

Active Nonlinear Mechanics of the Organ of Corti Including the Stereocilia-Tectorial Membrane Complex

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Key Words

Organ of Corti · Cochlear amplifier · Outer hair cell · Nonlinearity · Stereocilia · Tectorial membrane

Abstract

There is a large amount of knowledge about the different components of the organ of Corti (OC), but little is known about how these components act together in vivo. To clarify the complex mechanical behavior of the OC, anatomic results are carefully analyzed and used to develop a finite element model of a short section of OC, which includes 8 outer hair cells (OHC) and their supporting structures. The modal analysis shows the frequency-dependent phase reversal of the radial stereocilia displacement. The transient computation confirms the amplification of OC displacements when the ability of the OHC to contract and elongate is considered. The inclusion of a nonlinear function describing the mechano-electrical transduction in OHC amplifies and distorts the displacement of the OC when it is stimulated by a sinusoidal input pressure function. These results are in agreement with other psychoacoustic, electrophysiologic and otoacoustic measurements.

Introduction

Though intense research has been conducted on the micromechanics of the organ of Corti (OC) since its discovery [1], the in vivo behavior remains unclear. One of the reasons for this is that it is difficult to yield mechanical parameters, e.g. Young's modulus, of the heterogeneous cell composition, using in vivo measurements. In addition to that, modern computers are not able to calculate the biomechanics of the cochlea including the complete OC with its million degrees of freedom. Therefore, former simulations of cochlear mechanics either neglected known anatomical details or considered only a small number of cells from the complete system. To clarify the complex signal transduction process in the cochlea, we developed a three-dimensional finite element (3D-FE) model of the OC including the stereocilia (St) and the tectorial membrane (TM). While the study neglects wave propagation effects, it resolves details of the cochlear partition, which divides the fluid-filled channels scala media and scala tympani. The stereocilia displacement and the resulting mechano-electric transduction is caused by the shearing of the TM relative to the reticular lamina (RL) in the transverse direction, i.e. perpendicular to the main direction of wave propagation in the longitudinal direction of the cochlea.

The reader is referred to other contemporary literature concerning cochlear modelling [2, 3].

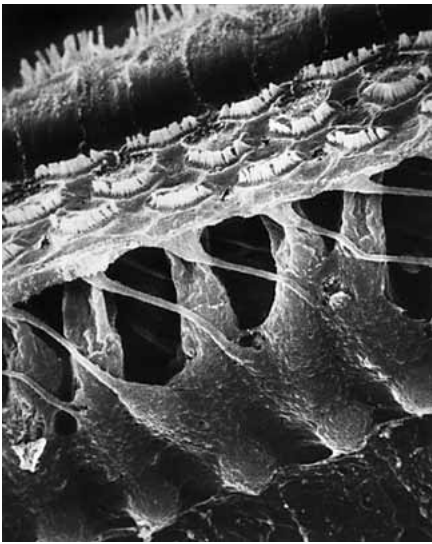


Fig. 1. SEM of OHC supported by Php of DC.

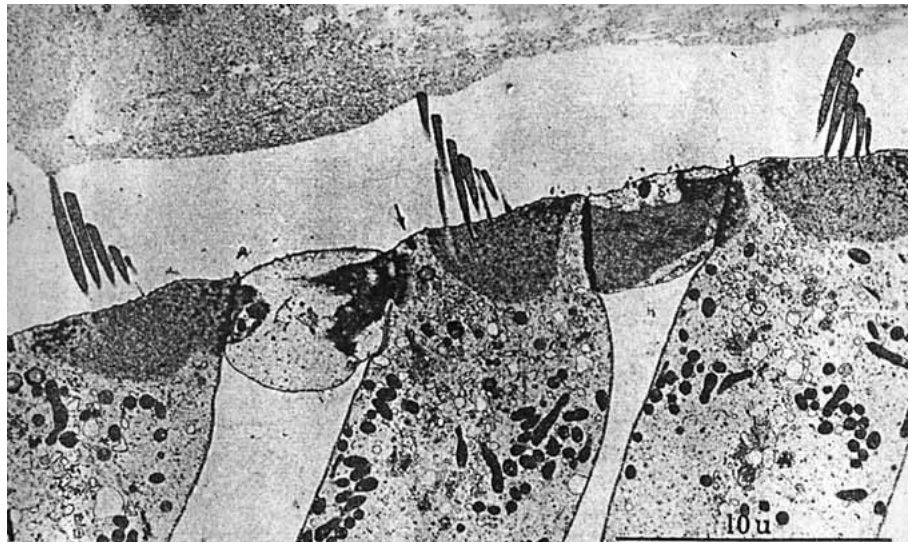


Fig. 2. Coupling of the longest St of OHC to the TM.

