



Synaptic Adaptation Stability ARC Therapy



The revolutionary technology in tinnitus reduction



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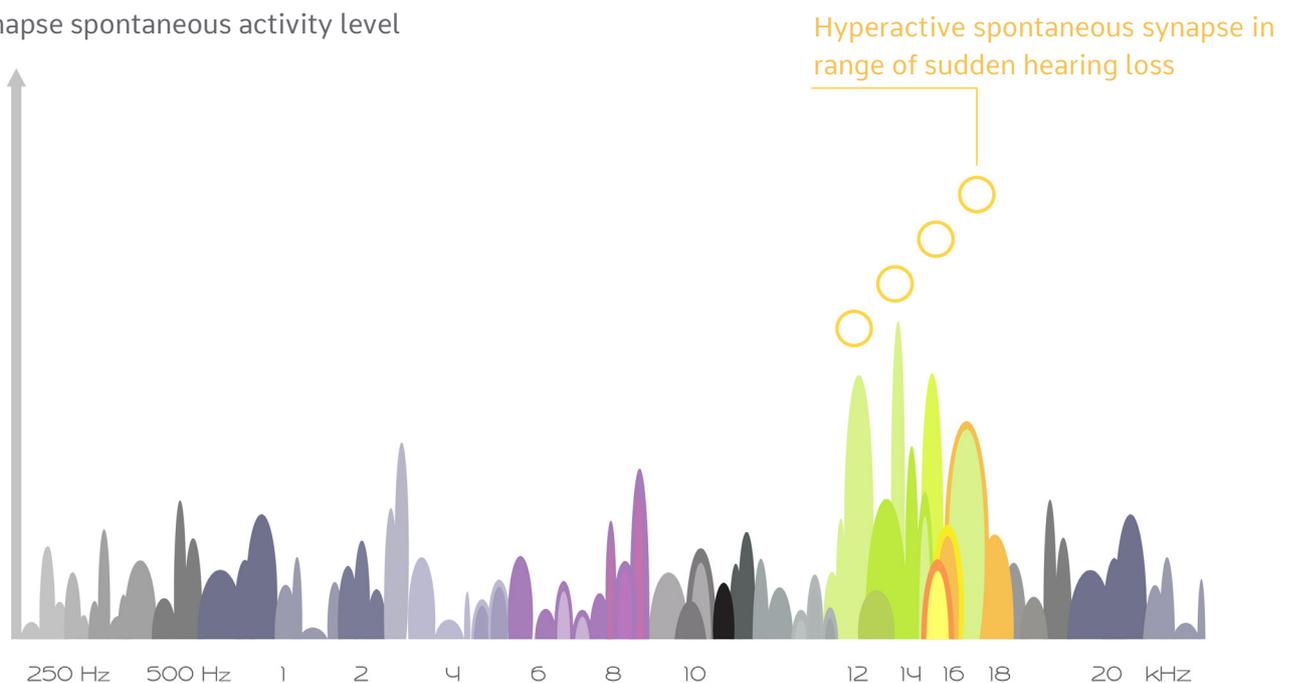
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1. The cause of tinnitus

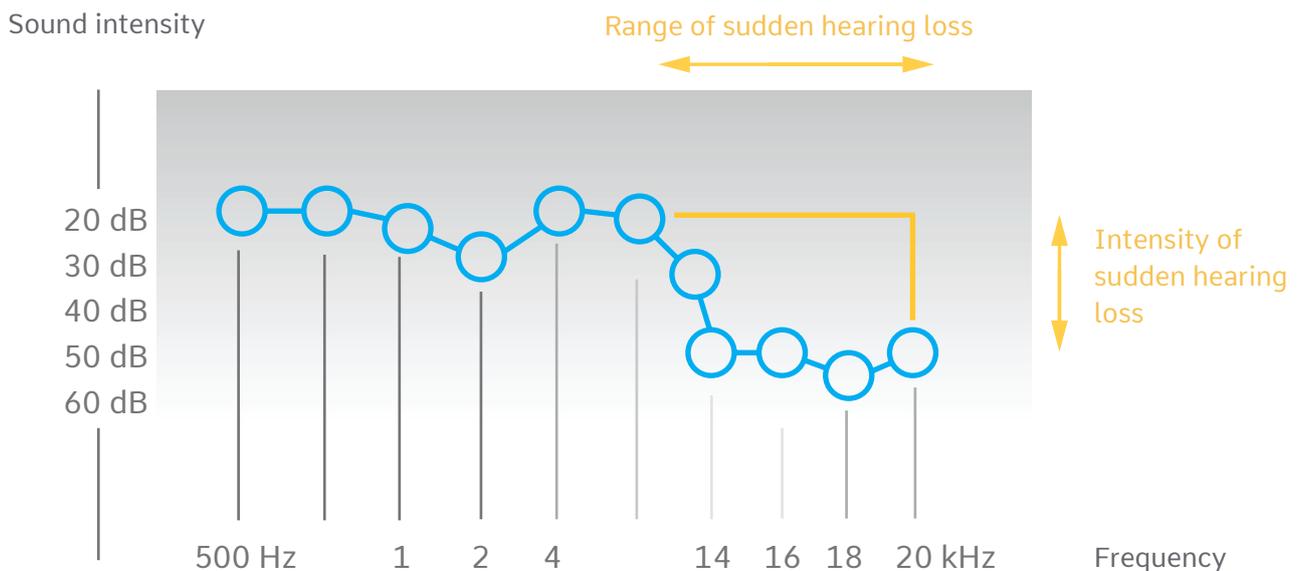
Lack of adaptation of auditory nervous system to sudden hearing loss

Tinnitus is a symptom of not adapted auditory nervous system after sudden hearing loss (sudden death of hearing hair cells that cause very rapid and fast decrease of input). This process itself manifest in well known process called synaptic scaling or homeostatic plasticity where one of synapse (post synapse) generate hyperactive and spontaneous activity that cause fast and often release of neurotransmitter after decrease input from pre synapse (cochlear nerve). Slow acting hearing loss don't cause tinnitus because of adaptation process of all auditory nervous system structure that has place always during long lasting hearing loss in slow decreasing of hair cells number. During this process Arc/Arg 3.1 protein is created. Arc is an immediate early gene that has been shown to be associated with neuronal activation and is also necessary for neuronal plasticity and change of neural number and synapse mass in deprivation process. In progressing hearing loss, nervous system have time to decrease number of neural units and synapse mass to less frequent and decrease stimulation from cochlear hair cells.

Synapse spontaneous activity level



A patient with a progressive hearing loss have high Arc / Arg 3.1 protein level that is slowly increasing with time during change in decreasing input stimulation level. Arc decrease synapses proportion to the level of the stimulation. The protein is released only at the moment when the nervous system is replaced by gradually decreasing stimulation over time. During sudden hearing loss (that usually occurs at the level of 4 to 20 kHz) there is a very high-speed external cellular destruction, which also involves the inability to adapt auditory nervous system in such a short period of time- to worse hearing. Studies confirm that during such rapid destruction, there is no production of the protein Arc / Arg 3.1 in auditory nervous system. resulting in any change in size and structure of the nervous system in a relation to the decline inner ear hair cells activity. The nervous system (which retains its size and the natural dynamics of working in silence and with limited stimulation from the outside) increases its activity on the quiet sounds in range of hearing loss resulting in hearing the higher gain and noise of synapse as tinnitus. No longer stimulation permanently opens the calcium channels at synapses that generate electrical discharge of spontaneous activity and stimulus-specific adaptation (SSA) in auditory memory that memorizes the level of synapse activity to no stimulation. Spontaneity activity and its volume depends on the depth of hearing loss, which affects a large number of synapses is left without adequate stimulation and is present in the range of hearing loss. Constantly stimulated synapses generate tinnitus, if cell destruction is broad, squeal if the sudden destruction of cells occurs in a narrow band.



