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MASTER'S THESIS

FUNCTIONAL-TECHNICAL EQUIVALENT CIRCUITS OF VESTIBULAR SYSTEM

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ABSTRACT

Key words: Functional-technical circuit, vestibular apparatus, vestibular implant, transfer function, mathematical modeling, biological tissue impedance, electrical equivalent circuit.

For the last 20 years research and development of vestibular implants have been actively carried out, but currently available samples of vestibular implants are still far from perfect. The reason for this is the fundamental problems related to the electrically conductive properties of vestibular labyrinth tissues that influence the change of characteristics.

The electrical impulses generated by the implant from the electrodes propagate through the tissues of the inner ear to the ends of the vestibular nerves and then to the brain, causing the corresponding vestibular reflexes to change the position of the body or head. Thus, the vestibular system (implant + vestibular labyrinth) is a biotechnical system with biological feedback, the effectiveness of which depends on the parameters of stimulating impulses (shape, amplitude, frequency, modulation depth) both from the electroconductive properties of the labyrinth tissues (specific resistance, capacity). The control of such systems is based on the theory of dynamic systems, the most important characteristic being the transfer function. The degree of adaptation of the biotechnical system to reality depends on the precision of the mathematical model describing the transformation of the electrical signal from the stimulating electrode to the vestibular nerve, and hence the dynamic characteristics of the transfer function.

In this connection, the **aim** of the master’s thesis is to improve the transfer function of the vestibular implant.

The object of research is the human vestibular organ.

The subject of the study is the electrophysical properties and the transfer function of the vestibular labyrinth.

Tasks:

1) anatomical research of the vestibular apparatus and the physical principles and mechanisms of its work;

2) to conduct a study of the electrically conductive properties of the tissues of the vestibular labyrinth;

3) the study of the foundations of the theory of control of dynamical systems;

4) development of a method for determining the transfer function of the vestibular organ;

5) measurement and calculation of the amplitude phase characteristics of the harmonic signal during passage of vestibular labyrinth tissues;

6) calculation of the transfer function of the vestibular labyrinth;

7) analysis of the dependence of the transfer function on the frequency of the stimulating signal.

Detailed studies of the electrically conductive properties of the tissues of the vestibular labyrinth have been carried out, formulae for calculating the impedance of the electrical circuit of the labyrinth and its transfer function have been obtained. Measurements and calculations of the amplitude-phase characteristics of a harmonic signal of various frequencies passing from the ampoules of the vestibular labyrinth of the guinea pig to the end of the vestibular nerve and to the adjacent electrodes were made. On the basis of measured output signal values at the end of the vestibular nerve, the transfer function of the vestibular labyrinth at nerve stimulation from the upper, horizontal and rear semicircular channels is calculated and its frequency dependence is investigated. It has been shown that when the frequency increases, the transfer function tends to its asymptotic value. The transfer function of the vestibular labyrinth for stimulating impulses from the electrode located in the vicinity of semicircular channel has been found to be significantly smaller than for stimulating pulses from electrodes, located in the upper and horizontal semi-circular channels. The proposed electrical model and the results of calculations can serve as a basis for diagnostics of vestibular labyrinth diseases and for design a new type of vestibular implants.

Research results are presented in the following publications:

1. Demkin V.P., Kingma H., Melnichuk S.V., Svetlik M.V., Rudenko T.V., Akinina M.D., Suyundukova A.T. Influence of leakage currents on the formation of electrical pulse to stimulate the vestibular nerve // Izvestiya vuzov. Fizika. 2019. № 12. P. 63–68. DOI: 10.17223/00213411/62/12/63 (in Russian)

2. Akinina M. D., Demkin V.P. The electrical model of the vestibular organ. – Abstracts, materials of the Twenty-Fifth All-Russian Conference of Physicists and Young Scientists (VNKSF-25, Crimea): conference materials, abstracts: V. 1. - Ekaterinburg - Rostov-on-Don-Crimea: ASF Russia Publishing House, 2019. – p. 296 – 297. (in Russian)

3. Akinina M. D. Biotechnical system of the vestibular organ // Abstracts, materials of the Twenty-Fifth All-Russian Conference of Physicists and Young Scientists (VNKSF-26, Ufa, Bashkortostan): conference materials, abstracts: V. 1. - Ekaterinburg - Rostov-on-Don – Ufa: “Altair”, 2020. – p. 247-248. (in Russian)

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LIST OF ABBREVIATIONS

VO – vestibular organ

VI – vestibular implant

VOR – vestibulo-ocular reflex

DVA – dynamic visual acuity

VSR – vestibulo-spinal reflex

CNS – central nervous system

TF – transfer function

BPPV – benign paroxysmal positional vertigo

VN – vestibular neuritis

MD – Meniere's disease

TIA – transient ischemic attack

EOCSPOM – exacerbation of chronic secondary purulent otitis media

G – transfer function

$Y(p)$ – Laplace converted output

$X(p)$ – Laplace converted input

Z – impedance of biological tissues

INTRODUCTION

Currently, for 30 million people in the world who have lost vestibular function, there is no effective treatment. This disorder, like blindness or deafness, significantly affects the quality of life and the ability to work. More than 70% of these patients lose their jobs, and their quality of life is estimated at 40% lower than before the onset of the disease [4]. In recent years, clinical neuro-vestibulology has attracted increasing interest among doctors of various specialties and among researchers. The reasons for the increased interest in diseases of the vestibular system are several. The most significant causes are the high prevalence of vestibular diseases, nonspecific clinical manifestations, the complexity of the diagnosis and treatment of various vestibulopathies [2]. All this led to the fact that neuro-vestibulology (otoneurology or neurootology) began to separate itself as a independent interdisciplinary area of medicine, combining the clinical interests of neurologists, otorhinolaryngologists, specialists in functional diagnostics and rehabilitation. Such important clinicians as R. Baloh, D. Zee, B. Cohen, C.C. played an important role in the development of neurovestibulology. Delia Santina in the USA, T. Brandt in Germany, A. Bronstein in the UK, N.S. Blagoveshchenskaya in Russia [7, 18] and other researchers.

The human vestibular system is one of the most complex sensory systems responsible for the generation and transmission to the brain of information about the position of the body in space and its movement. The absence of this information is caused by a different of diseases, a frequent cause of which are pathological processes in the organs of the inner ear.

An additional impulse for the development of neuro-vestibulology was the discovery, first, of the development mechanism, and then of the methods of effective treatment of the most common disease of the vestibular system – benign paroxysmal positional dizziness (BPPD) [11].

Dysfunction of the vestibular system causes postural instability, visual impairment during head movement and chronic imbalance. In the case of unilateral loss of vestibular function, compensatory restoration of it through the functioning of one of the vestibular organs is possible. In case of bilateral vestibular dysfunction, the only method of treatment is implantation with an artificial prosthesis, a type of bion ear, which is largely similar to a cochlear (snail) implant, which can restore hearing by electrical stimulation of the auditory nerve sites. With its help it is possible to partially restore the lost functions, allowing to lead a "normal life".

Despite the huge volume of fundamental and applied research conducted in the world on this topic, currently there are no effective treatments for vestibular dysfunction; An effective method for restoring vestibular function is to replace the vestibular organ with a vestibular implant - an artificial motion detector and an associated electrical stimulator that generates signals to the brain [2]. Diagnosis of the vestibular apparatus «*in vivo*» is very complicated, which complicates the diagnosis of vestibular diseases.

An effective method in this case is physical and mathematical modeling and subsequent comparison of calculation results with experiments on laboratory animals, based on the similarity of physiological processes in the vestibular labyrinth of animals and humans [4] and the influence of these processes on the electrical properties of biological tissues.

The idea of implementing a vestibular implant (VI) is to replace the labyrinth with an artificial motion detector and an associated electrical stimulator that is able to send signals to the brain to restore vestibular function. The construction of a functional analogue of the vestibular apparatus is in line with the general problem of total prosthetics of the human body, common for modern biomechanics, of expanding the possibilities of partial or complete replacement of certain human organs, depending on the requirements of a medical, biotechnological, military or other nature.

The quality of the vestibular implant depends on its transfer function (TF), the ability to transmit stimulating pulses from the stimulating electrode to the end of the vestibular nerve [8]. A stimulating electrical impulse from the electrode, passing through the tissues of the vestibular organ, is affected by the impedance of the biological tissue, which leads to a change in its amplitude-phase characteristics. The task of finding the optimal mode of electrical stimulation of the vestibular nerve: setting the shape and amplitude-frequency parameters of the current pulse to improve the transfer function, is by far the most urgent, because its solution makes it possible to improve the vestibular implant [14].

1 The human vestibular system

The vestibular organ of the inner ear is the main anatomical system for sensing movement. The vestibular organ located in the inner ear provides entry into the nervous system to move the head and orient the body in space, support body balance and steady vision [17]. This system compose of three orthogonal liquid-filled semicircular canals for determining the angular movement of the head and two otolith organs for determining horizontal and vertical linear acceleration [18].

The vestibular apparatus is an organ of balance located in the inner ear. Information that is transmitted to the nervous system from the vestibular apparatus about the position and movements of the head is processed, and the brain can automatically determine the state of the muscles when we are standing or walking, which helps us maintain balance.

The balance of the body depends on the precise control exercised by the central nervous system over the muscles and joints unconsciously, but constantly and dynamically. An exception is when the body is turned upside down or balance is required.

In this position, a certain pressure is maintained in the muscles of the hands, that is, they are tense, the body weight moves on them, and the leg muscles are relaxed.

In this and other cases, appropriate regulation must be made to complete the movement. In order to send a signal about the need for this regulation, the central nervous system must process information about the position of each individual and collectively parts of our body [1].

The receptors of the vestibular analyzer are designed so that, along with the movement of the body, the kinetic energy of the mechanical movement is converted into a nerve impulse. Such a “transfer” link is the hairs of the neurosensory epithelium, displaced during the movement of the endolymph.

