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Electrochemical Involvement in the Senses

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Abstract

There has been recent application of electrochemistry to unifying mode of action by odor and taste. This review extends the mechanistic approach to the other senses, namely touch, vision and hearing. A major difference among the senses is that molecules are initially involved in the case of odor and taste. The theory is based on a four-step process for odor and taste. The literature contains numerous reports dealing with electrochemistry in all cases, including electrical stimulation. The various factors involved are dipoles, electron transfer, receptor binding, radical species, neurochemistry and cell signaling. Other modes may be operative.

Keywords: Electrochemical; Five Senses

Abbreviations

EMF	:	Electromagnetic Field
ET	:	Electron Transfer
ROS	:	Reactive Oxygen Species
AO	:	Antioxidant
OS	:	Oxidative Stress
EOG	:	Electro-Olfactogram
DM	:	Dipole Moment

Introduction

Recent reviews provide extensive evidence for the importance of electrochemistry in living organisms. Electromagnetic Fields (EMFs) played an early role in living systems, as well as subsequent evolution [1]. The more recent literature on electrochemistry is documented, as well as magnetism. The large numbers of reports on interaction with living systems and the consequences are presented. An important aspect is involvement with cell signaling and resultant effects in which numerous signaling pathways participate. Much research has been devoted to the influence of man-made-EMFs e.g., from cell phones and electrical lines, on human health. The degree of seriousness is unresolved at present. The relationship of EMFs to Reactive Oxygen Species (ROS) and Oxidative Stress (OS) is discussed. There is evidence that indicates a relationship involving EMFs, ROS, and OS with toxic effects. Various articles deal with beneficial aspects of Antioxidants (AO) in countering the harmful influence from ROS-OS associated with EMFs. EMFs are useful in medicine, as indicated by healing bone fractures. Beneficial effects are recorded from electrical treatment of patients with Parkinson's disease, depression, and cancer.

Electrochemistry and cell signaling are widely involved in the operation of biochemical systems. A review [2] discusses the relationship of the two, as well as interconnection with a variety of other aspects, such as free radicals, receptors, and stereochemistry. Both endogenous and exogenous agents are involved. The electrochemistry deals with electrostatics, electron transfer, reduction potentials, as well as involvement in membranes, proteins and neurotransmission. Application of electrostatics is made to cell signaling involving receptor-ligand action, phosphates, sulfates, metal cations, and miscellaneous others. Apparently, energetics play a significant part. Practical and experimental aspects are addressed. The literature reveals an extensive involvement of electrostatics in biological systems [3]. In prior articles, supporting evidence was cited from volatile anesthetics, electron transport in photosynthesis and molecular electrostatic potential studies with DNA. The main focus is on energetics associated with bio-electrostatics. Examples include action of enzymes, such as, xylose isomerase, SOD and cytochrome c oxidase. In the membrane area, reports deal with the phospholipase-membrane and the nuclear membrane. Other categories are chromosomes, oxidation by hydroxyl radicals, Hofmeister effect, and histamine. In addition, electrostatic effects have been examined in the plant kingdom. There is relevant related material [4-9].

This report is unique in dealing in a unifying manner with electrochemical involvement in all senses, with application already made to smell [10] and taste [11]. Thus, the unifying aspect is novel in connection with touch, vision and hearing. Considering all of the senses, smell and taste differ from the others in that molecules initially participate. It is interesting that, with this difference, there is appreciable literature dealing with electrochemical effects in touch, vision and hearing. It is important to recognize that biological action is often multifaceted with various factors participating. A good example is smell in which extensive literature exists dealing with operation of vibration and shape, in addition to electrochemistry [10]. Other important aspects are cell signaling, receptors and redox.