2. Adaptive models auditory nervous system

Model of normal hearing

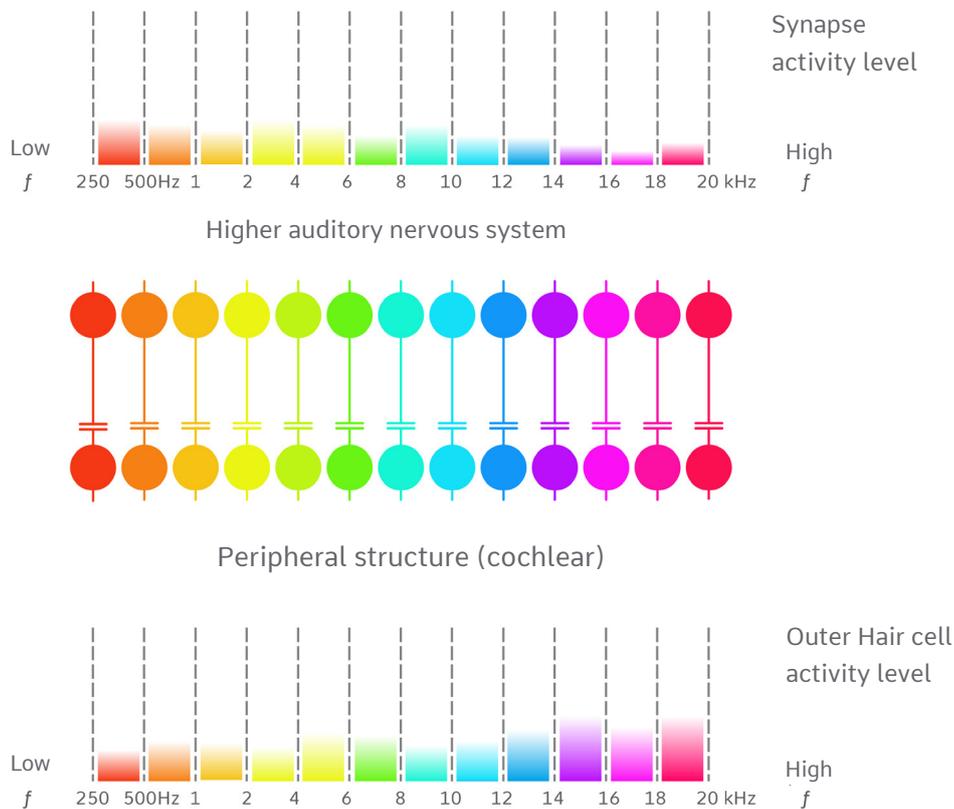


Figure No. 1 shows, such as the normal structures of the auditory pathway from the inner ear to the central nervous system. The activity of the hair cells of the cochlea at the same time regulates the activity and strengthen the work of synapses in the cochlear nucleus and higher neurons of the auditory pathway. If the activity of the inner ear hair cells in a low frequency range is decreased, synaptic activity in this band will be higher (synaptic scaling process). If the stimulation of the inner ear hair cells at high frequencies is increased in this band, synapses are reducing their own sensitivity to regulate the activity and (at the same time) protect the neurons in the auditory cortex before over stimulation and burnout. The process is known as synaptic scaling or homeostatic plasticity. Synapses in the central nervous system regulate their own activity and state of arousal in proportion to stimulate to the input. This process in prehistory protect us from danger as it managed very selectively hear the faintest sound and rustle against to present silence.

Model of progressing hearing loss

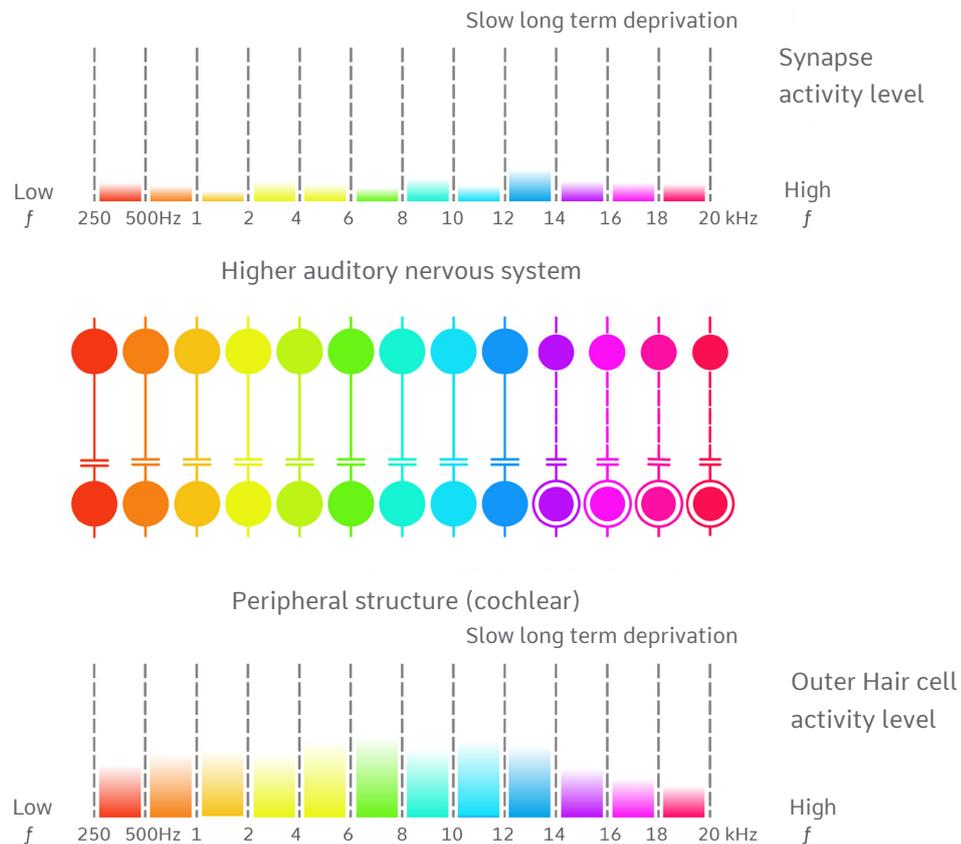


Figure No. 2 shows the process of adaptation of the auditory nervous system to slow decreasing stimulation in long lasting hearing loss. The long lasting decrease in hearing cell activity results in less release of glutamate from the inner hair cells in time. In effect the structure of pre and post synapses in the cochlear nucleus, the number of fibers sideband and the number of neurons in the auditory cortex, decreases and adapts to the progressive deprivation each week. During the decreasing stimulate the Arc receptors produce a special adaptive protein Arc / Arg 3.1 that reduces and prepares the construction and mass weakening of synapses proportionally to the decreased level of stimulation over time.

