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Clinical Endocrinology and Metabolism

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Review Article

Theories of Hearing: „A New Submolecular Perspective"

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Received date: 17 March 2025 | **Accepted:** 31 March 2025 | **Published:** 10 April 2025

Citation: Jan Myjkowski, (2025), Theories of Hearing: „A New Submolecular Perspective", *Clinical Endocrinology and Metabolism* 4(2): 10.31579/2834-8761/078

Abstract

The travelling wave theory was proclaimed by Georgy von Bekesy (1899-1972) in 1928. The author attempted to explain physiological processes by means of physics and mechanics alone. Bekesy's successors tried to modernise this theory. Not much attention has been paid to complex molecular processes in the receptor and auditory cells. This paper specifies certain fallacies of the travelling wave theory. Specific focus is given to mechanisms on a submolecular level related to the hearing process. The significance of transformations taking place in an auditory cell is emphasised. The essence of the new theory lies in a hypothesis of a changed pathway a sound wave takes to reach the receptor. The signal is transferred from the auricle, through the ossicles of the middle ear and the stapes to the receptor via the bony pathway. The study presents nanostructures and nanoprocesses related to the reception and processing of auditory information. Hence, the theory has been named the submolecular theory of hearing.

Keywords: datura stramonium; atropine; anticholinergic syndrome; devil's apple; pipe flower

Introduction

Bekesy's travelling wave theory is founded on the assumption that a wave is reflected by the cochlear fluid in 99.9%. Assumedly, this loss of energy is offset by amplification in the middle ear [1,2]. A sound wave hits the flexible tympanic membrane that reflects ca. 20% of the sound wave energy. The wave that reaches the tympanic membrane at the intensity of 90 dB = 500 nm, 1000 Hz – on the side of the tympanic cavity is 80 dB =100 nm, whereas on the stapedial footplate on the side of the inner ear, the amplitude of this wave is 60 dB = 11.7 nm, and in the fluid in the initial section of the vestibular duct ca. 25 dB = 0.275 nm. Here, the wave is not amplified 44 times = 33 dB. As for stapedotomy, the area of the tympanic membrane is 100 times bigger than that of the piston whose diameter is 0.4 mm. There is no description of a sound wave being amplified 100 times. The lever operating in the middle ear causes a decrease in the sound wave amplitude at the ratio of 1.3: 1, with the amplitude of a sound wave decreased 1.3 to 1. The threshold wave amplitude 8 pm is 6 pm for the input wave on the side of the tympanic cavity. The sound wave energy loss on the tympanic membrane is ca. 20-25%. This amplitude is decreased by means of the level mechanism to 5 pm. On its way to the receptor through the cochlear fluid, the sound wave amplitude becomes hundred times lower. Sounds like this can be heard by young healthy individuals. At high frequencies, there is no vibration of the ossicles as mass, the lever is not working, and the sound wave is not amplified. At this stage of the pathway, a sound wave with the amplitude of 5 nm cannot trigger a travelling wave on the basilar membrane, fluid movements, bending of hair cells. A wave like that cannot be amplified via a mechanical method as it is not received by the receptor.In an ECoG study, the time in which a signal reaches the measurement point from the external auditory canal is 1.5 – 1.9 ms. [3]. The time in which the signal is propagated through the basilar membrane and the cochlear fluid is estimated at 5-6 ms. A contraction of the cell takes place after the auditory cell is depolarised. Depolarization depends on the activity of ion channels. If depolarization pertains to the entire cell, that cell can shrink only ca. 250 - 300 times per second, since the ion channels are active in a cycle, ca. 4-5 ms. There is an opening stage, a closing stage, an inactivation stage, and a refraction stage. The depolarization of an entire cell would result in a spike discharge independent of the stimulus that triggers depolarisation. To confirm the frequency of OHC contractions, isolated auditory cells were subjected to testing by means of teasing with electricity. The activity of the ion channels was not taken into account. The activity of these channels in the side and bottom walls of the auditory cell restricts the frequency of simultaneous depolarization and contraction of the entire cell. In the situation of a limited depolarization, without a simultaneous contraction of the entire auditory cell, a problem arises regarding signal amplification by means of an OHC contraction and the pulling of the basilar membrane. OHC contraction after depolarisation is responsible for amplifying soft tones (40-50 dB). Depolarization of the cell causes the cell to contract regardless of sound intensity [4]. There is no mechanism that would determine which tone should be amplified. A tone that is below the excitability threshold cannot be amplified. A received tone causes receptor potential and then action potential is formed, which is transmitted to the centre. At this stage, a received tone does not require amplification. As for multi-tones, whereas a higher intensity tone is received and transferred to the centre, a soft tone needs to be amplified by means of pulling by the basilar membrane that overlap with another travelling wave on the basilar membrane. The mechanical amplification of soft tones by 40 dB causes signals below 40 dB to fail to reach the centre. An additional time of soft tone amplification is at least 0.25 ms; in that time, ca. 360 mm of the acoustic wave runs through the cochlear fluid, each millimetre of the wave carrying new information. This information overlaps with the amplified wave. An OHC contraction shortens it by 4%. The OHC length in the vicinity of the oval window is 1000 nm. If half of that shortened value of 4% is able to pull the basilar membrane by 20 nm, the tone is amplifyied by 60 dB. The OHC length in the viicinity of the cupula is 4,000 nm and the 4% contraction that pulls the

