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Compression, adaptation and efferent control in a revised outer hair cell functional model

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Abstract

In the cochlea of the inner ear, outer hair cells (OHC) together with the local passive structures of the tectorial and basilar membranes comprise non-linear resonance circuits with the local and central (afferent–efferent) feedback. The characteristics of these circuits and their control possibilities depend on the mechanomotility of the OHC.

The main element of our functional model of the OHC is the mechanomotility circuit with the general transfer characteristic $y = k\tanh(x - a)$. The parameter k of this characteristic reflects the axial stiffness of the OHC, and the parameter a working position of the hair bundle. The efferent synaptic signals act on the parameter k directly and on the parameter a indirectly through changes in the membrane potential. The dependences of the sensitivity and selectivity on changes in the parameters a and k are obtained by the computer simulation.

Functioning of the model at low-level input signals is linear. Due to the non-linearity of the transfer characteristic of the mechanomotility circuit the high-level signals are compressed. For the adaptation and efferent control, however, the transfer characteristic with respect to the initial operating point should be asymmetrical ($a > 0$). The asymmetry relies on the deflection of the hair bundle from the axis of the OHC.

Keywords: Cochlea; Outer hair cell; Mechanomotility; Motor protein prestin; Efferent synapse

1. Introduction

The role of the cochlea in mammalian inner ear is to transduce sound waves into action potentials (nerve pulses). This is done by the decomposition of a complex signal into constituent frequencies and the transduction of the filtered signals into a sequence of nerve pulses. The main role in the process of filtering is played by the outer hair cells (OHC). As a consequence of filtering, each sensory cell within the cochlea responds preferentially to sound energy within a limited frequency range. The cochlea, as a frequency analyzer, was compared to a bank of overlapping band-pass filters [1]. The function of the OHC in hearing is now perceived as that of a cochlear amplifier that refines the sensitivity and frequency selectivity of the mechanical vibrations of the cochlea [2–7]. The basis of the cochlear amplification is the ability of the OHC to change their length in response to changes in the membrane potential (MP) [8]. The OHCs length changes exert a force against the tectorial membrane (TM), amplifying the basilar membrane (BM) vibrations [8,9–11]. This phenomenon, called electro-motility, depends on the voltage-

Abbreviations: OHC, outer hair cell; IHC, inner hair cell; TM, tectorial membrane; BM, basilar membrane; MET, mechanical–electrical transduction; EMT, electrical–mechanical transduction; RP, receptor potential; MP, membrane potential; RMP, resting membrane potential; MMC, mechanomotility circuit; BPC, band pass circuit; LPC, low-pass circuit; CN, cochlear nuclei; MSO, medial superior olive; EST, efferent synaptic transducer; AST, afferent synaptic transducer; ENF, efferent nerve fibre; ANF, afferent nerve fibre; ES, efferent synaptic; ACh, acetylcholine; GABA, gamma aminobutyric acid; ac, alternating component; dc, direct component

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sensitive motor protein prestin embedded in the basolateral membrane of the OHC [12,13]. The motor protein is a direct voltage-to-force converter capable to operate at microsecond rates over the entire audible frequency range up to 20–50 kHz [14–16]. Various models for electro-motility have been proposed, based on structural and electrophysiological data related to the membrane and the motor protein [9,17–21].

The real functioning of the OHC cannot be clear without estimation of the influences of the local passive structures of the cochlea. The OHC, together with the local passive structures of the TM, BM and the passive cells of the organ of Corti, constitute (in the transverse direction) a closed filtering system with the feedback connections. Therefore an experimental investigation of the real functioning OHC in the cochlea is a quite difficult task. The results obtained in the isolated OHC with the hair separated from the TM [8,22–24] revealed important facts about transduction processes in these cells. However, the influence of the OHC on the BM and TM mechanics remains not completely clear [7,25]. Modelling establishes the rational basis for the extrapolation of data collected in isolated cells to physiological conditions [9,21,26–29].