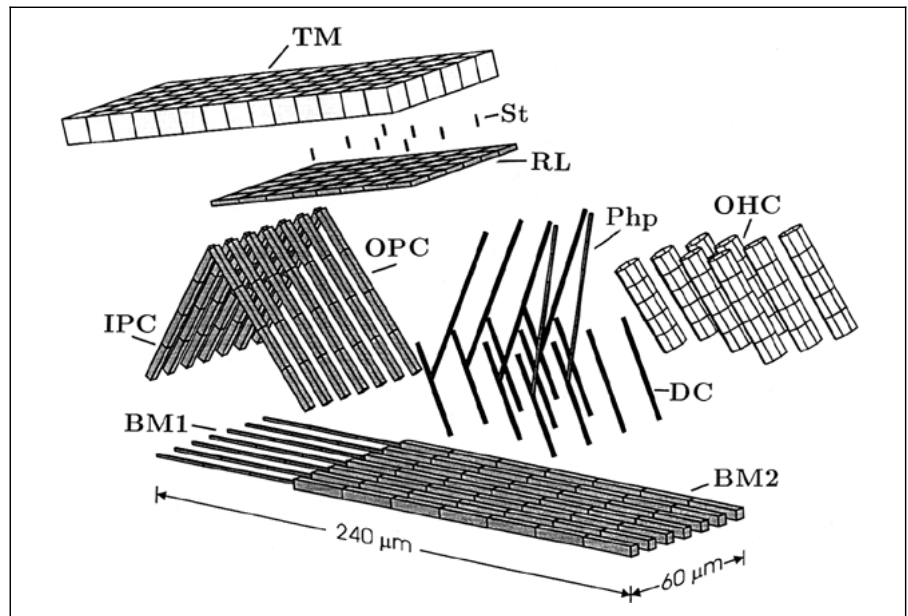


Fig. 3. Components of the FE model with 8 OHC.

Morphology and Methods

A small section of the OC that includes only 8 of the approximately 12,000 outer hair cells (OHCs) of a human cochlea is considered. The surrounding lymphatic fluid is not included in the model, but its mechanical effect is approximated by the symmetrical loading of the organ. Anatomical results used during the development of the FE model have been described previously [4]. Figure 1 shows a scanning electron microscopic (SEM) image of the OC, including the staggered positions of the OHCs. On top of each OHC, the w-shaped form of the stereocilia bundles can be seen. The phalangeal processes (Php) of

Deiters' cells (DC) are clearly visible. One Php runs from the head of an OHC to the base of the next but one OHC. The Php are slender bodies (length $\approx 70 \mu\text{m} \gg$ diameter $\approx 1 \mu\text{m}$) of fibers that are constructed with the protein f-actin. The junctions between the stereocilia of three OHC and the TM are shown at a high magnification in figure 2 [5]. Only the longest stereocilia of the bundles, i.e. those corresponding to the outermost row of bundles, are connected to the TM. Figure 3 shows the different components of the resulting FE model of the small section ($l = 60 \mu\text{m}$) of the OC.

The basilar membrane (BM) constitutes the base of the system on which the OC is located. To circumvent difficulties with the idealiza-

tion of the BM as an orthotropic shell, e.g. the unknown shearing modulus and Poisson ratios of the shell, it is represented by a set of 14 beams (7 pairs). Each transversal fiber is represented using two rectangular beams of different widths [1 μm (BM1) and 4 μm (BM2)] to reflect accurately anatomical results. The complete length of one beam pair is $l_{BM} = 240 \mu\text{m}$ representing a medial part of the human BM. Young's modulus of these beams is chosen as 1.7 GPa according to static point load measurements in the basal part of the guinea pig cochlea [6].

