Chapter 12

Cochlea – A Physiological Description of a Finely Structured Sense Organ

Raphael R. Ciuman

Additional information is available at the end of the chapter

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Abstract

The whole inner ear or the cochlea, responsible for hearing perception, represents a unique sense organ, including the organ of Corti and the inner ear endo- and perilymph. The fluid homeostasis of the lymph spaces with its parameters volume, concentration, osmolarity and pressure, as well as the finely aligned hair cell receptors, their supporting cells and structures embedded in these unique fluid spaces, corresponds to the specific necessities for adequate response to continuous stimulation and the outstanding discrimination capacity of the hearing system. The manuscript gives an overview and describes the structural characteristics and distinct physiological hearing qualities of the cochlea in comparison with the other human receptor cells and sense organs.

Keywords: cochlea, organ of Corti, endolymph, stria vascularis, inner hair cells, outer hair cells, stereocilia, supporting cells, efferent innervation

1. Introduction

The whole inner ear or the cochlea, responsible for hearing perception, can be described as unique sense organ, including the organ of Corti and the inner ear endo- and perilymph. The fluid homeostasis of the lymph spaces with its parameters volume, concentration, osmolarity and pressure corresponds to the specific necessities for adequate response to continuous stimulation and the outstanding discrimination capacity of the hearing system. Discrimination of loudness is regulated mainly by discharge intensity of stimulus transmission, rhythm by discharge duration and discrimination of frequency and tone colour timbre by harmonized fine regulation of the geometrically and functionally aligned hearing structures along the cochlear duct. Surrounded by endolymph, the inner and outer hair cells with their distinct

geometrically arranged finger-like processes, the stereocilia, are the mechanoelectrical transducers of the mechanoreceptor organ ear. The complex afferent and efferent innervation of the hair cells respond to further fine processing of the hearing stimulus. In this context, the efferent innervation supplies further qualities, in particular noise protection, mediation of selective attention and improvement of signal-to-noise ratio. It also supports adaptation and frequency selectivity by modification of the micromechanical properties of the outer hair cells. The past five decades of molecular biological research involved immense achievements in understanding of the physiological and biochemical mechanisms leading to current genetic-based, nanotechnology-based and stem cell research [1, 2].

2. Hearing system qualities

The human cochlea consists of about two and a half turns and is about 9 cm in length from the oval window to the helicotrema, corresponding to a frequency gradient starting with high frequencies at the base and proceeding to low frequencies at the apex.

The middle ear main function is to achieve mechanical gain by the ossicles as a lever and the tympanic membrane and oval window as a plane focuser. Besides, the middle ear makes the stimulus processable by harmonizing the sound wave resistance (impedance) of air and perilymph and the hair cells, respectively (**Figure 1**).

Adaptation mechanisms are characteristical for a sense organ, and as the cochlea has to process travelling waves continuously, it involves all molecular structures and biochemical processes of the inner ear. Adaptation lowers the system requirements, protects from overstimulation and reflects the environmental necessities of stimulus perception. In addition, it characterizes tone and music perception. Contrastingly, to the chemical receptors of the olfactory and gustatory system and the dermal mechano-, and thermoreceptors, sound adaptation does not lead to no stimulus perception at all. Generally speaking, the adaptation time constant is faster in hair cells at the high-frequency end than at the low-frequency end, what probably contributes to frequency selectivity [3].

Different adaptation mechanisms contribute to inner ear function, namely voltage-dependent hair-cell properties, structural hair-bundle characteristics and afferent transmitter release. Fast adaptation operates around the most sensitive portion of the hair cell activation, whereas larger displacements of the hair bundle induce slow adaptation [4]. Fast adaptation has been identified in both cochlear and vestibular hair cells, but is the main form of adaptation in cochlear hair cells. Slow adaptation has been identified in all but mammalian auditory hair cells, and is the predominant adaptation mechanism found in vestibular hair cells [5–7]. (Comparison of the adaptation mechanisms of the human sense organs and receptor cells is described at the end of the article in **Table 1**. Comparison of the perception qualities of the human sense organs and further comparison are listed in **Table 2**. Comparison of the structural characteristics of the human sense organs.)

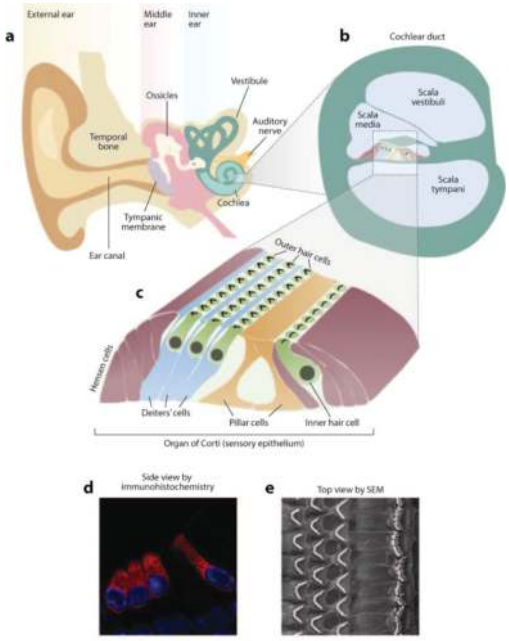

Figure 1. Schematic illustration of the human ear. (**a**) The ear consists of the outer, middle and inner ear. (**b**) A section through the cochlear duct illustrates the fluid-filled compartments of the inner ear. (**c**) The organ of Corti resides in the scala media, with sensory hair cells surrounded by supporting cells that include Deiters, Hensen and pillar cells. (**d**) Immunohistochemistry with the inner ear hair cell marker myosin VI, marking the cytoplasm of inner and outer hair cells, and 4,6-diamidino-2-phenylindole (DAPI), marking the nuclei. (**e**) Scanning electron microscopy image of the top view of the sensory epithelium reveals the precise arrangement of one row of inner hair cells and three rows of outer hair cells, separated by the pillar cells (with permission from Ref. [75]. Copyright © 2009, Annual Reviews. All rights reserved).

