



# About the Physiology of Hearing

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## Abstract

The membrana basilaris plays an important role in the theory of traveling wave. It originates from the ectoblast of the connective tissue, and is bereft of both afferent or efferent innervation. Vibrations of the membrana basilaris formed into a transverse wave occur together with the organ of Corti and a band of connective tissue on the inferior membrane surface. Vibrations take place in a fluid which has suppressive properties. The length and the mass of the membrana basilaris in mammals and birds are very different and there is no relationship between the membrana basilaris length and the length of the sound wave, especially in the range of low frequencies. Small sound intensities, supraliminal, have amplitudes within the limits of a few picometers upon the entrance into the auditory meatus. This amplitude disappears in cochlear fluids and cannot reach the receptor through cochlear fluids. It cannot be intensified by OHC contractions, since there is no depolarization of the external acoustic cell. Short sounds, whose duration time is equal to tenth parts of milliseconds, are perceived by the receptor and recognized is the frequency of those waves, although they do not generate any resonance with the membrana basilaris. Attention was paid to molecular, intracellular transformations responsible for the transfer of information and intracellular amplification. An important role in those processes is played by ion channels of sodium, potassium, calcium and chlorine in the lateral and inferior wall of the acoustic cell. They are responsible for the polarization and depolarization of a cell. Underlined is the role of calcium in the signal transmission and its amplification in an acoustic cell. Słowa kluczowe: Komórka słuchowa, wzmocnienie sygnału, receptor, kanały jonowe

**Keywords:** Acoustic cells; Amplification; Receptor; Ionic canals

## Mechanisms of Hearing

Bekesy's theory of traveling wave attributes a very important role to the basilar membrane. It originates from the ectoblast of the connective tissue as distinct from the acoustic cells originating from the ectoblast of the nervous tissue. The basilar membrane does not have either afferent or efferent innervation as distinct from other crucial organs. Neither is it able to change the tension; it separates two spaces with fluid of the internal ear with various concentrations of electrolytes and supports the organ of Corti with the spaces said, increasing the with mass of the vibrating conglomerate. A thin layer of the basilar membrane is unlikely to vibrate without vibrations of the organ of Corti and the band of connective tissue

on the inferior surface of the basilar membrane. Vibrations occur in a fluid endowed with suppressive properties. Inertia of a vibrating element is directly proportional to the vibrating mass and the wave amplitude and proportional to the squared frequency of the wave. Due to inertia, a transfer of high frequencies through the basilar membrane is problematic or incompatible with the rules of physics. A sound wave has no mass; while heading directly for the receptor through the osseous cochlear housing, it may convey frequencies of up to 200 kHz (bat). Irrespective of those objections, the basilar membrane is attributed with the following features: critical bands, frequency selectivity, time resolution, auditory filters, tuning curves, reception of a pitch, perception of timbres, resonance with

a sound wave and a share in signal amplification. Most of those actions do not depend on the basilar membrane, leaving aside that a traveling wave is generated on the basilar membrane with the organ of Corti; this wave depends on the difference of wave pressure in the vestibular duct and the scala tympani. This is caused by a difference in the elasticity of both the windows – oval and round. The round window is 20 times more elastic than the oval one. The pressure value in the vestibular duct is by 20 dB higher than the pressure in the tympanic duct. There will be generated a transverse wave moving from the cochlear base towards the cochlear apex at a speed approx. 200 times slower than the sound wave in cochlear fluids. Nearby the base, this wave has a speed of around 7 m/s and nearby the 2nd gyrus is 660 times slower than the sound wave, on an average 2.2 m/s. If a sound wave in fluid covers 145 mm in a 1 ms time, on the basilar membrane the wave travels 2.2 – 7.0 mm towards the apex. Those results concern experiments performed on animals. Each segment of a sound wave contains an information package. In what way is exactly the information conveyed to the basilar membrane at such a disproportion of speed? Such a dramatic release of information transfer is incompatible with the reaction speed of creatures whose existence depends upon the reaction speed. There is also some incompatibility of the waves. A sound wave is a longitudinal wave, while the wave traveling on the basilar membrane is a transverse wave. A balancing swing which remains under influence only of a lateral force will not take over such a new energy incompatible with the pendulum's direction.

