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Basilar Membrane and Reticular Lamina Motion in a Multi-Scale Finite Element Model of the Mouse Cochlea

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Abstract. A multi-scale finite element (FE) model of the mouse cochlea, based on its anatomy and material properties is presented. The important feature in the model is a lattice of 400 Y-shaped structures in the longitudinal direction, each formed by Deiters cells, phalangeal processes and outer hair cells (OHC). OHC somatic motility is modeled by an expansion force proportional to the shear on the stereocilia, which in turn is proportional to the pressure difference between the scala vestibule and scala tympani. Basilar membrane (BM) and reticular lamina (RL) velocity compare qualitatively very well with recent *in vivo* measurements in guinea pig [2]. Compared to the BM, the RL is shown to have higher amplification and a shift to higher frequencies. This comes naturally from the realistic Y-shaped cell organization without tectorial membrane tuning.

INTRODUCTION

Thousands of hair cells, embedded in the organ of Corti (OoC), are thought to amplify/detect sub-micron basilar membrane (BM) displacements. It is generally considered that the electromotility of the outer hair cells (OHCs) results in an amplification of BM motion [1]. The highly structured 3D orientation of the OHCs in relation to their surrounding supporting cells could play an important role in this amplification. An interesting geometrical feature is a lattice of Y-shaped structures between the reticular lamina (RL) and BM (Fig. 1C), formed by tilted electromotile OHCs and differently angled passive phalangeal processes (PhPs) connected to the BM through the Deiters cells (DC) [6]. In the feedforward/feedbackward (FF/FB) theory, it is hypothesized that this Y-shaped structure plays a key role in distributing forces that profoundly affect the cochlear amplifier [7, 8].

The goal of this paper is to test this hypothesis without using FF/FB but by modeling the cells explicitly. Therefore a multi-scale model is developed. In this model a macroscopic part, consisting of the fluid and membrane domains, is fully coupled with a microscopic OoC. As a first approximation, the modeled OoC consists of 1 row of OHCs, connected by PhPs forming the Y-shaped structures. Consequently, we do not only obtain results for BM displacement, but we can also calculate RL displacements. Moreover, when OHC force is activated, it does not only act on the BM, but also RL magnitude and phase is expected to change. Recently, this RL motion was measured simultaneously with the BM [2,3]. A good correspondence between the model results of the BM and the RL, to corresponding measurements would further strengthen the hypothesis that the Y-shaped elements of the OoC play a critical building block for the cochlear amplifier.

MATERIAL AND METHODS

A multi-scale finite element (FE) model of the mouse cochlea, based on its anatomy and realistic material properties is developed using COMSOL Multiphysics 4.4 (Fig. 1). The FE model is solved in the frequency domain. A three-dimensional (3D) unrolled box model of the mouse cochlea is used as the macroscopic part (Fig. 1A, B) of this multi-scale model. Notice the use of symmetry in the box model (Fig. 1A) to decrease the degrees of freedom by half and thus improve computational time by a fourth from that of the full model. In this macroscopic model a fluid domain for the fluid-filled scalae is fully coupled with the solid domain. Linearized Navier-Stokes equations are solved close (~20 um) to the BM to obtain the viscous damping. In the remainder of the fluid domain, Helmholtz equations are used to further reduce the computational cost. The solid domain consists of shell elements for the BM (orthotropic), RL and round window (RW) membrane. The surroundings of the OoC, situated in between the BM

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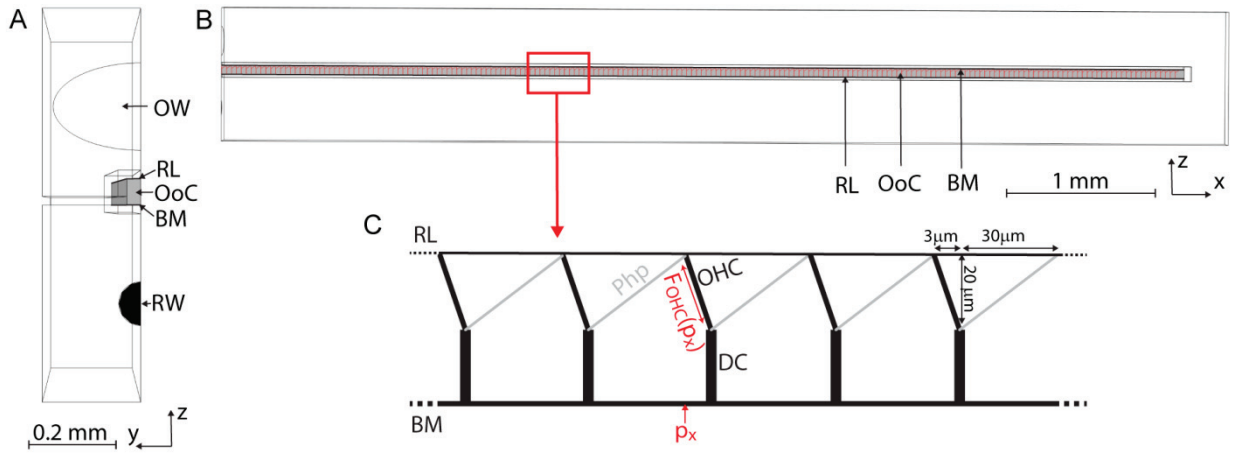