Odor

One of the main sense areas that receive extensive evidence for involvement of electrochemistry is odor. A recent review presents the various mechanistic aspects, which are summarized in the following four parts [10]. Part A shows that a correlation exists between odor and molecular dipoles, but of a limited nature. Compounds, such as hydrogen, nitrogen and oxygen, with no dipoles have no odors, in accord with the theoretical framework. Chlorine reacts rapidly at the receptor to produce odorous material. Alkanes have small Dipole Moments (DMs) e.g., propane (DM=0.08) [12] and relatively weak odors. Natural gas (methane) is diluted with strong odorant in order to aid leak detection. On the other hand, common perfumes contain functional groups (aldehyde, ketone, esters and nitrile) possessing higher DM values (1.75-3.92). However, this relationship alone is not sufficient in rationalizing the experimental data. A criticism of both Vibration and Electrochemistry theories is that vibrational energies can be small as in the case with some Dipole Forces (DFs) of odorant molecules. Is there sufficient energy to produce the observed result? Electrostatic forces can be relatively weak for dipoles, but stronger for ions. A recent study provides evidence for participation of small forces [13].

Part B deals with interaction of the odorant EF with those of the protein receptor. It is evident that the EFs alone of molecules are insufficient to rationalize the experimental observations. However, docking of the molecule into the receptor site brings the molecule EFs in contact with EFs of the receptor protein. There are many protein EFs of varying strengths associated with the numerous functionalities present. Some of the functional groups possess strong EFs, as with the ions derived from acidic and basic amino acids. The most prevalent dipole and a strong one (DM=3.68) is that of the peptide (amide) bond. Alterations can occur with interactions of dipoles or ions in the receptor, hydrogen bonding, ion formation with volatile acids and bases and covalent bonding. Thus, molecules with identical DMs and EFs can have different odors since binding to different receptors results in different EFs due to varied alterations. The important aspect of change in the strength of the odorant molecule EF field has received scant attention previously. There is considerable information concerning the olfactory receptors [10]. The altered EF then propagates the sequence by interaction with neurons in the olfactory system.

Part C comprises interaction of the receptor-ligand dipoles with olfactory neurons [10]. Various electrochemical interactions occur entailing the altered receptor-odorant EF and the neuronal system. Research quite relevant to the electrochemical approach involves Electro-Olfatograms (EOGS) which reflect electrical potentials of the olfactory epithelium that occur in reference to the olfactory stimulation [14]. The EOG represents the sum of the generator potentials of olfactory receptor neurons. This approach has been used extensively with animals, together with much lesser application to humans. A review outlines the following: (a) the cellular and physiological nature of EOG response, (b) odor selection and delivery and (c) application of EOG in humans, fish and insect olfaction and pheromonal responsivity [15].

An article discusses molecular mechanisms of smell and taste [16]. Emphasis is on the transformation into electrical signals. This important contribution, which has received scant attention, adds credibility to the electrochemical theme. In the initial process of chemoreception, a stimulatory substance absorbs onto a membrane. The olfactory cells are primary sensory cells connected to the end of the olfactory nerve, and they depolarize when a stimulating substance absorbs in a receptive membrane. Hence, an impulse is generated directly from the nerve without involvement of synapse. The olfactory nerves can be viewed as information converters for changing chemical information into electrical signals. Therefore, a large resting potential which is negative inside the cell is produced. An appreciable amount of attention has been paid to exposure of the olfactory system to external electrical stimulus. The results are in accord with an electrochemical approach to olfactory action [10]. Although the electrical stimulus and the odor molecule both provide electrochemical force, the stimulus is different in having mobile electrons as the source. Also, interaction of the external stimulus with the olfactory nerve is not the same as for the odor molecule.

The above important investigations clearly demonstrate the participation of bio electrochemistry in the olfactory process entailing response to binding with the receptor. Part D completes the sequence by transfer of information from Part C to the brain [10]. Since the brain is replete with electrochemical activity, it is not surprising that extensive, relevant literature pertains to the olfactory cortex [17]. This part of the cerebrum receives sensory input from the olfactory bulb. The events cause the membrane charge to become more positive, or depolarize, which travels down the axon of the olfactory receptor cells to the olfactory nerve. There is considerable literature documenting electrical effects in the cerebral olfactory cortex.

