Global Journal of Surgical Research

Original Article Open Access

New Submolecular Theory of Hearing

Myjkowski Jan[1] Karcz Jan[2]
1- Laryngology Mielec,

2- Medical University of Warsaw

Abstract

The paper presents a new hypothesis of the mechanisms of hearing. The new theory of hearing is: ***Submolecular theory of hearing.*** The main hearing processes take place at the molecular and electronic levels. A mechanism of information encoding within the sound wave and during signal transmission to the receptor has been proposed The transmission pathway of sound waves to the receptor undergoes changes. Attention was drawn to the importance of inertia in the middle and inner ear. The dissipation of sound wave energy from the external auditory canal to the round window has been described. The significance of the rocking movements of the stapes was discussed. An analysis was conducted of the resonance between the longitudinal wave in the cochlear fluid and the transverse wave associated with the natural vibrations of the basilar membrane. The operation of the mechanoreceptor and the auditory cell was presented, and the molecular processes of intracellular amplification were described.

Correspondence:

Myjkowski Jan
Laryngology Mielec,

Received Date: 30 May 2026

Accepted Date: 05 June 2026

Published Date: 10 June 2026

Citation: Myjkowski Jan. New Submolecular Theory of Hearing . Glob J Sur Res. 2026; 1(1): 1- 10

Introduction:

A sound wave consists of vibrations of particles of a medium that propagate through an elastic medium. The source of sound is a vibrating body that transfers vibrational energy to the particles of the medium, causing them to oscillate about their equilibrium positions. Sound is heard and recognized by humans when the wave frequency is between 16 Hz and 20 kHz.

Air plays a significant role in hearing as a medium for the propagation of sound waves. Air molecules are in constant motion, upon which the energy generated by the sound source is superimposed. Number of air molecules in 1 cm^3 = 2.7 x 10^{21}. The mean free path of an air molecule is on the order of tenths of a nanometer.

Air molecules are made of atoms, their diameter is 2 x 10^{-8} cm, and they have a minimum intrinsic energy. They are in constant motion, performing vibrations around their equilibrium position; these are oscillations of atoms which, when summed, form the oscillations of the molecule [1].

The second type of vibrations is the rotational motion of atoms, which leads to changes in chemical bond angles. Every change in oscillation, rotation, and bond angle is associated with a corresponding amount of energy responsible for a unit of information

transmitted by the sound wave. This is how the energy encoding information is transmitted from the sound source through the first molecules to the next molecules, up to the receptor. Each molecule has the ability to transmit an amount of information proportional to the square of the number of atoms in the molecule. A 10-atom molecule can simultaneously receive and transmit 10^{10} energy changes. A six-atom molecule can already transmit 1,000,000 units of information.

The generation of information encoded in the sound wave in voice emission and in music is at the same time, with different intensity and different amount of information. The amount of information produced is less than the capacity of the sound wave molecules to absorb information.

The transfer of information between molecules takes place at the electronic level (electron clouds). This process takes place on the attosecond timescale, i.e. 10^{-18} seconds. The ability to transmit this amount of information simultaneously makes it possible to listen to a symphony of 150 musicians producing thousands of pieces of sound information, at the same time, encoded in the sound waves traveling toward the ear. The information must reach the auditory receptor without alteration, it is received, analyzed in the auditory cell, sent to the brain, where it is decoded and stored.

The impulse (force impulse) imparted to the molecule by the sound source causes a change in the air molecule's momentum – a change in kinetic energy, a change in total energy. This change is equal to the acting impulse. The impulse (an integer multiple of the energy quantum) is added to the initial momentum of the molecule, to the basic energy. The change in momentum is equal to the added impulse passed on to the next air molecule. After transmitting the impulse, the molecule returns to its base energy level. The number of such molecular collisions is approximately one billion per second. Regardless of the number of collisions, the information encoding the information in the molecule does not change.

The sound wave impinges simultaneously on the auricle and the external auditory canal. Some of the wave energy is received by the auricles. The primary flow of energy comes through the external auditory canal to the tympanic membrane. Sound waves striking the human auricle are partially absorbed and partially reflected. The surface of the auricle is uneven, which causes scattering of reflected waves. Only a small portion of the reflected waves is directed into the auditory canal [2].