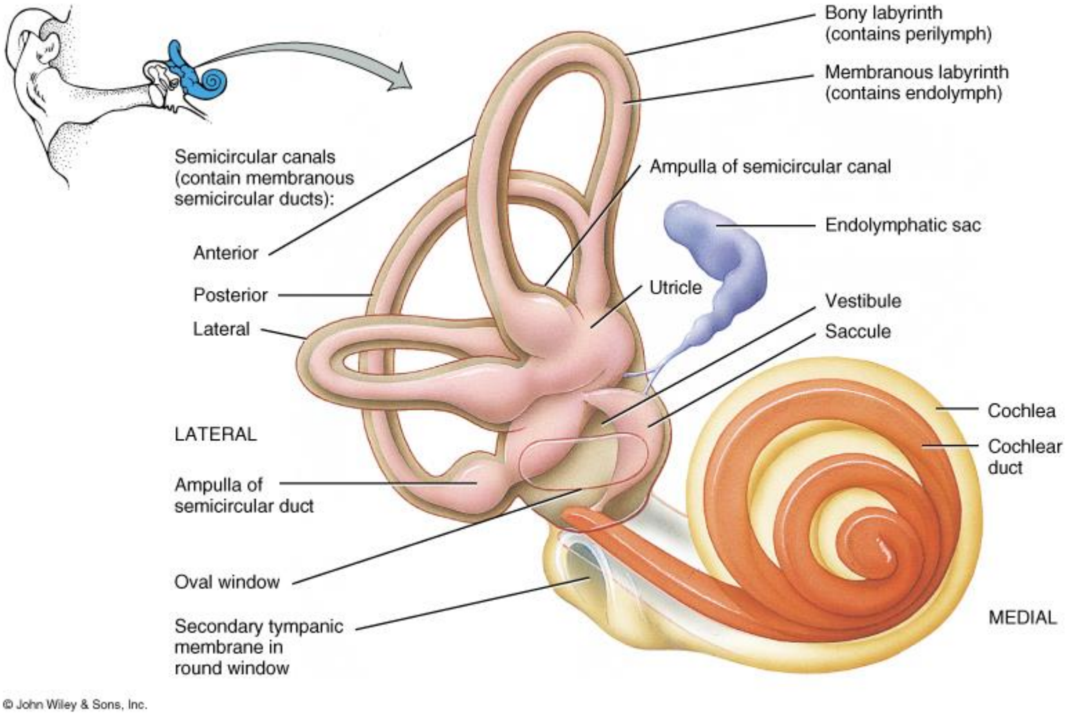


Figure 1.1 – The structure of the inner ear

Part of the inner ear (labyrinth) (Figure 1.1), is located in the depth of the temporal bone. The vestibular apparatus consists of bone and membranous labyrinths.

The bony labyrinth is a system of three semicircular canals and a cavity communicating with them - the vestibule. The semicircular canals are three curved hollow structures (“tubes”) located in three mutually perpendicular planes. Around the circumference of the ampoule there is a bone outgrowth inside the lumen - an ampullar scallop, “*crista ampularis*” [2, 11]. On the ambular scallop are neuroepithelial cells, or hair cells. Each cell has several hairs on the surface, the longest hair being called kinocilia, and the remaining hairs – stereocilia.

Kinocilia is located closer to the vestibule, it has the main functional value, because the current of endolymph, directed to the vestibule of the labyrinth (to the ampoule, ampulopetal current), it moves away from the rest, thereby opening the ion channel on the surface of the cell. The flow of ions into the cell leads to the depolarization of the neuroepithelium and the conduction of exciting signals along the nerve fibers.

At rest, when kinocilia and stereocilia are directed parallel to each other, ion channels work, but in rest mode. In this way they provide impulsation of rest from semicircular canals, i.e. in the absence of head and body movements, the central structures constantly receive information that there is neither excitation nor inhibition. Such a system of the vestibular analyzer opens two pathological pathways: inhibition or excitation of semicircular canals [9].

The semicircular channels of both labyrinths have the same impulse of rest, i.e. they are balanced. But the impulse of rest can vary from individual to individual, so vestibular tests perceive from most medical studies in the absence of a clear norm.

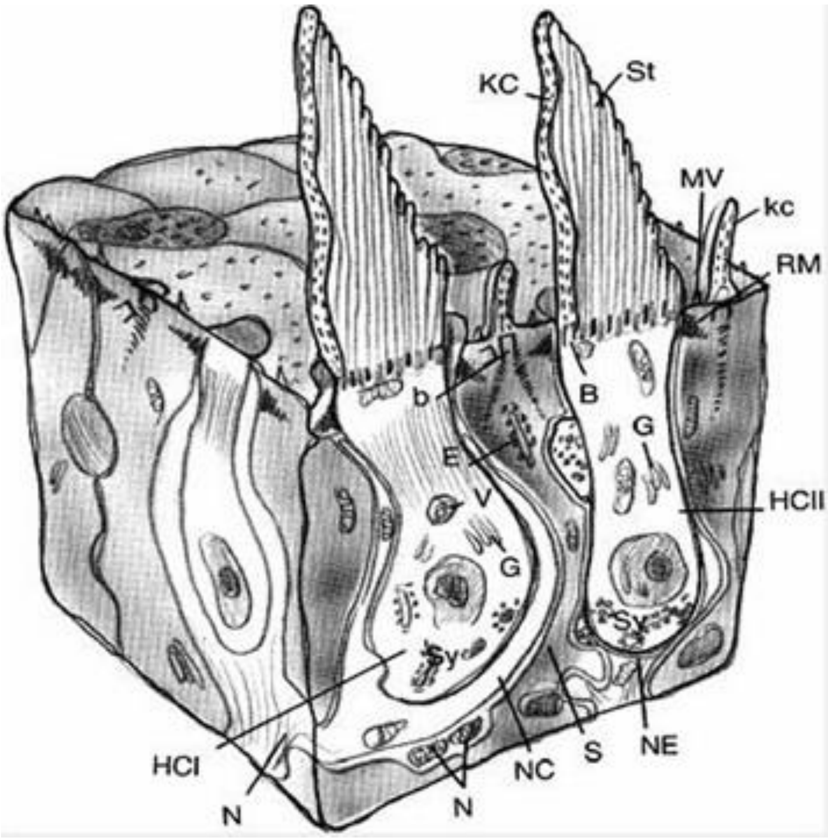


Figure 1.2 – Vestibular sensory epithelium

The vestibule includes two otolith organs - the utriculus (oval sac) and the sacculus (round sac). The utriculus, sacculus and semicircular canals consist of thin membranes forming closed tubes - a membranous labyrinth located inside the bone labyrinth and partly repeating its shape.

The anatomy of the sacs of the otolith apparatus is characterized in that the inertial mass here is the otoliths, which press on the gelatinous substance. The structure of the receptors themselves does not differ from those in the semicircular canals [7].

The receptors of the vestibular apparatus form five distinct areas: one in each semicircular canal and one in the vestibule sacs. Receptors are typical hair cells with directional sensitivity. In other words, they are excited only at a certain direction of fluid flow in the labyrinth.

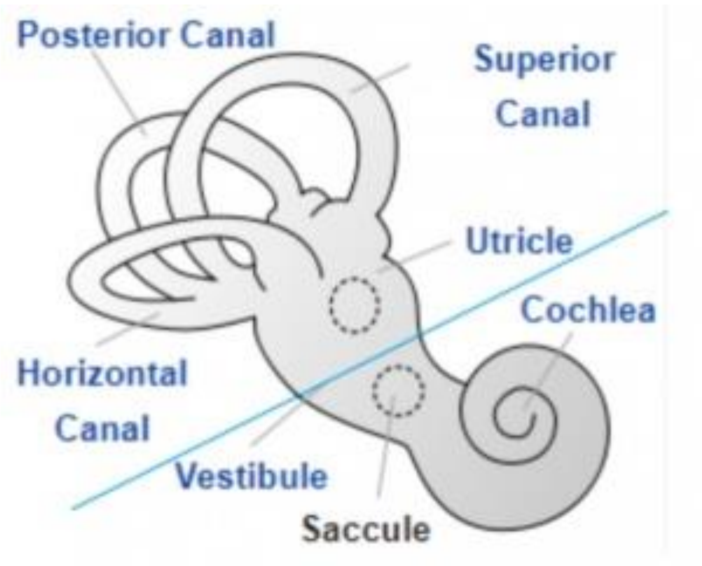


Figure 1.3 – The structure of the vestibular apparatus

One end of each semicircular canal widen to form an ampoule. In ampoules of semicircular canals is located on the bone scallop of the crescent shape. The membranous labyrinth and the accumulation of two rows of cells are directly adjacent to it: supporting, or sustaining, and sensitive, hairy, with 10-15 long hairs glued together on the upper end, glued together with a gelatinous substance in a brush, or shutter. The semicircular canals are filled with endolymph.

The vestibular apparatus (Figure 1.3) also includes two sacs: spherical – *sacculus* and elliptical, or uterus – *utriculus*. The first of them lies closer to the cochlea, and the second to the semicircular canals. The function of the *utriculus* and *sacculus* is the perception of linear accelerations. An effective incentive for them is gravity. *Utriculus* and *sacculus* to the left and right are located relative to the cranium in certain positions. With a direct position of the body and head, the *utriculus* is in the horizontal, and the *sacculus* is in the vertical position. The inclination of the head leads to the displacement of the sacs – the *utriculus* and *sacculus* – by a certain angle between horizontal and vertical position [18].

In each of the vestibule sacs there is a section in which receptor hair cells are collected. It is called the *macula* (*macula* - spot). In each ampoule, the receptors are also grouped and form a *crista* (*crista* - scallop). Above the receptors lies a jelly-like mass floating in the endolymph, into which the ends of the hairs of the receptor cells are immersed. n semicircular canals, this mass is called a cupule. In bags, the jelly-like mass contains crystals of calcium carbonate (otoliths) and is called the otolith membrane (Figure 1.3).

The functions of hair cells in ampoules and sucs are different due to the structural features of the vestibular apparatus. Macular receptors are gravitational receptors, i.e. gravity receptors. They respond to different tilts of the head. The macules in the round and oval sacs are located almost perpendicular to each other, therefore, with any orientation of the head, some of the receptors are excited. These receptors respond to the appearance of linear acceleration (i.e., to the displacement of the body back and forth, up and down, etc.). Receptors in cristae are excited at angular (rotational) acceleration, i.e. when turning the head [16]. An adequate stimulus for the hair cells of the vestibular apparatus is a shift in the jelly-like mass inside the cavity filled with endolymph. This shift occurs under the influence of inertia forces when our body moves with acceleration.

The orientation of the semicircular canals corresponds to three planes of the body. In membranous semicircular canals, filled, like the entire labyrinth, with a dense endolymph (its viscosity is 2-3 times greater than that of water). During the movement of the endolymph (during angular accelerations), when the hairs are curved to one side, the hair cells become excited, and when they move in the opposite direction, they are inhibited (Figure 1.4). This is due to the fact that the mechanical control of the ion channels of the hair membrane using microfilaments depends on the direction of the bend of the hair: deviation in one direction leads to opening of the channels and depolarization of the hair cell, and deviation in the opposite direction causes channel closure and hyperpolarization of the receptor [17].