3. Supporting structures

3.1. Communication routes of the inner ear filled with endo- or perilymph

The cochlea consists of three scalae that contain endo- and perilymph. The scala media contain endolymph, where osmotic and ionic characteristics are close to the intracellular hair cell milieu (high potassium content, K^+ = 144 mval/l), and the scala tympani and vestibuli contain perilymph, which can be compared to cerebrospinal fluid (high sodium content, Na^+ = 140 mval/l). There exist three communication routes between the intracranial spaces and the inner ear, the vestibular aqueduct, the cochlear aqueduct and the internal auditory canal [8]. The vestibular aqueduct contains the endolymphatic duct that begins with the union of the utricular and saccular ducts and ends in a blind pouch, the endolymphatic sac, which is embedded between two dural blades, located in the epidural space and shows immunological

competence. The cochlear aqueduct contains the perilymphatic or periotic duct and possesses communication with the subarachnoidal space (**Figure 2**).

The aqueducts provide functionality for continuous response to stimulation to both inner ear sense systems, the cochlea and the vestibular organs, maculae of the utricle and saccule and cupulae of the three semicircular canals, by pressure equilibrium, participate in inner ear fluid regulation, make longitudinal flow feasible and thus possess a key role in guaranteeing adequate response to stimulation. Pressure equilibrium is primarily the function of the cochlear aqueduct, whereas fluid circulation is dependent on an intact vestibular aqueduct, but various interactions exist.

The main drainage of the inner ear is maintained by two to four veins of the cochlear aqueduct, and to a lesser extent by one or more, usually two at the proximal termination-located vessels of the vestibular aqueduct [9–11]. The protein and ionic composition, the endolymphatic potential and resting potential of the hair cells show differences in the distinct parts of the endolymphatic fluid spaces. These gradients and the fluid circulation are essential for adequate response to stimulation. Procedures which expand the endolymphatic space induce endolymph flow towards the base of the cochlea, contributing to the removal of electrolytes and volume. Procedures which reduce cochlear endolymph volume lead to apically directed flow in the cochlea, contributing to the addition of electrolytes and volume [12].

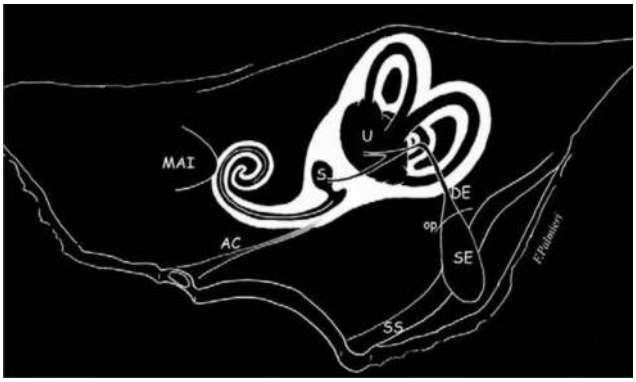

Figure 2. Schematic presentation of the labyrinth and aqueducts. AC: cochlear aqueduct; DE: endolymphatic duct; SE: endolymphatic sac; U: utricle; S: saccule; SS: sigmoid sinus; MAI: internal acoustic meatus. The white area represents the perilymphatic space; within it is the endolymphatic space in black. The endolymphatic duct is contained in the vestibular aqueduct; the perilymphatic or periotic duct is contained in the vestibular aqueduct; the endolymphatic sac protrudes from the vestibular aqueduct aperture protected by a bony operculum (op) and spreads out into the epidural space (with permission from Ref. [76]. Copyright © 2004, Springer-Verlag. All rights reserved).

3.2. Stria vascularis

The regulation of inner ear fluid homeostasis, with its parameters volume, concentration, osmolarity and pressure, is the basis for adequate response to stimulation [13]. The ion and water transport in the inner ear help maintain the proper potassium concentration required

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for hair cell function. Potassium is the major charge carrier for sensory transduction. It is ideal for this role, since it is by far the most abundant ion in the cytosol and responsible for the large endocochlear potential of 80 mV which is the driving force for mechanoelectrical transduction. Contrastingly, the endovestibular potential in the semicircular canals is ±1 mV [14].

The stria vascularis, located at the lateral wall of the cochlear duct, is the main structure responsible for endolymph secretion of the cochlea. It is connected to the spiral prominence, to Reissner's membrane and to the spiral ligament, which binds to the otic capsule. The stria vascularis represents one of the few epithelial types that contain capillaries. The stria vascularis has a higher oxygen consumption than brain tissue, and the strial capillaries are larger in diameter, with a higher haematocrit and a slower flow than the capillaries of any other tissue type [15]. The strial marginal cells show structural characteristics for fluid transport. They possess extensively infolded basolateral membranes with mitochondria providing the energy for active transport mechanisms, and microvilli located at the apical and basal sides increasing surface area. The stria vascularis consists of three cell layers: marginal cells, intermediate cells and basal cells. The intermediate cells, with their extensive, active transport mechanisms, are responsible for generating the endolymphatic potential. Consequently, the marginal cells possess a positive intracellular potential similar to that of the scala media [16].

A distinct pattern of tight and gap junctions, barrier and transport proteins maintains endolymph composition and generates endolymphatic potential, facilitating sensory transduction and reflecting fine regulation and a wide range of responses to stimulation. The transport proteins are regulated by purinergic, adrenergic and muscarinic receptors, steroids, vasopressin and atrial natriuretic peptide (ANP). There is evidence that the stress hormones noradrenaline and adrenaline, corticosteroids and mineralocorticosteroids possess a key role in inner ear homeostasis and sensory transduction. Besides, there exists a strongly expressed and largely non-overlapping distribution pattern for the different aquaporin (AQP) water channel subtypes in the inner ear, suggesting the existence of regional, subtype-specific water transport pathways [17–19]. The regulation of water transport in the inner ear probably requires concerted actions of multiple types of AQPs [20].