The wave energy received by the auricles is mainly used to recognize the direction from which the wave is coming. Dogs such as dachshunds, basset hounds, setters, and pointers have long, drooping ears that obscure the auditory canal. They hear perfectly, recognize directions well, and are hunting dogs. Cats possess 32 auricular muscles that adjust the position of the ear to optimize the direction of sound wave energy reception. They can change the position of the ear by 180°, which excludes the transmission of waves to the auditory canal. The auricles of these mammals are heavily hairy, which increases the absorption of wave energy. A sound wave incident on the auricle and the tympanic membrane encounters a new medium with greater resistance.

A fraction of the energy is reflected, and a fraction, in accordance with the transmission coefficient, is transmitted into the new medium. According to Huygens' principle (1629–1695), "every point in a medium reached by a sound wave becomes a source of a new spherical wave".

This allows the wave to propagate in any direction through the medium. Partial waves are generated, which are capable of interference with waves of the same frequency. Through the continuity of the tissues, the sound wave is transmitted to the temporal bone. It undergoes constructive interference with waves transmitted by the same mechanism from the tympanic membrane and the auditory ossicles of the tympanic cavity to the temporal bone. The largest portion of the sound wave energy transmitted to the temporal bone comes from the stapes plate, which is connected to the temporal bone at the oval window. The energy of the waves transmitted to the temporal bone is amplified during each constructive interference and travels directly to the receptor at a speed of up to 4000 m/s. This is confirmed by experimental studies. The receptor potential is generated within 1.5 ms after the signal reaches the external auditory canal.

The main portion of sound wave energy entering the external auditory canal causes the tympanic membrane to vibrate, transmitting energy through the ossicles of the middle ear to the oval window. Vibrometric studies do not confirm the amplification of the wave in the middle ear described by Bekesy. A 90 dB - 800 Hz wave with an amplitude

of 500 nm, in the middle ear near the tympanic membrane has an amplitude of 100 nm, and at the stapes plate it has an amplitude of 11.7 nm. Bekesy already observed that the malleus, at frequencies above 2400 Hz, does not vibrate in accordance with the frequency of the sound wave [3]. Above the limit of approximately 3000 Hz, the sound wave is transmitted without vibration of the ossicles. What matters is the inertia of the vibrating system that has mass. Inertia, and the energy necessary to generate a wave, equal to inertia, is directly proportional to the vibrating mass and to the wave amplitude and proportional to the square of the frequency.
The inertia for wave motion is calculated according to the formula: $(2\pi \times \text{frequency})^2 \times \text{amplitude} \times \text{mass}$ in Newtons. N = 1 kg x mass/sec.

The vibrating mass of the middle ear ossicles, and the tympanic membrane, was assumed to be 70 mg. The amplitude of a 60 dB sound wave was taken as 10 nm.
For 60 dB - 2400 Hz - inertia = 1.59×10^{-5} N.
For 60 dB - - 100 Hz - inertia = 2.76×10^{-7} N.
For 60 dB -- 1000 Hz - inertia = 2.76×10^{-5} N.
For 60 dB - 10,000 Hz - inertia = 2.76×10^{-3} N.

For the same vibrating mass and amplitude, a 10-fold increase in frequency causes a 100-fold increase in inertia = energy necessary to generate the wave. High-frequency sounds are transmitted through the middle ear to the oval window without ossicular vibration. Low-frequency sounds transmitted to the oval window generate a sound wave in the vestibular fluid, which travels to the cap and through the tympanic canal to the round window, where they are annihilated. The energy of these waves reaches the receptor through the cochlear fluid and the bony casing of the cochlea. The same mechanism exists in the case of a child's hearing in the mother's womb in the second half of pregnancy. The baby hears the mother's speech, heartbeat, and intestinal movements. A vibrating tuning fork placed against the knee is perceived in the ear. All body tissues conduct sound waves at different speeds.

During the wave's transmission from the external auditory canal to the round window, the amplitude of this wave decreases 1000 times, and the energy of this wave decreases a million times. The 800 Hz wave at the input of 90 dB = 500 nm has an amplitude of 0.5 nm at the round window [4,5]. Low frequencies on their way to the receptor, which are supposed to generate a traveling wave, reach the region of the cap (according to the traveling wave theory). It should be assumed that the amplitude loss of this wave is greater than 500-fold. This means that the wave energy decay is more than 250,000 times. The explanation for such a large energy loss is absorptive damping, reflective damping, and interference damping in the narrowing, spirally coiled vestibular duct. In addition, wave dispersion in the fluid also occurs.