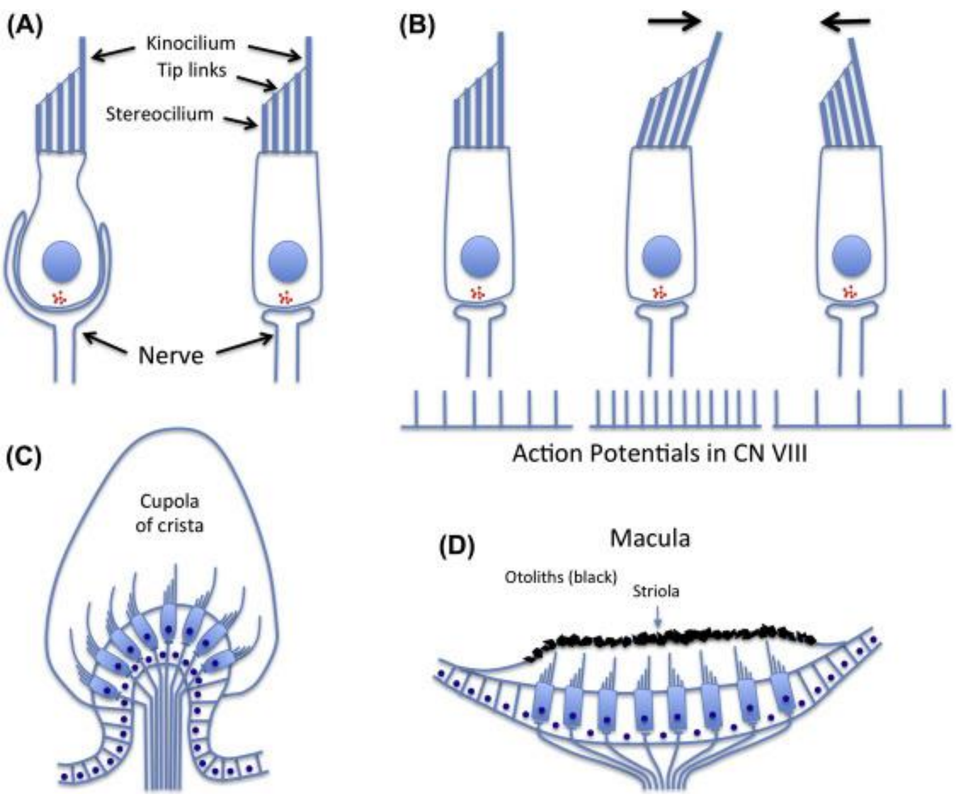


Figure 1.4 – Vestibular receptors in the macula and cristae

The orientation of the cells within the scallop is the same. Excitation of receptor cells causes impulses in afferent nerve fibers. In the hair cells of the vestibule and ampoules, when they are bent, a receptor potential is generated that enhances the release of acetylcholine and activates the ends of the vestibular nerve fibers through synapses.

The vestibular nerve (*N. vestibularis*) (the vestibular part of the VIII pair of cranial nerves) is formed by axons of the vestibular ganglion cells. Most fibers of this nerve end at four vestibular nuclei located on each side at the border of the medulla oblongata and the bridge. These are the upper core (Bechterev`s nucleus), lateral (Deiters), lower (Roller) and medial (Schwalbe). From here, signals are sent to many parts of the central nervous system: spinal cord, cerebellum, oculomotor nuclei, cerebral cortex, reticular formation and ganglia of the autonomic nervous system.

Fibers from the vestibular nuclei go to the cerebral cortex, as in other sensory systems, through the thalamus (through the motor projection nuclei). Due to this, conscious orientation in space is carried out. The vestibular zones in the cortex are located in the posterior part of the postcentral gyrus and the lower part of the precentral gyrus.

The impulses coming from the vestibular receptors do not provide the central nervous system with complete information about the position of the body in space, since the position of the head does not always correspond to the position of the body. Therefore, orientation in space is carried out with the complex participation of a number of sensory systems, primarily muscular-articular and visual [9, 18].

Works with the vestibular system became very active after the start of flights into space, since in weightlessness the vestibular apparatus was largely turned off. However, according to astronauts, getting used to this condition is fast, in just a few days. Apparently, in this case, the work of the vestibular analyzer begins to be performed by other sensory organs, which indicates the plasticity (flexibility) of the NS.

The information provided by the vestibular apparatus implements the functionality of the vestibulospinal, vestibuloocular and vestibulo-cerebellar systems.

The vestibulospinal system ensures the stability of the head with respect to the center of gravity of the body. With each movement, the head remains motionless in relation to the surrounding space, while the body moves smoothly. The movements of the head, trunk and limbs are coordinated thanks to cervical reflexes.

The vestibulo-ocular system is a reflex, where activation of the vestibular system causes eye movement. It serves to stabilize the image on the retina during head movement, producing eye movements in the opposite direction to the head movement, thus preserving the image in the center of the field of view of the physiological reflex of the deviation of the trunk and extremities to the side with irritation of the receptors of the vestibular analyzer [4].

The vestibulo-cerebellar system provides sensorimotor coordination. Part of the fibers from the vestibular nuclei goes to the cerebellar neurons, and from them back to the same nuclei. Thus, the cerebellum performs fine-tuning of the vestibular reflexes. In violation of these connections, a person is not able to maintain balance, his movements acquire increased amplitude, especially when walking.

1.1 Connections of the vestibular analyzer and pathological symptoms realized through them

The vestibular nerve receives fibers from the vestibule of the labyrinth and semicircular canals, combines with the cochlear and in the form of the vestibule-cochlear nerve, passes through the internal auditory canal into the cranial cavity. Then it passes through the bridge-cerebellar angle and enters the brain stem, branching into separate bundles to the four vestibular nuclei lying on the bottom of the fourth ventricle. Fibers of the VIII pair are partially crossed, i.e. fibers from labyrinths on both sides approach the vestibular nuclei of one side. From the vestibular nuclei, the fibers go as part of the conduction paths to various structures of the central nervous system.

1. Vestibulo-ocular connections

They are realized through pathways going from the vestibular nuclei to the nuclei of the oculomotor nerves, which lie in the midbrain (Figure 1.5). When one of the labyrinths is excited or suppressed, the resulting imbalance manifests itself in the form of nystagmus through the vestibuloocular pathways [10].

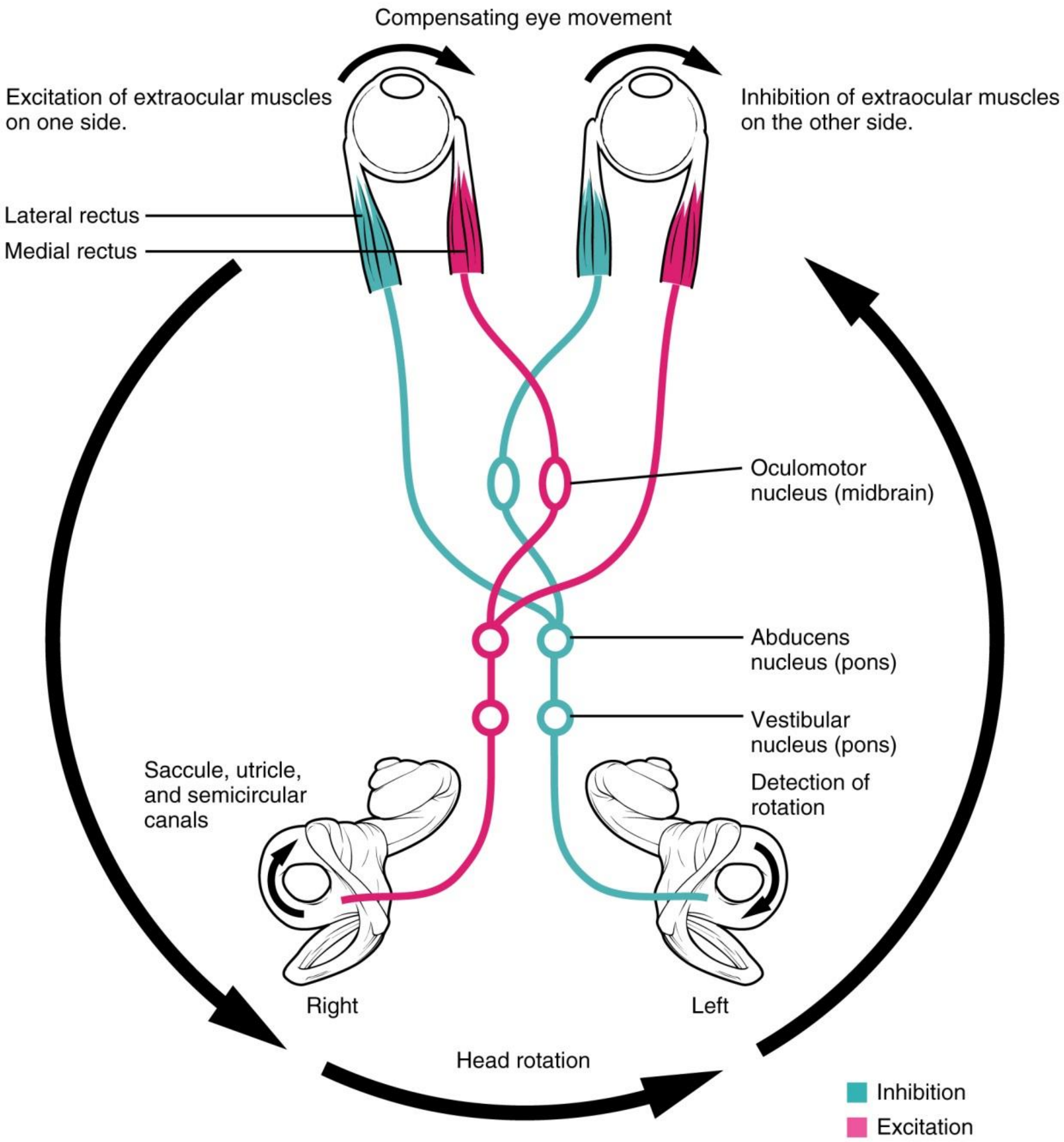


Figure 1.5 – Scheme of the vestibulo-ocular reflex

Nystagmus is an involuntary two-component movement of the eyeballs, which has a slow and fast phase, directed in opposite directions. Nystagmus can be spontaneous, always indicative of pathology, and induced, which can be physiological and pathological. Nystagmus as a pathological reaction does not always have a vestibular origin.

Vestibular nystagmus is divided into 3 degrees. First degree nystagmus characterizes a weak excitation of the labyrinth. When looking directly, he is not. To identify it, it is necessary to create such conditions that the "confrontation" between the cortex and the labyrinth is maximum. Thus, if the slow component of nystagmus, due to the imbalance between the labyrinths, should be directed to the left, and the fast component to the right, then for maximum counteraction the eyes should be asked to move to the right. Nystagmus of the first degree – nystagmus that occurs when looking towards the fast component. II degree nystagmus – nystagmus that occurs when looking towards the fast component and directly. III degree nystagmus - nystagmus that occurs when looking towards the slow component, directly and towards the fast component [4].

2. Vestibulospinal connections. Vestibulo-cerebellar connections

These two ways allow the vestibular analyzer to control the tone of the limbs. In the pathology of the labyrinth, the body deviates from the midline, the limbs deviate during pointing tests in the direction of the endolymph current. Thus, the following symptoms are included in vestibular symptoms: discoordination of movements, imbalance in the standing position (astasia), impaired walking (ataxia). Dysequillibrium is more often observed with bilateral damage to the inner ear than with a unilateral one.