Model of progressing hearing loss

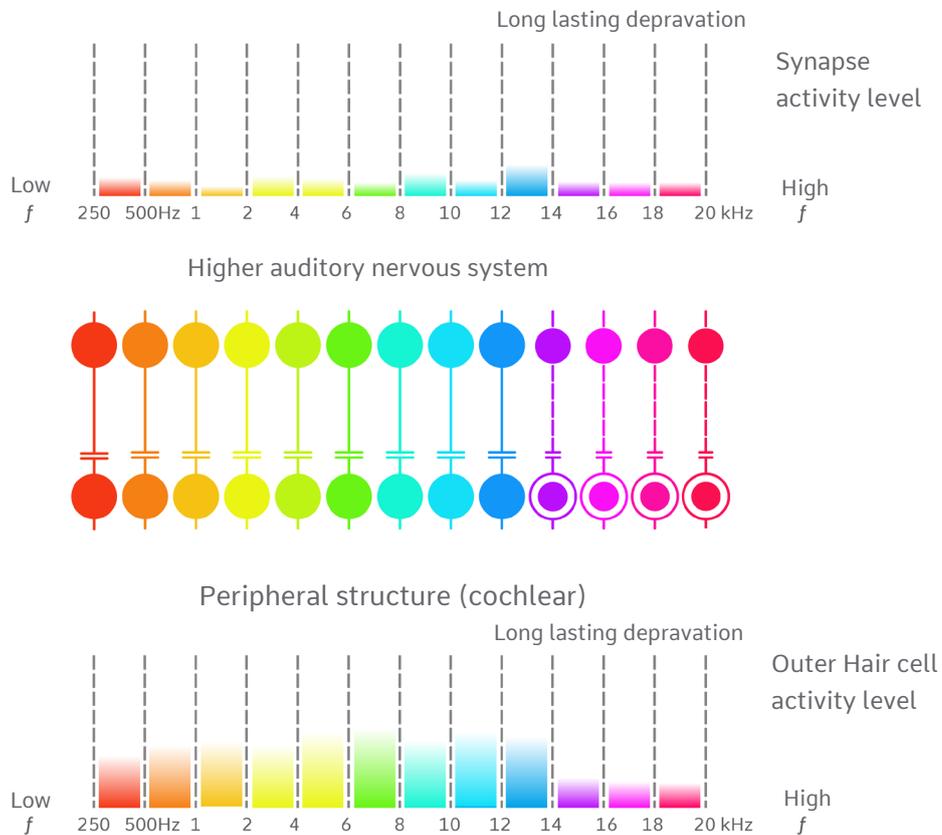


Figure No. 3 shows the process of adaptation of the auditory nervous system to gradually decreasing the stimulation of outer hair cells. A larger decrease in the activity of cells (in the further process of progressive hearing loss) causes weaker and weaker release of glutamate from the inner hair cells. In effect the structure of synapses in the cochlear nucleus, the number of fibers sideband and the number of neurons in the auditory cortex, is further weakening process and adaptation. During the hearing loss growing, stimulation decline in activity and stimulate the Arc receptors to produce an increasing amount of protein Arc / Arg 3.1 which further regulates the construction and mass of synapses to degraded hearing in deeper adaptation process.

Model of progressing hearing loss

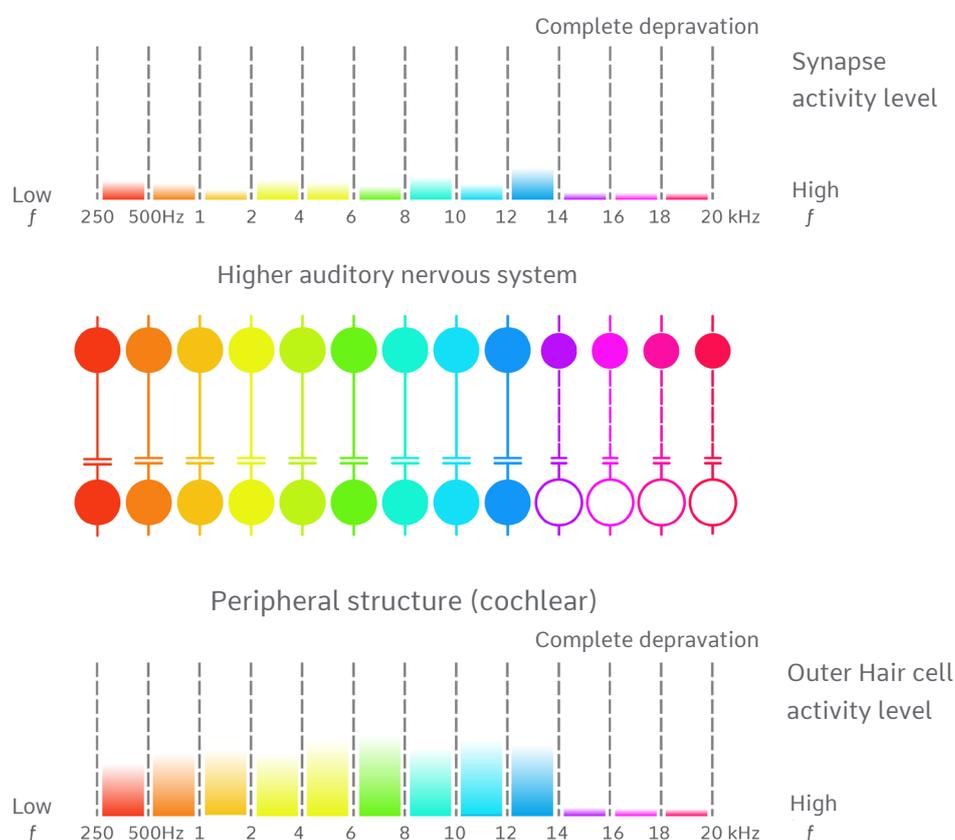


Figure 4. Shows completed process of adaptation of the auditory nervous system to long lasting decreased acoustic stimulation. In the cochlea there was a total destruction of the three rows of outer hair cells. The inner auditory cell is at rest, and can be activated only by a very loud sound. Even so, auditory nervous system for the duration of weakening the stimulation occurred adapt its structure. Synapses reduced their weight and structure size to complete lack of stimulation above hearing threshold and are almost complete deprived. The amount of fiber has been decreased. The neurons in the auditory cortex began the process of reorganization and migration to another side of structure that is active and has access to stimulation. The whole way the auditory undergone successful adaptation process, maintaining the correct ratio of each element and stimulate the auditory pathway to the level of stimulation of the inner ear without causing tinnitus.