basilar membrane by 2% (one end of the OHC) is 80 nm, which is ca. 70 dB. Amplitudes of these overlapping waves are added together. On the lower OHC pole there is a network of synapses of afferent and efferent innervation. A synapse is a nanoprocessor that is 50 nm in diameter – a space filled with a fluid that a transmitter is injected into. An OHC contraction whose frequency is up to 100 kHz causes the basilar membrane to be pulled by these delicate structures.

The immobilisation of the basilar mambrane by means of introducing about 20 electrodes into the tympanic duct in a surgery for partial deafness has no negative effect on the existing hearing ability [5]. In rehabilitation of patients following the cochlear impact surgery undergone due to partial deafness, an air conduction hearing aid is applied for accelerating rehabilitation. The patient receives sounds without the basilar membrane vibrating. The basis of the travelling wave is hydrodynamics of the cochlear fluid[,The vibrating stapedial footplate causes the fluid inside the vestibular duct to vibrate and a change in pressure on both sides of the basilar membrane, leading to the formation of the travelling wave on the basilar membrane. According to the theory, the fluid wave runs from the oval window to the cupula and further to the round window, where the sound wave energy becomes dampened. This is not the pathway that a signal takes to reach the receptor. In his estimates, Bekesy turns the cochlea into a straight line, removes Reissner's membrane so that the sound wave runs on both sides of the basilar membrane. Resonance involving the sound wave and the frequencies of the natural vibrations of the basilar membrane is taking place. The wave goes through the cochlear fluid and the tegmental wall, via the fluid under that membrane, the wave reaches the auditory cells of the organ of Corti without transferring the information to the receptor. The wave propagates towards the basilar membrane to trigger a travelling wave on that membrane. Allegedly, the greatest displacement of the formed travelling imposes a flow of the fluid in the cochlear duct that bends or tilts hair cells to tension fibres that connect adjacent hair cells. The cadherin fibres pull on the basilar membrane of an adjacent hair cell. This tip-links mechanism supposedly determines the coding and transfer of amplitude, frequency, phase shifts, quantitative, accent and melody. Pulling with a link up to 100 kHz is responsible for gating mechanically-activated potassium ion channels that determine the depolarisation of an auditory cell. At low frequencies, the stapedial footplate makes a piston motion and transmits the sound wave energy to the cochlear fluid. Low frequencies are well conducted by all tissues. This is evidenced by a child's hearing in the womb in the second half of pregnancy. The outer ear and the middle ear are not functioning – the child can hear, recognize the mother's voice and remembers that voice after birth. The elephant can receive low-frequency sounds that propagate on the earth with its feet. At medium frequencies, the stapedial footplate vibrates in the transverse axis of the stapes. At high frequencies, the footplate vibrates in the longitudinal axis of the stapes. When one half of the footplate is generating forward motion, at the same time, the other half of the footplate is generating regressive motion. A loss of energy occurs due to the friction of opposite currents in the fluid and due to destructive interference of waves. The resulting altered wave cannot cause resonance with the basilar membrane, and a travelling wave cannot be formed. A well-educated musician can distinguish up to 3,000 frequencies. If wave resonance and the greatest displacement of the travelling wave determines the coding of a frequency, the section of a basilar membrane that is responsible for identifying differences in the sound wave frequencies is 0.0106 mm. Sound waves that last for tenths of ms are recognized when the energy is transferred by one or two periods of the wave. A wave resonance is a transfer of energy in time. A signal that is that short reaches the receptor and is recognized via a different way. A transfer of a sound wave energy is a transfer of pressure, that is, a maximum amplitude of a wave in every period of that wave. A wave length is the quotient of the speed of the wave in the medium and its frequency. For the frequency of 100 Hz in the cochlear fluid and the speed of 1450m/s, the length of a sound wave is 1450 cm. The maximum displacement of the wave occurs halfway the length of the wave, that is, at 725 cm of the wave period – every 1450 cm. Resonance on the basilar membrane that is 3.2 cm long in humans is unlikely. The pigeon can hear a sound wave at the frequency of 10 Hz. The wave length in the cochlear fluid is 145 metres with the length of the basilar membrane ranging from 5 to 7 mm. The western barn owl can hear sound waves whose input amplitude is 1 picometer. That wave is up to 300 times smaller than the diameter of the atoms that the basilar membrane comprises. The input amplitude of that wave is 100,000 times smaller than the diameter of hair cells it allegedly bends or tilts. A wave that small becomes about 100 times smaller on its way via the cochlear fluid. Laser vibrometry studies have shown that a sound wave of 800 Hz, 90 dB with the amplitude of 500 nm in the hearing canal that is examined in the round window is 0.5 nm long. The amplitude becomes 1000 times lower [6]. The energy of the wave is proportionate to the amplitude squared. The pathway to the round window is not the pathway to the receptor; however, on the pathway of the fluid to the cupula, during the formation of wave resonance, the highest loss of energy occurs due to absorption damping, reflective damping, interferential damping, and wave dispersion in the fluid caused by the presence of electrolytes and other microparticles. Instead of 90 dB, the input value of the wave was specified as 60 dB. Using the available method, no wave on the round window has been recorded. What pathway do 10dB or 20dB waves that are audible to us take to reach the receptor? There is no explanation as to how each travelling wave on the basilar membrane grows with the growing distance from the oval window – even if resonance is not possible. There is no explanation as to how the information is transferred from a longitudinal wave in the fluid to the transverse wave of the basilar membrane where vectors of the forces are perpendicular. Each wave frequency has a different speed at which a travelling wave propagates from the oval window to the cupula. A sound wave in a fluid runs at the speed of 1450 m/s. Resonance of this wave and a travelling wave that runs at a variable speed from 50 m/s in the vicinity of the oval window up to 2.9 m/s in the vicinity of the cupula is unlikely. Assuming that at a certain distance from the cupula, the speed of the travelling wave is 10 m/s, that wave is 145 times slower than the wave imposing resonance. Importantly, on 1 mm of the reflected wave the information of 145 mm of the incident sound wave is recorded. This compression of the data is transferred to the cochlear fluid, hair cells, cadherin fibres, and the receptor.