3. Vestibulovegetative connections

The vestibular nucleus are connected by pathways to the reticular formation and the hypothalamus, which regulate the vegetative nervous system. With irritation of the labyrinths, vegetative symptoms are represented by nausea, vomiting, change in blood pressure, increased heart rate, sweating, cold extremities, whiten of the skin. The entire spectrum of vegetative reactions is clearly manifested in seasickness as a result of vestibular apparatus irritation.

4. Vestibulocortical connections

When the equilibrium is shifted between the labyrinths, the cerebral cortex responds to the resulting imbalance with dizziness. Dizziness is a symptom of many neurological diseases, but only vestibular dizziness is systemic, i.e. described as a sensation of rotation of objects around a patient or a sensation of rotation inside. Systemic dizziness is more common with unilateral pathology of the inner ear (or bilateral, but with a predominance of one labyrinth over another) as a reflection of the reaction of the cortex to an imbalance between the labyrinths.

1.2 Major vestibular diseases

1.2.1 Benign paroxysmal positional vertigo (BPPV)

The etiology and pathogenesis of the disease consists in the migration of otoconia (otoliths of the elliptic sac, detached from the gelatinous substance as a result of trauma, infection or age-related degeneration) into the posterior semicircular canal (Figure 1.6) Over time, the otoconia dissolve in the endolymph, but so far they exist when moving with the head endolymph displacement in the affected labyrinth is much stronger than in the healthy one. As a result, a short-term episode of dizziness occurs until crystals of calcium carbonate settle.

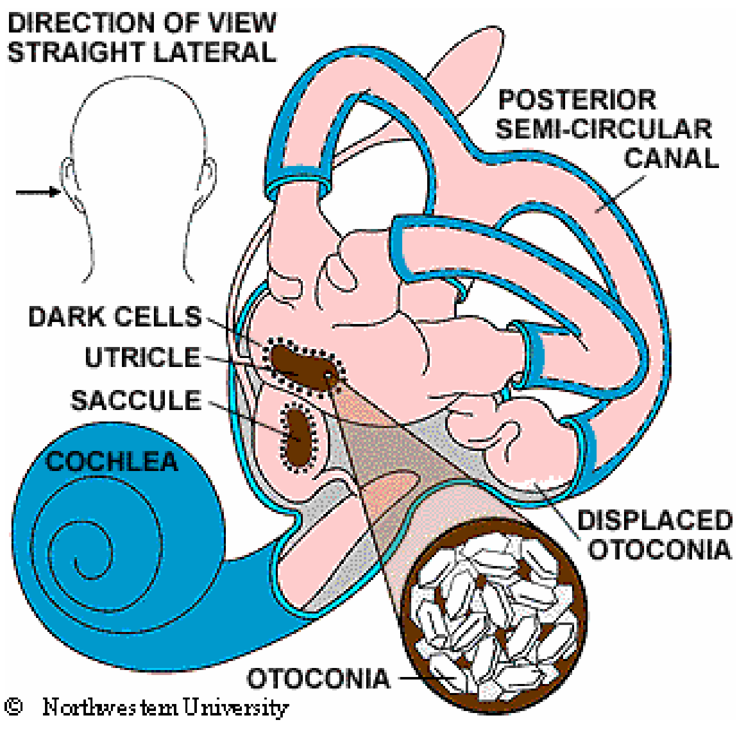


Figure 1.6 – The mechanism of the course of the disease

BPPV occupies 20% in the structure of all causes of dizziness. With age, the occurrence of BPPV increases, although the disease can occur in children. The classic BPPV is due to the ingress and free flotation of the otoconia in the smooth knee of the posterior semicircular canal. This form is also called posterior canalolithiasis.

Otoconia can fall much less frequently into other semicircular canals, in which case the anterior or horizontal canalolithiasis will develop (2% of cases of BPPV). In 5% of cases, bilateral posterior canalolithiasis is observed [17].

Sometimes, the otoconies caught in the semicircular channel are fixed to the cupula, this condition is called cupulolithiasis (5% of cases of BPPV). This form of BPPV is much more difficult to treat due to the difficulties of separating calcium crystals from the cupula.

The manifestations of BPPV consist of a brief bout of systemic dizziness (from a few seconds to five minutes), which can be accompanied by movement coordination disorders, ataxia, nausea and vomiting. Usually the trigger factor is the displacement of the head at an angle to the gravitational force vector. The trivial name «Upper Regiment Disease» was given by the BPPV, because tilting the head to look up is the trigger factor of the attack. It is also common for patients to mention the bending of the bed as trigger factors.

The following features are characteristic of the cupulolithase. When the cupula is in a horizontal position, there is no movement of the otoconia. When it is in a different position, and this happens with almost any head movement, the labyrinth is irritated and dizziness occurs. This results in almost constant dizziness and nausea, as well as in some cases spontaneous nystagmus [5]

If dizziness first appeared less than 2 months ago, the BPPV is often described as a self-limiting disease, i.e. symptoms decrease or disappear within 2 months. This is related to the dissolution of calcium carbonate crystals in the endolymph. For this time the patient should be advised to sleep in elevated position on several pillows, avoid sleeping on the «sick» side, resist from active movement of the head and physical tension, not bend when lifting objects from the floor, but to squat.

1.2.2 Vestibular neuronite (Neuritis)

Vestibular neuronite (VN) – damage to the vestibular part of the pre-door snail nerve or one of its branches.

Etiology and pathogenesis. At the moment, it is generally accepted that VN is a viral nerve disorder. The most common pathogens are *Herpesviridae*: *Herpes lex virus* I-II, *varicella zoster virus*. This theory of the origin of the disease is disputed by some authors, because no randomized controlled trial has shown that antiepretic drugs have a placebo effect.

The virus infects the nerve, causing all the symptoms of inflammation. Edema leads to compression of nerve fibers with further death, disruption of conductivity of vestibular impulses. As a result, there is an imbalance in central structures between the afferent impulses of the two labyrinths, which manifests itself in dizziness, ataxia, discoordination of movements, nausea, and vomiting.

The nerve may not be fully involved. The lesion of the upper vestibular nerve, which departs from the frontal, horizontal semicircular canals and the elliptic sac, or the lower branch, which innervates the sagittal semicircular canal and the spherical sac, may cause the features of the vestibular passport [11].

Vestibular neuritis is a classic example of one-sided vestibular insufficiency found in all vestibular examination tests.

Dizziness is systemic due to its peripheral origin. It is accompanied by a nystagmus directed towards a healthy ear. The labyrinth involved is depressed. The dizziness lasts for hours-days, accompanied by nausea, vomiting, disturbance of body balance. The resolution of the attack comes in 2-3 days. There may be residual phenomena in the form of some instability, some light dizziness.

The diagnosis of VN can be made on the basis of an objective examination. The use of hardware-based research methods can confirm the diagnosis, verify the affected branch of the vestibular nerve (when the lower branch of the VEMP is damaged, it is asymmetric), exclude diseases with a similar symptom complex (Meniere's disease, migraine, acoustic neurinoma, TIA or stroke). The neurological examination reveals a pronounced one-sided peripheral vestibular deficiency, lack of hearing disorders, absence of diseases of the middle ear.

1.2.3 Labyrinitis

A labyrinitis (L) is an inflammatory disease of the inner ear of different etiology.

In the English-speaking literature, this disease is considered a disease of predominantly viral etiology (*Herpesviridae family*), diagnosed with a combination of symptoms of VN and ipsilateral acute of sensual tuberous disease. In this paper, we will consider the domestic approach to the etiopathogenesis and classification of the disease.

Labirnitis can be developed in several ways:

1) tympanogenic – with exacerbation of chronic secondary purulent otitis media (EOCSPOM), less often with acute purulent otitis media;

2) hematogenous;

3) meningogenic;

4) traumatic.

A limited and diffuse labyrintis is distinguished in terms of the prevalence of the process, and an exudate is characterized by its serous and purulent nature.

The most frequent route of infection through the inner ear is the thympanogenic pathway. Initially, a limited labyrintis is formed due to bone fracture by a caryosis process. At this point, osteosite develops, and the inflammation locus is then limited by granulation. This prevents bacteria from penetrating the inner ear. This form is most often not available. If granulations do not tightly cover the formed window in the bone labyrinth (most often in the horizontal semicircular channel), the manifestation of the limited labyrinth is the symptoms of perilymphatic fistula. At any exacerbation of EOCSPOM, the penetration of bacteria and/or their products into the inner ear will lead to the development of a diffuse labyrinth. Often, inflammatory products and bacterial toxins with the development of serous labyrinthitis penetrate the labyrinth first. This increases the vascular permeability of *stria vascularis*, which causes an increase in endolymph production. Increased pressure in the inner ear leads to the inhibition of the receptors of the analyzers in it – acute neurosensory silence, ear noise, dizziness, disequilibrium, nausea/vomiting develop. If the process stops there without the addition of bacterial flora, the receptor function may recover over time. If the exudation in the inner ear leads to a rupture of the snail windows from the inside, the bacterial flora penetrates the labyrinth and inflammation takes on a purging character. At the same time, vestibular and auditory receptors are completely destroyed, with total neurosensory refraction and unilateral vestibular deficiency. Vestibular symptoms in 6-12 months will be compensated to varying degrees by the neuroplastic properties of the CNS.

A special form is the necrotic labyrintis, which is usually viral. In addition, thromboses in the inner ear develop with total receptor death. The process has a lightning current.

The classical path of labyrinthitis has 2 phases: the phase of irritation, which lasts from several minutes to several hours, and the phase of oppression, which lasts days or weeks. Because in both cases there is an imbalance between the patient and the affected ear, clinically they will proceed identically, the only difference is the direction of nystagmus. In the phase of irrigation, nystagmus is directed toward the affected ear, and in the phase of depression, towards the healthy ear.

The dizziness of the labyrintis is systemic, accompanied by nausea, vomiting, disequilibrium of the body, discoordination of movements.

Nystagmus has a peripheral vestibular characteristic. The developing attenuation is sensual, accompanied by ear noise.

Sometimes, the contraction of the facial nerve passing through the labyrinth causes a pair of facial muscles of half the face, which is also peripheral. In the peripheral pair of the facial nerve all branches are involved, in the central process there is an asymmetry of only the lower half of the face, because the upper part has cross-innervation [17].

While the labyrinth is overwhelmingly a secondary disease, the symptoms of the primary process (perforation of the eardrum and excretion, meningeal signs, signs of fracture of the pyramid of the temporal bone, etc.) are attached to the labyrinth.

The purulent labyrinth causes characteristic changes in the blood and fever.