According to the tonotopy of the cochlea, potassium concentration and circulation are generally stronger at the cochlear base, and these gradients are maintained by extensive potassium recirculation cycles (**Figure 3**). In the auditory system, potassium circulation begins with the entrance of potassium into the sensory cells via the apical transduction channel. After entering the inner and outer hair cells, potassium recirculates mainly by a medial and a lateral pathway, and further smaller pathways through Reissner's membrane and the outer sulcus cells [21–23]. The medial pathway from the inner hair cells and the inner radial nerves involves inner sulcus cells, limbal fibrocytes and interdental cells. The lateral pathway from the outer hair cells consists of potassium delivery into the perilymph, absorption by the spiral ligament cells and entrance into the stria vascularis via strial intermediate cells [24, 25].

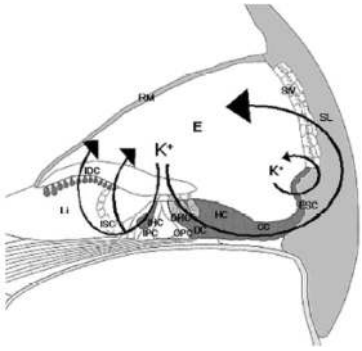

Figure 3. Schematic representation of a cochlear turn with the most significant recycling pathways of K^+ ions. Furthermore, it depicts the organ of Corti composed of sensory inner (IHC) and outer (OHC) hair cells and supporting cells. Inner pillar cells (IPC), outer pillar cells (OPC), Deiters cells (DC), Hensen cells (HC), Claudius cells (CC), external or outer sulcus cells (ESC), internal or inner sulcus cells (ISC), spiral limbus (Li), interdental cells (IDC), Reissner's membrane (RM) and stria vascularis (StV) adjacent to the fibrous spiral ligament (SL) (with permission from Professor G. van Camp, University of Antwerp, Belgium modified by Ref. [77]. Copyright © 2004, Springer-Verlag. All rights reserved).

3.3. Supporting cells

The organ of Corti encloses the outer hair cells and the inner hair cells, which are stabilized by inner sulcus and inner and outer pillar cells. The outer hair cells are placed on top of one Deiters cell each. Besides, the organ of Corti encloses two small endolymph spaces, the Nuel space and the outer tunnel, and one perilymph space, the inner tunnel. The inner sulcus cells and the interdental cells terminate the organ of Corti into the spiral limbus and the tectorial membrane. The outer sulcus cells connect to the stria vascularis and spiral ligament (**Figure 3**).

The secretory stria vascularis, the vestibular dark cells and endolymphatic sac and the non-secretory vestibular transitional cells, the Reissner's membrane, the sulcus cells, the spiral limbus cells, the Deiters cells and the lateral or outer supporting cells (Hensen and Claudius cells) are responsible for fine regulation of inner ear fluids including the maintenance of ion and osmolarity gradients and potassium recirculation. The lateral or outer supporting cells are located between the outer hair cells and outer sulcus cells. The necessity for precise fine regulation of the endolymph is underlined by the fact that basally to the Hensen cells, Boettcher cells and medioapically to the Hensen cells cover or tectal cells were distinguished [26].

4. Inner and outer hair cells – the mechanoelectrical transducers

4.1. Stereocilia

The stereocilia of the inner ear hair cells are microvilli-derived and unique cell structures that represent the gate for stimulus detection and correlate anatomically with distinct cochlear functions, including mechanoelectrical transduction, cochlear amplification, adaptation,

frequency selectivity and tuning [27]. The stereocilia have a typical staircase arrangement connected with lateral and tip links stabilizing the mature hair-bundle structure. The number of stereocilia on each hair cell decreases in a linear fashion with distance from the base of the cochlea. However, stereociliary length increases as a hyperbolic function of distance along the cochlear duct [28]. Contrastingly, in the vestibular organs one kinocilium is bound to the tallest of 50–80 stereocilia, arranged in a distinct geometrical alignment [29]. Differences in ciliary gradation also exist between the three rows of stereocilia on outer hair cells and the two rows on inner hair cells, with the tallest row positioned laterally [30]. The longest stereocilia layer left imprints on the undersurface of the tectorial membrane at the region known as Hardesty's or Kimura's membrane [31]. The stereocilia of the inner hair cells do not have the same firm attachment to the tectorial membrane as the stereocilia of the outer hair cells suggesting different modes of mechanical coupling between the tectorial membrane and the inner and outer hair cell stereocilia [30].

The term stereocilia does not reflect their origin, as these microvilli-derived structures should be clearly distinguished from microtubule-based, true cilia. Stereocilia are constructed of cross-linked actin filaments in a parallel, paracrystalline array, giving stereocilia their stiffness, are rich in fimbrin and their stereociliary rootlets contain actin and tropomyosin [32]. The actin filaments insert with an electron-dense rootlet into a fibrous-anchoring structure, the cuticular plate. The cuticular plate is a network of actin filaments, which also contain myosin, α-actinin, fimbrin, tropomyosin, fodrin and calcium-binding proteins [33, 34].

When sound is induced, fluids move through the cochlear duct and vibrate the basilar membrane with the sensory hair cells against the tectorial membrane, which leads to deflection of the stereocilia and activation of the mechanoelectrical transduction channels gated by the tip links. They are extracellular, cell surface associated, fine filaments, gating the mechano-transducer channel by deflecting the hair cell bundle towards the taller row, depolarizing the hair cells and enabling potassium influx. A deflection in the opposite direction leads to hyperpolarization [35].