The tympanic membrane exhibits a differentiated structure on either side of the handle of the malleus. This causes the movements of the malleus at high frequencies to be rocking in nature. Such movements are transmitted to the stapes plate. Depending on the frequency, the plate vibrates in accordance with the frequency along the transverse or longitudinal axis of the plate. These movements disrupt the transmission of high-frequency information. When one part of the plate generates forward motion, the other part of the plate simultaneously generates a backward motion. Friction of wave streams and destructive interference eliminate high-frequency waves [6].
Evidence of the lack of transmission of high frequencies is provided by stapedotomy surgery.

Degraded waves are unable to resonate properly with the transverse waves of the basilar membrane's natural vibrations. The traveling wave cannot be properly formed on the basilar membrane. There is no proper transmission of auditory information. The natural vibrations of the basilar membrane have been incorrectly calculated. The basilar membrane does not vibrate independently, but together with the organ of Corti, forming a system of considerable mass. It vibrates in fluid characterized by high energy damping, which results in substantial inertia. The vibrating mass was used to calculate the energy required to amplify soft sounds by 40 dB, mechanically, by pulling on the basilar membrane of the contracting OHCs. Vibrating mass of the basilar membrane with the organ of Corti 250 mg, (for calculations), wave amplitude 1 nm for 40 dB.

250 mg ---40 dB = 1 nm ---100 Hz ----98.7 nano N
250 mg ---40 dB = 1 nm ---1000 Hz ---9.88 micro N
250 mg—40 dB = 1 nm—10,000 Hz - 98.7 mili N
250 mg -100 dB = 1000 nm - 10,000 Hz -- 0.988 N

It is difficult to imagine a wave on the basilar

membrane when the massive organ of Corti lies on it along its entire length.

Bekesy found that the pressure in the vestibular duct is 20 dB higher than the pressure in the tympanic duct. The wave deflections together with the entire organ of Corti occur toward the region of higher pressure, which is inconsistent with the laws of physics. Bekesy's paradox.

The amplitude of the threshold wave is 0.01 to 0.05 nm. The energy of this wave is smaller than the damping of the vibrations of the basilar membrane connected to the organ of Corti. In such a system, wave resonance is not possible. Yet such tones are heard. Through a different pathway.

A 20 dB wave at the input has an amplitude of 0.1 nm — a magnitude comparable to the diameter of a hydrogen atom. Such a wave is perceived according to Bekesy's theory and creates a wave traveling in the region of the cap. The amplitude of this wave is reduced by approximately 500-fold along its path from the external auditory canal to the point of resonance with the natural vibrations of the basilar membrane. The amplitude of this wave is 0.005 nm – it is 250 times smaller than the average size of the atoms that make up the basilar membrane. Such a wave does not have the ability to generate fluid flows to bend hairs of hair cells, which have a diameter of 100-200 nm. Such a wave cannot be received by the receptor and cannot be amplified. We hear – in a different way.

The receptor receives sounds with only 1 or 2 wave periods [7]. Resonance of such waves with full transmission of auditory information is impossible. A serious problem in Bekesy's theory is created by the difference in the speed of the sound wave in the cochlear fluid of 1450 m/s and the variable speed of the traveling wave – 50 m/s in the area of the oval window and 2.9 m/s in the area of the cap (according to Bekesy). The compression of transmitted information varies from 29 times in the area of the base of the basilar membrane to 500 times in the area of the cap. Each wave frequency in the fluid, through resonance (according to the traveling wave theory), produces the greatest deflection of the basilar membrane at a different place and at a different time – a different wave path. A polytone with numerous harmonic components is received along a large section of the basilar membrane, resulting in subsequent deflections on the basilar membrane? These maximum deflections of the basilar membrane in the organ of Corti, connected to the basilar membrane, are supposed to generate cochlear fluid flows?

It is impossible to amplify soft sounds by 40-50 dB by pulling on the basilar membrane of contracting OHCs. A lot of energy is required, which prestin does not have. It is considered a molecular motor, similar to dynein or kinesin, but does not have the ability to use ATP energy. The inverse piezoelectric effect is unlikely. Using the electrochemical energy of the cell membrane is impossible. Creating energy de novo is also impossible. An excitable cell, such as an auditory cell, when deprived of part of its energy, loses its viability. The electric field produced does not create as much new energy.

Energy required to amplify a silent wave by 40 dB in the inner ear, according to traveling wave theory:

40 dB ---100 Hz ----98.7 nano N - energy required for amplification
40 dB ----1000 Hz ---9.88 micro N - energy required for amplification
40 dB —-10,000 Hz - 98.7 mili N - energy required for amplification.