The disease consists of the presence of symptoms of the primary process, unilateral vestibular deficiency detected by the vestibular examination, and acute neurosensory acuity.

1.2.4 Meniere’s disease

MD is a disease of the inner ear with unknown etiology, in which the pathogenesis of great importance is endolymphatic hydrops (watery labyrinth), resulting in the impairment of the function of all the labyrinth receptors (Figure 1.7).

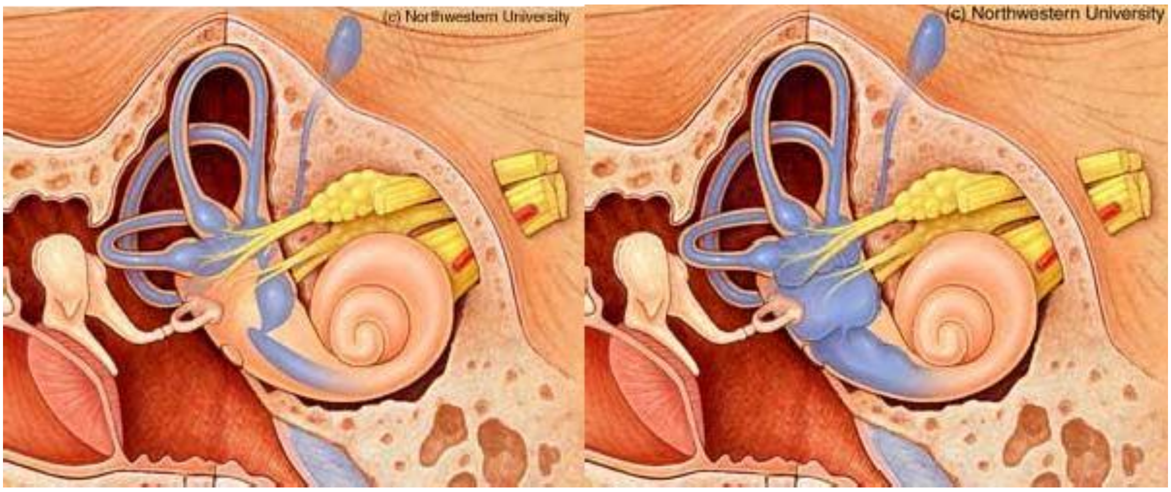


Figure 1.7 – Healthy ear (left), watery maze (right)

On the left is a normal labyrinth, on the right is a water labyrinth (dilation of the membrane labyrinth with increased fluid).

Etiology and pathogenesis. It is known that traditionally MD is considered as endolymphatic hydrops as a result of the hyperproduction of the endolymph stria vascularis or the disruption of the flow of endolymph into the endolymphatic sac for unknown reasons. But, according to autopsy data, 6% of people who have never had a menyero-like complaint in their lifetime have endolymphatic hydrops. MD prevalence in the population is 0.2%, which is much lower than postmortem studies. From this it can be deduced that besides the watering of the maze there must be some other factors that lead to the development of MD.

Recently, the autoimmune etiology of MD has been actively discussed. This statement is supported by the frequent incidence of autoimmune thyroiditis in patients with MD (about 25%). In a 2002 Ruckenstein study, the authors determined in the blood of patients with unilateral MD the markers of autoimmune reactions: antinuclear antibodies, anti-Shegren antibodies, rheumatic factor, antiphospholipid antibodies, complement, heat shock antibodies (anti-heat shock protein).

An increase in antiphospholipid antibodies was found in 27%. Heat shock proteins were found in 6%. Perhaps the indicators would be even higher for patients with bilateral MD. More sensitive markers are being sought.

At the moment, the cumulative view is that the development of endolymphatic hydrops is a universal response of the inner ear to any damage, be it trauma, infection (often DNA is found in the inner ear of the patients, 1% of MD is otopiphilis) allergies or autoimmune inflammation. Autoimmune theory, so popular today, states that the target of autoantibodies is an endolymphatic sac, which is a «lymphatic node» of the inner ear. The developing inflammation is blocking its function of labyrinth fluid pressure support. Cytokines, biogenic amines produced during the inflammatory reaction strengthen the production of endolymphs.

When the MD is acute attacked, the overflowing labyrinth is filled with endolymph, and the walls of the labyrinth are microfractured with disruption of the ion potentials of the inner ear fluids. As a result, the inner ear receptors (Cortes of the organ, the otolite apparatus, and the amplum receptors) are unable to function normally. A small part of the receptors dies during the attack, most of them atrophy gradually from the pressure of the continuously existing hydrops [12].

The hair cells of the cochlea are the most sensitive to the ongoing processes, so hearing is lost in the first 5-10 years of illness. The receptors of the vestibular apparatus are more resistant to such damage.

At first one ear is affected, but after 30 years, 50% of patients develop bilateral MD.

The classic picture of an acute MD attack is: an acute attack of dizziness, hearing loss, noise in the ear, which is preceded by a feeling of fullness in the ear.

1) Dizziness during a BM attack is systemic, accompanied by severe autonomic symptoms (nausea, vomiting), nystagmus. It usually lasts 2-4 hours, after which patients feel tired and need sleep. An acute episode of dizziness can take the form of a “Tumarkin otolith crisis”, in which a sharply developing edema of the vestibule of the labyrinth presses on the sacs and causes a sudden activation of vestibular reflexes with imbalance and subsequent fall. Most patients in the interictal period feel healthy, while some still have some dysequillibrium.

2) The patient sharply loses hearing during an attack, hearing loss is neurosensory in nature. After an attack, the hearing is restored, but each subsequent attack causes the death of a certain number of receptors, so hearing loss is fluctuating, progressive in nature. First, the patient loses hearing at low frequencies. Five years later, the audiogram becomes flat - the patient loses hearing at all frequencies, but within 50-60 dB. After 10 years, deafness develops in the affected ear [9].

On the basis of the literary data it can be concluded that the choice of this object (the vestibular system of a human) is due to the scientific and practical significance of the development of methods for correcting disturbances of vestibular apparatus in people.

The scientific results obtained at this stage are the basis for further work on obtaining new knowledge on mechanisms of stimulation of vestibular nerves, on interaction of sensory signals and their interference, which will improve the vestibular implant and consequently the quality of life of patients with vestibular dysfunction.

2 Vestibular implant

The main idea of the vestibular implant is the direct electrical stimulation of the vestibular nerve with the help of electrical impulses of a certain shape, frequency and amplitude. It is based on the fact that the labyrinths of a healthy person encode information about the position of the head with the help of electrical impulses generated by receptors (hair cells) of the vestibular system.

The new type of bionic ear is very similar to the cochlear (snail) implant, which restores hearing by electrically stimulating areas of the auditory nerve. It restores the sense of equilibrium by stimulating the vestibular nerve, which transmits signals from the vestibular labyrinth to the brain. The electrical contact with the nerve provided by the implant makes it possible to bypass the damaged vestibular system [7]. Normally, the labyrinth has two important functions. One of them is to record the angular movement of the body. This information is necessary to maintain equilibrium and position [5].

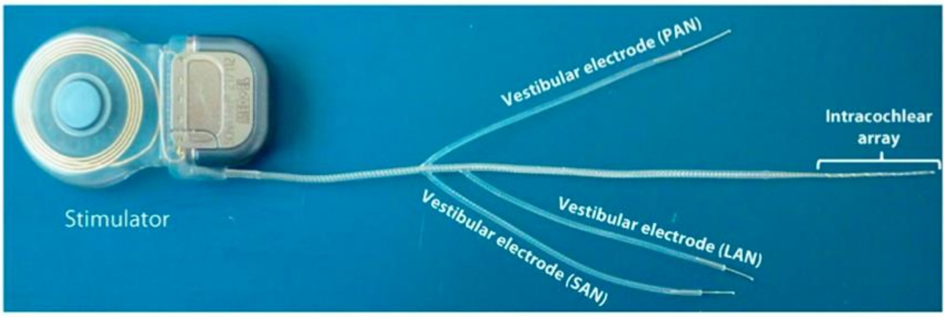


Figure 2.1 – The vestibular implant

The second function is to react to head rotations and to provide a fixed view of the desired object. For example, in response to the rise of the head, the maze sends signals to the oculomotor muscles, causing the eyes to descend at the same speed. As a result, the image of the object on the retina is not moved. Without this reflex, we would see the world around us as if we were looking at it through a moving video camera «there-there» camera. This defect is precisely one that can be corrected with a bionic prosthesis, but the sense of equilibrium is not fully restored. The vestibular labyrinth responds to angular movements using three fluid-filled structures called semicircular canals. They are located in the inner ear at certain angles to each other and control the rotation of the head in three-dimensional space [14].

The prosthesis itself comprises a control chip, a battery and, primarily, motion sensors parallel to the semicircular channels of the inner ear (Figure 2.1).

The signal generated by the circuit is transmitted through eight electrodes implanted in the patient’s inner ear to the vestibular nerve endings [7].

The processor, using the original program developed by Santina and his colleagues, forms millisecond impulses that simulate similar impulses in the form of a real inner ear [1].

Thus, the device completely replaces the damaged vestibular apparatus, creating a sense of movement in the head.

Despite the fact that the vestibular apparatus contributes to the work of many systems of the human body (about 70% of the information entering the cerebellum comes from the vestibular apparatus), it was decided to highlight the most important functions that make the greatest contribution to well-being and daily activities. The bulk of patients' complaints relate to oscillopopsia (impaired dynamic visual acuity and vestibulo-ocular reflex) and equilibrium (impaired motion perception and vestibulo-spinal reflex). Thus, by focusing on the four vestibular functions described: a vestibular-ocular reflex, a vestibular-dorsal reflex, a dynamic acuity of sight and perception of movement; it is possible to significantly improve the quality of life of the vestibular patients.

Research has shown that direct impulse stimulation of the vestibular nerve, simulating a natural frequency-modulated neural reaction to head movement the defective vestibular organ, produces a similar effect of motion [14].

Thus, the vestibular prosthesis can be an effective way to restore the equilibrium function. The vestibular implant will be able to sense head movement with sufficient accuracy and deliver a signal to the central nervous system, corresponding to the signal that is generated by the natural organ, simulating dynamic vestibular function.

2.1 Transfer function of vestibular implants

One of the main issues in the area of vestibular prostheses is the optimization of electrical impulses and the reduction of electrical noises. By electrical noise is meant the spread of current beyond the region stimulated by a specific electrode. For example, while stimulating the forward semicircular channel, there may be partial excitation of the lateral semicircular channel.

During the last 20 years research and development of vestibular implants have been actively carried out, unfortunately the samples of vestibular implants that are available today are far from perfect. The fact is that, in addition to solving technical problems in perfecting the implant, there are fundamental problems related to the electrically conductive properties of the tissues of the vestibular organ, which influence the modification of the characteristics of the stimulating pulse, its amplitude-frequency and phase parameters [11].