Other aspects

It is well established that ET processes play important roles in biology and medicine [18]. The negative electron in motion creates an electric field that can interact with others. Reviews discuss involvement of ET with receptor binding [5,18]. Hence, one can imagine participation of ET in the electrochemical phenomena taking place in the olfactory system. A book also touches upon the aspect [19]. ET commonly occurs in the receptor protein [18]. The role played by EFs, such as those associated with the dipolar peptide bond, is discussed. The ions and positive or negative dipoles interact with the negative electron involved in ET.

Cell signaling (signal transduction) plays an important role in biology and medicine, in which there is involvement of electrochemical effects [1-9]. Animals, including humans, can be regarded as complex electrochemical systems which evolved over billions of years. Organisms interact with and adapted to an environment of electrical and magnetic fields. Humans are now immersed in a man-made atmosphere of such fields whose long-term effects are unknown. The reviews provide much evidence linking cell signaling with electrical effects, including ET. There is considerable literature dealing with electrochemical effects associated with cell signaling in the olfactory system, providing further support for the theoretical framework.

Zinc has been implicated in several of the theoretical frameworks. A role for binding to zinc was outlined in the Vibration theory approach [20]: "The involvement of zinc in or near the active site of the olfactory receptor might account for the anomalous strength of certain classes of odorants. Thiols, nitriles and isonitriles, some of which are among the strongest odorants known, coordinated to zinc readily. Indoles bind to zinc and are very strong odorants, as are oxathianes, diketones. and furanones. Binding of these molecules to the zinc ion at or near the electron tunneling site will increase their effective concentration at the receptor and, all other things being equal, allow their detection at lower partial pressures."

Zinc involvement can also be accommodated within the electrochemistry framework [7], The review addresses an electrostatic mechanism for metals cations in receptors and cell signaling. Important involvement of bioelectrical effects in olfaction had previously been recognized [1]. There are proposals linking odor and taste mechanistically [10,16]. Other modes of action have been the center of attention, namely shape and vibration of the odorant [19-21]. Although shape has lost favor in recent years, there can be no doubt that it plays an important role in receptor binding, namely the well known "Lock and key" concept. The vibration debate continues [22] involving both pro [23] and con [24] evidence. There are more recent reports on the controversy [25,26].

Taste

This portion represents a highlight of a recent review on the mechanism of taste based on electrochemistry, receptors and signal transduction [11]. The mode of action is similar to that presented in the prior section on smell.

Part A. Tastant Molecules and Electromagnetic Fields (EFs): Limited Correlation

There is some correlation between molecular dipoles with associated EFs, and taste. Molecules with no dipoles, such as hydrogen, oxygen and nitrogen exhibit no taste. Appreciable Dipole Moments (DMs) [27] are linked to substances in the main taste classes. For example, in the case of sour taste, acetic acid (vinegar) has DM of 1.70. The data for sweetness are as follows: sugars, e.g., sucrose (alcohols 1.58-1.69 DM; aldehyde, 2.75 DM; ketone 2.88 DM; ether 1.10 DM; amine, 1.19 DM; amide, 3.68 DM; ester, 1.72 DM; toluene, 0.27 DM), higher DMs are limited to quinine (bitter taste), salty taste (NaCl), and ionic acids and bases.

Part B. Interaction of Tastant Molecule EF with Receptor EFs

Interaction of the tastant as ligand with the receptor plays an important role. It is evident that the EFs alone of molecules are insufficient to rationalize the experimental observations. However, docking of the molecule into the receptor site brings the molecular EFs in contact with EFs of the receptor protein. There are many protein EFs of varying strengths associated with numerous functionalities present. Some of the functional groups possess strong EFs, as with the ions derived from acidic and basic amino acids. The most prevalent dipole and stronger one (DM-3.68) is that of the peptide (amide) bond. Alterations can occur with interactions of dipoles or ions in the receptor, hydrogen bonding, ion formation with acids and bases and covalent bonding. Thus, molecules with identical DMs and EFs can have different taste since binding to different receptors result in different EFs due to varied alterations. The important aspect of change in the strength of the tastant molecule EF field has received scant attention previously. The altered EF then propagates the sequence by interaction with neurons in the olfactory system.