Small mammals and birds have a basilar membrane 1 mm long and can perceive sounds from 2 Hz onwards (pigeon). The length of a sound wave in cochlear fluids for 10 Hz is 145 m. A resonance of such a wave in cochlear fluids with the basilar membrane is unlikely to occur; hence, no frequency resolution is possible according to this rule. The internal ear of a barn owl is like in all mammals, but the bird can perceive sounds of minus 20 dB, which corresponds to a 0.001 nm wave amplitude in the external auditory meatus. Such a wave will disappear in cochlear fluids few hundred times. Therefore, it will not reach the receptor through cochlear fluids. Nor can it be amplified by OHC contractions, since there is no OHC depolarization. Such a signal is received by the receptor. It implies that there is another signal path to the receptor. Plants receive the energy of sound waves directly through receptors susceptible to sounds. When little plants hear vibrations of the water running nearby, they will direct their roots thereto. Standing at water we cannot hear a voice generated in it. All we should do is entering the water up to a knee-high level, and we can receive sounds from the water, previously inaudible. Vibrations are conducted through the human body directly to the internal ear, to the receptor. A child in its mother's womb can hear the mother's voice and her heartbeat from the 2nd half of gestation onwards, when the child's middle ear is not active yet. After birth, the child will remember its mother's timbre. It can also hear music and reacts to it. Yet, not each kind of music is received identically. The auditory receptor receives short sounds whose duration time is of an order of tenth parts of ms. In that time, only a part of a wave period, viz. 1 or at most 2 will act upon the basilar membrane, upon the transverse wave, according

to the frequencies. It is not enough to generate a resonance of a longitudinal wave in cochlear fluid with the transverse wave of the basilar membrane. It is unlikely to occur at low frequencies, e.g. in a pigeon which receives frequencies of 2 Hz with its short basilar membrane – the wave length in cochlear fluids is 725 m. A signal reaches the receptor; recognized is the frequency, without any resonance with the basilar membrane. Bekesy's theory of traveling wave, like a dogma gives a theorem [quotation]: 'the area of the longest basilar membrane displacement changes in line with the sound wave. High pitched sounds generate a 'short' traveling wave which does not run beyond the basilar cochlear gyrus. Stimuli with medium and low frequencies have their maximum deflection, respectively, closer to the cupola'. The length of a sound wave in cochlear fluids at a frequency of 10 kHz is 145 mm. 1/14.5 part of one wave period falls for the first 10 mm of basilar membrane at its base. At a frequency of a sound wave of 1,000 Hz, the wave length in cochlear fluids is 1,450 mm. The entire basilar membrane is only ~1/40 part of one sound wave period. There is something absurd in a pigeon - since 1/20,000 part of the length of one period of a wave with a frequency of 2 Hz resonates with the basilar membrane nearby the cochlear apex. How to explain the resonance of such a short wave segment with the basilar membrane? The submolecular theory assumes that sounds with various frequencies and intensities act upon the specific phonoreceptors - like the organ of Corti - arranged in an ordered way along the basilemma, from the cochlear base towards its apex.