The quality of this signal determines the quality of the vestibular reflexes. The majority of complaints from patients with vestibular system disorders are related to oscillopopsia (impaired dynamic visual acuity and vestibular-ocular reflex) and equilibrium (impaired motion perception and vestibular-spinal reflex). Therefore, when testing the quality of the implant, it is necessary to focus on the four described vestibular functions: a vestibular ocular reflex, a vestibular-spinal reflex (VSR), dynamic visual acuity and motion perception, which are the criteria for the perfection of the transfer function of the vestibular implant.

One of the approaches that determine the functional improvement of the implant is the approach based on the theory of dynamic systems. The dynamics of such systems are described by linear differential equations with constant coefficients, based on the physical laws that determine the process of converting the input signal generated by the implant into the output signal, as a response result (reflex) sensor system. Then the functional efficiency of the implant can be described by the transfer function, defined as the ratio of the Laplace converted output signal of the system to the Laplace transformed image of the input signal. Thus, applying the operating calculus apparatus to a certain electrical substitution scheme and arrangement of stimulating electrodes, which are based on the mathematical model of the vestibular organ, It is possible to calculate the transfer function and find optimum parameters of the stimulating impulse in order to obtain a vestibular-ocular reflex, sense of motion, dynamic visual acuity and control of equilibrium.

The implant of vestibular apparatus replaces the natural labyrinth, the output signal of the implant by passing the pathological areas of the vestibular labyrinth, is connected at the level of the nerve fibers to the vestibular system, replacing the natural output of the labyrinth [3]. Therefore, the main task in developing the implant is how to form the optimal electrical signal of the VI based on the natural transfer function. Therefore, the mathematical model should include all the stages of the electrical current through the tissues of the vestibular organ and take into account all the processes influencing the change of the stimulating impulse.

For a better understanding the mechanism of the response the vestibular nerve to the electrical stimulation of the implant and determination of the transfer function, we developed a physical and mathematical model of the current distribution through the tissues of the vestibular labyrinth using a detailed anatomical model of the vestibular labyrinth and a mathematical description of the physical processes of the flow of electric current in the labyrinth tissues [3, 12].

In order to study the transit of a stimulating current pulse from electrodes located in ampoules to the body of the vestibular nerve, we measured the amplitude-phase characteristics of a harmonic signal of different frequencies, we measured the amplitude-phase characteristics of the harmonic signal of different frequency. A comparison has been made of the characteristics of the currents from the ampoules of the porpoise vestibular apparatus at the end of the vestibular nerve, and measurements have been made of the amplitude-phase characteristics between the stimulating electrodes.

3 Elements of dynamic systems control theory

The transfer function is one of the main dynamic characteristics used in the theory of autonomous control of dynamic systems. The main mathematical apparatus in the study and study of control systems is the apparatus of differential equations.

A mathematical description of an autonomous control system is a description of the processes that take place in a system in a mathematical language. The physico-mathematical description of dynamic systems is based on the model of physical processes occurring in the system.

In the general case of the equations of the mathematical model of the system, the regard between the input and output variables are established, and are called equations of motion [19].

In control theory, linear systems are usually those in which the processes are stationary and described by linear differential equations with constant or time-dependent coefficients. An important feature of such systems is their consistency with the principle of superposition. Therefore, the definition of a linear system is generally given in the following variant: linear systems are systems that obey the superposition principle, which is that the system’s response to the sum of two input signals $\Sigma xi(t)$ is the sum of the reactions to each signal separately for any $xi(t)$. Since most control systems are nonlinear, under certain conditions non-linear characteristics can be approximated by linearization of nonlinear dependencies [20, 22].

One of the most common methods of linearization is the decomposition of a non-linear function into a Taylor`s series in the vicinity of a given point and the elimination of non-linear decomposition terms.

The most interesting is the dynamic behavior of the linear system, which is generally shown in figure 3.1.

x(t), y(t) – the input and output signals of the system.

Figure 3.1 – The structure of the linear control system

The main task of studying the dynamic behavior of a linear system is to be able to calculate the output signal *y(t)* for any known input signal *x(t)*. It is therefore necessary to have a mathematical apparatus for the investigation of the linear system [12].

In this case, there are stationary systems, the coefficients of the differential equations of which do not change over time, and non-stationary systems, in which the coefficients change over time, for example, a change in the physical properties of the system.

Most control systems are unsteady, however, their rate of change is less than the speed of adjustment, so such systems can be approximated as stationary for a certain period of time in the calculation of the control algorithms, for which the properties of the system do not change significantly.

Next we will consider linear stationary systems with concentrated coordinates, which are described by ordinary differential equations with constant coefficients.

Let the behavior of the system be described by a linear stationary differential equation of order n:

$$a_n \frac{d^n y(t)}{dt^n} + a_{n-1} \frac{d^{n-1} y(t)}{dt^{n-1}} + \cdots + a_1 \frac{d^1 y(t)}{dt^1} + a_0 y(t) = b_n \frac{d^n x(t)}{dt^n} + b_{n-1} \frac{d^{n-1} x(t)}{dt^{n-1}} + \ldots + b_1 \frac{d^1 x(t)}{dt^1} + b_0 x(t) \quad (1)$$

where *x(t), y(t)* – input and output signals, depending on the time.

Apply the Laplace transform (2) to the left and right of equation (1)

$$F(p)=\int_0^{\infty} f(t)e^{-pt}dt\,, \qquad (2)$$

where F(p) is an image of a function *f(t); p=s+iω* is a complex number.

Then equation (1) is converted to:

$$\left(a_n p^n + a_{n-1}p^{n-1} + \cdots + a_1 p^1 + \mathrm{a}_0\right)Y(p) = \left(b_n p^n + b_{n-1}p^{n-1} + \cdots + b_1 p^1 + \mathrm{b}_0\right)X(p)\,, \qquad (3)$$

or

$$Y(p)=\frac{\left(b_n p^n + b_{n-1}p^{n-1} + \cdots + b_1 p^1 + \mathrm{b}_0\right)}{\left(a_n p^n + a_{n-1}p^{n-1} + \cdots + a_1 p^1 + \mathrm{a}_0\right)}X(p) = G(p)X(p)\,, \qquad (4)$$

where

$$G(p)=\frac{Y(p)}{X(p)}=\frac{\left(b_n p^n + b_{n-1}p^{n-1} + \cdots + b_1 p^1 + \mathrm{b}_0\right)}{\left(a_n p^n + a_{n-1}p^{n-1} + \cdots + a_1 p^1 + \mathrm{a}_0\right)}, \qquad (5)$$

G(p) is called the transfer function of a system and is expressed through the ratio of the Laplace- converted output signal of the system *Y(p)* to the Laplace-converted input signal *X(p)* under zero initial conditions. If the transfer function of the object system is known, then the output image of the object *Y(p)* is the product of the transfer function on the input image *X(p):*

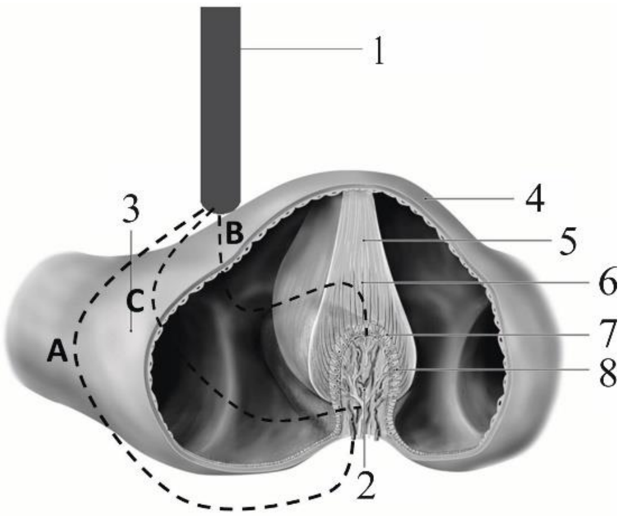
$$Y(p)=G(p)X(p)\,. \qquad (6)$$

Formula (6) is the basis for determining the value of the output signal according to the transmission function of the dynamic system.

3.1 Experimental study of electric current through the tissues of the vestibular labyrinth

When the vestibular apparatus is prosthetic, three electrodes are used, said electrodes being introduced into the cavity of the fenestrated ampule in the immediate vicinity of the crista of the semicircular channels and, accordingly, near the extremities of the vestibular nerves. Consequently, the stimulating current pulse from the electrode to the vestibular nerve passes a certain distance which will depend on the position of the electrodes (Figure 3.2).

The tissues of the vestibular labyrinth have electroimpedance characteristics relative to current pulses emanating from electrodes. As a result, the amplitude and shape of the current pulse that the afferent nerve perceives will differ from their original values.

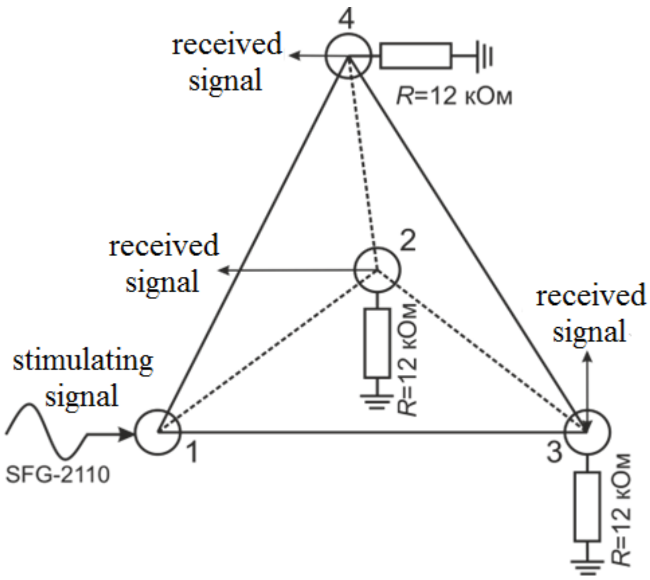


1 – electrode; 2 – vestibular nerve end; 3 – ampoule mouth; 5 – cupula;
6 – kinocilia; 7 – hair cells; 8 – supporting cells.

Figure 3.2 – Electrical current distribution scheme for the vestibular labyrinth

The measured amplitudes of the input and output signals can be used to find the transfer function using formula (5). In this work, we measured the amplitude-phase characteristics of a harmonic signal of various frequencies passing from electrodes located in ampoules of the vestibular organ of a guinea pig to the end of the vestibular nerve, and also measured the amplitude-phase characteristics between the stimulating electrodes.

For measurements, the electrodes were inserted into ampoules of the upper, horizontal and rear semicircular canals of the vestibular labyrinth, the fourth recording electrode was fixed at the end of the vestibular nerve. Taking into account the miniature size of the vestibular organ of the guinea pig (the linear dimensions of the vestibular apparatus are ~ 2 mm), the implantation of the electrodes was carried out under the control of an MBS-10 optical microscope at 28.6x magnification. When the electrodes were immersed in the ampoules, the presence of contact was monitored by an oscilloscope signal, which corresponded to the repeat by the recorded signal of the form of the initial signal. The test was carried out with the calcified electrodes 0.4 mm in diameter.