The stereocilia, together with the structures of the hair cell body, probably contribute actively and/or passively to cochlear amplification. They also influence the amplification properties of the outer hair cell body enabled by bending leading to a membrane potential change in outer hair cells and causing length changes [36]. These length changes feed force back to the basilar membrane on a cycle-by-cycle basis and so tune its otherwise shallow vibrations to the characteristic frequency [37]. At low frequencies, the stereociliary sensitivity is proportional to the cube of the heights of their hair bundles, whereas at high frequencies the sensitivity is proportional to the inverse of their heights [38]. Frequency and stiffness are proportional to each other [39] correlating with the height of the stereocilia [40]. The cochlear amplifier gain is the difference between the peaks in the sensitivity functions for low- and high-intensity tones [41].

4.2. Inner hair cells

The tip links of the stereocilia of the inner hair cells are the location for the mechanoelectrical transduction of the cochlea, long searched for. There exist about 3500 inner hair cells that are

grouped in one row, in contrast to about 12000 outer hair cells that are grouped in three rows. 90–95 % of all innervation supplies the inner hair cells and each inner hair cell has contact with about fifteen to twenty neurons, of which about 90 % are afferent neurons [42, 43].

Inner hair cells show a characteristic 'flask' shape, displaying a constriction in the neck region. Relative to the surface of the organ of Corti, the cell body is angled towards the centre of the cochlear spiral (the modiolus) and away from the supporting pillar cell. The apical half of the cell contains the nucleus, and the infranuclear region shows an extensive and seemingly continuous network of intracellular endoplasmic reticulum membranes, associated with mitochondria and cytoplasmic vesicles. The afferent nerve endings form characteristical ribbon synapses around the entire baso-lateral region below the level of the nucleus [42]. Ribbon synapses are specialized for the precision and speed required to process auditory information and show tonotopical variation in function and form along the cochlear duct [44].

The inner hair cells are embedded for stabilization between inner sulcus cells and inner pillar cells, which shape the stiffness and elastic reactance of the travelling wave-processing structures [45]. Already, the basilar membrane and the inner and outer hair cells with their receptor potentials show tuning characteristics similar to the characteristical tuning of the cochlear afferent neurons [46].

4.3. Outer hair cells

The inner ear is not just a mechanoreceptor, but is capable to an active processing by the outer hair cells. The active component can be up to more than 100 times larger than the classical basilar membrane vibration. The outer hair cells enhance and focus the amplitude of the travelling wave by its contractions at sound pressure levels up to 60 dB (cochlear amplification) [47]. But the outer hair cells with their W-pattern-aligned stereocilia are not just a cochlear amplifier; they are three-dimensionally regulators for bone conduction and the natural exposition to bone vibrations.

To process the sound waves three-dimensionally, the outer hair cells are positioned on Deiters cells. Corresponding to the necessity for continous fast and active response to stimulation, they are surrounded by two endolymph spaces, the outer tunnel and the Nuel space.

The outer hair cells with their micromechanical properties enhance frequency selectivity and the tone intensity range. Stimulus protection, distance adjustment and sharpness enhancement in the eye are executed by the micromechanical light accommodation of the lens and the pupils and the biochemical and electrophysiological light accommodation by variation of the amount of photopigment and the open probability of transduction channels by the photoreceptors.

Hyperpolarization mediated by specific $GABA_A$ receptors (gamma aminobutyric acid A) causes expansion of prestin molecules, which elongates the outer hair cell [48]. Stimulation of ACh receptors (acetylcholine) leads to opposite outer hair cell changes [49]. Those outer hair cell changes can be measured as otoacoustic emissions (OAEs, spontaneous and evoked).

Contrastingly to the innervation of inner hair cells, the afferent nerve-receptor cell ratio is with about 1:10 negative [43, 50].

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5. Afferent and efferent innervation

5.1. Afferent innervation

90–95 % of innervation to the hair cells is afferent, and 90-95 % are bipolar afferent type I neurons, which are organized in the spiral ganglion and form single ribbon synapses under inner hair cells. These specific synapses are found in retinal photoreceptors and bipolar neurons. Outer hair cells are innervated by type II afferent neurons, which are ribbonless and only excited with maximal synaptic stimulation, suggesting to be part of the sensory drive for the medial olivocochlear reflex protecting from acoustic overstimulation [51]. But the majority of outer hair cell innervation is efferent and about 90% of all efferent innervation terminates on outer hair cells [43, 52].

The first neurons of all parts of the vestibulocochlear nerve are truely bipolar, formed to the spiral ganglion in the bony modiolus, and leave the vestibule through the lamina cribrosa, which is a thin bony plate that is penetrated by the neural structures and blood vessels originating in most cases from the anterior inferior cerebellar artery. The lamina cribrosa is medially covered by dura mater and arachnoidea and forms a barrier between the inner ear and the subarachnoid space.

The excitatory afferent transmission of the auditory system is regulated by various types of glutamate receptors, ionotropic glutamate receptors of the N-methyl-D-aspartic acid (NMDA) and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) type as well as group I and II metabotropic glutamate receptors, and inhibitorily efferent modulated by GABA and dopamine [53].

Complex neural processing between afferent and efferent fibres is found in the spiral ganglion and the ventral cochlear nucleus (VCN) [54]. Not just tonotopical place coding but also periodical time coding make the signal robust, relevant for complex sounds when afferent excitation is saturated [55–57].

5.2. Efferent innervation

The efferent system of the cochlea provides stimulus protection and fine regulation, in particular noise protection, mediation of selective attention and improvement of signal-to-noise ratio, by innervating the same structures that are responsible for stimulus perception, the inner and outer hair cells. The efferent system also supports adaptation and frequency selectivity by modification of the micromechanical properties of outer hair cells. The efferent system as well as the entire human auditory system is susceptible to strengthening by training and it could be shown that efferent suppression is stronger in musicians [58].