For each frequency, a different additional energy is required. A 10-fold increase in wave frequency causes a 100-fold increase in the energy required. By this method, a wave below the hearing threshold cannot be amplified. The received wave does not require amplification, the signal is transmitted to the brain via afferent innervation. An external wave is amplified, which at that time, according to the traveling wave theory, propagates slowly along the basilar membrane. The amplitude, frequency, phase, aliquots, length of sound, and accent of this wave are unknown. Every sound wave contains this information. OHC does not have a direct connection with the basilar membrane, hence doubts regarding the exact transmission of information. The pulling up of the basilar membrane causes the organ of Corti and all the hair cells to pull up simultaneously. The cochlear fluid moves, which is supposed to encode all the sound wave information. By pulling up the basilar membrane, the OHC pulls up itself along with the hairs of the hair cell. If the cochlear fluid that is supposed to activate the tip-link mechanism moves in sync with the hair cells, there is no bending of the OHC hairs.

The cadherin filaments do not become tensioned and do not regulate the molecular gating

mechanism of mechano-dependent potassium ion channels.

Another problem with amplifying quiet sounds mechanically by pulling on the basilar membrane concerns high frequencies. The frequency of depolarization and contraction of OHCs depends on the functioning of the ion channels of the cell wall. If all voltage-dependent channels of a cell operate in the same rhythm with absolute and relative refractory periods and ion channel inactivation times, the frequency of cell depolarization is limited. The entire cell cannot contract at a frequency of 50 kHz simultaneously. When examining the frequency of OHC contractions, an electric current was used, which is misleading - the decisive role of ion channels in cellular depolarization was excluded [8].

I propose to take into account limited OHC depolarization and limited OHC contraction. This excludes the possibility of mechanical amplification of sound by 40–50 dB, which is therefore questionable. This thesis is confirmed by the presence of numerous afferent synapses on the lower and lateral walls of the cell. In the case of uniform depolarization of the entire cell, one synapse is sufficient to transmit the depolarization energy.

Mechanoreceptor [9]

The mechanism of converting the mechanical energy of a sound wave transmitting encoded information into the chemical energy of the receptor and then into the energy of the chemical bonds of the intracellular information transmitters takes place at the submolecular and electronic level. Transmission of frequency and intensity is not a problem.
The problem is caused by harmonic tones, phase shifts, length of sound and accent.

The adequate stimulus for the hearing organ is the energy of the sound wave. All molecules as well as all atoms in the molecule of the sound wave transmitted through the medium and the molecules and atoms that make up the hearing receptor are in constant motion. It is a progressive movement - oscillatory and rotational, or a mixture of these movements. The kinetic energy of molecules is associated with the motion. Supplying external energy – in the case of the hearing receptor – a sound wave, to the acceptor molecule (hearing receptor) causes an increase in the internal energy of the molecule receiving the signal.

The vibrating particles of a sound wave have encoded energy, depending on the vibration speed and vibration frequency, as well as electronic energy in the form of electron clouds of the molecules. Every atom has electrons that form an electron cloud around the nucleus of the atom. The size of this cloud depends on the number of orbits in which the electrons are arranged. The closer to the nucleus, the greater the energy of the electron. An electron can change orbit, but to move to an orbit closer to the nucleus it must receive additional energy. Changing 1 orbit from 2 to 1 requires 3.4 eV. Such transitions are quantized, meaning that the jump either occurs or does not occur. If an atom in an acceptor molecule receives a quantum of energy from another atom or molecule (of a sound wave), the acceptor electron jumps to an orbit closer to the nucleus - its internal energy increases - in a stepwise - quantized manner. An excited state of the atom is formed, which, unlike the ground state, is unstable. Such a state is unstable and immediately tends to return to the ground state by emitting a single photon of energy when the transition involves one atom and a one-orbit change. If there are numerous such transitions between a receptor molecule and sound-wave energy — including transitions involving two or more orbits — then in a molecule consisting of 20 atoms there may exist on the order of 10^{20} possible modes of transmission of different forms of quantized energy. This allows for an infinite amount and diversity of transmitted information. This energy transfer reaches the molecules inside the potassium ion channel responsible for regulating the openness of the ion channel. These molecules form the activation gates of the potassium channel. The channel activation gate together with the inactivation gate determines the channel's conductance depending on the sound wave energy. The wave energy acts on the molecules that gate the ion channel, called sound-sensitive molecules. There are changes in the rotation of atoms, changes in bond angles, and oscillations, which lead to conformational changes in the molecules, and the resulting conformers perform the work of closing and opening the ion channel.
This activity is very precisely regulated by the information encoded in the sound wave.

