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**Review Article**

# Amplification of the Auditory Signal on the Way to the Center

**Myjkowski Jan1\***

1. Retired physician, Specialist in otolaryngology, pensioner, Myjkowski Jan, Poland

**\*Corresponding Author:** Myjkowski Jan, Retired physician, Specialist in otolaryngology, pensioner, Myjkowski Jan, Poland,  
Tel: +48782449179, Email: janmyjkowski@poczta.onet.pl

## 1. Abstract

A person receives auditory information from the environment in terms of sound intensity between 0 dB = 10-12 W/m<sup>2</sup> and 120 dB = 1 W/m<sup>2</sup>. The difference in intensity levels is a trillion times. Converted into the amplitude of the sound wave, it ranges from 8 pm to 10,000 nm. The pain threshold of 130 dB is 10 W/m<sup>2</sup>. Hearing loss 140 dB = 100 W/m<sup>2</sup>. Destruction of the ear, rupture of the eardrum 160 dB = 10,000 W/m<sup>2</sup>. The difference between hearing threshold and eardrum destruction is 15 orders of magnitude - a quadrillion. Waves that are above the auditory threshold are received without amplification of the signal before the receptor. According to the traveling wave theory since the 1980s, it is believed that quiet tones are amplified in front of the receptor by 40 dB, thanks to the contractions of the OHC, which are supposed to be an amplifier for the IHC. According to other views, sounds are amplified in the hair cell and further to the center, the energy of which is too low to reach the CNS. This takes place at the level of molecular changes.

## 2. Signal Gain

According to the traveling wave theory for quiet tones, the auditory signal reaching the receptor is amplified by 40 dB. The mechanism of this amplification is believed to be the pulling up of the basement membrane by contracting OHCs during depolarization of the hair cell [1,2]. If we assume that each OHC depolarization causes cell contraction, there is no explanation at what level the decision is made which waves are to be amplified and to what extent. Loud sounds also cause OHC contractions, which can also pull up the basement membrane. Increasing the sound intensity by 40 dB, i.e. 10,000 times, increases the energy of the wave heading towards the center. The original energy of a sound wave cannot be the source of such a large portion of energy. What remains is the OHC contraction energy. If each OHC contraction is a source of this energy, the question arises what happens to this energy in the case of loud sounds.

The second question concerns the source of energy necessary for OHC contraction. Conformational changes of Prestin particles, responsible for shortening OHC by approximately 5%, are regulated by changes in the level of chlorine or chlorides on both sides of the cell

membrane. during depolarization. Changes in chlorine levels occur during each depolarization. Therefore, each depolarization should result in contraction of the OHC and pulling up of the basement membrane. Quiet tones that have not been received cannot be amplified using this method. The wave must first be received for the OHC to depolarize and contract. If the wave is received, the information reaches the brain through the afferent innervation of the OHC. There is no need to amplify such a wave at this stage. Even if a quiet tone is amplified, this process is time-consuming and after a fraction of a millisecond, pulling up the basilar membrane will disrupt the traveling wave caused by a much later, foreign sound wave.

In 0.1 ms, a sound wave travels 145 mm in the fluid and transmits information to a traveling wave at a speed of 2-50 m/s, which travels 0.2-5 mm in 0.1 ms. There is a large disproportion in wave speeds, inconsistent direction of the resonant waves and compression of the transmitted information. The transmission of information is disrupted by the traction of the basilar membrane by the OHC contraction of the wave that has passed and cannot be amplified by this method.

When a quiet tone has harmonic components and phase shifts, the formation of a traveling wave is problematic.

Such a wave traveling through the basilar membrane is disturbed by the traction of the basilar membrane, an earlier silent, amplified wave. What information is transmitted to stimulate the IHC and further to the center? If the quiet, amplified wave came from a multi-tone, then the information about the loud tones was separated and sent to the center earlier? Without silent tone information? Nature could not accept such an illogical mechanism.

There is an intracellular, molecular mechanism for amplification of the auditory signal, the same as in other sense organs [3,4]. If a sound intensity level of 10 dB with an amplitude of 0.05 nm is increased by 40 dB, the amplitude increases 100 times and the sound intensity increases 10,000 times. The power of this sound increases from  $10^{-11}$  W/m<sup>2</sup> to  $10^{-8}$  W/m<sup>2</sup>. It's hard to explain the fact that we still hear these quiet sounds 10,000 times amplified - as still quiet.

The energy of sound waves received by the auricle, especially in animals with a large number of ear muscles that adjust the ears like a radar to the direction of sound waves, is transmitted to the skull bone [5]. The eardrum receives the energy of waves coming through the ear canal. It transmits the energy of the waves to the bones, but part of the energy is transferred from the eardrum directly to the bone [6]. The bones of the tympanic cavity vibrate and transfer energy to the stapes plate and the skull bone. The stapes plate, making piston movements, transfers energy to the fluid of the vestibular duct, but part of the energy is transferred through the tendinous ring to the cochlear housing bone. At high frequencies, the stapes plate makes a rocking movement, transferring more energy to the oval window case. The movements of the plate take place in the longitudinal or transverse axis of the plate. Part of the plate generates a forward wave in the fluid, while at the same time the other part of the plate generates a backward wave. At the same frequency and in the opposite direction, destructive interference occurs, significantly disturbing the transmission of auditory information. Quiet high-frequency sounds cannot be transmitted through the cochlear fluids and basement membrane because they are subject to decay and destructive interference. We hear them, so we should assume that they go to the receptor via a different route [7]. Information transmitted to the bone and the bony casing of the cochlea undergo constructive interference at a speed of 3-4 thousand times. m/s are transmitted to the receptor. A sound wave that has no mass, except for environmental particles vibrating around a central position with an amplitude depending on the energy of the wave. This vibrating mass is at the level of atomic masses and does not play a significant role in the inertia of wave motion, such as vibrating elements having a large mass, e.g. the ossicles of the middle ear.