The multipolar lateral efferent neurons originate from the lateral superior olive (LSO) and the multipolar medial efferent system from the periolivary region (medial, ventral and anterior) around the medial superior olivary (MSO) complex and the trapezoid body [59] (**Figure 4**). In human, there is no nucleus trapezoid body and the lateral efferent component is relatively small compared with other species [60–62]. By contrast, the medial superior olivary nucleus

reflects a steady increase in primates corresponding to the capability of low-frequency hearing [63].

The well-developed human medial olivary nucleus seems to be the basis for extraction of interaural time and phase differences, whereas the smaller human lateral olivary nucleus probably functions in the analysis of interaural differences in frequency and intensity. The lateral and medial nuclei together form the basis for localization of a sound stimulus and enable us to function in a three-dimensional auditory world [64, 65].

The myelinated medial fibres, which innervate outer hair cells, project ipsi- and contralateral and the unmyelinated lateral fibres, which innervate the dendrites of afferent nerve fibres, project mainly ipsilateral [66]. There exists distinct but complex geometrical and functional alignment of the efferent fibres, their connections and neurotransmitters [67].

Neurotransmission of the efferent system takes place by inhibitory and excitatory transmitters reflecting fine regulation. The numerous neurotransmitters provide for the auditory system a wide operating range to enhance or depress environmental stimuli and can be co-localized as well. The neurotransmitter of the medial olivocochlear fibres includes ACh (acetylcholine), GABA (gamma aminobutyric acid), CGRP (calcitonin gene-related peptide), ATP (adenosine triphosphate), enkephalins and NO (nitric oxide) [68, 69]. The transmitter of the lateral efferent system includes ACh, GABA, CGRP, dopamine, serotonin and opioids such as dynorphin or enkephalin [70–72].

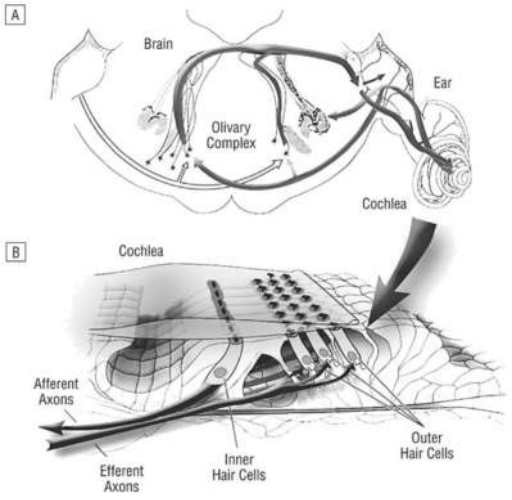

Figure 4. Course of the medial and lateral efferent systems. (**A**) The auditory brainstem section. Sound representations from the ear ascend to the olivary complex via the ventral afferent pathway and project back to the ear via dorsal crossed and uncrossed medial and lateral efferent fibres. (**B**) Cross-sectional view of the inner ear. The major ascending afferent pathway arises from inner hair cells. Descending olivocochlear projections terminate on inner and outer hair cells (with permission from Ref. [78], © 1990, Elsevier; and Ref. [79], Copyright © 2004 American Medical Association. All rights reserved).

6. Conclusion

The cochlea is a unique sense organ with regard to its qualities in continuous stimulus perception and stimulus discrimination capacity. This corresponds to the finely aligned hair cell receptors, their surrounding supporting cells and structures embedded in unique fluid spaces, and to further afferent and efferent neural processing.

	Cochlea
Perception characteristics	- continuous response to stimulation due to extensive homeostasis of the inner ear lymph spaces with a driving force of endocochlear potential of about 80 mV; - tonotopical place coding of the basilar membrane, the hair cells and the cochlear nerve (additional periodical time coding); - ossicles (lever), tympanic membrane and oval window (plane focuser) enhance the sound pressure (22–25 *x*) and together with the lymph spaces accommodate the impedance between air and receptor cells before sound stimulus perception of the mechanoreceptoric hair cells; - stimulus localization is made possible by the outer ear and bone conduction by interaural time/phase and intensity differences of both ears with up to 3° and 1 dB, respectively; - outer hair cells are the counterparts of a unique active sense organ that are not just cochlear amplifier, but three-dimensionally regulators for bone conduction and the natural exposition to bone vibrations; - predominantly fast adaptation;
Perception range	- 18 Hz to 20 kHz (acoustical fovea is 200–4000 Hz); - at 1000-Hz sound pressure levels (SPL) between 2×10^{-5} Pa = 0 dB (hearing level/HL) and 2×10^{2} Pa = 140 dB (pain threshold);
Discrimination capacity	**- frequency, colour timbre** with characteristical tuning and most sensitive areas for high-frequency sound at the cochlear base and for low-frequency sound at the cochlear apex; **loudness** by intensity (number of discharges of the hair cells and afferent nerves), **rhythm** by discharge duration of the hair cells;
Further qualities	- noise protection, mediation of selective attention and improvement of signal-to-noise ratio by efferent innervation;
	Vestibular organ
Perception characteristics	- secondary sense organ as adequate stimulation has to be centrally processed with optical or proprioceptic inputs (exception gravitation as kind of linear acceleration); - continuous response to stimulation due to extensive homeostasis of the inner ear lymph spaces with an endovestibular potential of ±1 mV; - stimulation of the vestibular organs of one site leads to contralateral inhibition with central processing; - cupula organ and endolymph have the same specific gravity; - predominantly slow adaptation in human (cupula organ needs 10–30 s to get back in resting position);
Perception range	- cut-off frequency of the semicircular canals circa 0.03 Hz for the yaw rotation [73]; yaw rotation detection threshold about 1.45 ± 0.81 °/s (3.49 ± 1.95 °/s^2) and absolute nasooccipital translation detection threshold about 2.93 ± 2.10 cm/s (7.07 ± 5.05 cm/s^2) [74];
Discrimination capacity	- perception of **linear acceleration** by macula organs in the saccule and utricule; perception of **angular acceleration** by cupula organs in the semicircular canals; **spatial resolution** by position of the semicircular canals, the saccule and utricle and the position and alignment of their hair cells, stereocilia and kinocilium;
Further qualities	- unique response to inadequate caloric stimulation, which is used for investigations;
	Optical system
Perception characteristics	- cornea, lens and vitreous body refract and accommodate the light waves before stimulus perception of the receptor cells;