Submolecular theory of hearing

The auditory information coded by quantized energy of a sound wave are transmitted from the auricle, the middle ear and the bone capsule of the oval window onto the bony labyrinth of the cochlea, to crista spinalis and to the hearing receptor. The transmission occurs by means of a sound wave that transmits the encoded information to the receptor that receives the signals and forwards them to the auditory cell. Further analysis and processing of the information takes place in the auditory cell [7]. Low frequencies are easily transmitted via all the media, and are also transmitted via the cochlear fluid with the reservation that the information is forwarded by a sound wave without the mass of the environment being moved. The mechanism for receiving and processing the information operates on a submolecular and electron level. A stimulus adequate for the hearing organ is the energy of a sound wave transmitted via the vibrating particles of the medium to the receptor. All the atoms in the matter of the medium that the sound wave propagates in and the molecules and atoms that form the hearing receptor are in constant motion. It is a progressive motion – oscillatory and rotary motion or a combination of the above. Motion is related to kinetic energy of molecules, which also have potential energy that is the energy of chemical bonds, electrostatic attraction forces, and electromagnetic interactions. The sum of these energies forms the inner energy of a molecule. The total inner energy is also determined by temperature and the mass of a molecule. Providing external energy – sound wave energy specifically when it comes to hearing – to the molecule of the hearing receptor causes a rise in the internal energy of a sound-sensitive molecule that receives the signal [8]. The vibrating particles of a sound wave in a medium have either a positive charge, a negative charge or a neutral charge. Neutral ones transfer potential energy determined by the speed of vibrations and frequency, as well as electron energy by means of contact between electron clouds of molecules. Electrons form an electron cloud around a nucleus of an atom. The size of that cloud depends on the number of orbits that electrons are situated on. An electron can change an orbit; however, in order to go to an orbit that is closer to the nucleus, an electron needs to receive additional energy. Going from orbit 2 to orbit 1 requires 3.4 eV. These jumps are quantized, meaning that there is either a jump or no jump – without any transitional option. If an