The inner (IPC) and outer pillar cells (OPC) are idealized as straight elastic beams (length = 71.8 μm , width = 3 μm).

The DC support the OHC and are represented as thin (1 μm) beams. They consist of Deiters' rods ($l_{rod} = 38.5 \mu\text{m}$) and their Php ($l_{php} = 62.9 \mu\text{m}$). Their average Young's modulus was recently determined again ($E_{DC} = 45 \text{ MPa}$) [7].

The OHC are idealized as straight isotropic elastic pipes with wall thicknesses of 0.1 μm and $E_{OHC} = 45 \text{ kPa}$ [8]. The average length is 55 μm . Their natural ability to elongate and contract is modelled by heating and cooling according to a thermal expansion coefficient $\alpha = 10^{-4}$. This feature can be switched on or off to simulate the active or passive OC, respectively. To yield an effective gain of 40 dB for the displacement of the RL, an OHC gain of $g \approx 2$ (i.e. the ratio of somatic OHC length change to stereocilia bundle displacement; fig. 4) is chosen. This reflects other experimental results [9].

The RL consists of the endings of the OHC and the Php and the junction between the upper parts of the IPC and OPC. It is idealized as an isotropic plate ($A = 60 \times 104 \mu\text{m}$, $E_{RL} = 1.7 \text{ GPa}$). The head of the IPC and OPC is firmly attached.

The TM is idealized as a structural solid and discretized with 3D 8-node finite elements with three displacements and three rotations per node. Its Young's modulus is chosen as $E_{TM} = 30 \text{ kPa}$ which is the value given for the TM of the bobtail lizard [10]. The density is $\rho_{TM} = 1 \text{ mg/mm}^3$ as it is in all other cases. Therefore, the mass of the TM is included.

The St are covered as elastic beams whose Young's modulus is 20 MPa and their lengths and diameters are 4 and 0.2 μm , respectively.

The complete system of equations used to calculate the 3D-FE model contains 2,298 variables, which are displacements and rotations. For the transient computation (see Results) a symmetric external load is used. It consists of a pressure acting on top of the TM surface and 11 forces acting on the nodes of the BM beams.

Nonlinear OHC Function

The nonlinear processing of acoustic signals by the ear has been verified by psychoacoustical observations, electrophysiological examinations and the analysis of the saturating behavior of evoked otoacoustic emissions, but the sources of the nonlinearities remained unidentified. Possible sources include: material, geometrical (the dependence of the stiffness on the displacement) and state-dependent nonlinearities of mechanical structures, the nonlinear mechano-electrical transduction process of auditory hair cells and nonlinear neural coding of information, e.g. rate intensity functions. A mixture of all these nonlinearities is effective in vivo and it is difficult to distinguish separate causes. Because geometrical nonlinearities are expected to be relevant at high levels (>80 dB SPL) and material nonlinearities are not yet quantified, the nonlinear OHC function is solely used in the present study.

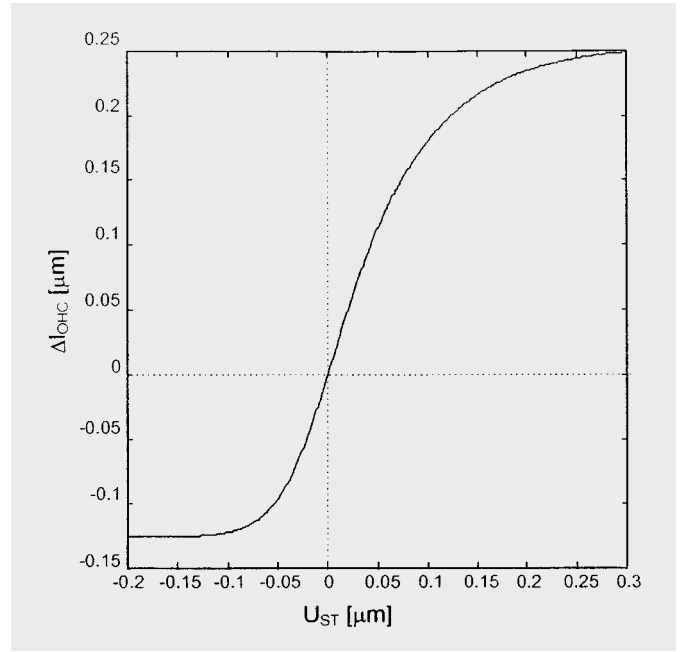


Fig. 4. Asymmetric nonlinear transfer function of the OHC length to the St displacement.