	- single sense organ where receptor potential is hyperpolarization; - dark adaptation of the fovea centralis in 5–10 min, extrafoveal 45–100 min; - adaptation to darkness by the iris with its muscles sphincter and dilator pupillae, increased photopigment and spatial and time summation in the afferent nerves; in darkness the photoreceptors increase light sensitivity by increased opening of Na^+ channels;
Perception range	- 400–700 nm (highest absorption maximum for blue, 440 nm; green, 540 nm; red, 570 nm); detection threshold 1–2 nm; - flickering until 65–80 pictures/s; in darkness 20–25 pictures/s;
Discrimination capacity	- **sharpest vision** at a small area of the macula lutea, the fovea centralis, which contains only cone cells that are longer than in the periphery; sharpest vision decrease to the periphery of the retina; - **colour vision** by cone cells which decrease to the periphery of the retina and have either one of three different photopigments; neuronal processing of opposite colours already starts in the retina (colour vision and opponent colour vision theory); - **black and white vision (night vision)** by rod cells that are more light sensitive than cone cells; - **light accommodation** by different light sensitivity of the cone and rod cells and excitation of on-center (light-on) and off-center (light-off) neurons; - **contrast enhancement** by lateral inhibition (horizontal processing) of neuronal horizontal cells in the retina, but already the first step of central processing of **form and motion**;
Further qualities	- convergence reflex of the eye bulbi due to the bilateral pupil reflex and the external eye muscles; - light accommodation by the lens and the pupils for protection, sharpness, distance adjustment (comparable to the function of outer hair cells and the stapedius reflex);
	Olfactory system
Perception characteristics	- chemical receptors are slower in their time characteristics than mechano- and photoreceptors; - chemical stimulus pre-processing by dilution in the mucoepithelial film; - smell is perceived by form and size of the molecules that bind to the cell membrane (key-lock principle); - adaptation leads to no stimulus perception at all;
Perception range	- absolute threshold of about 10^7 molecules/ml; - only soluble molecules (e.g. dental metal alloy cannot be perceived) and specific molecules (key-lock principle) can be perceived; consequently absolute and relative perception thresholds are dependent on humidity and temperature;
Discrimination capacity	- perception of a few thousand smell qualities; for testing 20 standard qualities;
Further qualities	- no perceived smells can have a behavioural impact (pheromones); - trigeminal nerve for thermal and pain perception and a, hot, burning, astringent, tingling or cooling sense perception; - continuous neurogenesis of the primary sensory neurons in mammals;
	Gustatory system
Perception characteristics	- chemical receptors are slower in their time characteristics than mechano- and photoreceptors; - chemical stimulus pre-processing by dilution in seromucous saliva; - taste is perceived by form and size of the molecules that bind to the cell membrane (key-lock principle); - adaptation leads to no stimulus perception at all;
Perception range	- absolute threshold of about 10^{16} molecules/ml; - only soluble molecules (e.g. dental alloy cannot be perceived) and specific molecules (key-lock principle) can be perceived; consequently absolute and relative perception thresholds are dependent on humidity and temperature;
Discrimination capacity	- **bitter, sour, salt, sweet** with areas of highest sensitivity on the tongue; many various biochemical molecules can simulate one of these four qualities;

Further qualities	- trigeminal nerve for thermal and pain perception and a, hot, burning, astringent, tingling or cooling sense perception;
	Dermal receptors
Perception characteristics	- mechanoreceptors: pressure receptors are basically intensity receptors (proportional receptors), touch receptors are basically speed receptors (differential receptors) and vibration receptors are basically acceleration receptors (differential receptors), temperature receptors are proportional-differential receptors (PD receptors); - adaptation for touch leads to no stimulus perception at all; - adaptation is faster for vibration than touch and is slowest or not at all for pressure receptors; temperature receptors with few and pain receptors with no adaptation at all; - perception transmission fastest in Pacinian corpuscles (richly myelinated afferent axons) and slowest in temperature and pain receptors (poorly myelinated or unmyelinated afferent axons);
Perception range	- 40–1000 Hz for vibration (Pacinian corpuscles);
Discrimination capacity	- perception of **pain is a non-specific sensation** and can be triggered by pressure, temperature, chemicals; - **temperature/warm receptors** (40–47°C) can be triggered non-specifically by, for example, pepper; - **temperature/cold receptors** (17–36°C) can be triggered non-specifically by, for example, menthol; - **tactile sensation/pressure** by Merkel cells and Ruffini corpuscles; - **tactile sensation/touch** by Meissner tactile corpuscles and free nerve endings at hair follicles; - **tactile sensation/vibration** by Pacinian corpuscles; - **spatial resolution** by density of receptors and afferent nerves, smallest sensoric areas in tongue, lips, fingers and hands with highest number of receptor cells and amount of afferent innervation;
Further qualities	- gustatory papillae regenerate after destruction and reinnervation;

Table 1. Comparison of the perception qualities of the human sense organs.

