cilia separated by spaces of 0.1 μm or less. A glass micropipette having this diameter would have a resistance of from ten to several hundred megohms, (Frank and Becker, 1964). Thus for practical purposes, the majority of current which crosses the ciliary membrane should traverse only that portion of the membrane which is openly exposed to the endolymph.

During excitatory stimulation however, such as simulated in Figs. 4 and 5, rows of cilia are spread open, and the electrical resistance of the channels between the hairs is greatly reduced. This allows access for the ions to portions of the cilia which had previously been obscured, effectively increasing the surface area through which the ions can flow. If the stimulation is in the opposite direction, then the channels between the rows of hairs will be diminished, increasing the effective resistance, thus decreasing the current in the circuit. This modulation of a standing current would alter the electrical potential of the interior of the hair cell, presumably effecting the release of neurochemical transmitter from the hair cell and thereby modulating the train of action potentials in the subsequent neurons. This change of electrical potential within the hair cell would be enhanced if the ions were cleared from the cell by a pump which worked at a comparatively steady rate, instead of by a passive system whose motive force was the changeable electrochemical gradient.

The author has calculated from the models that the maximum change in free surface area of the cilia, from the condition where the rows are spread open to that where the rows are closed tight is from 30 to 60% of the resting surface area. This was found to be the case for all three types of hair cell. Johnstone et al. (1966) made a very careful measurement of the resistance change of the scala media of the guinea pig when it was stimulated with a 5-kHz tone 95 dB above threshold. They observed a change in the resistance across the basilar membrane of about 10%. They point out that some of the change could be due to current leaking through or between the Claudius and Hansen cells and if this were so, the change in resistance of the hair cells would be considerably higher. They went on to calculate that the minimum resistance of a single hair cell is of the order of 48 MΩ.

It is quite instructive to consider, at least qualitatively, the response of this proposed mechanism of transduction to the expected range of inputs. A large excitatory stimulus will cause the rows of cilia to spread apart to such an extent that a further increase in stimulus will not expose more ciliary surface area to the endolymph. The mechanism is said to be "saturated." In the same fashion, a strong inhibitory stimulus will cause the rows of cilia to come together to such an extent that they are all touching one another.

Further stimulation cannot bring them any closer and once again the mechanism is saturated. During this latter condition however, less current will be flowing into the cell and the cell will therefore not be so depolarized as in the former condition. Between these two extremes, the current flowing into the cell will be a linear function of the shearing force acting upon the cilia. The electrical potential within the cell is a function of the current flowing into the cell and this potential will govern the rate of release of neurochemical transmitter which modulates the action potential frequency in the first-order neurons. If one plots the output of the cell as a function of the shearing force on the cilia as input, one predicts that the curve will have an "S" shape, saturated at the extremes and linear in the midrange. These qualities correspond precisely to the known characteristics of the sensory cells of the organs of balance as reviewed by Trincker in 1962.

It is evident from the physical considerations discussed above that the stimulation of the hair cells will be proportional to the velocity of the fluid surrounding the cilia and thus to the relative velocity of the moving parts of the organ. Trincker (1962) has shown however, that the signals from the gravity receptors are proportional to the displacement of the otoliths with respect to the sensory epithelium. It is also well known that some of the signals from the semicircular canals are proportional to the angular velocity of the skull. However, because of the mechanical damping of the fluid within the canals, the displacement of the cupula from its resting position is also proportional to this same angular velocity (Jones and Milsum, 1965). Thus, in at least these two organs, one must explain how some neural signals from the hair cells could be proportional to the displacement of the moving components rather than the velocity of these components.

Some workers contend that the tops of the longest cilia are in physical contact with the moving components of the organ, (Hawkins, 1964; Iurato, 1967; Marco et al., 1971). Whether or not this is actually the case, it is not so for the shorter cilia which outnumber the longest cilia in these organs. This would mean that the response from an individual cell would be a complex function of both the velocity and the displacement of the moving components of the transducer. While this complex type of behaviour was actually observed by Fernandez and Goldberg (1971) and Goldberg and Fernandez (1971 a, b) who recorded from single vestibular units of the squirrel monkey, other investigators (Precht et al., 1971) observed that some units in the frog responded to the apparent motion of the cupula while other units responded only to its displacement. The second-order neurons observed by Melvill Jones and Milsum (1970) in the cat responded only to the apparent displacement of the cupula.