The alternating component of the receptor potential ΔV_r as a function of the stereocilia displacement u_{St} is given by a second-order Boltzmann function, which was developed based on statistical considerations [11]:

$$\Delta V_r = \frac{V_{SS}}{1 + e^{-C_1(u_{St} - u_1)/kT} (1 + e^{-C_2(u_{St} - u_2)/kT})} - V_H \quad (1)$$

V_{SS} is the peak-to-peak value and V_H is the membrane potential for maximal hyperpolarization. The constants C_1 and C_2 were determined as $C_1 = 60 \text{ fN}$ and $C_2 = 120 \text{ fN}$ and $u_1 = 56.8 \text{ nm}$ and $u_2 = 27.3 \text{ nm}$, respectively [12]. The product kT can be calculated with the Boltzmann constant k and the temperature T . Taking the multiple elementary motor model of the OHC wall into consideration [13], an axial length change as a function of the alternating receptor potential ΔV_r is given by:

$$\Delta l_{OHC} = c_0 L_0 N \left(\frac{1}{1 + e^{-\Delta V_r a_0 + b_0}} - \frac{1}{1 + e^{b_0}} \right) \quad (2)$$

with $L_0 = 55 \mu\text{m}$ the OHC (quiet)-length, $N = 80 \mu\text{m}^{-1}$ the packing density of elementary motors and three constants $a_0 = 0.009 \text{ mV}^{-1}$, $b_0 = 1.45$ and $c_0 = 0.18 \text{ nm}$. Figure 4 shows the asymmetrical transfer function of the OHC length change Δl_{OHC} as a function of the stereocilia displacement, which may be approximated by a linear function of slope $s = 2$, equivalent to the gain, g , in its origin.

According to the low frequency cut-off of the receptor potential of the mammalian OHC, filters with different low frequency cut-offs were included in the feedback path of the active system. Though the stability of the system depends on this parameter, the results shown in figures 7–9 are calculated without the use of frequency-limiting filters.

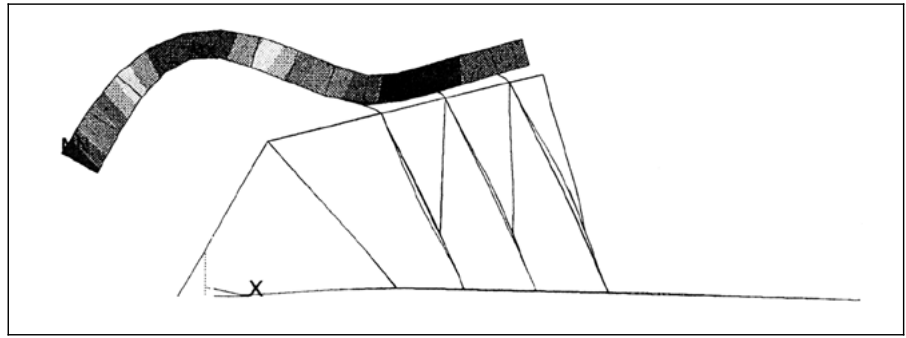


Fig. 5. Displaced structure (first eigenfrequency $f_1 = 3,585.7$ Hz).