Model of sudden hearing loss and tinnitus formation

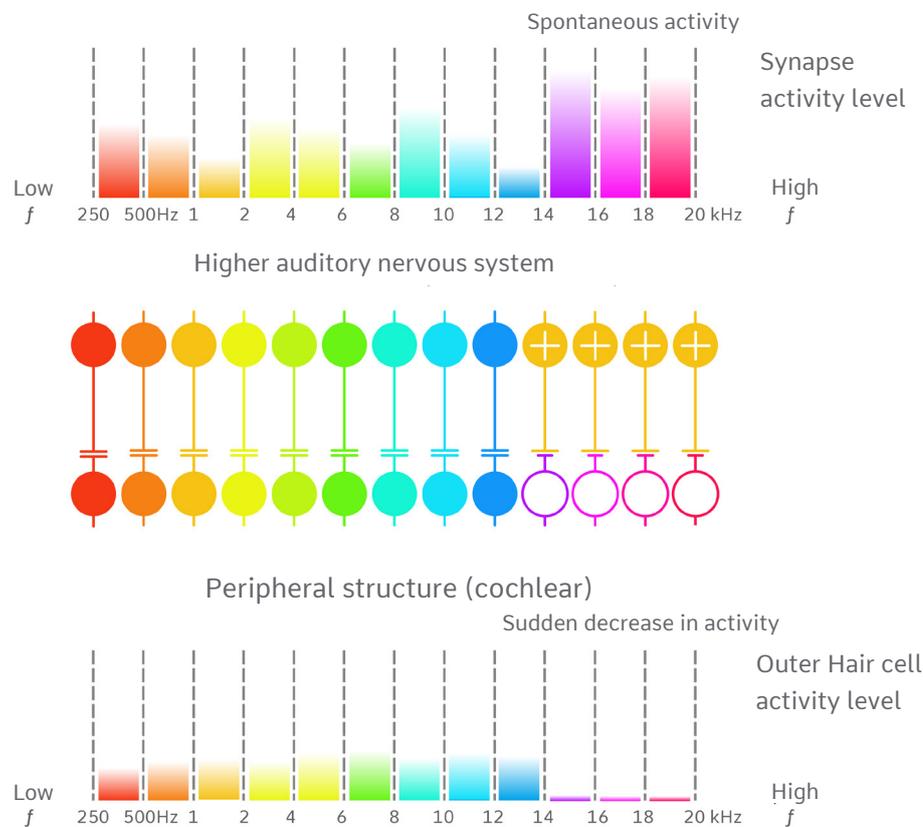
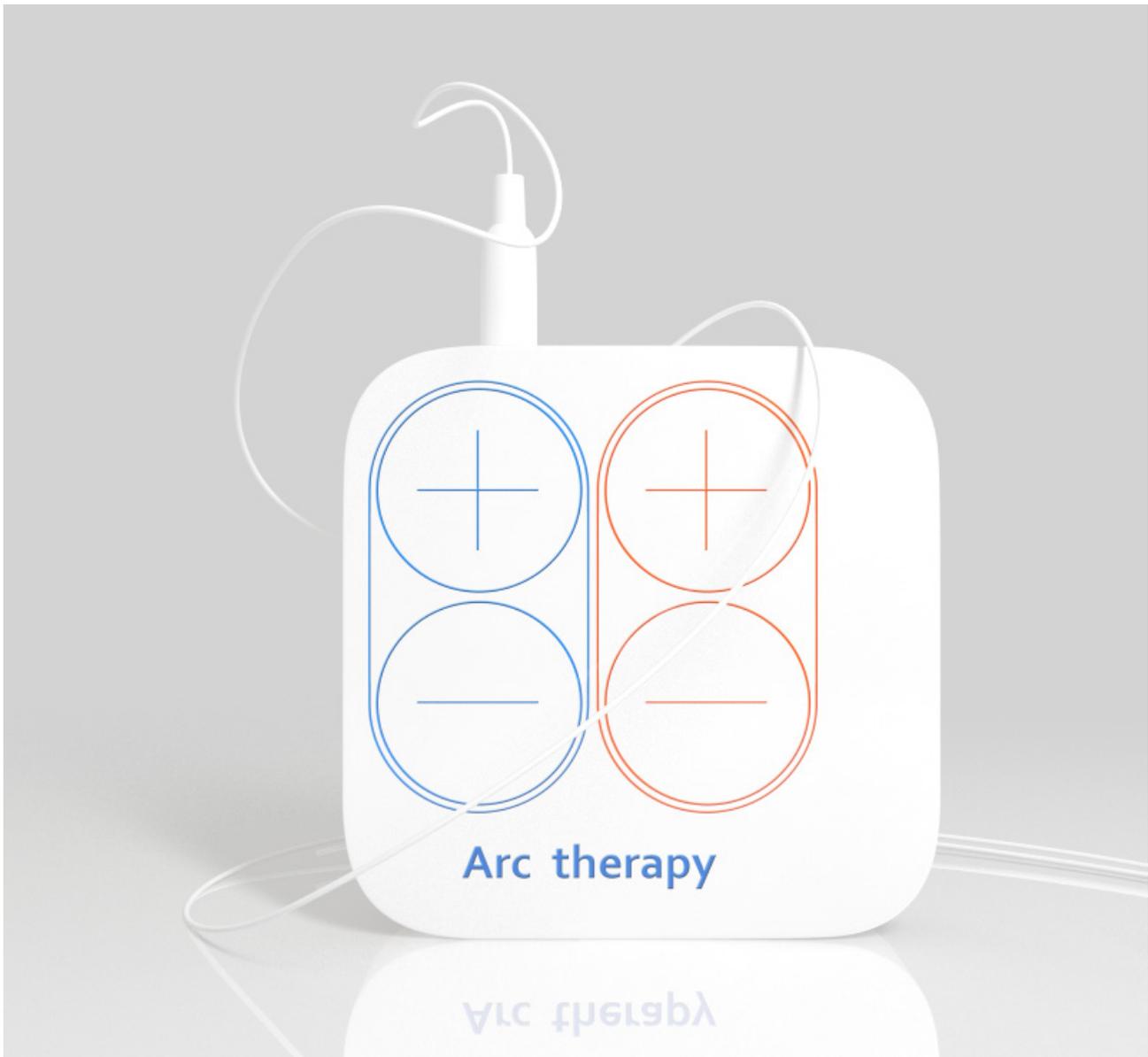


Figure 5. presents a model of sudden hearing loss, in which neurons and synapses in auditory pathway suddenly lose high level of stimulation from hair cells in cochlear. In this model all three rows of outer hair calls died very fast in the same time in 1 hour. The nervous system devoid of such a high level of stimulation in such a short time increases and it act as if there were a sudden silence in environment automatically increase gain and sensitivity amplification of synapse in band of high frequency affected sudden hair cells death . This generates more noisy synapses work which is manifested in the form of a heard a squeak or broadband noise. During such rapid changes in the level of stimulation does not occur to produce a protein Arc / Arg 3.1 which is manifested by the fact that in spite of the reduced activity of the inner ear structure nervous system is not in deprivation mode. The nervous system adapts, but in a different direction. If the neurons in a specific band that is in silence does not receive a suitable activity in longer period of time, they develop structure called axon initial segment, additionally by increasing axonal mass neurons are more responsive and sensitive to the quiet ambient sounds which increases the volume of the noise or squeak as tinnitus.

3. The termination and reduction tinnitus by using synaptic adaptation stability therapy ARC



The complex technology in a simple device

At first look synaptic stabilizer resembles a simple mechanism and MP3 player functionality. But inside we use unique technology that is complex and complicated as the nervous system.

For successful tinnitus reduction the time is a key factor

Time To decrease synapses activity permanently the synapse need to reduce their own mass and size to the current level of decreased stimulation affected by sudden hearing loss (a natural deprivation process). To accomplish this, inner auditory hair cell need to released progressively less and less glutamate (neurotransmitter) in the time, despite the presence of current hearing loss. The only solution to this problem is to use artificial environment that will reproduce the process were inner hair cell becoming less stimulated by decreasing acoustic stimulation in band were sudden hearing loss is. By this process we can imitate the long lasting outer hair cells death with high accuracy that leads in to increased Arc/Arg 3.1 production and the same process that begins in deprive and adapting nervous system to less acoustic stimulation from cochlear in progressive hearing loss.

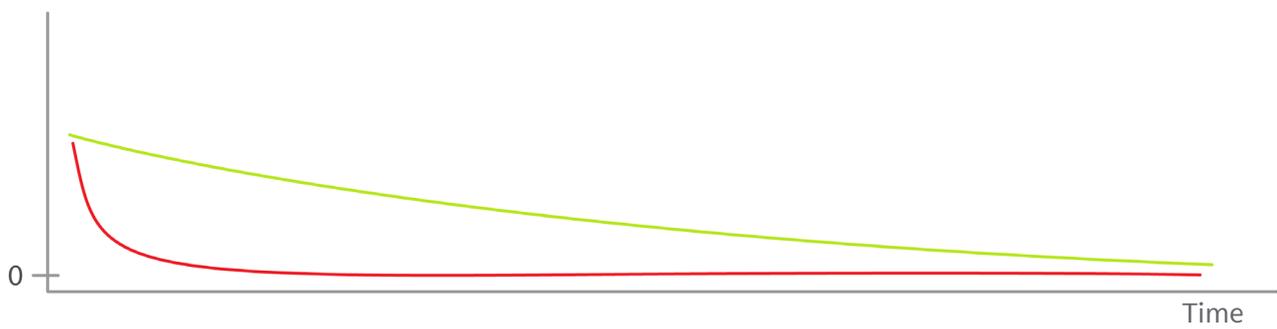
Decreasing stimulation over time

To restore the process of deprivation of the auditory pathway and simulation of production in the nervous system adaptive Arc protein, we used a unique technology which automatically reduce the frequency of administration time signal. This means, that the device based on a preset course of therapy itself automatically knows when and at what point in the therapy, to reduce stimulation so that it led to the mapping of the process that occurs when naturally increasing hearing loss over time. The result of this process is reduced tinnitus that the patient hears.