	Cochlea
Receptor cells	- about 3500 inner and 12000 outer hair cells; - inner hair cells are the mechanoreceptors; active elongation of outer hair cells enhances the sound stimulus at sound pressure levels up to 60 dB (cochlear amplification); - inner hair cell stereocilia show linear alignment and outer hair cell stereocilia show a W-pattern; tip links of the stereocilia are the location of mechanoelectrical transduction;
Supporting structures	- supporting cells for stabilization of the inner hair cells (inner sulcus and inner and outer pillar cells) and outer hair cells (Deiters cells), which shapes the stiffness and elastic reactance of the travelling wave-processing structures; - the supporting cells of the cochlea participate in endolymph production, its fine regulation of ion and osmolarity gradients and potassium recirculation; - the stria vascularis is the main structure responsible for endolymph secretion of the cochlea; - the vestibular and cochlear aqueduct provide functionality to the cochlea and the vestibular organs by pressure equilibrium, participate in inner ear fluid regulation, make longitudinal flow feasible; pressure equilibrium may be primarily attributed to the cochlear aqueduct, whereas fluid circulation is dependent on the vestibular aqueduct;
Afferent innervation	- 90–95% of the neurons of the cochlear nerve are afferent and of them 90–95% supply inner hair cells, and only 5–10% outer hair cells; - inner and outer hair cells with bipolar afferent neurons; - Type I myelinated afferent neurons supply inner hair cells; type II myelinated afferent neurons constitute the sensory drive for the medial olivocochlear (MOC) efferent reflex on outer hair cells;

Efferent innervation	- 5–10 % of the neurons of the cochlear nerve are efferent, which predominantly terminate on outer hair cells; - medial efferent neurons that project ipsi- and contralateral and terminate directly under outer hair cells are myelinated; lateral efferent neurons that project mainly ipsilateral and innervate the dendrites of radial afferent fibres under inner hair cells are unmyelinated; - efferent innervation for noise protection, mediation of selective attention and improvement of signal-to-noise ratio; - it also supports adaptation and frequency selectivity by modification of the micromechanical properties of the outer hair cells;
	Vestibular organ
Receptor cells	- on the hair cells 50–80 stereocilia are aligned to one kinocilium; movement of the stereocilia to the kinocilium leads to neural depolarization; movement of the stereocilia into the opposite direction leads to neural hyperpolarization; - two types of hair cells with different innervation characteristics; the wider and taller type I vestibular cells possess more, taller and thicker stereocilia and a thicker cuticular plate compared with type II cells;
Supporting structures	- vestibular endolymph production and fine regulation of ion and osmolarity gradients by secretory dark cells, potassium recirculation by non-secretory transitional cells, calcium homeostasis by melanocytes; - the vestibular and cochlear aqueduct provide functionality to the cochlea and the vestibular organs by pressure equilibrium, participate in inner ear fluid regulation, make longitudinal flow feasible; pressure equilibrium is primarily the function of the cochlear aqueduct, whereas fluid circulation is dependent on the vestibular aqueduct;
Afferent innervation	- receptor cell-afferent nerve ratio of 3:1 in the cupula organs and 5:1 in the macula organs; - bipolar afferent neurons that may end as a button, dimorphic or as a cup; - excitatory glutamatergic afferent transmission;
Efferent innervation	- 5–10% are efferent neurons; - efferent nerve with direct contact to type II hair cells, but indirect contact upon afferent neuron dendrites to type I cells;
	Optical system
Receptor cells	- about 120 million rod cells and six million cone cells; - receptor cells are unipolar neurons (primary sensory cells); no elongation of receptor cells in mammals proven; - photoreceptors are characterized as well as inner hair cells by ribbon synapses with excitatory glutamatergic transmission;
Supporting structures	- supporting cells of the retina for stabilization due to localization of the first three neurons of afferent innervation within the retina; - melanin-containing cells of the stratum pigmentosum retinae increase sharpness by absorbing scattered light and extend with high light intensity deep into the photoreceptor layer;
Afferent innervation	- photoreceptor cells represent the first neuron; the second and third neurons are located in the retina as well; - one million afferent nerves with decreasing sensitivity to the periphery; photoreceptor cells in the central fovea connect to one single neuron; in the periphery up to 500 photoreceptors converge to one neuron; - the macula possesses a separate afferent nerve bundle;
Efferent innervation	- efferent innervation for light adaptation, light reflex and lateral inhibition;
	Olfactory system
Receptor cells	- receptor cells are bipolar neurons (primary sensory cells); - about 10^7 receptor cells; - 5–20 kinocilia per receptor cell;
Supporting structures	- supporting cells for stabilization, basal cells for regeneration; - Bowman glands for mucous secretion;
Afferent innervation	- the mitral cells (second afferent neuron) has contact with about 1000 primary afferent neurons (receptor cells);

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Efferent innervation	- in the bulbus olfactorius, where the fila olfactoria terminate as primary afferent neurons is complex efferent inhibition localized as adaptation leads to no stimulus perception at all; the dendrites of the mitral cells can be specifically inhibited by two cell types, the periglomerular cells and granule cell interneurons (partial inhibition), which are innervated by efferent neurons;
	Gustatory system
Receptor cells	- taste perception by vallate, fungiform and foliate papillae; filiform papillae have no sensoric qualities; single gustatory papillae can be found at the soft palate, the hypopharynx and the epiglottis as well; - the gustatory papillae are formed of about 20 receptor cells;
Supporting structures	- supporting cells for stabilization; - salivatory glands for seromucous saliva production;
Afferent innervation	- about 50 afferent nerves per gustatory papilla; - facial nerve (chorda tympani) supplies the first two-thirds of the tongue; glossopharyngeal nerve (mainly bitter perception) supplies the last tongue third;
Efferent innervation	- taste adaptation after physiological food and saliva cleaning in about 5 s; efferent control dependent on concentration (salty food with longer aftertaste) and food aversion (unphysiological food such as pure vinegar with longer aftertaste); (own experiments)
	Dermal receptors
Receptor cells	- enclosed corpuscles and not enclosed free nerve endings (alone or at hair follicles); - Merkel cells are located in the corium; Ruffini corpuscles are located in the corium and the subcutis; Meissner tactile corpuscles are located in the dermal papillae; Pacinian corpuscles are located in the subcutis; free nerve endings alone or at hair follicles are located up to the highest corium layers; cold receptors are located higher in the corium than warm receptors;
Supporting structures	- Merkel cells are modified epithelial cells which are covered on the apical side by a touch meniscus representing the terminal swelling of a nerve fibre; - Meissner corpuscles are ovally formed structures built by lamellarly in layers arranged cells and surrounded by a capsula; one or more nerve fibres enter this structure and its terminating swellings are the receptoric parts; - Pacinian corpuscles are ovally formed lamellarly in layers arranged organs surrounded by a capsula, which is entered by a nerve fibre; the unmyelinated termination of the nerve fibre is the receptoric part;
Afferent innervation	- one to seven afferent nerves insert at the enclosed dermal receptors; - non-specific pain sensation and the receptoric free nerve endings with highest number of discovered different transmitters and neuropeptides (glutamate, aspartate, CGRP-calcitonin gene-related peptide, Substance P, Neurokinin A, Somatostatin, VIP-vasoactive intestinal peptide);
Efferent innervation	- indifference temperature between 31 and 36°C with few activated cold and warm receptors and efferent overweight; temperatures beneath 20°C and above 40°C lead to receptor activation and afferent overweight;