The operation of the ion channel selectivity filter is very important, as it is responsible for the passage of one type of ions that have been dehydrated in the central part of the channel. The sound wave regulates the flow of K+ ions. When the ion channel

is fully open, 6 million ions flow through the channel in 1 second. The entrance to the potassium channel is 1 nm in diameter, while the central part, narrowed to 0.3 nm, determines the specificity of the passing ions.

Hair cell: [10,11]

The influx of positively charged K+ ions into the interior of the hair cell initiates its depolarization. If the change in membrane potential exceeds approximately 10 mV, voltage-dependent Ca++ ion channels are activated. Local depolarization increases, and further depolarization-dependent Ca++ channels and Na+ channels on the lateral surface of the hair cell open. The interior of the cell has a negative potential of -80 mV, due to the large number of negatively charged proteins and the constant operation of sodium-potassium pumps that export 3 sodium ions out of the cell in exchange for 2 potassium ions transported into the cell. Outside the cell there are high levels of Na+, Ca++ and Cl-, which together with the high electrical potential create a high electrochemical potential for sodium and calcium ions. The wave of Ca++ ions flowing into the cell causes the release of calcium ions from the mitochondria, endoplasmic reticulum and cell nucleus. The level of calcium outside the cell is 10,000 times higher than the basic calcium level within the cell, which can increase by up to 100 times. When stimulated, the membrane potential changes into a receptor potential. In the cell, calcium binds to calcium-dependent proteins, altering their properties. The most important of them is calmodulin.

Information is divided into constitutive activities related to normal cell functioning and regulated activities related to the production, transport and synaptic release of neurotransmitters. Once calcium levels are increased and the information is transmitted, the calcium level is rapidly reduced. Calcium pumps and ion exchangers function to extrude calcium ions from the cell, while a portion of the calcium is redistributed back into the mitochondria, endoplasmic reticulum, and nucleus. The lower the intracellular calcium concentration, the greater the cell's sensitivity to receiving a new signal. Intracellular messengers, variations in calcium concentration, and the actions of intracellular proteins are responsible for intracellular signal amplification.

An important factor in the generation of membrane potential is the different permeability of the membrane to various ions. At rest, the cell membrane exhibits the highest permeability to potassium ions, therefore the value of the resting membrane potential is close to the resting potassium potential. The natural tendency to equalize concentrations and electrical potentials across the membrane, in accordance with the second law of thermodynamics, results in the dissipation of the membrane potential. This process is opposed by ion pumps and ion transporters, which constitute an active mechanism responsible for maintaining concentration gradients and electrical potential differences across the membrane. They establish chemical and electrical gradient.

The intracellular space has a negative potential of approximately -80 mV, relative to its surroundings. It was assumed that the cell's surroundings, used as the reference point, have a potential equal to zero.

In the case of hair cells, there is a special situation because the lateral and basal walls of these cells are in contact with the perilymph or interstitial fluid with a low potassium and high sodium concentrations (K^+ 7-8 mEq/l, Na^+ -140 mEq/l), whereas the hairs of the hair cells and the apical part of the hair cell are surrounded by endolymph with a very high potassium and low sodium concentrations (K^+ -150 mEq/l, Na^+ -15 mEq/l). This is extremely important in the reception of auditory information.

The functioning of ion channels can be influenced by a number of factors, such as: phosphorylation and dephosphorylation of channel proteins, ATP concentration inside and outside the cell, cAMP and cGMP levels, cell pH, mechanical energy (sound wave), osmotic pressure, oxidation-reduction potential, and the presence of ligands.

A very important mechanism for the hearing process is located in stereocilia, these are proteins - molecules sensitive to a given frequency and intensity of a sound wave, genetically determined, reacting to an appropriate stimulus.

The energy of the sound wave causes an influx of potassium ions into the cell. A too small influx of K^+ ions through mechanosensitive potassium channels in the hair cells of auditory cells does not disturb this equilibrium. Exceeding a defined threshold induces a cascade of intracellular events within the auditory hair cell.

Positively charged potassium ions flowing into the cell from the endolymph cause its depolarization, which initiates conformational changes in calcium and sodium ion channel proteins in the lateral and basal parts of the cell.