1, 2, 3 – ampullas of the vestibular organ; 4 – end of the vestibular nerve;

R – shunt resistance.

Figure 3.3 – Electrical measurement circuit

The measuring diagram presented in figure 3.3 contained bypass resistors R=12 kOm located between the recording electrodes and the general «zero» electrode. The stimulating sinusoidal voltage $U0$=200 mV was supplied from the signal generator SFG-2110 alternately to each of the electrodes corresponding to the upper (1), horizontal (2) and rear (3) semicircular channels. The voltages from the recording electrodes of the adjacent ampoules and at the end of the vestibular nerve were together detected by the four-channel electron oscillograph RIGOL DS1074B. The amplitudes U of the received signals and their phase shift φ relative to the stimulating signal according to the frequency: 0.1, 0.2, 0.4, 1, 1.5 kHz were measured.

The results of the measured amplitude phase characteristics of the signal at the vestibular nerve are presented in Table 3.1. The values φ, U are given relative to the stimulating signal given to the electrode in the first, second and third ampules respectively.

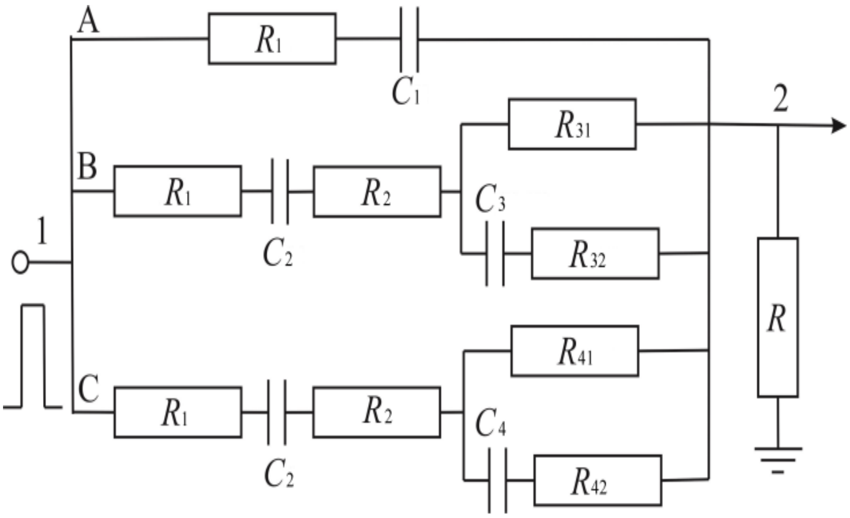
Table 3.1 – Amplitude phase characteristics of the received signal at the end of the vestibular nerve

Frequency, Hz	First ampoule		Second ampoule		Third ampoule	
	φ, degree	U, мV	φ, degrees	U, мV	φ, degrees	U, мV
100	-18	123	-19	117	-26,2	88
200	-13,1	126	-13,6	127	-19,6	94
400	-8,6	132	-9,3	139	-13,0	104
1000	-6,2	143	-6,6	147	-10,8	108
1500	-5,4	147	-5,2	151	-10,9	109

3.2 Vestibular transfer function simulation

The replacement of the vestibular organ with an implant, an artificial motion detector and an associated electrical stimulant, which generates electrical signals in the vestibular nerve for transmission to the brain, allows for the partial restoration of the vestibular function of the human being. Today’s vestibular implant samples are far from perfect. One reason for this is the imperfection of the transfer function, which reflects the quality of the electrical signal received into the vestibular nerve from the stimulating electrode. The stimulating electric pulse from the electrode, passing through the tissues of the vestibular organ, is influenced by the impedance of the biological tissue, which leads to a change in its amplitude-frequency characteristics. The problem of finding the optimum mode of electrical stimulation of the vestibular nerve - the task of determining the shape and amplitude-frequency parameters of the current pulse for improving the transfer function - is currently the most topical, Its solution allows to improve the vestibular implant.

Despite the abundance of research in this field, the study of the electrophysiological mechanisms of stimulating impulse formation *in vivo* is very difficult. In such cases, physical and mathematical modelling and the subsequent comparison of the results with laboratory animal experiments, based on the similarity of physiological processes occurring in the vestibular labyrinth of animals and humans, and the effect of these processes on the electrical properties of biological tissues. In the work of [22] we propose an electrical model of current spread through the tissues of the vestibular labyrinth of a person on the basis of a five-element Maxwell`s equivalent circuit.



1 – stimulating electrode; 2 – the end of the vestibular nerve; R1 – the resistance of the perilymph; C_1 – the capacity of nerve isolation; R_2 – the resistance of endolymph; R_{31} – resistance of the membrane of hair cells; R_{32} – resistance of the cytoplasm of hair cells; R_{41} –the resistance of the membrane of basilar cells; R_{42} – cytoplasmic resistance of basilar cells; C_2 – the capacity of the membrane separating

perilymph and endolymph; C_3 –capacity of the membrane of hair cells; C_4 – the membrane capacity of basilar cells; R is the load resistance.

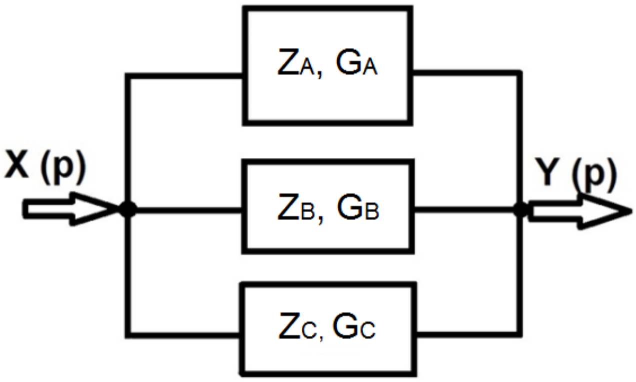
Figure 3.4 – Detailed electrical equivalent circuit of the vestibular labyrinth

Detailed electrical equivalent circuit of the vestibular labyrinth (Figure 3.4). In order to assess the effect of cell structures on the impedance of the tissues of the vestibular labyrinth, sections of the circuit containing the electrophysical parameters of hair and basilar cells are identified in the diagram. The number 1 marks the electrode through which a current pulse is supplied to stimulate the vestibular nerve. The number 2 indicates the position of the recording electrode, which can control the amplitude-phase characteristics of the signal after passing the electric circuit from point 1 to point 2, which corresponds to the passage of the stimulating pulse through the tissues of the vestibular labyrinth.

Table 3.2 – Electrophysical characteristics of the vestibular labyrinth

Electrical parameter	Value [*R*]= kΩ, [*C*] = nF
Perilymph resistance (R_1)	129.0±20
Endolymph resistance (R2)	155.0±20
Resistance of cupula hair cells (R3)	3.7±1
Resistance of basilar cell cupula (R4)	2.4±1
Vestibular Nerve Isolation Capacity (C1)	8±4
Capacity of the membrane separating perilymph and endolymph (C2)	100.0±40
Capule hair cell membrane capacity(C3)	62.0±30
Capillary Basilar Cell Membrane Capacity (C4)	94.0±30
Load resistance (Rn)	12.0

Table 3.2 shows the integrated values of the electrical parameters of the equivalent circuit of the vestibular labyrinth of the guinea pig, calculated from the specific characteristics of the conductivity and capacity of biological tissues and taking into account the detailed anatomical structure of the labyrinth of the guinea pig. To calculate the transfer function from all the links of a given electrical circuit, we will present it in the form of the following structural diagram (Figure 3.5).



Z_A, Z_B, Z_C – impedances of sections (A), (B) and (C) of the electrical equivalent circuit; GA, GB, GC - transfer functions corresponding to (A), (B), (C) electric current paths.

Figure 3.5 – Block diagram of the electrical circuit

The calculation of the impedance of the electrical equivalent circuit of the vestibular maze was carried out in the representation of complex numbers $Z = T + i \cdot W$ for each section of the electrical circuit shown in Figure 3.5. Given the parallel connection of the sections of the circuit, the total impedance of the circuit was calculated by the formula (7) $\frac{1}{Z} = \frac{1}{Z_A} + \frac{1}{Z_B} + \frac{1}{Z_C}$, where Z_A, Z_B, Z_C – values of the impedances of the circuit sections corresponding to the directions of current flow.

$$Z_A = \sqrt{R_1^2 + \left(\frac{1}{\omega C_1}\right)^2}, \quad (7a)$$

$$Z_B = \sqrt{(R_1 + R_2 + R_3)^2 + \left(\frac{C_2 + C_3}{\omega C_2 C_3}\right)^2}\ , \tag{7b}$$

$$Z_B = \sqrt{(R_1 + R_2 + R_4)^2 + \left(\frac{C_2 + C_4}{\omega C_2 C_4}\right)^2}\ . \tag{7c}$$

The resulting transfer function for this circuit will be equal to the sum of the transfer functions for each section of the chain (Figure 3.5).

$$G(p) = \frac{Y(p)}{X(p)} = G_A + G_B + G_C\ . \tag{8}$$

where G_A, G_B, G_c – transfer functions corresponding to electric current paths: A, B, C (Figure 3.4).

Using Kirchhoff's rules for alternating current and applying the Laplace transform formulas, we can obtain expressions for G_A, G_B, G_c

$$G_A = \frac{\omega}{\left(p + \frac{1}{R_1 C_1}\right)}\ , \tag{8a}$$

$$G_B = \frac{\omega}{\left(p + \frac{C_2 + C_3}{(R_1 + R_2 + R_3)C_2 C_3}\right)}\ , \tag{8b}$$

$$G_C = \frac{\omega}{\left(p + \frac{C_2 + C_4}{(R_1 + R_2 + R_4)C_2 C_4}\right)}\ . \tag{8c}$$

The expression for the complete transfer function can be found by adding formulas (8a), (8b), (8c). As a result, the stimulating current pulse coming from the electrode will incure a change in amplitude and phase due to the influence of tissue impedance of the vestibular organ, and the magnitude of these changes depends on the electrical conductive properties of the tissues.

Designate: $\eta = p/\omega$, then from formulas (8) and (8a) - (8c), taking into account the values of the parameters of the electrical equivalent circuit (Table 3.2.) we obtain the equation for determining the parameter η:

$$G(p) = \frac{Y(p)}{X(p)} = \frac{1}{(\eta + \frac{1.5}{k})} + \frac{1}{(\eta + \frac{0.15}{k})} + \frac{1}{(\eta + \frac{0.12}{k})}, \qquad (9)$$

where $k=f/100$ – reduced frequency relative $f=100$ Hz.