Synapse activity level



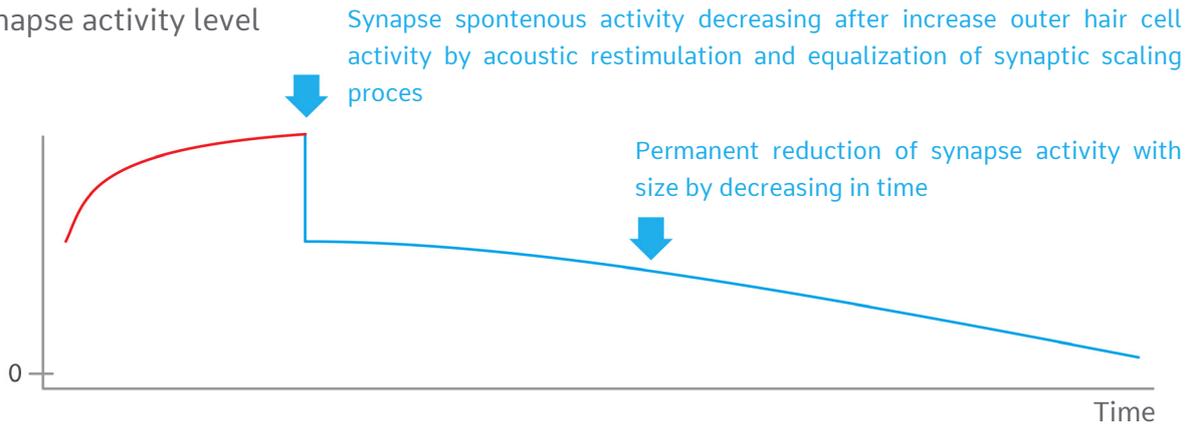
Outer hair cell activity level



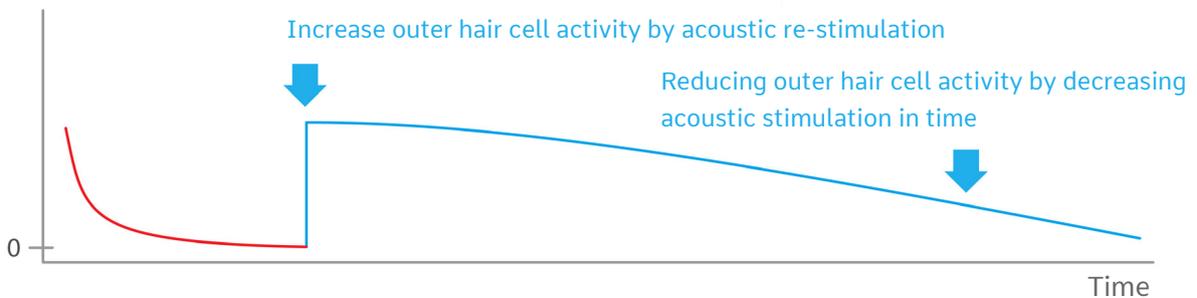
- Sudden hearing loss
- Progressing hearing loss

The use of replacement acoustic environment that adapt the nervous system to the already existing hearing loss.

Synapse activity level



Outer hair cell activity level



— Sudden hearing loss

— Synaptic adaptation stability Arc therapy stimulation replacement

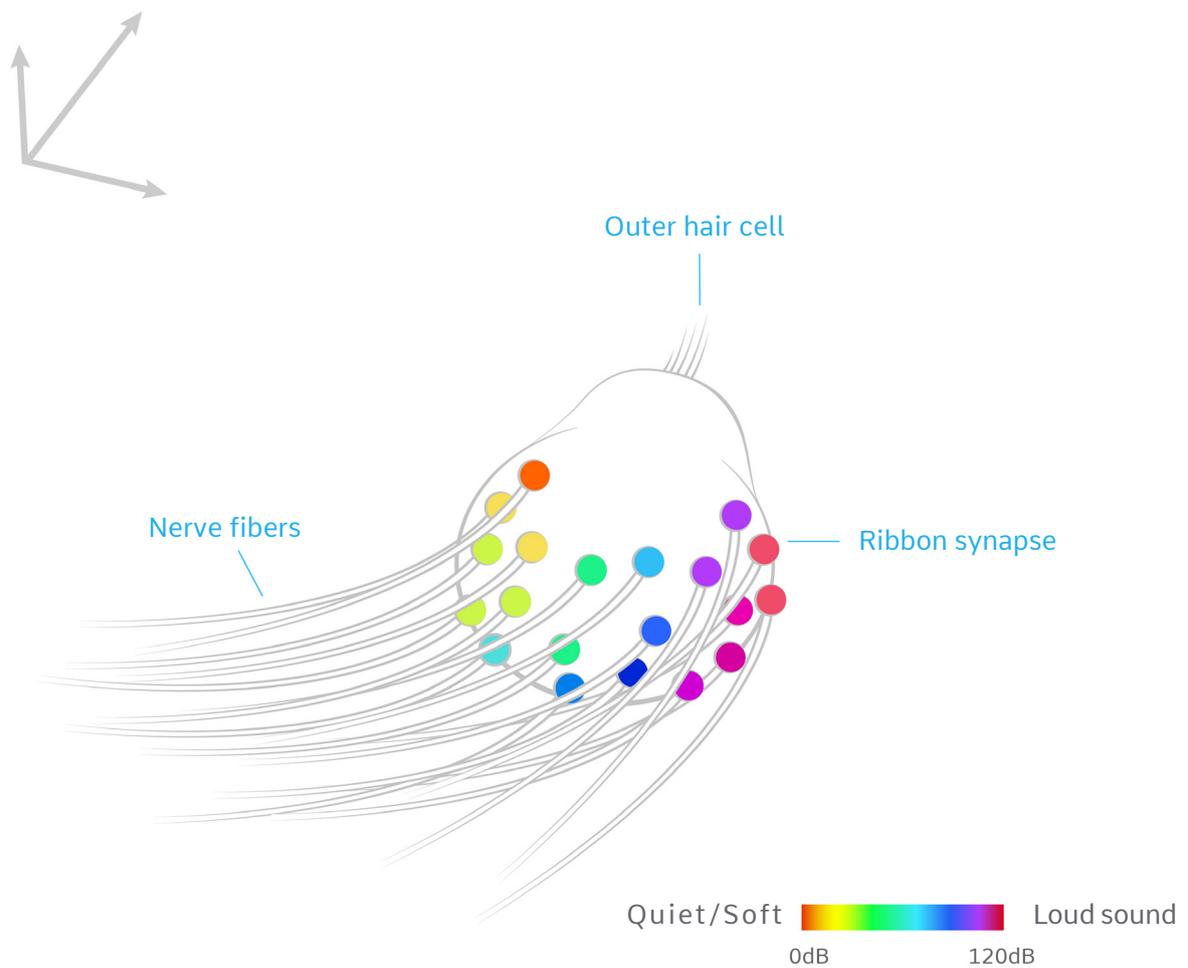
Adapting the nervous system in three dimensions

Time is the key to effectively reducing tinnitus by correctly due process of adaptation and production of a protein Arc / Arg 3.1, however, there cannot be the only factor causing the positive adaptation of the nervous system. For this, our technology stimulation is programmed in different intensity threshold.