Part C. Receptors, Electrochemistry, Cell Signaling and Nerves

A 1984 book provides general fundamentals and also includes some of the rudimentary aspects of the electrochemical theory [28]. The structural basis of taste discrimination must be sought in all probability at a molecular level of receptor organization. Pfaffmann and his colleagues pioneered the electrophysiology of taste [11].

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They recorded the neural responses of taste receptors to various chemical stimuli and found that individual nerve fibers showed responses to two or more types of stimuli. A taste bud consists of a cluster of cells many of which have intimate connections with nerve endings. The taste buds are possible taste receptor cells since they have extensive contacts with five nerve processes. At least two of these are taste receptor cells.

The AH, B theory was advanced in order to rationalize the sweet taste [11]. The hydroxyl groups, common in sugars, comprise the AH portion. Very close to hydrogen, there must exist another electronegative atom (B), such as O or N. The gap between the hydrogens and B is crucial. The AH, B grouping is necessary for the locking together of the sweet tastant molecules and the membrane receptor. The theory also rationalizes other sweet substances based on the AH, B pattern. A protein, bound to the membrane, is the tastant receptor. Evidently all sweet stimuli act by a common receptor mechanism.

A 1984 article provides information that is highly relevant to the electrochemical approach [29]. The gustatory cells in vertebrates are secondary sensory cells that are formed by the differentiation of epithelial cells, and are connected to the gustatory nerve via a chemical synapse. A stimulating substance adsorbs onto a microbilimembrane. As a result, the potential of the gustatory cell is changed into the direction of depolarization, and the conductor is discharged. The conductor acts on the end of the gustatory nerve to produce an impulse. The gustatory nerves are information converters for changing chemical information into electrical signals. If a stimulant is given to gustatory cells, a potential change in the direction of depolarization takes place. A large resting potential which is negative inside the cell is produced. If the nerve is stimulated, the sodium channel opens and ions outside flow inside. Opening of the channel greatly lowers membrane resistance. The potential change makes the inside more positive. The receptor potential of the gustatory cell is fundamentally the same as that of the olfactory cells. The membrane potential change occurs in the presence of various types of stimulants. When a stimulant is absorbed on the surface of gustatory cells, the membrane potential changes. There is change in membrane conformation resulting in alteration in the arrangement of charge transfer complexes and dipoles of the membrane resulting in change of membrane potential. This change is propagated by electrons to the synapse region or impulse generating position. The membrane depolarization is propagated to a synaptic gap and the potential-dependent calcium channel is activated. The calcium flow into gustatory cells result in discharge of norepinephrine.

Roper has contributed to cell signaling, neural involvement and other aspects [30-38], as has Kinnamon [39-48]. There are numerous other reports dealing with electrochemical effects in this connection [11]. A recent review deals with receptors that have been identified for various tastes [49]. Many other reports involve signal transduction [11].

Part D. Brain function

Subcortical connections route incoming signals from the receptors to brain stem regions, such as the medulla and cerebellum [28]. Higher vertebrates may respond to taste in two disparate ways. Evidence suggests that frontal brain electrical activity reveals asymmetries in activation in responses to taste stimuli [50]. Findings indicated that the electrical effect is present at birth. Other pertinent information in this category is available [11].

Investigations of electrical taste have been made. Electric taste may be described as the perception of a taste produced by passing a small current through the tongue [51]. The response profiles indicate a ion specificity for electric taste. The electrochemical theory derives strong support from the many studies that associate electrochemistry with taste.