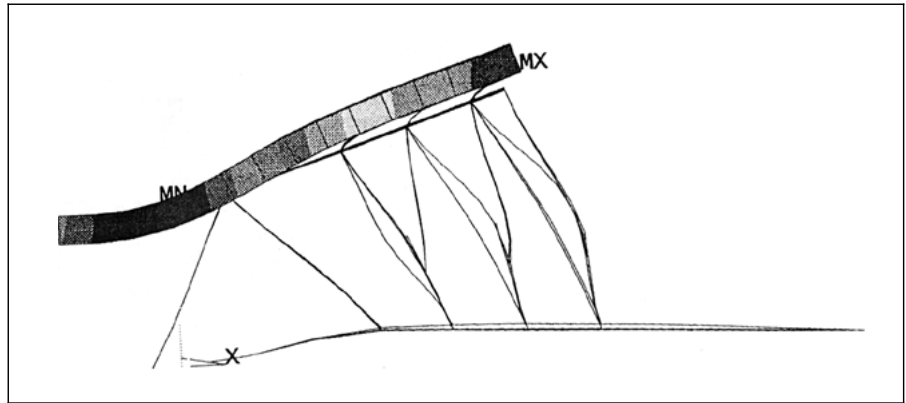


Fig. 6. Displaced structure (second eigenfrequency $f_2 = 6,841.8$ Hz).

Results

Modal Analysis

In order to calculate eigenfrequencies and eigenvalues of the system with 8 OHCs, a damped modal analysis is used. The damping is included by material damping for all elements (damping factor $\beta = 10^{-5}$). Figure 5 shows the displaced system (eigenvalues) for the first eigenfrequency ($f_1 = 3,585.7$ Hz). The displacement of the BM towards scala vestibuli (up) results in the stereocilia heads being deflected to the left (negative x -direction), whereas the direction of the stereocilia heads deflection is reversed when the eigenvalues of the second mode ($f_2 = 6,841.8$ Hz) are used (fig. 6). This result is in agreement with the former proposal of Zwislocki [14], who suggested a phase reversal by interpreting neurophysiological data. As shown in figure 6, the displacement of the TM in z -direction is maximal at the place of the stereocilia of the inner hair cell. This result may differ if additional coupling structures are included here. Hints for this anatomical detail concerning the coupling of the stereocilia of inner hair cells to Hensen's stripe of the TM were given by Lim [15], but the real in vivo conditions remain controversial, at least for the human cochlea.

Transient Computation

In figures 7–9, respectively, the displacements of the RL (z -direction, near the outermost OHC, gray), the displacements of the BM (z -direction, center of the BM plane, black), and the horizontal deflection of the stereocilia head of an OHC (x -direction, light gray) are shown in case of a switched sinusoidal excitation ($L = 40$ dB SPL). In the passive case, using the frequency $f_{ext} = 1,000$ Hz (fig. 7), the deflection of the BM towards scala vestibuli (up) results in a deflection of the stereocilia head to the right (positive x -direction); this corresponds with the classical shearing between TM and RL originally proposed by ter Kuile [16] and given later in a clear representation [17]. In this passive case, with the frequency of excitation below the first eigenfrequency, the amplitude of the RL displacement is 0.22 nm.

When the organ is excited with an external signal of the first eigenfrequency ($f_1 = 3,585.7$ Hz), the amplitude of the RL displacement increases to 1.5 nm due to resonance and the displacement of the stereocilia head changes its sign relative to the BM displacement in the z -direction (fig. 8). When the activity of the OHC is considered, a further increase of the RL displacement (40 dB, amplitude = 160 nm) results (fig. 9), and a considerable amount of dis-