Replacing in the formula (9) the ratio of the output signal to the input through $\frac{U_{out}}{U_{in}}$ – the ratio of the measured voltage amplitudes at the end of the vestibular nerve *Uout* to the voltage on the stimulating electrode *Uin* = 200 mV, we can calculate the value of the parameter η (Table 3.3) and, accordingly, the value *G* (η, ω).

Table 3.3 – The Dependence of the parameter η and the transfer function G (η, ω) of the frequency of the stimulating signal

Frequency, Hz	First ampoule		Second ampoule		Third ampoule	
	p/ω	$G(\eta,\omega)$	p/ω	$G(\eta,\omega)$	p/ω	$G(\eta,\omega)$
100	4.35	0.62	4.50	0.59	6.25	0.44
200	4.50	0.63	4.50	0.63	6.10	0.47
400	4.40	0.66	4.10	0.70	5.75	0.52
1000	4.10	0.72	4.00	0.74	5.00	0.54
1500	4.01	0.74	3.90	0.76	5.40	0.55

Table 3.3 shows the dependence of the calculated values of the parameter $\eta = \frac{p}{\omega}$ and G (η, ω). Table 3.3 shows that the transfer function of the electrically conductive tissues of the vestibular labyrinth for stimulating pulses issue from an electrode located in the rear semicircular canal is much smaller than for stimulating pulses from the electrodes located in the upper and horizontal semicircular canals. This should be taken into account both in the design of the vestibular implant and in its tuning in clinical trials.

An analysis of Table 3.3 shows that the parameter p increases linearly with increasing ω. Therefore, and as follows from formulas (8a) - (8c), the frequency dependence of the vestibular implant transfer function has the form:

$$G(\omega) = \frac{\omega}{\alpha + \beta\omega} \tag{10}$$

where α and β are constants determined by the electrophysical parameters of the tissue of the vestibular labyrinth (electrical equivalent circuit), the form of which is given by formulas (8a) - (8c). The growth of the transfer function with increased frequency is due to the reduction of the reactive portion of impedance tissues of the vestibular labyrinth, and in the limit $\omega \rightarrow \infty, G$ is asymtotic to the limit of $\frac{1}{\beta}$. Thus, the value of the transfer function is a personified characteristic depending on the electrophysiological properties of the tissue of the vestibular labyrinth. The physico-mathematical modeling of the transfer function is the basis for determining the optimum characteristics of the electrophysical parameters R and C of the electrical substitution scheme, as well as amplitude-frequency characteristics of the stimulating pulse to find the maximum value of the transfer function.

CONCLUSION

In this work, studies of the electrical conductive properties of the tissues of the vestibular labyrinth, have been carried out and formulas for the impedance for the impedance of the electrical circuit of the labyrinth and its transfer function have been obtained.

The main results of the study are:

1) Anatomical structure of the vestibular apparatus and physical principles and mechanisms of its work were studied.

2) The conductive properties of the tissues of the vestibular labyrinth were studied and their ohmic and capacitive characteristics were determined.

3) An equivalent electrical circuit for the replacement of the vestibular labyrinth has been developed.

4) The foundations of the theory of dynamic systems management have been studied.

5) A method for determining the transfer function of the vestibular organ has been developed.

6) Measurements and calculations of the amplitude-phase characteristics of the harmonic signal passing through the vestibular organ of the guinea pig were made.

7) Formulas for impedance have been obtained and the transfer function of the vestibular labyrinth has been calculated.

8) The analysis of the transfer function dependence on the frequency of the stimulating signal outgoing from electrodes arranged in three ampullae of semicircular channels is carried out.

The obtained formulas and the calculations of the amplitude and phase characteristics of the stimulating current based on experimental data on the electrophysical and anatomical characteristics of the tissues of the vestibular labyrinth of guinea pigs made it possible to determine the patterns of current propagation through the tissues of the vestibular labyrinth.

On the basis of measured output signal values at the end of the vestibular nerve, the transfer function of the vestibular labyrinth at nerve stimulation from the upper, horizontal and rear semicircular channels is calculated and its frequency dependence is investigated. It has been shown that when the frequency increases, the transfer function tends to its asymptotic value. The transfer function of the vestibular labyrinth for stimulating impulses from the electrode located in the vicinity semicircular channel has been found to be significantly smaller than for stimulating pulses from electrodes, located in the upper and horizontal semi-circular channels. These features, due to the anatomical structure and electrophysiology of the vestibular labyrinth, need to be taken into account both for the design of the vestibular implant and for its tuning during clinical trials. The results obtained in this work can be used in the development of new models of vestibular human implant, as well as for the diagnosis of diseases of vestibular labyrinth.

REFERENCES

1. A Multichannel Semicircular Canal Neural Prosthesis Using Electrical Stimulation to Restore 3-D Vestibular Sensation. Charles C. Della Santina et al. in IEEE Trans actions on Biomedical Engineering. –Vol. 54.–No. 6. – P.1016–1030.

2. Asadi H., Mohamed S., Chee Peng Lim C.P., et al. A review on otolith models in human perception // Behavioural Brain Research. – 2016. – Vol. 309. – P. 67–76.

3. Chenkai D. Effects of vestibular prosthesis electrode implantation and stimulation on hearing in rhesus monkeys. / Chenkai D., Gene Y., Della Santina C. // Hearing Research. – 2011. – № 277. – P. 204–210.

4. Cohen, B. Eye movements induced by ampullary nerve stimulation/Cohen, B. and Suzuki, J. // The American journal of physiology. – 1978. – № 204.- P. 347–351.

5. Daniel Q. Sun, Mehdi A. Rahman, Gene Fridman, Chenkai Dai,1 Bryce Chiang, and Charles C. Della Santina. Chronic Stimulation of the Semicircular Canals Using a Multichannel Vestibular Prosthesis: Effects on Locomotion and Angular Vestibulo-Ocular Reflex in Chinchillas//Conf Proc IEEE Eng Med Biol Soc. 2011; 2011: 3519–3523. doi: 10.1109/IEMBS.2011.6090584

6. Davidovics N. Effects of Biphasic Current Pulse Frequency, Amplitude, Duration and Interphase Gap on Eye Movement Responses to Prosthetic Electrical Stimulation of the Vestibular Nerve. / Fridman G., Della Santina C. // TNSRE-2009-00234.

7. Della Santina C. Current and Future Management of Bilateral Loss of Vestibular Sensation – An update on the Johns Hopkins Multichannel Vestibular Prosthesis Project / Della Santina C., Migliaccio A., Hayden R., and others // Cochlear Implants Int. – 2010. – 11(Suppl 2). – P. 2–11.

8. Demkin V.P., Melnichuk S.V., Shchetinin P.P., Kingma H., Van de Berg R. Electrophysical Properties and Determination of the Impedance of Vestibular

Labyrinth Tissues // Russian Physics Journal. – 2019. – V. 61. – P. 2019–2027. DOI:10.1007/s11182-019-01632-z

9. Fawzy M., Khater A. Bilateral vestibulopathy treatment: Update and future directions // Egypt J Otolaryngol. – 2016. – Vol. 32. – P. 83–92.

10. Fornos A.P., Guinand N., van de Berg R.,et al. // Frontiers in Neurology. – 2014. – Vol. 5. – P. 1–10.

11. Kosivtsova O.V., Yavorskaya S.A., Fateeva T.G. Vestibular vertigo treatment in a polymorbid patient.//Neurology, neuropsychiatry, psychosomatics. 2018;10 (1):96–101.

12. Momani A. and Cardullo F. A Review of the Recent Literature on the Mathematical Modeling of the Vestibular System. AIAA SciTech Forum. 8–12 January 2018. Kissimmee, Florida. –P. 1-35.

13. Perez Fornos, A.; Guinand, N.; Van De Berg, R.; Stokroos, R.; Micera, S.; Kingma, H.; Pelizzone, M.; and Guyot, J. (2014). Artificial balance: restoration of the vestibulo-ocular reflex in humans with a prototype vestibular neuroprosthesis // Frontiers in Neurology 5.

14. Rubinstein, Jay T. Postural responses to electrical stimulation of the vestibular end organs in human subjects / Rubinstein Jay T. // Experimental Brain Research. – 2013. – № 229. – P. 181–195.

15. Straka H., Zwergal A., Kathleen E. Cullen K.E. Vestibular animal models: contributions to understanding physiology and disease // J. Neurol. – 2016. – Vol. 263. – P. 10–23.

16. Van de Berg, Guinand N.,Nguyen T.A.K. //Frontiers in System Neyrosciense. – 2012. – Vol. 8. – P. 1–12.

17. Ward B.K, Sun D.Q, Santina C.C.D., et al. / The 7th International Symposium on Meniere's Disease and Inner Ear Disorders, At Rome, Italy. – October 2015. P. 343–347.

18. Watanuki K., Gottesberge A.M. zum. Light Microscopic Observations of the Sensory Epithelium of the Crista Ampullaris in the Guinea Pig // Ann. Otol. Rhinol. Laryngol. 1971. Vol. 80, № 3. P. 450–454.

19. Akulov S. A., Fedotov A.A. Fundamentals of the theory of biotechnological systems. – M.: PHYSMATHLIT, 2014. – 259 p. (in Russian)

20. Antonenko S. V. Mathematical modeling of biological objects by the method of physical and technical functional analogy / S. V. Antonenko, A. F. Belyanskaya, I. S. Lebedenko // Bulletin of new medical technologies. Electronic edition. - 2013. - No. 1 (in Russian)

21. Demkin V. P. Electric Current Transmission Through Tissues of the Vestibular Labyrinth of a Patient: Perfection of the Vestibular Implant / V. P. Demkin, S. V. Melnichuk, P. P. Schetinin, G. Kingma, R. Van De Berg // Russian Physics Journal. – 2018. V. 60. P. 2019–2024. DOI:10.1007/s11182-018-1318-5

22. Demkin V.P., Melnichuk S.V., Svetlik M.V., Shchetinin P.P., Kingma H., Van de Berg R., Demkin O.V., Udut E.V. Experimental Investigation of Electric Signal Transmission Through Vestibular Organ Tissues // Russian Physics Journal. – 2019. – V. 61. – P. 2264–2267. DOI: 10.1007/s11182-019-01665-4

23. Demkin V. P., Melnichuk S. V., Schetinin P. P., G. Kingma, R. Van De Berg, Demkin O. V., Udut E. V. Experimental Investigation of Electric Signal Transmission Through Vestibular Organ Tissues // Russian Physics Journal. –2019. – V. 61. – P. 2264–2267. DOI: 10.1007/s11182-019-01665-4

Отчет о проверке на заимствования №1

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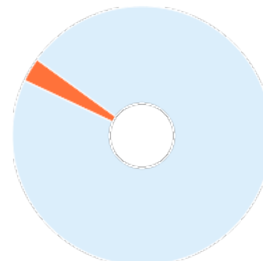

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