Touch

This sensory perception mainly deals with the skin. Since evidence indicates involvement of electrochemistry in the other senses, it is reasonable to assume the possibility of participation in the sense of touch. The act of touch induces transmission of an impulse in the nervous system to the brain. There are reports on a role for electrochemistry, although this aspect has attracted little attention. A crude hypothesis for ET involvement in neurotransmission was advanced in 1983 [52]. Later, electron translocation brought about by redox reactions was visualized as being the primary mechanism whereby electric fields are generated in the living cell [53]. Fast movement of electrons results in polarization, which establishes an electrical gradient. Electron migration conceivably progresses by means of radical intermediates. In 1996, the ET concept was applied to regulatory action of NO in neurotransmission, toxicity, and immunological reactions [54].

A 2004 review summarizes the present status of electrophysiological effects, and deserves special attention [55]. After a burst of research dealing with electrical coupling, gap junctions became less popular among the neurobiologists vs. the ionic approach. Recent reports have brought gap junction back into the spotlight, suggesting that this type of cell-cell signaling may be interrelated with, rather than an alternative to, chemical transmission. The thesis is credible because the electromagnetic effects of electrons and radicals in motion should have an influence on positive and negative charges associated with the Central Nervous System (CNS). The generally accepted view of neurotransmission entails movement of ions in channels and gap junctions. This movement results in establishment of an electrical field. However, this aspect has attracted scant attention. The presence of these fields could well play a role.

A report deals with electrical stimulation of the skin [56]. When a sensor contacts the skin, an electrical stimulation translates the acquired information into a tactile sensation, such as pressure or vibration. In relation to skin receptor types, there

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are four mechanoreceptors, namely Meissner corpuscles, Merkel cells, Ruffini endings and Pacinian corpuscles. An electrical current from surface electrodes generates an electrical field inside the skin, inducing nerve activity. If the current flows from a central electrode, acting as an anode, it elicits an acute vibratory sensation. A cathodic pulse seems to selectively stimulate nerve fibers connected to Merkel cells, whereas an anodic pulse activates nerve fibers connected to Meissner corpuscles. Electrophysiological studies support this selective stimulation. Mathematically, analysis of a nerve-fiber electrical model revealed that a cathodic pulse selectively stimulates nerve axons running parallel to the skin's surface, whereas an anodic pulse efficiently stimulates vertical oriented nerves.

Various studies are reported on electrical stimulus of the skin. An example is the effect of pulse height and pulse width on the magnitude sensation of electrocutaneous stimulation [57]. Experiments were performed to determine the relationship between the pattern of stimulus of nerves and the size of action potentials in frog's skin [58]. The stimulating effect was determined of electric alternating impulses on the skin sensitivity of man [59]. An electrochemical stimulator system was used for neurophysiological and psychophysical studies of pain involving the skin surface [60]. A survey was performed comprising electrical stimulation of sensory nerves with skin electrodes for research, diagnosis, communication and behavioral conditioning [61]. Exposure to oscillating magnetic fields influences sensitivity to electrical stimuli of the skin [62]. Weak alterations of the magnetic field may induce hyperalgesis in humans. Frequency-related effects were determined in the optimization of magnetic stimulation of the nervous system in the skin [63]. Changes were identified in human skin electrical properties due to long-term neuromuscular electrical stimulation [64]. Intermittent stimulation delays adaptation to electrocutaneous sensory feedback [65]. The effect of stimulation waveform on pattern perception was investigated on a fingertip electrocutaneous display [66]. Data show that electrovibratory perceptual sensitivity to positive electrical pulses is less than that for negative pulses [67]. The disparity may be due to the asymmetric electrical properties of human skin. A study was made of pulse electrical stimulation on cells involving skin wound healing [68]. A report deals with vulnerability of skin to electric current perception [69]. This susceptibility condition to various exogenous factors suggests the intervention of neuropeptides and other neurobiological mediators.