Mucopolysaccharides

These apparently anomalous properties of the vestibular apparatus can be explained if one considers the gel often seen in the inner ear. Vilstrup and Jenson (1953 a, b, 1960), reported on a mucopolysaccharide in the vestibular apparatus which they believed was either hyaluronic acid or chondroitin sulphate. Von Békésy (personal communication) often noticed that the scala media of the guinea pig was filled with a gel when it was carefully opened. The present author has found that the ampulla of the frog is filled with a gel which can be visualized under a polarizing microscope when the canal is very gently perfused with methyline blue. Under these conditions, what corresponds to the cupula appears to be a large "plug" of gel, which nearly fills the ampulla. If an extremely small displacement of the dye is caused (of the order of 5×10^{-8} liters), this plug of gel surrounded by blue dye moves through the ampulla. It is seen to be quite flexible, and can be moved back and forth through the ampulla. If the motion is made just a little too vigorously, the plug of gel seems to suddenly disappear, as if it turned to liquid in one quick stroke.

Dohlman (1970) injected pigeons with radioactive sulfur compounds and found that a gel-like substance took up the sulfur in the vestibular apparatus. Most interestingly, he has electron micrographs which show large molecular fibers between the cilia which he has identified as being a mucopolysaccharide (personal communication). The author believes that this gel is most likely to be composed, at least in part, of chondroitin sulfate, since this can bind with protein, take up radio-sulfur and react with testicular hyaluronidase such as was used by Vilstrup and Jenson, (1953 a, b, 1960) (see Stacy and Barker, 1962; Quintarelli, 1965).

In concentrations greater than about 0.1%, mucopolysaccharides form what is known as a "thixotropic" fluid. Such fluids exhibit non-Newtonian characteristics such as having a viscosity which is a function of shear rate. Typically, for high shear rates, the fluid behaves much like ordinary water, but as the shear rate becomes quite small, the viscosity quickly increases to very high values, and as the shear rate approaches zero, the fluid gels, taking on properties of a plastic solid.

The presence of such a non-Newtonian fluid between the cilia can explain much of the anomalous behaviour of the vestibular transducers. Stimulations which produced low shear rates in the fluid surrounding the cilia would cause these cilia to move as a function of the displacement of the moving parts of the organ. On the other hand, stimuli that produced high shear rates would cause the gel to become "liquid," and the hair cells would then be stimulated as a function of the relative velocity of the moving parts.

For example, in the semicircular canals one might expect that there would be a smooth transition from that of angular velocity transducer to one of angular acceleration as the velocity of the stimulus increased. This would seem to correspond to the observations of Goldberg and Fernandez (1971 b) and Fernandez and Goldberg (1971) who noticed that as the frequency of sinusoidal oscillations increased, the responses of single units became more and more phase advanced. These authors pointed out that this advancement corresponds to the sensing mechanism of the canals changing from being sensitive to the displacement of the cupula to becoming sensitive to the velocity of the cupula. This might also explain some of the large phase advancements noted by Löwenstein and Roberts (1950) while recording from the gravity receptor organs in the ray.

The fact that the spaces between the cilia might contain such a gel would not alter the proposed mechanism of transduction described above. Laurent (1966) has developed an empirical relation between the drag on an ion and that ion's diameter for a gel of hyaluronic acid. This acid is closely related to chondroitin sulphate and the relationship of Laurent shows that no significant effect is to be expected from the matrix of the gel on the mobility of hydrated cations. The matrices are so flexible that one can expect that their presence will not interfere with the relative movement of the cilia during stimulation.

SUMMARY

The transduction mechanism that has been proposed would work in the manner of a very simple amplifier. A standing electrical current, the energy for which is derived ultimately from metabolic sources, is modulated by the simple physical movement of a resistive element in the circuit. The energy required as input to this device is only that necessary to move the miniscule cilia on the hair cells, while the output is the neurochemical transmitter that modulates the train of action potentials in the subsequent nerve fibers. A thixotropic gel which appears to surround the transducers is seen to be a coupling device which not only helps restore the system to its resting position in the absence of stimulation, but in some cases works as a mathematical integrator, altering the phase angle of the output as a function of the amplitude and frequency of stimulation.