High pitch tones are received by the receptors in the initial segment of the basilar membrane, and lower and lower tones are received while moving towards the cupola. This is tonotopy responsible for the frequency resolution. For the intensity resolution responsible are the quantity and the degree of stimulated receptors, the receptor field as well as temporal and spatial summation. Quiet tones are received and amplified by intracellular mechanisms. The greater wax moth (*Galleria mellonella*), a moth, can hear sounds of up to 300 kHz. It means that the molecular processes related to the reception of sound wave energy are efficient for such a frequency. Instead, there is no place and time for the operation of the basilar membrane or a signal amplification reaching the receptor, which entails an extra time. A quiet signal may be amplified only on the molecular way only with prior reception – in the acoustic cell. It is worth noticing that in the case of directional hearing in humans, the time difference of the wave reaching each ear is 0.0006 s. Decisive are both the speed of a sound wave in the air and the distance between the ears. In small animals, the interaural distance and birds is considerably smaller and the recognizable difference in time and energy reaching each ear is smaller. It is hardly believable that quiet tones, which play a very important role in the life of animals, might be amplified mechanically on the way to the receptor, which entails an extra time. It is hard to imagine a time-consuming mechanical amplification in the case of echolocation. Intracellular amplification of tones needing an amplification upon signal reception, on the way to the center, occurs on the molecular level in a time of an order of picoseconds. The time of simple chemical reactions is as short as 10<sup>-12</sup> - 10<sup>-15</sup> second.

The crucial part of the internal ear is an acoustic cell where occur processes on both the molecular and atomic levels; hence, the postulated name of the theory: 'Submolecular theory of hearing'. As this theory has it, the potential energy of a possible sound wave is converted into electric potential of the transmitters of intracellular information. Subsequently, in a chemical synapse chemical energy is converted into post-synaptic electric potential conducted in dendrites without myelinated sheaths (a slower transfer) to a nervous cell in the spiral ganglion, where generated is the action potential of the auditory nerve, then conducted to the center. In billions of creatures on the earth, bereft of the basilar membrane, the energy of a sound wave acts directly on the hearing receptor. In the course of evolution developed was a specific sensitivity of the receptor, respectively, to light beams in the eye and to sound waves in the ear. The wave energy acts upon the protein sound sensitive molecules, bringing about spatial changes in them. Due to changes in chemical bonds, vibrations of ions and particles and modified actions of enzymes there occur conformational transformations of proteins. Proteins, sensitive to sound wave energy, change their sizes, perform some work and are responsible for the gating of mechanosensitive channels in an acoustic cell. Those are chiefly potassium channels through which in a 1 ms time the cell is reached by up to 10,000 potassium ions. Nowadays described is only one mechanosensitive channel on one hair of the acoustic cell, which is rather unlikely. On each hair there should be arranged thousands of channels, responsible for the frequency resolution according to the location on the basilar membrane – in compliance with the tonotopy principle. They are responsible for the intensity resolution through the number of the stimulated receptors as well as the size and opening time of mechanosensitive channels. An important role is played by the receptor fields, like in other sense organs.

In endolymph, the K<sup>+</sup> concentration amounts to 158 mM, whereas in an auditory cell – to 140 mM. Such a concentration difference in conjunction with a positive endolymph potential and a negative potential inside the auditory cell is the driving force for the migration of potassium ions towards the cell when the potassium channel remains open. When the threshold of the change of negative potential inside the cell is exceeded by approx. 10 mV due to inflowing positive ions, the voltage-gated Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>++</sup> and Cl<sup>-</sup> channels in the lateral and inferior cell area will be activated. Sodium channels act faster than potassium ones; sodium ions arrive at the cell. Increased is depolarization which accelerates the activation of a larger number of sodium channels. Active is a positive feedback - the higher the depolarization, the more sodium channels are active. But ion channels have a limited time of action. A short time of channel opening is followed by inactivation and the channel is closed. Only a fall in the potential of the cell membrane will restore the channel's sensitivity to stimulation, which triggers off a transit of the channel from inactivation to a simple closing state, sensitive to a new stimulation.