Vision

Rhodopsin

Electrical phenomena may be found operating in the rhodopsin portion of the eye. Neural ectopic wiring in retinal degeneration, such as retinitis pigmentosa, may form functional synapses between cones and rod bipolar cells that cause atypical signal processing [70]. In a study, the multifacial Electroretinography (ERG) of an animal model, the rhodopsin P347L transgenic pig, were measured to examine the source and nature of altered signal processing. A report deals with ERG changes along with rhodopsin content in the isolated retina and eye cup of rats during retinal degeneration [71]. A comparison was made of electrically evoked and channel rhodopsin-evoked postsynaptic potentials in the pharyngeal system of *Caenorhabditis elegans* [72]. A report deals with rhodopsin and the electrical activity of the retina in congenital night blindness [73]. In a study of rhodopsin, a link appears to exist between chemical and electrical processes following light absorption [74]. An electrical approach was used to investigate rhodopsin activation [75]. The electrical properties of proton pumping rhodopsin have been examined [76]. Electrostatic interactions appear to play a critical role in rhodopsin activations [77]. There appears to be electric-field control of the bacteriorhodopsin photocycle, which has functional relevance [78].

There are other relevant aspects in the biochemistry of vision. Much attention has been devoted to light-induced cis-trans isomerization of the photosensitive rhodopsin. However, evidence also supports the involvement of ET and electrical phenomena. Upon photoexcitation of the chromophore, energized electron density in the highly unsaturated retinal chain is redistributed to the iminium end, causing a variety of events including cis-trans isomerization. The phenomena have been designated sudden polarization [79,80]. The evidence, including theoretical studies, points to a fundamental role in the initial stage of the visual process for ET in the retinal iminium moiety of rhodopsin. Electron migration of the negative charge cancels the positive charge on nitrogen. The generated radical cation on the retinal portion is delocalized. More than 30 years ago, the suggestion was made that this polarization is a crucially primary event in the overall mechanism leading to vision. Movement of electrons and positive charges during photo-induced ET is equivalent to establishment of an electrical current. The electrical signal triggered by light may, in turn, bring about a change in ion permeability of the disk membrane.

In most cases of ET, the process is intermolecular, in contrast to the intramolecular nature for rhodopsin. Establishment of the carbocation and loss of charge on nitrogen necessitate adjustments involving counterions. Electrostatic interactions were noted between electron deficient sites in the chromophore and charged or dipolar groups in the opsin [81]. The negative point charges were located near delocalized positive regions at C-12 and C-14.

Eye Illnesses

There is widespread participation of electrochemistry in eye insults. Electroretinography (ERG) is valuable for evaluation of visual function of animal models [82]. Both naturally occurring, and genetically-manipulated animal models of human retinal and optic nerve diseases have been studied in this manner. ERGs have proven to be quite useful for investigating visual functions in animal models of these human eye diseases. A novel experimental technique involving spectral electrical impedance was used to examine eye ulcers in animals [83]. The method may be helpful in diagnosing ocular surface diseases, such as dry eye syndrome. In ERG studies, some patients with acute zonal occult outer retinopathy show symptomatic acute visual impairment in one eye only, but electrophysiological abnormalities in both eyes [84]. The technique of axonal electrovisiogram can be considered to involve a visual evoked potential capable of recording the electrical activity of the optic nerve and inner retina [85]. The method may be useful as an electrophysiological test in the diagnosis of neuroretinal diseases. Electrophysiological testing is the preferred tool for examination of functional visual loss following chemical eye burn [86]. Various investigations were carried out involving electrical stimulation of the eye. Electrical stimulus was used in a study of eye movements [87]. A report deals with intraoperative monitoring of visual function using cortical potentials after electrical epidural stimulation of the optic nerve in connection with tumor removal [88].