The nervous system not only analyzes the signal based on the difference octave in pitch, frequency tone but also analyzes based on intensity octaves. It is associated with the independent internal auditory electric level potential processing by Ribbon synapses in every inner hair cell nucleus which is converted into information which the intensity of the sound is heard.

This is an amazing importance in grouping and sorting of sound in space. The process of hearing independently in different intensities allows to distribute the signal loud and silent partnership in the given frequency range.

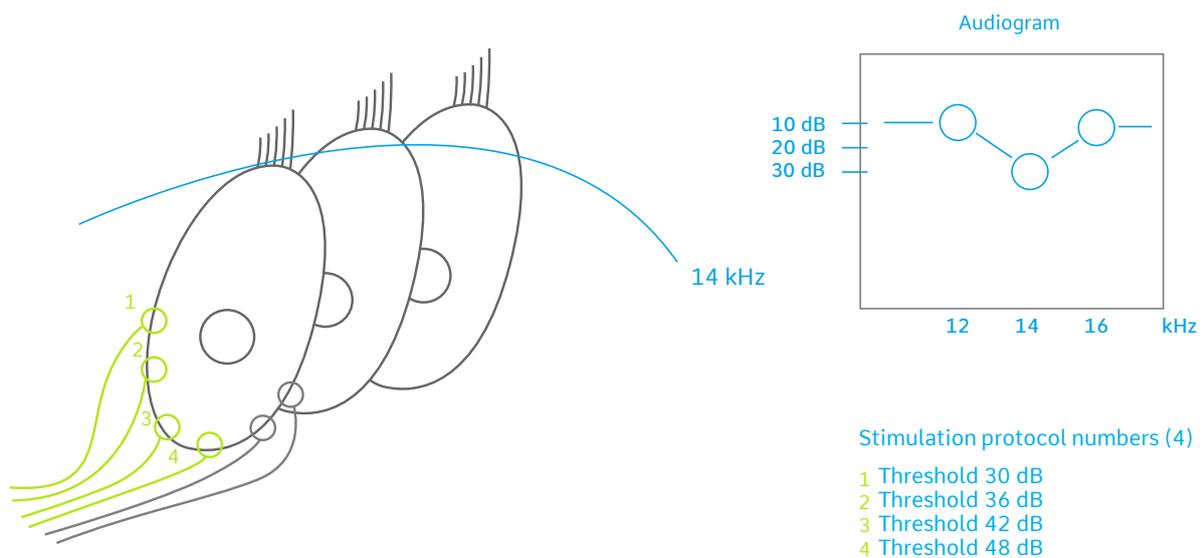
Under each outer hair cell nucleus we will find 20 Ribbon synapses. Each single ribbon synapse is involved in transmitting 6 dB of sound level intensity. This covers the whole dynamic level in sound intensity from 0 dB to 120 dB.



Adjusting the amount of stimulus protocols to the depth of hearing loss

Depending on how profound hearing loss occurs is matched individual number of protocols stimulus whose task is independent adaptation of framing each band sound intensity at a given frequency.

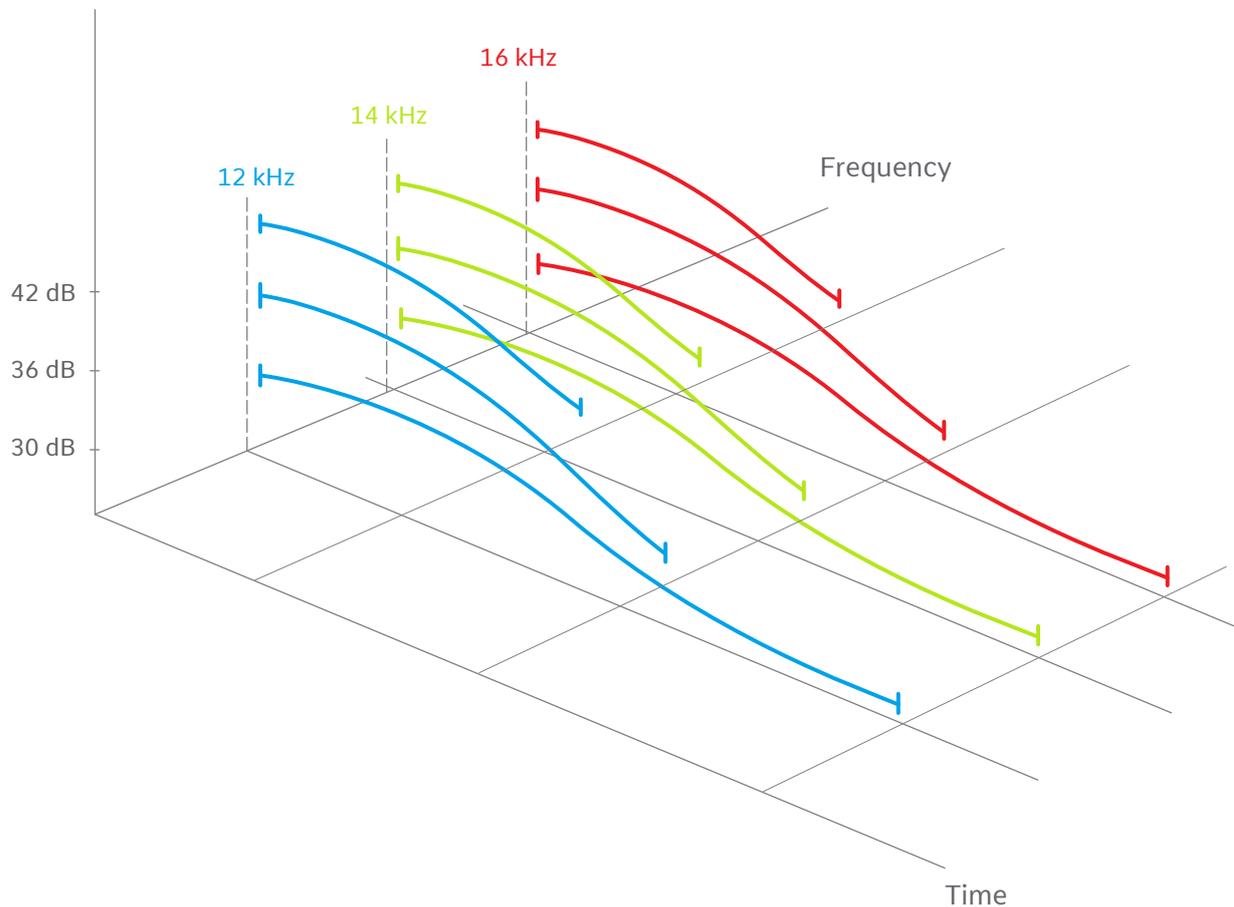
Model of sudden hearing loss on 30 dB threshold level and 5 synapses require adaptation process



— Synapse that doesn't have access to stimulation after sudden hearing loss and require adaptation process to decrease hyperactivity

The device is programmable in terms of width and depth of hearing loss, hearing loss (ratio of inactive synapses to that protocols stimulus measures). The profound hearing loss the greater the number of synapses adapted, longer duration of treatment.