Sodium channels respond to stimulation faster than potassium channels, so the cell membrane first becomes permeable to sodium ions. The electrochemical potential is much higher for sodium ions than for potassium ions. Increasing depolarization promotes the opening of more and more sodium channels. A positive feedback mechanism occurs, in which influx of sodium ions enhances depolarization, and depolarization in turn promotes the opening of new ion channels. The membrane potential approaches the equilibrium potential for sodium ions and the electric potential - which is the driving force for these ions - approaches zero. The driving force for potassium ions increases. The opening of more and more voltage-gated potassium channels causes inhibition of depolarization. The factor that rapidly inhibits depolarization is the phenomenon of inactivation of Na^+ ion channels. Approximately 1–2 ms after channel opening, inactivation occurs, rendering the channel closed and insensitive to further stimulation. The influx of potassium through the potassium channels of the lateral wall of the cell and the inactivation of sodium channels leads to the reversal of the situation – the cell repolarization occurs, and finally to hyperpolarization, which is a stimulus to close the potassium channels and return to the equilibrium state. Repolarization and hyperpolarization cause sodium channels to transition from an inactivated state to a closed state, sensitive to new stimulation. The membrane potential returns to equilibrium level.

The full cycle of the sodium ion channel (activation, opening, closing, inactivation) is approximately 4-5 ms, which makes it possible to receive information carried by a sound wave up to a frequency of 250 Hz, assuming that the entire auditory cell is depolarized simultaneously. To receive higher frequencies, a larger number of ion channels activated at different times are necessary, transmitting information to the synapse without simultaneous depolarization and contraction of the entire hair cell.

A wave of Ca++ ions flows into the hair cell through calcium channels in the lateral wall. The calcium concentration in the auditory cell is approximately 100 nM/L, while in the interstitial fluid it is approximately 1,200,000 nM/L. Most of the calcium in a cell is stored in the endoplasmic reticulum and cell organelles. Cell depolarization and calcium influx are signals for its release from intracellular stores.

Calcium flowing through ion channels, together with calcium released from cellular stores, quickly spreads throughout the interior of the hair cell. An increase in the concentration of cytoplasmic calcium ions leads to their binding with specific proteins, which are thus activated, increasing the activity of various protein kinases.

For this mechanism to operate, a mechanism must exist that enables rapid reduction of intracellular calcium levels following signal transmission. This is carried out by a pump that transports Ca^{2+} ions out of the cell in exchange for two H^+ ions transported into the cell. $Ca^{2+}H^+$ATPase works, deriving energy from ATP. The second mechanism that lowers calcium levels in the cell is antiport transport, which depends on the Na+ ion concentration, which exchanges two Na^+ ions from the extracellular space for one Ca^{2+} ion that is exported from the cell. The third mechanism is ion pumps that move calcium ions from the cell fluids to the organelles, mainly mitochondria, the endoplasmic reticulum and the nucleus.

Calcium is a regulator of many intracellular mechanisms, but its most important tasks include participation in the transmission of intracellular information, its amplification and distribution. This involves the effect of Ca^{2+} ions on enzymes such as adenylate cyclase, phosphodiesterase, phospholipase A_2, and protein kinase A.

Calcium ions are a second messenger and are involved in the formation of other second messengers such as cAMP, cGMP, IP3 and DAG Intracellular amplification acts through second messengers and Ca^{2+} receptor proteins. After binding calcium, these proteins change their biological properties and interact with other proteins, thereby influencing cellular reactions. There are many Ca^{2+} receptor proteins, and special role is played by calmodulin, which has four Ca^{2+} ion binding sites. The binding of successive ions to the binding domains causes conformational changes in the calmodulin molecule, increasing its ability to bind enzyme molecules.

Enzyme activation occurs after the binding of at least three Ca^{2+} ions. At an intracellular calcium concentration of 10^{-6} mol/l, the activity of the calmodulin-calcium complex is 10,000 times greater than the activity of calmodulin alone. This is one of the most important elements of intracellular amplification. This complex acts either directly on enzymes or indirectly via stimulation of calmodulin-dependent protein kinases, which phosphorylate

enzymatic proteins and thereby convert them into their active forms. The calmodulin-related information transfer stage in the hair cell leads to the separation of the signal into different directions. The amplified signal continues in the centripetal direction, but at the same time calmodulin activates many so-called constitutive processes, i.e. those occurring in the unstimulated cell.

Other cellular proteins whose function is dependent on the level of calcium in the cell include gelsolin, troponin C, and parvoalbumin. After binding calcium, they activate other cellular proteins. The activity of some enzymes increases in the presence of calcium ions. These include mitochondrial enzymes such as pyruvate dehydrogenase and alpha-ketoglutaric acid dehydrogenase, and the calpain-calpastin protein system, responsible for the proteolysis of many cellular proteins.