Macular Degeneration and Retinal Pigmentosa

There is increased risk of degenerative diseases that affect the retinal cells with increasing age. Age-related macular degeneration, the loss of cells in the macula-near the center of the retina, affects millions of people around the world. Symptoms start with loss of fine vision, but can lead to declining vision and ultimately blindness in many cases. Retinitis pigmentosa is a genetic disorder that primarily affects photoreceptors in the retina, leading to incurable blindness. Symptoms include decreased night vision, decreased peripheral vision, and decreased central vision. Electrical stimulation of the retina and other technological approaches have become increasingly researched areas for restoring vision [89-94]. A review deals with electrical stimulation of the retina using implantable microelectrode array [95]. In both types of defects, the retina stays intact, but the light sensing photoreceptors do not function. A potential solution to the problem is retinal prosthesis. The implant is placed beneath the retina to essentially replace photoreceptors with connection to electrodes and the nerve center [96-98]. In a second type, the implant is placed on the surface of the retina.

Facial Nerve Paralysis

Facial nerve paralysis is a common problem which is caused by Bell's palsy, trauma, tumor compression, or infection. Patients with facial nerve paralysis lack control over important muscles involved in facial expression. Blinking, rapid closing and opening of the eye spread tears over surface of the cornea, which is a necessary function to keep the eyes lubricated. Electrical stimulation in eyelid reanimation was shown to be potential treatment for facial nerve paralysis [99]. This portion is also relevant to electrochemical involvement in illnesses.

Hearing

Considerable research has been done on electrical involvement with hearing, much of which deals with electrical stimulation. The general participation of electrical phenomena in the CNS, discussed in the Touch section, is also applicable to the auditory nerve. There is appreciable literature dealing with electrical stimulation of the ear which suggests a role for electrochemistry on operation. Also, there is a unifying theme since the technique has been used in the study of other senses, particularly smell and taste (see earlier sections).

Electrical stimulation of the cochlea is known to cause auditory sensations in humans and other animals [100]. It has been shown to produce emissions of sound from the inner ear. The relationship between electrically induced motion of the Basilar Membrane (BM) and production of otoacoustic emissions was studied. The hypothesis was tested that electrical current-induced movements of the Outer Hair Cell (OHC electromotility) result in intracochlear acoustic pressure which causes traveling waves on BM. Results provide direct support for a mechanism of cochlear sensitivity and tuning involving high-frequency OHC electromotility. Moreover, the data also indicate that any intra- or extracochlear electric current which affects the electric polarization of OHCs could induce BM traveling waves and cause 'Electronic hearing'. This form of hearing would be one component under the more general definition of the electophonic effect.

Application of electric stimulation to the cochlea induces an acoustic emission in the ear canal [101]. These emissions are produced by basilar membrane motion, and have been used to suggest a corresponding acoustic sensation termed "Electromotile hearing" which has been attributed to electric stimulation of Outer Hair Cells (OHCs) in the organ of Corti. Electric stimulation of the cochlea results in perception of a tonal sound at a frequency of 8 Hz or above. Mammalian OHCs convert electrical energy into mechanical energy [102]. The significance of this electromotility rests in the ability of the OHCs to modulate the vibrations of the cochlea partition in vivo. Electrical stimulation of the guinea pig cochlea induces a mechanical response of the basilar membrane for frequencies to at least 100 kHz. The OHCs play a critical role in mammalian hearing [103]. OHCs enhance basilar membrane motion through a mechanical feedback process within the cochlea, called the cochlear amplifier. The basis of the cochlear response is believed to be a voltage-dependent electromotile factor. This response to sound stimulation appears to enhance the sensitivity and selectivity of the cochlea [104]. These OHC mechanical changes feed energy back into the cochlea before completion of the transduction process by the inner hair cells. OHC electromotility may depend on certain transmembrane proteins. The electromotile response is thought to underlie the sharp tuning and sensitivity of the mammalian inner ear, and contributes to the production of Electrically Evoked Otoacoustic Emissions (EEOAEs) [105]. Results suggest a biological origin of the EEOAE in the cochlea, which could involve electrically-evoked stereocilia bundle movements. The OHCs of the cochlea have an electromotility mechanism, based on conformational changes of voltage-sensitive motor proteins in the lateral plasma membrane [106]. The translocation of electrical charges across the membrane during electromotility induces a voltage dependency to the membrane capacitance. Two different calcium-dependent pathways may control the OHC motor output. One route shifts the voltage sensitivity of the OHC electromotile mechanism. A salient feature of peripheral sound processing in the mammalian cochlea is high-frequency resolution [107]. The sensitivity originates in amplification of the wave on the basilar membrane by OHCs, where electrically induced mechanical action of the OHCs is believed to be the crucial component. The electromechanical process of the OHCs possesses the ability to bring about amplification of the traveling wave. The OHCs are believed responsible for the high sensitivity and selectivity of mammalian hearing [108]. Molecular motion appears to cause the electrically-driven length change (electromotility) of the OHCs.