Sound intensity in dB

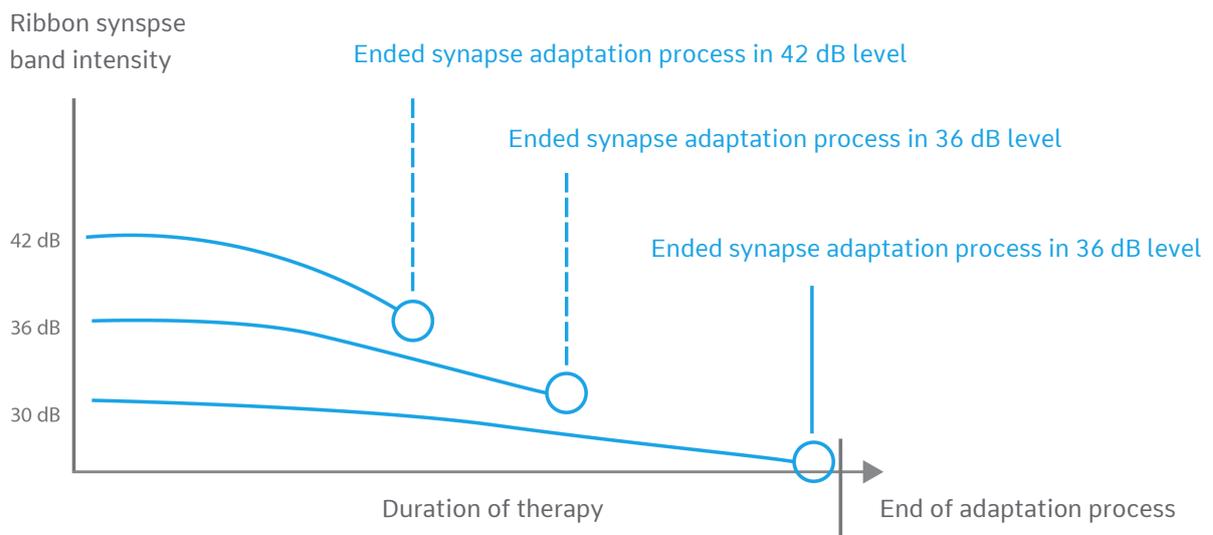


Above we have an example, in which we use adaptation technology for hearing loss 20 dB level and a wide sudden hearing loss frequency band from 12 to 16 kHz. Each frequency band receives three stimulation protocols on three different sound level intensity. These intensities respectively stimulate the shift in dynamic intensity of three synapses under each hair cell in the range of 12 to 16 kHz and in the range from 0 to 20 dB. Stimulation is programmed so that none of the stimulus protocols do not overlap in time, giving the impression of a natural environmental background noise in soft middle and loud sounds. Each of intensity protocols are automatically removed from the programmed cycle of therapy after each month, which creates the impression of turning down the environment in intensity and reinforces the effect of adaptation on each band.

The duration of treatment w the example used protocols

Hearing loss level	Frequency range	Number of synapse	Duration of therapy	Numbersm of protocols
30 dB	20 kHz	5	5 month	5
30 dB	12- 16 kHz	30	12 month	15
60 dB	20 kHz	10	10 month	10

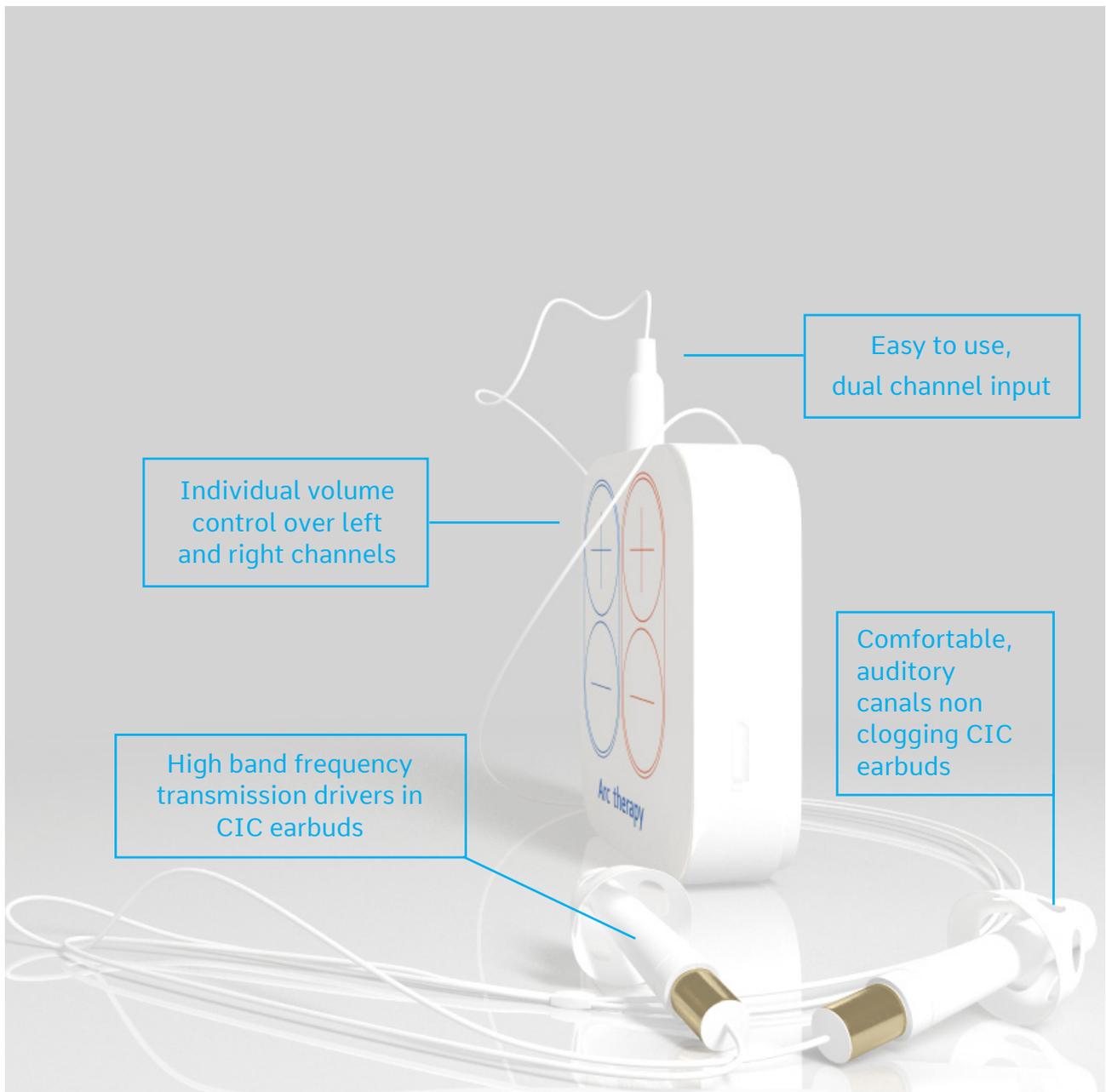
Here is an example of steps to reduce ended adaptation processes protocols of individual synapse fibers above each auditory hair cell. This example illustrates the range of 12 kHz frequency and three threshold levels which are reduced in time from circulation the programmed therapy.



4. Technology

Construction of the equipment

To cover such a complex acoustic stimulation needs we created specialized device used only for our therapy.



The device is programmed by an audiologist in the range of hearing loss and hearing loss threshold level . The specialist also can set independently time of each stimulation protocol even in 8 independent channels for the left and right ear, which gives 16 independently operating device settings.

The device has a memory and resource multiple independent axis of their work, which means that the protocol set to run automatically on a given day or week, no matter how long the device is used.