A sound wave has quantized energy [8], which means

that differences in intensity can only exist as an integer of the smallest portion of energy, called an energy quantum. This energy encodes information and is transferred to receptor molecules sensitive to a specific energy, called sound-sensitive molecules.

“A molecule is a collection of atoms connected by bonds of various lengths. They have different mass and different numbers of protons and electrons. Atoms vibrate at different frequencies. Electrons in orbits give rise to electronic energy, electrostatic energy. Dipoles are formed due to atomic bonds. In addition to the translational motion of atomic nuclei, there is also rotational motion. Atomic bonds create angles between bonds - valence and rotational. Each bond, each oscillation, has its own energy, which, when added up in the molecule, gives the molecule's own energy. Each atomic bond of elements has a specific frequency of natural vibrations. There are 3-4 times more bonds than atoms in molecule. The number of such atomic bonds in 1 mm<sup>3</sup> molecule has been calculated, and there may be about  $10^{18}$  of them. Each atom with  $n$  electrons has a specific energy. Valence angles and rotational angles influence (their change) the change in total energy. There are isolated molecule vibrations, stretching vibrations, bending vibrations, and intermolecular vibrations. According to the law of Nature, molecule searches for the bottom of the well, i.e. the lowest possible total energy. It has the ability to emit energy in the form of photons in order to absorb the lowest possible energy at a given temperature. A molecule that has received energy from a sound wave (sound-sensitive molecule), has increased total energy, tries to return to the basic energy, transferring the obtained energy to an adjacent molecule through photon radiation, through oscillations, vibrations or through its own conformational changes acting through contact on the adjacent molecule. This molecule, by obtaining quantized energy originally derived from the sound wave, creates a new conformer, capable, thanks to the energy received, of regulating the mechanism responsible for gating the potassium mechanosensitive channels of the hair cell wall. The rate of energy absorption and transfer by molecule is approximately  $10^{15}$ /s. Through the open potassium channel, 6000 K<sup>+</sup> ions/ms pass from the endolymph into the cell, starting the cell's depolarization. At the electronic, atomic and molecular level, the information contained in the sound wave is transferred to the hair cell. The work of the hair cell with the mechanism of intracellular amplification, producing a transmitter, was discussed in the paper “Submolecular theory of hearing”. Intracellular amplification is a whole complex of molecular factors such as: phosphorylation and dephosphorylation of ion channels responsible for the conductivity of cell membranes, ATP concentration, cAMP and cGMP levels, cell's pH, osmotic pressure, and the presence of ligands. It is related to the regulation

of calcium levels in the cell, with the work of proteins binding to calcium, where calmodulin plays an important role, influencing the production and breakdown of cAMP and cGMP. It activates protein kinases and phosphatases and regulates the functioning of the calcium pump. It affects the contraction of muscle and non-muscle cells by activating the cAMP-independent myosin light chain kinase. Calmodulin affects exocytosis. Saturation of the 4 domains of calmodulin increases its effect up to 10,000 times. Calmodulin, together with calcium that changes level during stimulation, affects metabolic processes in the cell by affecting the so-called key enzymes. The interaction of all cell organelles is regulated. The process of enzyme production or the rate of their degradation is regulated. Calcium is the second transmitter of information in cell, acting faster than the other second transmitters: cAMP, cGMP, DAG, IP<sub>3</sub>, which are produced in connection with an increase in calcium levels or activated by G-protein. The stage of generation of second transmitters is one of several mechanisms of intracellular amplification. One enzyme molecule can produce several hundred second transmitters” [9].

In response to sound, the hair cell releases a transmitter to the synapse, where an excitatory postsynaptic potential is created and conducted to the nerve cell [10]. Information flows to this cell through axons from many synapses, and information converges. After integrating this information with information from other nerve cells, an action potential is created and is conducted along the axon in the auditory nerve to the center. If the signal from a single dendrite is too small to cause depolarization of the nerve cell, the energy of the axons that successively reach the nerve cell is combined - this is called time summation.

The second mechanism is spatial summation, when the energies of neighboring axons at a given time are summed up. The resulting action potential runs in the myelinated nerve from the junction of Ranvier to the constriction, where it is amplified by subsequent depolarization, thanks to the action of ion pumps driven by the energy of ATP decay. Receptor fields, collateral inhibition, presynaptic and postsynaptic inhibition, the rate of production and breakdown of enzymes and other proteins, production and transport of transmitters and cotransmitters, and the entire general operation of the hair cell at the constitutive and regulated level are important in signal conduction to the center [11]. If our hearing has a billion levels of sound intensity from the hearing threshold to 120 dB, then no single mechanism can be responsible for the transmission or amplification of the signal. Each mechanism has its own regulation at the molecular level. Only good cooperation of all mechanisms ensures good hearing.

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