Parallely with a decreased activity of sodium channels increased is the activity of potassium channels, and K<sup>+</sup> ions pass from the inside outside the cell. After depolarization, repolarization of the cell will begin. Active are sodium-and potassium pumps

which, despite the electrochemical gradient, transport 3 sodium ions outside the cell and simultaneously 2 potassium ions inside the cell. This way generated is a negative potential inside the cell. The calcium level outside a cell is 10<sup>-3</sup> mole and inside an excitable cell at rest it is as high as 10<sup>-7</sup> mole. Calcium channels are mainly voltage-gated and Ca<sup>++</sup> flows into a cell upon depolarization. Moreover, released are calcium ions from the endoplasmic reticulum and mitochondria. Those channels may be controlled by a ligand, or calcium ions enter the cells through non-specific channels. After each depolarization, any calcium excess is removed actively from the cell by means of the calcium ATPase pumps as well as through a system of antiporter with Na<sup>+</sup> ions. It is also shifted to the endoplasmic reticulum and mitochondria. So that an acoustic cell should react to a new signal, the calcium level must be reduced as much as possible. The lower the calcium level in the cell, the higher the sensitivity to a new stimulation. Calcium ions act as an intracellular signal and enable the transmission of signals among cells, control the contractions of muscular and non-muscular cells. Calcium acts as a secondary transmitter by controlling the activity of numerous enzymes, ion channels, and expression of rapid response genes.

The Ca<sup>++</sup> concentration in the intercellular space is 10,000 thousand times higher than in the cell itself. Such a high gradient causes an unceasing migration of Ca<sup>++</sup> on various paths inside the cell and the necessity of its removal. Calcium is particularly predestined to the role of an intracellular signal. Some calcium salts are easily soluble, a calcium ion is not large, and thus it diffuses rapidly in the cytoplasm. Its level is strictly controlled, and its excess is eliminated almost immediately. This enables a rapid signal processing, which is significant in the case of high sound frequencies. Eventually, calcium becomes bound with proteins changes their conformations, so it can be used for the activation of numerous cellular enzymes. Such an ability of being bound with various proteins, which alters their properties, constitutes the base for an amplification of an intracellular signal, and therefore, a molecular signal amplification on the path from the receptor to the centre. The amplification mechanism is connected, among others, with calmodulin whose activity is increased 100 times when it binds 4 calcium ions. A calcium signal is cheap in view of energy - there is no need of synthesis of a signal transmitter; some problem is, yet, with the calcium removal from a cell after each depolarization. The inflow of calcium ions to the cell must be accurately controlled. When the cell membrane is no longer able to counteract an inflow of calcium ions for various reasons (trauma, toxins etc.), the calcium ions flowing into a cell activate proteolytic enzymes causing thus a destruction of intracellular mechanisms, which eventually leads to the death of a cell. Those disorders are on the molecular level, and to a lesser extent they bring about tinnitus. The reasons for such noises are not recognized and are treated with TRT method, which is not in line with the new philosophy of hearing - viz. causal treatment. When the nanostructures and nanoprocesses are unknown, it is hard to apply any causal treatment. The ascertainment of such changes is not simple, since the conductivity of calcium current passing through the cell membrane is of an

order of picoamperes, whereas the conductivity of the channel - of an order of picosiemens. The  $Ca^{++}$  level in a cell is 10,000 times lower than outside the cell, and in consequence, the calcium inflow into the cell may raise the  $Ca^{++}$  level in the cell even 100 times. The calcium level in a cell controls the production, transport and release of a transmitter into a synapse. Depolarization of a cell, within a time of an order of picoseconds, will open  $Ca^{++}$  channels, fusion of synaptic vesicles with the presynaptic membrane and release of a transmitter into the synaptic cleft. Such a presynaptic region acts as a nanoprocessor controlling the information flow. A neurotransmitter is released (fusion of the vesicle with the presynaptic membrane and its evacuation) with a 0.2 ms long time after the start of  $Ca^{++}$  inflow. The release of a neurotransmitter is caused by an increased level of calcium ions in the presynaptic region within a time shorter than milliseconds. Sensor proteins - sensors of the calcium level - act as intermediaries in the control of the effect of a change in the calcium level upon the cell operation viz. the transmitter's exocytosis. They are able to generate a selective response, proportional to a determined signal level and depending upon  $Ca^{++}$  which, in turn, depends upon the primary signal of a sound wave. Those proteins have a high affinity to  $Ca^{++}$  and an ability to conformational changes after being bound with calcium. That is why a rapid release of a neurotransmitter is connected with the presence of proteins to be bound with calcium on the membrane of synaptic vesicles. A transmitter is generated and packed into vesicles in the Golgi apparatus. Kinesin, a molecular motor, is responsible for the anterograde transport. Instead, dynein, a molecular motor is responsible for the retrograde transport of membranes of waste synaptic vesicles. Calcium ions and enzymes and proteins being bound with calcium control the transmitter production, both the anterograde and retrograde transport as well as processing of waste, emptied synaptic vesicles in a cell (recycling).