Table 2. Comparison of the structural characteristics of the human sense organs.

Cochlea Glossary

afferent innervation	*innervation that projects centrally from the effector/sense organ to the brain*
basilar membrane	*structure beneath the Corti organ consisting of the basilar lamina and a supporting fibral tissue layer*
cochlear aqueduct	*bony canal of the perilymphatic duct*
Corti organ	*all cells, tissue structures and their enclosed lymph spaces that participate in mechanoelectrical transduction, namely hair cells, supporting cells, basilar membrane, tectorial membrane, inner tunnel, outer tunnel and Nuel space*

cribrose lamina	*thin bony plate that forms the barrier between the vestibule of the inner ear and the internal auditory canal and is pierced by neurons of the cochlear nerve and blood vessels*
efferent innervation	*innervation that projects peripherally from the brain to the effector/sense organ*
endolymph	*lymph fluid in its composition close to the intracellular hair cell milieu that fills the medial scale and the outer tunnel and Nuel space in the Corti organ*
endolymphatic duct	*endolymph space that originates from the utriculosaccular duct and provides fluid circulation to the endolymphatic sac*
endolymphatic sac	*blind pouch of the endolymphatic duct with immune competence participating in the endolymph homeostasis*
helicotrema	*cochlear peak with confluence of tympanic scale and vestibulic scale*
inner hair cell	*receptor cell of the cochlea responsible for mechanoelectrical transduction*
inner tunnel	*perilymph space within the Corti organ between inner and outer pillar cells*
medial scale	*endolymph space containing the Corti organ*
modiolus	*bony spiral backbone of the cochlea*
Nuel space	*perilymph space within the Corti organ between outer pillar cells and outer hair cells*
olivocochlear bundle	*efferent innervation of the cochlea within a medial and lateral bundle can be distinguished*
outer hair cell	*receptor cell of the cochlea responsible for amplification and three-dimensionally focusing of basilar membrane vibration*
oval window	*membrane between the vestibule and the stapes*
outer tunnel	*endolymph space within the Corti organ between outer hair cells and lateral supporting cells*
perilymph	*lymph fluid in its composition close to cerebrospinal fluid that fills the tympanic scale and vestibulic scale and the inner tunnel in the Corti organ*
perilymphatic duct	*or periotic duct that originates from a pouchlike extension of the round window, containing a mesh of arachnoid-like tissue, providing communication with the subarachnoidal space and mainly pressure equilibrium to the inner ear*
reunion duct	*canal that connects the cochlear duct with the saccule*
Reissner's membrane	*cell barrier membrane between the medial scale and the vestibulic scale connected to the spiral ligament laterally and the spiral limbus medially canal that connects the cochlear duct with the saccule*
round window	*barrier membrane between the tympanic scale and the middle ear*
saccule	*vestibular endolymph space that contains one of the two macula organs and is origin of the saccular duct that combines with the utricular duct to the utriculosaccular duct, which itself is origin of the endolymphatic duct*
spiral ligament	*fibral tissue at the lateral wall of the medial scale connecting the vascular stria to the otic capsule*
spiral limbus	*fibral tissue at the medial wall of the medial scale connecting to the tectorial membrane by interdental cells and to the inner sulcus cells by forming the inner sulcus*
spiral ganglion	*first ganglion of the truely bipolar cochlear neurons located in the bony modiolus*

spiral prominence	*ledge of the lateral wall of the medial scale located at the connection between outer sulcus cells and vascular stria*
stereocilia	*microvilli derived finger-like processes of the hair cells connected by various links and location of the mechanoelectrical transduction channels within the tip links*
supporting cells	*cells within the medial scale that are located on the basilar membrane and responsible for hair cell stabilization and inner ear fluid homeostasis, comprising from medially to laterally inner sulcus cells, inner and outer pillar cells, Deiters cells, and the lateral supporting cells, namely Claudius cells, Hensen cells, Boettcher cells, tectal or cover cells and outer sulcus cells*
tectorial membrane	*structure of fibral tissue loosely covering the stereocilia of the hair cells*
tympanic scale	*perilymph space between the helicotrema and the round window*
utricle	*vestibular endolymph space that contains one of the two macula organs and is origin of the utricular duct that combines with the saccular duct to the utriculosaccular duct, which itself is origin of the endolymphatic duct*
vascular stria	*epithelial layer of the lateral wall of the medial scale between Reissner's membrane and spiral prominence covering the spiral ligament*
vestibular aqueduct	*bony canal of the endolymphatic duct*
vestibulic scale	*perilymph space between the vestibule and the helicotrema*
vestibule	*extension of the vestibulic scale between oval window and the saccule*

Author details

Raphael R. Ciuman

Address all correspondence to: ciuman.raphael@cityweb.de

Otorhinolaryngology, Natural Medicine Science, Pharmaceutical Medicine, Uranusbogen, Mülheim an der Ruhr, Germany

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Complementary Literature to Table 1. and Table 2.

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