atom in a molecule of the acceptor receives a quantum of energy from another atom or a particle (from a sound wave), then the electron of the acceptor jumps to an orbit that is closer to the nucleus – its inner energy increases – incrementally – in a quantized manner. This puts the atom in the so-called excited state which, unlike the ground state, is impermanent as it lasts ca. 10-8 of a second, followed by an immediate attempt to return to the ground state by means of emitting 1 photon of energy – in situations where the issue pertains to 1 atom jumping 1 orbit. If in a combination of a receptor molecule + energy of the sound wave there is an unlimited number of such jumps, then there is 1020 combinations of various kinds of quantized energy being transmitted. This gives an unlimited number and variety of transmitted information. The time required for simple changes in energy between the molecules is 10-14 s. More complex conversions take 1000 times longer; nonetheless, that is still 10-11 s. The energy that codes the information of sound-sensitive molecules that receive this information from a sound wave is forwarded to molecules responsible for gating mechanically-activated potassium ion channels. The transferred energy acts on the activation and inactivation gates of the potassium channel that determine the influx of potassium from the endolymph to the auditory cell. Sound wave energy causes changes in the rotation of atoms, alters angles in the bonds, oscillation, leading to changes in the conformation of molecules; by means of changing their size and dimensions, the conformers that are formed fulfil a role consisting in closing and opening of an ion channel. The mechanically-activated potassium channel has a selectivity filter that ensures inflow of potassium ions only. With the potassium channel fully open, in 1 ms, as many as 6,000 potassium ions flow from the endolymph into the auditory cell. The influx of K+ ions inside the cell triggers its depolarisation. With the threshold of 10 mV exceeded, potential-dependent Ca++ ion channels are activated. Local depolarisation increases, more and more Ca++ channels dependent on depolarisation and voltage-dependent Na+ channels on the lateral surface of auditory cells open up. The interior of the cell has a negative charge of - 80 mV owing to a high number of proteins whose charge is negative and continuously active sodium potassium pumps. Outside the cell, the level of Na+, Ca++ and Cl- is high which combined with a high electric potential forms a high electrochemical potential for sodium and calcium ions. The influx of Ca++ ions into the cell causes a release of calcium ions from mitochondria, the endoplasmic reticulum and the nucleus of the cell. The calcium level outside the cell is 10,000 higher than the baseline calcium level inside the cell, which can become even 100 times higher inside the cell. Following excitation, membrane potential changes to receptor potential. Inside the cell, calcium is combined with calcium-depended proteins, thus altering their properties. The information is split between constitutive activities related to regular work of a cell and to regulated ones which are related to production, transport, and release of the transmitter. Once the calcium level has been increased and the information has been transferred, the calcium level inside the cell is rapidly reduced. Calcium pumps are and ion exchangers that expel calcium ions outside the cell are working, and some of the calcium is transported to mitochondria, the endoplasmic reticulum, and the nucleus. Intracellular messengers, varying calcium levels, and the activity of intracellular proteins are responsible for intracellular amplification. The cellular membrane at rest is most permeable for potassium ions and for that reason, the value of the resting potential of the cell membrane is close to the resting potential of potassium. The natural drive to balance out the concentration and the voltage on both sides of the membrane, which is consistent with the second law of thermodynamics, consequently eliminates the membrane potential. This is counteracted by the presence of ion pumps and ion messengers, the active mechanism that creates a difference in voltage and potential on both sides of the membrane. This produces a chemical and electric gradient. In the case of auditory cells, there is a unique situation since the side and bottom walls of these cells are in contact with the perilymph or the interstitial fluid characterised by a low potassium ion level and a high sodium ion level (K+ 7-8 mEq/l, Na+ -140 mEq/l), whereas auditory hair cells and the top part of the auditory cell are surrounded by the endolymph with a very high potassium concentration and a low sodium concentration (K+ -150 mEq/l,Na+ -15 mEq/l).The activity of ion channels is affected by phosphorylation and dephosphorylation of channel proteins, ATP concentration inside and outside the cell, cAMP and cGMP levels, and the cell's pH, mechanical energy (the sound wave), osmotic