A change in the membrane potential - OHC depolarization - depends upon the operation of ion channels in the lateral and inferior cell. Most important are sodium, potassium and calcium channels. Also, Cl anions participate in it. The chlorine level in an auditory cell is approx. 4 mM, in endolymph - 130 mM, in perilymph - 125 mM. During the cell depolarization, Cl ions and anions arrive at the cell due to the SEM of the cell membrane. Anions and intracellular chlorine ions act as sensors dependent upon voltage; they become bound with prestin and bring about its conformational modifications responsible for OHC contractions. A OHC contraction itself occurs within a time of an order of microseconds. Instead, changes to the OHC membrane potential depend upon the operation of ion channels which are considerably slower than possible prestin contractions. There is why investigations into the frequency of OHC contractions, stimulated with electric current indicate possible a possibility of OHC contractions of up to 60 kHz, or more. Such investigations do not regard free work of ion channels. It can be deemed that an amplification of such high frequencies due to OHC contractions is doubtful or unfeasible. The operation of ion channels limits the frequency of OHC contractions.

A signal amplification may be performed only on a tone already received in the receptor; after amplification, such a tone amplified 1,000 times is superimposed with delay on a completely new, unknown sound wave (according to the theory of traveling wave). If such a new wave should carry a record of a loud sound, the amplification of the preceding wave due to an OHC contraction will alter the information transfer. While listening to quiet sounds with different intensities and harmonic frequencies, such an amplification of a preceding sound mixed up with a new one will disturb the reception of sounds which we should still hear in compliance with the sound wave pattern. In the laboratory sensible is amplification of a simple, harmonic tone of a constant, low intensity. Amplified is the second wave, the same as the first one. In the case of multitones with various intensities and harmonics with different frequencies, it is rather unlikely that the precision of transmission in line with the sound wave record could be maintained.

The threshold of hearing does not consist in a possible generation of a traveling wave, wave resonance or mechanical amplification due to OHC contractions. The threshold of hearing is a portion of energy of a sound wave in the form of a wave amplitude which can release the gating mechanism opening a  $K^{+}$  mechanosensitive ion channel, which, after its opening, will let pass a quantity of potassium ions causing the depolarization of an acoustic cell of an order of 10 mV. When the value of 10 mV is exceeded, the cell depolarization will be dramatically increased. There is no partial depolarization. There will occur the problem of conveying the sound intensity. It is probable that of importance is the number of channels as well as the size of receptor fields and the time in which mechanosensitive ion channels, which can receive the given frequency of a sound wave, remain open.

## Conclusions

New investigations, papers and analyses entail a reconsideration of all circumstances related to the reception, processing and transfer of auditory information. Emerging is a new vision of another signal path to the receptor, apart from the concept referred to as a traveling wave, described by Bekesy in 1928, which is corroborated by the facts presented in this study as well as by the cochlear implant, the lack of any improvement of high frequencies after stapedotomy, hearing of very quiet and very short sounds which cannot reach the receptor and cannot be amplified mechanically through an OHC contraction. Too little importance is attached to the operation of the acoustic cell itself. Into consideration should be taken the inertia in the middle and internal ear, especially for high frequencies. A better knowledge about the physiology of hearing may have a beneficial effect upon the therapeutical effects in the treatment of hearing disorders.

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## Conflict of Interest

No Conflict of interest.