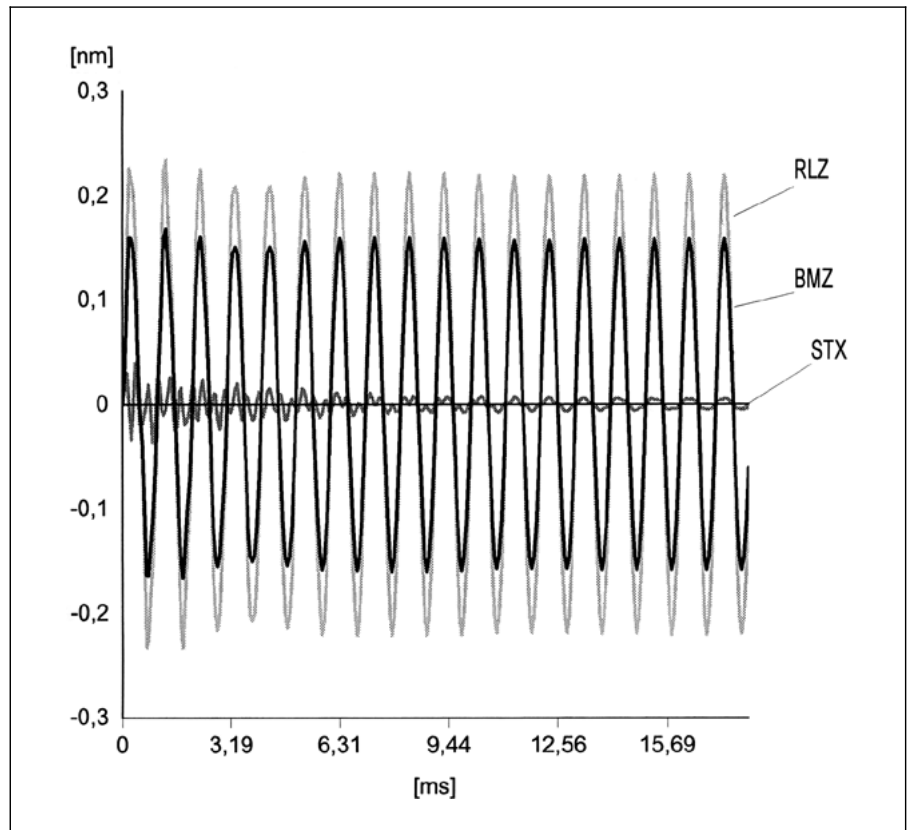


Fig. 7. z-Displacement of the BM (BMZ), RL (RLZ) and x-displacement of St (STX) for $f_{ext} = 1,000$ Hz of the passive OC.

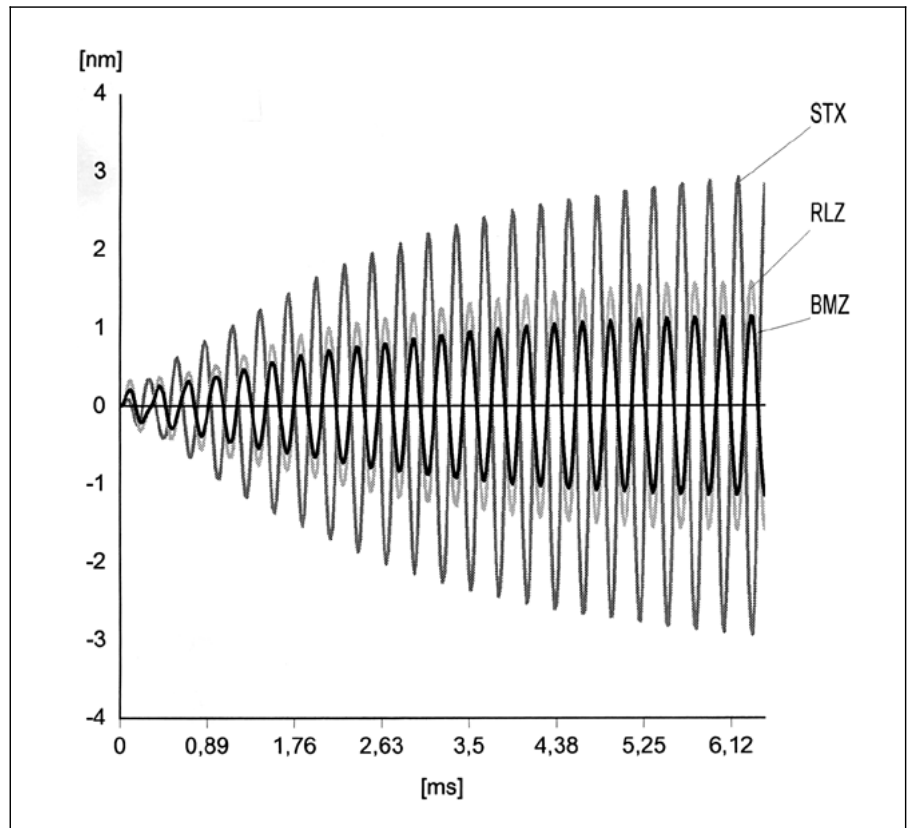


Fig. 8. z-Displacement of the BM (BMZ), RL (RLZ) and x-displacement of St (STX) for $f_{ext} = 3,585.7$ Hz of the passive OC.