The second system activated by the calcium-calmodulin complex involves the regulation of the interaction of all cellular organelles.

The third system, relatively slow, involves the regulation of protein production, especially enzymatic ones. The process of enzyme production or the rate of their breakdown may change. Enzyme activators and inhibitors also influence the reaction rate.

These three process regulation systems interact with each other, being responsible for the cooperation of constitutive and regulated processes.

The mechanical energy of the external signal, which is only the trigger for a cascade of intracellular reactions, causes the initiation of constitutive and regulated processes in the cell. Their intensity is proportional to the energy of the external signal. Intracellular information transmission pathways are activated. Second messengers are water-soluble and have the ability to move rapidly within the cell. The processing of information in the cell and its further transmission is associated with the reversible formation and hydrolysis of phosphate-ester bonds. Kinases are responsible for bond formation, phosphatases are responsible for hydrolysis. Each cell has a set of approximately 1,000 different kinases, indicating that the kinases are major components in intracellular signaling. Kinases are responsible for the phosphorylation of proteins, which undergo conformational changes, become active, and stimulate subsequent proteins, creating a wave of activation along the signaling pathway. Phosphorylation is an 'on–pass it on' type of action, whereas phosphatases, of which there are as many in the cell as kinases, act on an 'off—end of signal' principle. Information transfer is an endergonic process and requires the supply of energy from the breakdown of a high-energy compound such as ATP or GTP. Two types of hydrolytic enzymes are active: ATPases and GTPases, which are proteins that are intracellular molecular switches. They take an active part in the transmission of intracellular information.

The auditory cell operates according to two programs: the first is related to the cell's life as the basic unit of the organism, and the second is related to the processing of auditory information. Both programs function together, often using the same information transfer pathways, the same substrates and the same enzymes. The functioning of the second program depends on the proper functioning of the first one.

The mechanical energy of the external signal, converted into the electrical energy of the membrane potential and subsequently converted into the chemical energy of ionic and covalent bonds and intracellular messengers, is amplified and distributed to both systems. The degree of amplification increases as the energy of the external signal decreases. High-intensity sounds are associated with adaptation and inhibitory processes. The final product of these transformations (the transmitter) functions as an element of the information transmission system. Product synthesis and storage are controlled by the first (constitutive) system, while transmitter release into the synapse belongs to the second, regulated system. If a threshold-level external signal produces a receptor cell membrane potential on the order of 10^{-9} V, this energy must be amplified many times to be transmitted to the central nervous system.

The signal in a cell – a portion of energy – travels as a wave at a speed of about 0.5 millimeters per second. The frequency of the calcium waves encodes information related to the frequency of the sound wave, while the energy transferred corresponds to the sound intensity. A rise in calcium concentration in the presynaptic region serves as a signal for the release of transmitter into the synapse. The amount of transmitter is proportional to the sound intensity – to the energy released by synaptic vesicles. These vesicles undergo anterograde transport at the moment when calcium-activated proteins disrupt the protein linkages that anchor the vesicles to the

cytoskeleton. The molecular motor that moves vesicles towards the presynaptic membrane is kinesin. A protein complex in the presynaptic region promotes vesicle docking to the presynaptic membrane, their fusion, and the formation of a channel connecting the vesicle lumen with the synapse. The dynein protein is responsible for retrograde transport. These recycling membranes are reutilized for the formation of new synaptic vesicles. This is called cell membrane recycling. The release of the transmitter into the synapse is associated with the transmission of information about the intensity and frequency of the signal. The synaptic cleft, about 50 nm in width, is filled with fluid through which the transmitter diffuses from the presynaptic to the postsynaptic membrane, subsequently binding to specific ion channels and inducing their opening. The transmitter remains active only for a period of about 1 millisecond, after which it detaches from the ion channel and is degraded by enzymes present in the synaptic cleft. The transmitter concentration rapidly declines, after which ion channels regain sensitivity to a new influx of the transmitter. A depolarizing potential, the so-called excitatory postsynaptic potential, is created at the postsynaptic membrane. If a depolarization threshold of approximately 15 mV is exceeded, the depolarization propagates along the afferent nerve to the next synapse, namely to the spiral ganglion cell.

Synaptic transmission is associated with numerous regulatory mechanisms, including pre- and postsynaptic inhibition and summation, spatial and temporal summation, enzymatic degradation, and transmitter reuptake.