Electrokinetic effects might also play a role. A study showed that chlorpromazine in large doses may decrease hearing or otoacoustic emissions [109]. In the process OHCs electromotility is altered. In the mammalian cochlea, the basilar membranes mechanical responses are amplified, and frequency tuning is sharpened through feedback from the electromotile OHCs [110]. OHCs undergo elongation-contraction cycles when stimulated by electricity [111]. This electromotile response is believed to underlie the high sensitivity and frequency selectivity of amplification in mammalian cochlea. In an investigation of OHC electromotility, DC electrical pulses either elongate or shorten the cell and electrical stimulation results in mechanical oscillations [112]. Cell turgor is required so that pressure gradients associated with the electromotile responses can be communicated to the ends of the cell. Loss in cell turgor lessens the electromotile response. Basilar membrane vibrations induced by direct current are similar to those brought about by acoustic stimulation, which can transfer to other organ parts by traveling waves [113]. The electromotile properties of OHCs contribute largely to hearing sensitivity and frequency selectivity, leading to generation of otoacoustic emissions [114]. Cochlea OHCs in humans showed electromotility in voltage steps similar to that in rodent models [115]. Electrically evoked oto-acoustic emissions are sounds evoked in the canal when AC current is led into the cochlea [115]. The result is attributed to activation of fast electromotile responses in OHCs. Acoustic enhancement occurs when the emission amplitude is increased by moderate-level sound. A report deals with the radial pattern of basilar membrane motion evoked by electric stimulation of the cochlea [116]. There are related reports on electrochemistry [117-122].

The literature contains other reports dealing with hearing and electrical effects. Electropuncture therapy is used for sudden hearing loss [123] and in chronic pain patients [124]. Research was done on inner ear metabolism and electrical physiology of autoimmune sensoneural hearing loss [125]. A stochastic model was used for electrically stimulated auditory nerve pulse-train response [126]. A study involved the effects of electric stimulation on the electrically evoked compound action potential [127]. Electrophysiological evidence was obtained for “Streaming” in auditory evoked potentials [128]. An investigation dealt with changes in speech with electric sound amplification [129]. Electrophysiological evidence exists for response priming and conflict regulation that are consistent with an information processing model [130]. Loudness-coding mechanisms were inferred from electric stimulation of the human auditory system [131]. Results indicate that, as suggested by depolarization models, in vivo electrical stimulation-mediated neuroprotection requires the activation of voltage-gated calcium channels [132]. Electrophysiological evidence is reported for prefrontal cortex involvement in preattentive auditory deviance detection [133]. Other electrophysiological approaches suggest that the mismatch negativity is generated by a temporofrontal network subserving preattentive auditory change detection. A study was made to determine the usefulness of electrostimulation in treatment of persistent noise-induced cochlea lesion tinnitus [134]. Low frequency acoustic and electric stimuli produced similar auditory perceptions [135]. Electrocochleography and auditory brain stem response were examined in relation to Ramsay Hunt syndrome [136]. The exact mechanism by which the basilar membrane movement excites the hair cells is the subject of lively controversy and many theories [137]. It is likely that bending or shearing movement of the hairs relative to the apex of the cell induces a change in the difference in electrical charge between the contents of the cell and its surroundings. This change, technically a depolarization, will in turn stimulate the release of a chemical transmitter, probably glutamic acid. The substance initiates nerve impulse in the sensory nerve that has connections with the hair cells.

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