pressure, the oxidation-reduction potential, or the presence of ligands. A mechanism of great importance for hearing is proteins – sound-sensitive molecules sensitive to a given frequency and intensity of a sound wave, genetically conditioned, which react to an adequate stimulus – the sound wave energy that codes all the information. The energy of a sound wave causes an influx of potassium ions into the cell but at the same time, these ions are flowing outside the cell via potassium leak channels in the side wall of the cell. A specific balance in the K+ levels is preserved. An overly low inflow of K+ ions through the mechanically-activated potassium channels of the hair cells does not affect this balance. Once a certain limit called the threshold is exceeded, a cascade of consequences occurs inside the cell alone. The higher the density of potassium ion channels on the hair cells and in the top part of the auditory cell, the lower the excitation threshold for that auditory cell is. It is doubtful whether only one potassium channel is used for every two hair cells [9]. Potassium ions with a positive charge that flow into the cell from the endolymph cause depolarisation, which is a factor that triggers conformation changes in proteins that are responsible for the transport capacity of voltage-dependent calcium and sodium ion channels in the side wall and the bottom part of the cell. Sodium channels react to an excitation in a much quicker way than potassium channels; hence, the cell membrane becomes permeable for sodium ions first. The elctro-chemical potential is much higher for sodium ions than potassium ions. The force that drives ions is greater and affects the speed of the sodium ion influx into the cell. The growing depolarisation is conducive to opening of more and more sodium channels. A positive feedback loop occurs: the inflow of sodium ions increases depolarisation and depolarisation causes new ion channels to open up, resulting in a swift depolarisation of the auditory cell. The membrane potential nears the balance potential for sodium ions, whereas the electric potential – which is the force that drives these ions – ears zero. The force that drives potassium ions grows. The opening of more and more voltage-dependent potassium channels obstructs depolarisation. The factor that rapidly obstructs depolarisation is the phenomenon of inactivation of Na+ ion channels. After about 1-2 ms from the opening of the channel, they are inactivated – at that time, they are being closed and rendered unsensitive to stimulation. The inflow of potassium via the potassium channels in the side wall of the call and the inactivation of sodium channels lead to a reverse situation, where the cell is repolarised and hyperpolarisation occurs, which is a stimulus for closing the potassium channels and a return to a balanced state. Repolarisation and hyperpolarisation cause sodium channels to go from the inactive state to the closed state, sensitive to re-stimulation. The membrane potential goes back to the balanced state. A full work cycle of a sodium ion channel (activation, opening, closing, inactivation) is ca. 4-5 ms, which offers the possibility to receive the information carried by the sound wave to the frequency of 250 Hz, assuming that at the same time the entire auditory cell becomes depolarised. Receiving higher frequency sounds requires a higher number of ion channels activated at various points in time that transfer the information to the synapse without the auditory cell undergoing depolarisation and contraction all at once. The calcium channels in the side wall of the auditory cell is where the influx of Ca++ ions makes its way into the cell. The calcium level inside the auditory cell is ca. 100 nM/l, whereas in the interstitial fluid, it is ca. 1,200,000 nM/l. The vast amount of the calcium in the cell is stored in the endoplasmic reticulum and the organelles of the cell. The depolarisation of the cell and the inflow of calcium is a signal for it to be released from the intracellular reserves. The calcium inflowing through the ion channels along with the calcium released from the cellular storage sites spreads inside the auditory cell. As a result of the growing concentration of cytoplasmic calcium ions, they are bound with specific proteins that are activated in this manner, thus increasing the activity of various protein kinases. For this mechanism to be able to work, there needs to be a mechanism responsible for reducing the calcium level inside the cell in a very swift manner decrease after the information is transferred. This is the task of the pump that discharges the Ca2+ ion outside the cell in return for 2 H+ ions that are imported into the cell. The Ca2+H+ATPase is working, which derives energy from ATP. Another mechanism that lowers calcium levels in the cell is counter-transport dependent on the concentration of Na+ ions, which exchanges two Na+ ions from the extra-cellular space for one Ca2+ ion that is discharges outside the cell. The third mechanism is