In the synapse, the energy of the transmitter's chemical bonds is converted into the electrical energy of the postsynaptic potential transmitted to the central nervous system. The process of encoding transmitted information takes place in the synapse. Encoding involves the organization of the number and amplitude of impulses within a nerve fiber or a bundle of fibers as a function of sound intensity and frequency. At each subsequent synapse, information undergoes decoding, involving conversion of the electrical signal into the chemical energy of the neurotransmitter, integration of the primary synaptic input with additional interneuronal signals, and reconversion of chemical energy into the electrical energy of the excitatory postsynaptic potential, accompanied by simultaneous encoding.
After traversing several synapses and intersynaptic segments, the information reaches the central nervous system in the form of energy pulses. The information is decoded, subjected to processing analogous to Fourier analysis, and compared with information stored in long-term memory. An auditory representation is formed and stored in memory, making it possible to reproduce it even years later.

Signal amplification in the auditory hair cell [12]

In the auditory hair cell of the ear, regulated intracellular amplification occurs at the molecular level. Most chemical reactions and energy transfer between small molecules take place within 10^{-14} s. These are reactions at the atomic and electronic level. “Slow” reactions proceed 1000 times slower, yet still occur on a timescale of 10^{-11} seconds.

Intracellular amplification comprises a range of factors, including: phosphorylation and dephosphorylation of ion channels responsible for the conductance of cell membranes, ATP concentration, cAMP and cGMP levels, cell pH, osmotic pressure, presence of ligands, and the operation of Ca++ATPase pumps. These membrane-bound pumps play an important role in maintaining fluctuating calcium levels within the cell. Intracellular amplification is also related to the activity of calcium-binding proteins, where calmodulin plays an important role, influencing the production and breakdown of cAMP and cGMP.

Calcium acts as a second messenger of information within the cell, operating faster than other second messengers, including cAMP, cGMP, DAG, and IP_3, which are generated in response to elevated calcium levels or through G-protein activation. The generation of second messengers represents one of several key mechanisms of intracellular signal amplification. One enzyme molecule can produce several hundred second messengers. Received tones whose energy is too low to reach the brain are amplified. Intracellular signal amplification is one of the main pillars of the "Submolecular Theory of Hearing."

Bibliography:

1. Piela L, Idee chemii kwantowej, PWN, Warsaw 2022, p. 1300.
2. Myjkowski J, The Truth about Hearing, WebLong Journal of Otolaryngology. Published Date 02. Mar 2026, WebLong J Otolaryngol. Wjot 2026 c 205.
3. Pruszewicz A, Zarys Audiologii Klinicznej, Wydawnictwo Akademii Medycznej w Poznaniu, 2000, p. 65.

4. Wysocki J, Kwacz M, Mrówka M, Skarżyński H, Comparison of round-window membrane mechanics before and after experimental stapedotomy. Laryngoscope, 2011:121 (9): 1958-1964.
5. Kwacz M, Marek P, Borkowski P, Mrówka M, A three-dimensional finite element model of round window membrane vibration before and after stapedotomy surgery. Biomed. Model Mechanobiol. 2013: 12 (6) 1243 – 1261.
6. Myjkowski J, The secrets of hearing, Journal of Current Trends in Clinical Case Reports, J Cur Tre Clin Case Rep, 2025, 6 (5): 1-3.
7. Martinson K, Zieliński P, Kamiński T, Majka M, Dyskryminacja czasu trwania ultrakrótkich impulsów akustycznych. Postępy Akustyki, Otwarte Seminarium Akustyki, Instytut Fizyki Jądrowej, Cracow 2018.
8. Myjkowski J, The Vulnerabilities of Bekesy's Traveling Wave Theory, Biomedical Research and Clinical Advancement. August 2024, I(1):5DOI:BRCA-24-RA-05.
9. Myjkowski J, Mechanoreceptor of the Hearing Organ, Biomedical Journal of Scientific & Technical Research, Biomed J Sci & Tech Res 58 (3)-2024.
10. Alberts B, Bray D, Johnson A, Lewis J, et al. Podstawy biologii komórki, Wydawnictwo Naukowe PWN, Warsaw 1999.
11. Matthews HR, Friedland RA, Miesfeld RL, Biochemistry and Molecular Biology in Outline, Translated by Prószyński and Company, Warsaw 2000.
12. Myjkowski J, A new theory of hearing Submolecular theory of hearing, International Journal of Reproductive Research, Published 31 August 2024, 2 (2), 1-3.