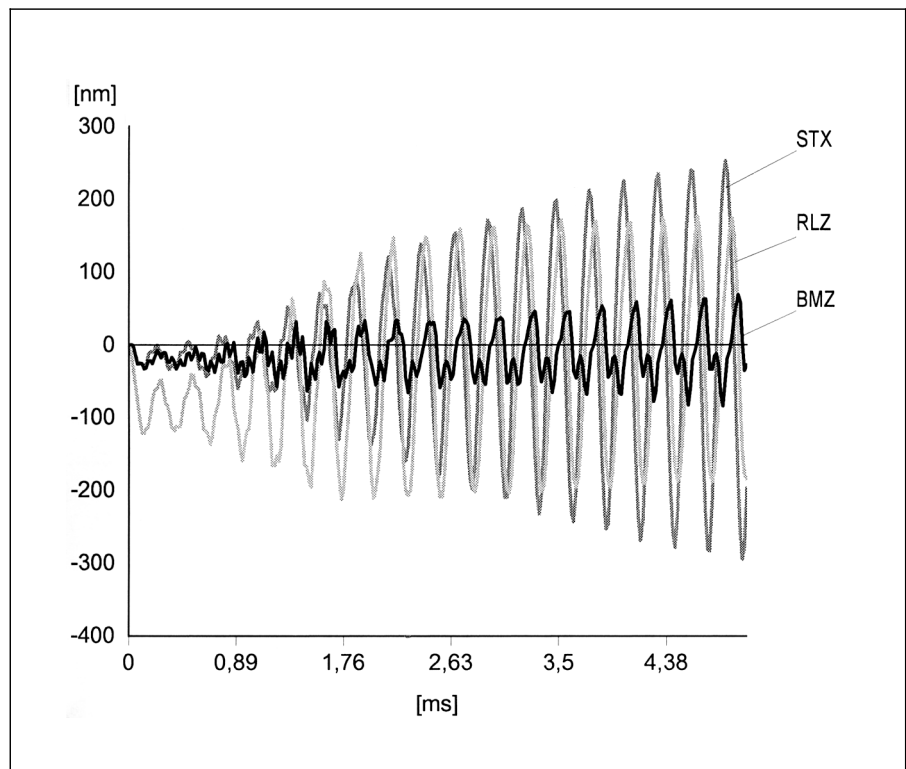


Fig. 9. z-Displacement of the BM (BMZ), RL (RLZ) and x-displacement of St (STX) for $f_{ext} = 3,585.7$ Hz of the active OC.

tortion, especially of the BM motion, can be seen. Thus, the displacement of the OC is amplified and distorted by the active processing of the OHC.

Discussion

The results of this study support the hypothesis of the cochlear amplifier [18, 19]. The inclusion of the OHC as active mechatronical elements in a FE model produces a 40 dB amplification of the displacement of the OC. This amplification is achieved though the OHC gain (or mechanomotility) is only $g \approx 2$. In order to explain this, it may be useful to consider the involved energies. While only a small amount of energy is necessary to displace the heads of the stereocila bundle, considerably more energy is needed to displace the whole OC. Because the cochlear partition realizes a positive feedback system for specific places and frequencies, an amplification of energy occurs. As a result, the activity enables the OC to overcome internal friction and viscous forces; this is a necessity for hearing at very low sound pressure levels. The energy is provided by the biological battery located in the stria vascularis.

The amplification is reduced by the destruction or pathologies of the OHC. This is in agreement with cochlear hearing losses when the OHC are damaged and fail to amplify. The psychoacoustic consequences are threshold increase and loudness recruitment. Though the non-linear OHC transduction process is considered in this study, the resulting nonlinearity could only be presented very roughly in form of the distorted time signal (fig. 9). To further our understanding of how the OC components function, spectral analyses, variations of the external levels and nonlinear oscillations need to be studied.

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