ion pumps that move calcium ions from the cellular fluids to the organelles, mainly mitochondria, the endoplasmic reticulum, and the nucleus. Calcium regulates numerous intracellular mechanisms, its key task being taking part in the transfer of the intracellular information, as well as amplifying and disseminating it. This consists in Ca2+ ions affecting the following enzymes: adenylyl cyclase, phosphodiesterase, phospholipase A2, protein kinase A. Calcium ions are the second messenger and participate in the forming of other second messengers such as cAMP, cGMP, IP3 , and DAG. Intracellular amplification works by means of second messengers and Ca2+ receptors. Once bound with calcium, these proteins change their biological properties and affect other proteins thus impacting cellular reactions. There are many Ca2+ receptors; a particularly significant one is calmodulin, which has four calcium-binding sites. With subsequent ions connecting to the binding domains, conformational changes in the calmodulin particle occur, thus increasing its ability to bind with enzyme particles. Enzyme activation takes place once at least three Ca2+ ions are connected. At the calcium level of 10-6 mol/l inside the cell, the activity of the calmodulin-calcium complex is 1000 times greater than the activity of the calmodulin alone. It is one of the key elements of intracellular amplification [10]. This complex acts directly on enzymes or indirectly by stimulating calmodulin-dependent protein kinases that by means of enzymatic protein phosphorylation transform them into an active form. The stage of transferring the information in the auditory cell related to calmodulin leads to the signal being split in different directions. The amplified signal continues to be forwarded towards the centre but at the same time, calmodulin is activating many so-called constitutive processes, that is, processes that occur in a non-excitable cell. The second system activated by the calmodulin-calcium complex consists in regulating the co-activity of all the organelles of the cell. The third one, relatively slow, consists in regulating the production of proteins, particularly enzymatic proteins. Changes can affect the process of generating enzymes or the speed at which they are broken down. The speed of the reaction is also affected by enzyme activators and inhibitors. These three process regulation systems cooperate to ensure that constitutive and regulated processes are well coordinated. Calcium is an information transmitter that precedes the formation of other second messengers (cAMP, cGMP, DAG, IP3) that are produced by enzymes stimulated by a spike in the calcium levels or activated by proteins G. The stage of producing second messengers is one of several mechanisms of intracellular amplification. A single particle of the enzyme can produce hundreds of second messengers. The energy of aexternal signal that triggers a chain of intracellular reactions causes constitutive and regulated processes in the cell to be launched. Their intensity is proportionate to the energy of the external signal. Pathways for transmitting intracellular information are started. Second messengers are water-soluble and can rapidly move inside the cell. The processing of the information in the cell and transferring the information forward is related to the reversible formation and hydrolysis of phosphodiester bonds. The forming of bonds is the task of kinases, whereas hydrolysis is the responsibility of phosphatases. Each cell has a set of ca. 1000 various kinases. Kinases are tasked with protein phosphorylation that alters conformation of these proteins, thus rendering them active and capable of stimulating other proteins, generating a wave of protein activation on a signalling pathway. Phosphorylation is an “activate and forward”-type of activity, whereas when it comes to phosphatases, which are just as abundant in the cell as kinases are, they operate on a “deactivate-end of information” principle. Information transfer is an endergonic process that requires an input of energy from a high-energy compound such as ATP or GTP being broken down. Two types of hydrolase enzymes are operating, namely, ATPases and GTPases, proteins acting as intracellular molecular switchers. An auditory cell functions in line with two programmes; the first one involves the cell living as the baseline unit of the body; the other one concerns processing auditory information. Both these programmes