REFERENCES

Von Békésy, G. 1951. The coarse pattern of the electrical resistance in the cochlea of the guinea pig. (Electro-anatomy of the cochlea). *J. Acoust. Soc. Am.* 23:18.

Von Békésy, G. 1953. Description of some mechanical properties of the organ of Corti. *J. Acoust. Soc. Am.* **25**:770.

Bredberg, F., H. W. Ades, and H. Engström. 1972. Scanning electron microscopy of the normal and pathologically altered organ of Corti. *Acta Oto-laryngol. Suppl.* **301**:3.

Davis, H. 1957. Biophysics and physiology of the inner ear. *Physiol. Rev.* **37**:1.

Dohlman, G. F. 1970. Investigations on the presence of acid mucopolysaccharides in the endolymph of pigeons. Proceedings Barany Society, First Extraordinary Meeting, in Amsterdam-Utrecht. Congress Bureau InterScientias Inc., The Hague, The Netherlands. pp. 5–20.

Dohlman, G. F. 1971. The attachment of the cupulae, otolith and tectorial membranes to the sensory cell areas. *Acta Oto-laryngol.* **71**:89.

Engström, H., B. Bergström, and H. W. Ades. 1972. Macula utriculi and macula sacculi in the squirrel monkey. *Acta Oto-laryngol. Suppl.* **301**:75.

Fernandez, C., and J. N. Goldberg. 1971. Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. II. Response to sinusoidal stimulation and dynamics of peripheral vestibular system. *J. Neurophysiol.* **34**:661.

Frank, D., and M. C. Becker. 1964. Microelectrodes for recording and stimulation. *In* Physical Techniques in Biological Research, vol. 5. W. Nastuk, editor, Academic Press, Inc., New York.

Goldberg, J. M., and C. Fernandez. 1971 *a*. Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. I. Resting discharge and response to constant angular accelerations. *J. Neurophysiol.* **34**:635.

Goldberg, J. N., and C. Fernandez. 1971 *b*. Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. III. Variations among units in their discharge properties. *J. Neurophysiol.* **34**:676.

Hawkins, J. E., Jr. 1964. Hearing. *Annu. Rev. Physiol.* **26**:453.

Iurato, S. 1967. Chapter V, Cochlear duct (section 3, Organ of Corti). Submicroscopic Structure of the Inner Ear. Pergamon Press Ltd., Oxford.

Johnstone, B. M., and A. J. F. Boyle. 1967. Basilar membrane vibration measured with the Mössbauer technique. *Science.* (*Wash. D.C.*). **158**:389.

Johnstone, J. R., and B. M. Johnstone. 1966. Origin of summating potential. *J. Acoust. Soc. Am.* **40**:1405.

Johnstone, B. M., J. R. Johnstone, and I. D. Pugsley. 1966. Membrane resistance in endolymphatic walls of the first turn of the guinea pig cochlea. *J. Acoust. Soc. Am.* **40**:1398.

Johnstone, B. M., and P. M. Sellick. 1972. The peripheral auditory apparatus. *Q. Rev. Biophys.* **5**:1.

Johnstone, B. M., K. J. Taylor, and A. J. Boyle. 1970. Mechanics of the guinea pig cochlea. *J. Acoust. Soc. Am.* **47**:504–9.

Jones, G. M., and J. H. Milsum. 1965. Spatial and dynamic aspects of visual fixation. *IEEE Trans. Bio. Med. Eng.* BME **12**:54.

Katsuki, Y., K. Yanigasawa, and J. Kanzaki. 1966. Tetraethylammonium and tetrodotoxin: Effects on cochlear potentials. *Science* (*Wash. D. C.*). **151**:1544.

Kimura, R. S. 1966. Hairs of the cochlear sensory cells and their attachment to the tectorial membrane. *Acta Oto-laryngol.* **61**:55.

Kurokawa, S. 1965. Experimental study on electrical resistance of basilar membrane in guinea pig. *J. Oto-Rhino-Laryngol. Soc. Jap.* **68**:1177.