Many different models of biological filtering structures of the cochlea and the fibres of the auditory nerve were proposed for the purpose of creating or improving the cochlea prosthesis and the systems of speech recognition. The models are designed on the basis of the observations of the oscillations of the BM and TM [11,25,30–35], physical and psychophysical data [7,18,36,37], firing properties of the auditory nerve fibre [38–41], otoacoustic emission (OAE) [1,42,43], neurophysiology and neurochemistry of the signal transduction and adaptation in the hair cells [4,10,12,44–50]. In addition to models of the filtering structures, biophysical models [51], piezoelectric models [17–19] and flexoelectric models [9] were proposed for the explanation of the electro-motility.

The functional models of the OHC should include not only the active non-linear elements but also the passive linear elements of the cochlea [52]. Moreover, such models should explain processes of the adaptation and efferent control. In this paper, we propose a revised adaptive non-linear functional model of the OHC with efferent control possibilities. The modelling results obtained by the computer simulation contribute to a better understanding of the real functioning of the OHC and the whole filtering system of the cochlea.

2. A biological background of the model

The OHC of the cochlea of the inner ear are located on the BM and the tips of their longest hairs are embedded in the TM. The initial stimulation of the OHC is produced by a shearing motion between the TM and the BM in the transverse direction evoked by the longitudinal–transverse pressure changes. The deflection of hairs of the OHC back and forth opens and closes K^+ ion channels of the cell and produces the receptor potential (RP) [39,53,54]. This mechanical–electrical transduction (MET) process is non-linear and very fast [14–16].

A shift in the MP in the OHC evokes shortening of the cell when depolarized and lengthening when hyperpolarized [8]. This electrical–mechanical transduction (EMT) is performed by the protein prestin located in the lateral wall of the cell [12,13,55]. The conformation changes of prestin in response to changes in the electrical field affect the length and axial stiffness of the cell [56]. The MET followed by the EMT comprise the mechanomotility of the OHC. The deflection of the bundle toward the tallest ciliary row yields somatic shortening while the deflection in the opposite direction produces lengthening of the OHC [22]. This mechanomotility of the OHC affects the local oscillations of the TM and BM supposedly amplifying them. Therefore, the interaction of all OHC with the passive structures of the BM and TM is the basis of the cochlear amplifier.

Changes in the MP of several OHC transduced into the nerve pulses are transmitted by an afferent nerve fibre (ANF) to the cochlear nuclei (CN). The efferent nerve fibres (ENF) from the medial superior olive (MSO) branch into the terminals and make up synapses with the OHC. Thus, the feed-forward and feedback connections with the higher auditory centres are realized in the cochlea [21,47,57–59]. When the ENF are activated, the neurotransmitter acetylcholine (ACh) is released in the synapse at the base of the OHC and the membrane channels are opened. Calcium ions enter through the non-specific channels and open Ca^+-dependent K^+ channels leading to the efflux of K^+ and hyperpolarization [54]. A change in length of the cell will evoke a change in working position of the hair bundle. The time of the response depends on the inertia of the hairs and associated structures of the TM.

While slow changes in membrane potential evoked by ionotropic efferent synaptic (ES) action should change the length of the cell and consequently the position of the hair bundle, the even slower metabotropic changes (evoked by ACh and GABA) do not change the cell length [60], but change the amplitude of fast oscillations [21,56,61]. This means that metabotropic action of ACh changes the axial stiffness of the cell. Thus the mechanisms of fast (mechanically evoked) and slow (synaptically evoked) movements of the cell are different. The mechanisms of the efferent control are also different. Taking into account the established non-linearity of the MET and EMT processes and new data on functioning of the OHC [21,45,47,49,50,56] makes it possible to refine and improve our previous non-linear filtering model of the OHC [52] by realizing the possibilities of adaptation and efferent control.

A revised model of the really functioning OHC in the cochlea is shown in Fig. 1. The basic function of the model is the non-linear filtering. This function is realized by the filtering loop consisting of the feed-forward linear passive circuit (BPC) and the feedback circuit. The BPC models the filtering properties of the local passive structures of the BM, TM and the organ of Corti. The feedback circuit consists of the MET, EMT and LPC and represents the isolated OHC.