cooperate, often using the same information transfer pathways, the same substrates, and the same enzymes. The mechanical energy of the external signal, conversed into the electric energy of the membrane potential, and then transformed into the chemical energy of ionic and covalent bonds, and intracellular messengers, becomes amplified and split into two systems. The lower the energy of the external signal the greater the amplification. A high-intensity sound is accompanied by the phenomena o adaptation and inhibition. The end product of these transformations (a transmitter) serves as a tool in the information transfer system. The forming and storing of the product are regulated by the first system (the constitutive system), whereas the discharge of the transmitter to the synapse is part of the other system – the regulated system. If an external signal that is above the threshold intensity generates a 10-9 V potential on the membrane of the receptor cell, then that energy must be amplified many times to make it capable of reaching the central nervous system. The signal inside the cell – which is a portion of energy – moves in the form of a wave at the speed of ca. 0.5 millimetre per second. The frequency of calcium waves codes the information related to the frequency of the sound wave, while the transferred energy is consistent with the intensity of the sound. A rise in the calcium level in the presynaptic area serves as a signal for releasing a portion of the transmitter into the synapse. The amount of the transmitter is proportionate to the intensity of the sound. Synaptic vesicles are moved by means of anterograde transport in the moment when calcium-activated proteins break down the protein bonds that fix the vesicles to the cytoskeleton. The molecular driving force that moves the vesicles towards the presynaptic membrane is kinesin. The protein complex in the presynaptic area facilitates contact between the vesicles and the presynaptic membrane, the bonding of the two and the forming of a channel that links the interior of a vesicle with a synapse. Retrograde traffic is the task of a protein called dynein. These membranes that are moving back are used for creating new synaptic vesicles. This is called cell membrane recycling. The discharge of a transmitter to a synapse involves a transfer of a bit of information whose intensity and frequency match that of the signal. A synaptic gap about 50 nm wide is filled with a fluid in which the transmitter moves from the presynaptic membrane to the postsynaptic membrane, and then connects to specific ion channels causing them to open. The transmitter is active only for a period of ca. 1 millisecond, after which it disconnects from the ion channel and is broken down by the enzymes present in the synaptic gap. The level of a transmitter falls rapidly, after which ion channels become sensitive to a new influx of that transmitter. On the postsynaptic membrane, a depolarising potential is formed, the so-called excitatory postsynaptic potential (EPSP). If a given depolarisation threshold is exceeded, which is ca. 15 mV, then this depolarisation moved along the afferent nerve to the next synapse, towards the ganglion cell. Synaptic transmitting is related to many regulatory mechanisms such as pre- and post-synaptic inhibition and aggregation, spatial aggregation, temporal aggregation, enzymatic degradation, and transmitter reabsorption. In the synapse, a process of encoding the transferred information occurs. The encoding consists in arranging the quantity and size of impulses in a nervous fibre or a bundle of fibres depending on the intensity and the frequency of the sound. In each subsequent synapse, the information is then decoded, the electric signal is transformed into the chemical energy of the transmitter, the basic information that reaches the synapse is integrated with the additional information from interneurons, the chemical energy is converted into electrical energy of the postsynaptic stimulating potential with simultaneous coding. Having crossed though several synapses and intrasynaptic sections, the information in the form of energy pulses reaches the central nervous system. It is the decoded, subjected to an analysis similar to Fourier analysis, and compared with the information recorded in long-term memory. An image of hearing is recorded in the memory, which can be re-accessed even many years later.

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