Laurent, T. C. 1966. In vitro studies on the transport of macro-molecules through the connective tissue. *Fed. Proc.* **25**:1128.

Lindeman, H. H. 1973. Anatomy of the otolith organs. *Adv. Oto-Rhino-Laryngol.* **20**:405.

Lindeman, H. H., H. W. Ades, G. Bredberg, and H. Engström. 1972. The sensory hairs and the tectorial membrane in the development of the cat's organ of Corti. *Acta Oto-laryngol.* **72**:229.

Löwenstein, O., and T. D. M. Roberts. 1950. The equilibrium function of the otolith organs of the thornback ray. *J. Physiol.* (*Lond.*). **110**:392.

Marco, J., J. M. Sanchez-Fernandez, and J. M. Rivera-Pomar. 1971. Ultrastructure of the

otoliths and otolithic membrane of the macula utriculi in the guinea pig. *Acta Oto-laryngol.* **71**:1.

MELVILL JONES, G., and J. H. MILSUM. 1969. Neural response of the vestibular system to translational acceleration. Proceedings Symposium on "Systems Analysis Approach to Neuro-Physiological Problems." Brainerd, Minn., Supplement p. 8.

MELVILL JONES, G., and J. H. MILSUM. 1970. Characteristics of neural transmission from the semicircular canal to the vestibular nuclei of cats. *J. Physiol. (Lond.).* **209**:295.

MONEY, K. E., L. BONEN, I. D. BEATTY, L. A. KUEHN, M. SOKOLOFF, and R. S. WEVER. 1971. Physical properties of fluids and structures of vestibular apparatus of the pigeon. *Am. J. Physiol.* **220**:140.

OMAN, C. M., and L. R. YOUNG. 1972. The physiological range of pressure difference and cupula deflections in the human semicircular canals. *Acta Oto-laryngol.* **74**:324.

PRECHT, W., R. LLINAS, and M. CLARKE. 1971. Physiological responses of frog vestibular fibers to horizontal angular rotation. *Exp. Brain Res.* **13**:378.

QUINTARELLI, G. editor, 1965. *Int. Symp. Chem. Physiol. Mucopolysaccharides.* Little, Brown and Company, Boston, Mass.

RHODE, W. S. 1971. Observations of the vibration of the basilar membrane in squirrel monkeys using the Mössbauer technique. *J. Acoust. Soc. Am.* **49**:1218.

SMITH, C. A., H. DAVIS, B. H. DEATHERAGE, and C. F. GESSERT. 1958. D.C. Potentials of the membranous labyrinth. *Am. J. Physiol.* **193**:203.

STACEY, M. T., and S. A. BARKER. 1962. Carbohydrates of Living Tissues. Van Nostrand (D.), Co. Ltd. London.

TRINCKER, D. 1962. The transformation of mechanical stimulus into nervous excitation by the labyrinthine receptors. *Symp. Soc. Exp. Biol.* **16**:289.

VISLTRUP, T. 1951. Structure and Function of the Membranous Sacs of the Labyrinth in Acanthus Vulgaris. Munksgaard, A/S, Copenhagen.

VILSTRUP, T., and C. E. JENSEN. 1953 *a.* On the chemistry of the endolymph: does the endolymph contain hyaluronic acid? *Acta Oto-laryngol. Suppl.* **109**:200.

VILSTRUP, T., and C. E. JENSEN. 1953 *b.* Liquefaction of endolymph from sharks by hyaluronidase. *Acta Chem. Scand.* **7**:1128.

VILSTRUP, T., and C. E. JENSEN. 1960. On the chemistry of human cupulae. *Acta Oto-Laryngol.* **52**:383.

WERSÄLL, J., A. FLOCK, and PER-G. LUNDQUIST. 1970. Christmas card of the Otologic Research Group at the Dept. of Otolaryngology, Karolinska Hospital and King Gustav V Research Institute

WERSÄLL, J., and PER-G. LUNDQUIST. 1966. Morphological polorization of the mechano-receptors of the vestibular and acoustic systems. Second symposium on "The role of the vestibular organs in space exploration" NASA SP-115, pp. 57-72.

WEVER, E. G. 1971. The mechanics of hair-cell stimulation. *Ann. Otol. Rhinol. Laryngol.* **80**:786.