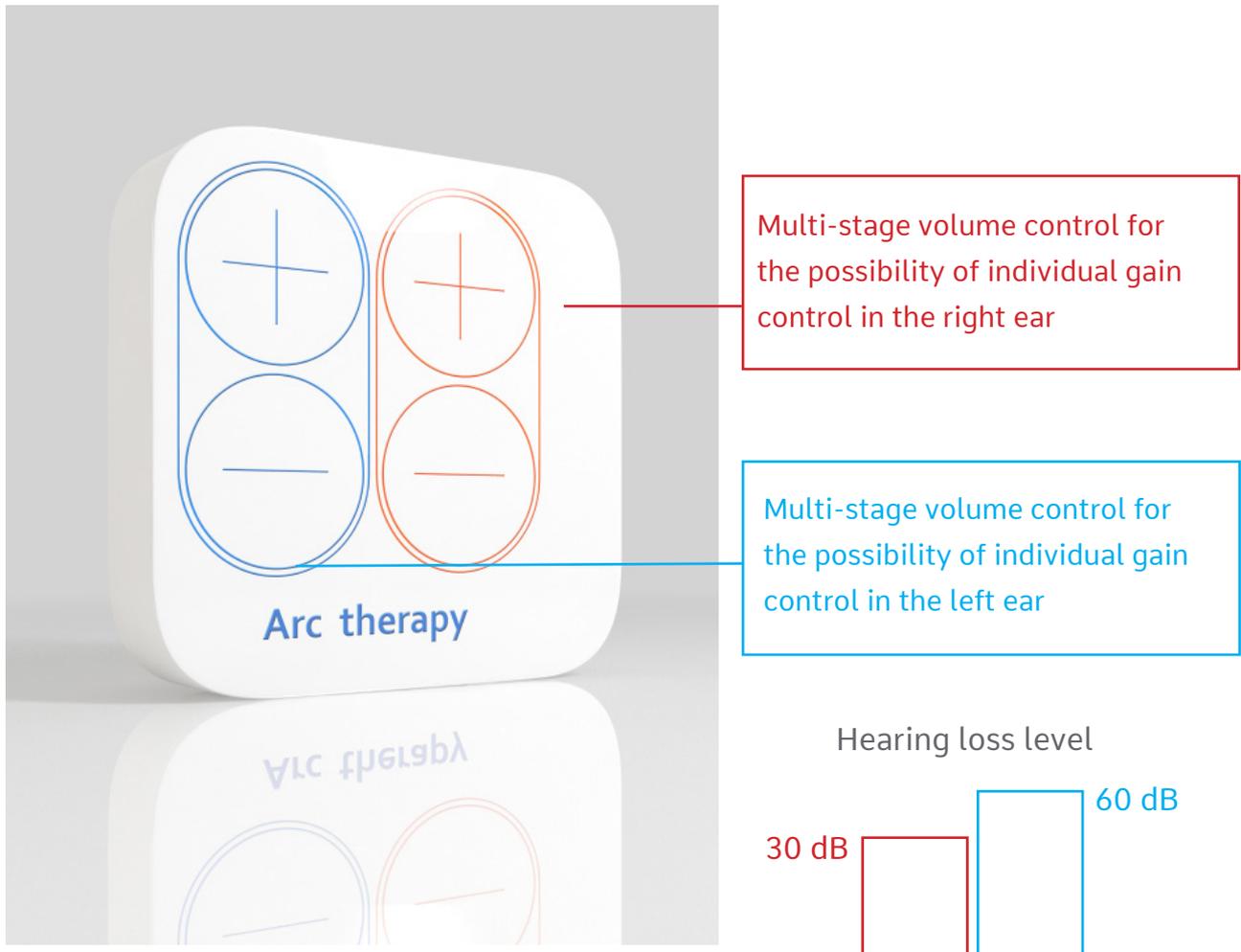
Data loggin

The audiologist wants the patient to wear the device as often as is possible for the best results. For this our processor has the data logging program that monitor time were stimulation in device were used.

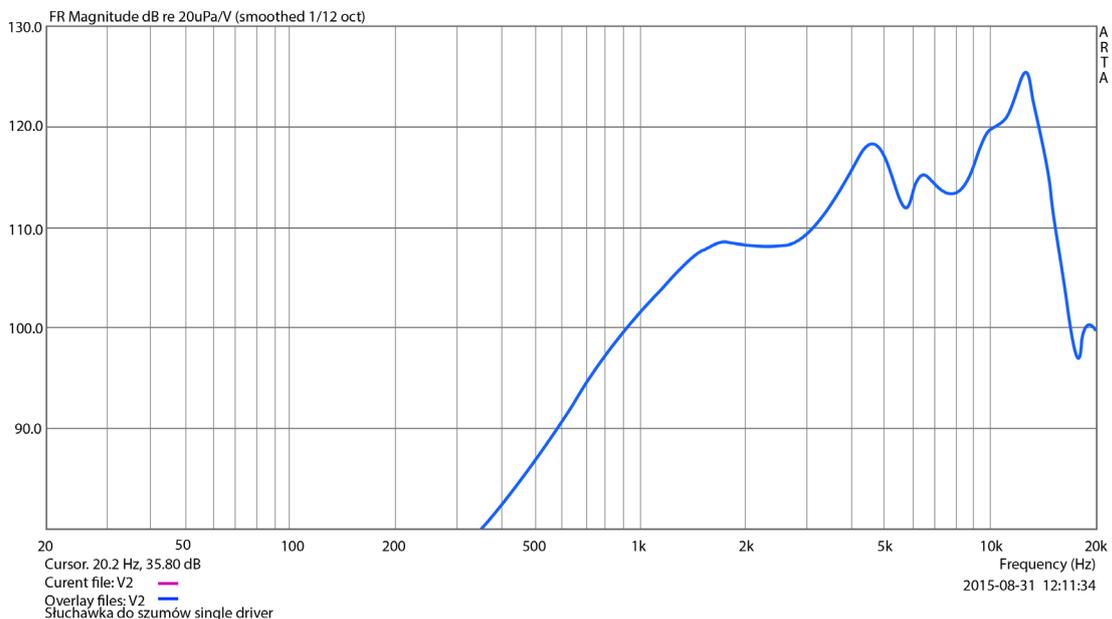
This is particularly important in order to continue the course of therapy to know how long the patient must wear the device to complete the full process of adaptation.



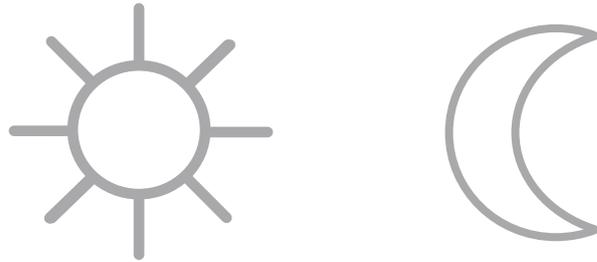
Individual volume controls on the right and left ear



The high gain range of amplification for the left and right ear of wide band achieved through headphones CIC

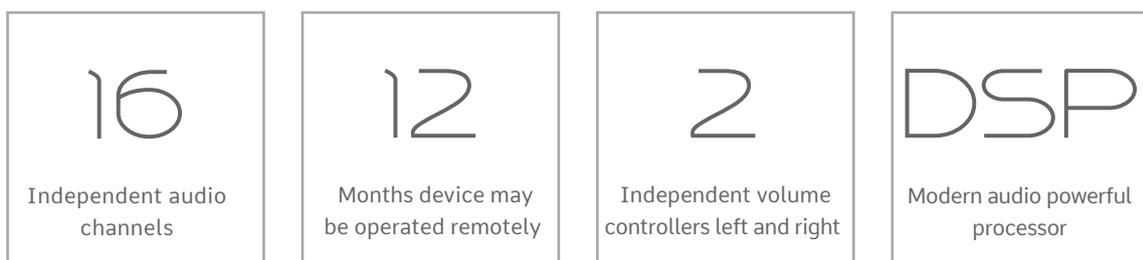


The maximum time during which the machine can automatically control the course of treatment is up to 12 months. During this period, the device automatically controls the therapy parameters of the working time of each stimulation. The task of the patient is only verify the volume of the right and left channel and observe standards using the device.



The device is small and mobile so a patient can use the device throughout the day and even the night and enjoy the silence.

The complex technology in a simple device





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creative audiology solution

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