FIGURE 1. Overview of FE model geometry: (A) Radial side view and (B) longitudinal side view of the macroscopic box model with symmetry used in the y-direction. (C) Microscopic OoC model showing a simplified representation of the cytoarchitecture. The apically directed OHC expansion force $F_{OHC}(p_x)$ is linear with pressure on the BM at position x.

TABLE 1. Overview of material parameters used in FE model for solid/shell materials, beam elements and fluid domain. Density (ρ) and elastic parameters are given for solid materials. For shell elements also the thickness is given. Orthotropic parameters are given for the BM (see Fig. 1 for x, y, z directions), arrow indicates changing values going from base to apex. Macroscopic OoC is nearly incompressible (K-modulus = 2.2 GPa). Beam elements have a pipe cross section with inner (r_{inner}) and outer (r_{outer}) radius. Fluid parameters are speed of sound (c), dynamic viscosity (μ) and density (ρ).

Solid/shells	**E-modulus (MPa)**	**ν**	**G-modulus (MPa)**	**Thickness (um)**	**ρ (kg/m^3)**
BM	[0.5,100→ 10,0.5]	[0,0,0.5]	[1e-2, 10→1,1e-4]	15→ 5	1000
RL	1	0.3		0.1	1000
RW	10+5i	0.4		10	1000
Macro OoC	3e-6		1e-6	n/a	1000
Beam elements	**E-modulus (MPa)**	**ν**	**r_{outer} (um)**	**r_{inner} (um)**	**ρ (kg/m^3)**
OHC	0.1	0	2.5	2.5-25e-3	1000
PhP	1e3	0	1	-	1000
DC	10	0	3.5	3.5-25e-3	1000
Fluid	**c (m/s)**		**µ (Pa s)**		**ρ (kg/m^3)**
Water	1484		7e-4		1000

and RL, are simulated as a gelatinous nearly incompressible but highly compliant solid box, attached to the BM and RL with a height of 60 um. As input to the model, a planar sinusoidal pressure wave (1 Pa) is presented at the oval window (OW). Output velocities are normalized by the OW velocity. An overview of the material parameters is given in Table 1. Material parameters were not fine-tuned at this stage because the model will be compared with guinea pig data [2].

Next, a microscopic model of the key cells that determine the behavior of the OoC is added. As a first approximation a single row of 400 overlapping Y-shaped elements is considered (2 times as much OHC as shown in Fig. 1C). Cells are modeled as beam elements to drastically reduce the number of degrees of freedom and computational cost. Material parameters used in the microscopic model are summarized in Table 1. OHC somatic motility is modeled by expanding OHCs. The expansion force is linear with the shear on the stereocilia. Since stereocilia and tectorial membrane (TM) are not modeled explicitly, this ciliary shear was approximated by the pressure difference over the BM at that longitudinal position [6], resulting in following expansion force at a given

position x: $F_{OHC}(x) = \alpha * p_x * length_{cochlea} / \#OHC * widthBM/2$, with gain factor α that depends on the input SPL (e.g., 0 for high input level corresponding to the passive case, 0.05 for medium input level, 0.1 for low input and high amplification), p_x pressure at longitudinal position x, $length_{cochlea}$ equals 6.5 mm and number of OHCs equals 400. The microscopic model (beam element displacement) is fully coupled to the macroscopic OoC. Consequently, an OHC expansion will change the RL and BM displacement and fluid pressure in the macroscopic model. BM and RL velocities are recorded at the 'middle turn' (4 mm from the base), normalized to OW velocity, and presented for different frequencies in the following results section.

RESULTS AND DISCUSSION

Magnitude and phase for BM and RL velocity of the model (left panels) are presented in Figs. 2-4 and compared to published guinea pig data (right panels) [2]. Displacement results of Chen et al. [2], measured at the base, are presented as normalized velocity (divided by input pressure). Notice the bigger frequency interval chosen for the model plots in A to allow comparison across a wider frequency range for the two different mammals (BM and RL from the same animal was not available). Good comparison is obtained between model and experimental BM results for both zero and high amplification (Fig. 2, solid line and Fig. 3). The first conclusion is that our simple model based on physical parameters and with the Y-shaped structures included allows us to get good correspondence with *in vivo* data (and with previous published FF/FB [6]) for the BM motion in the active and passive cochlea.

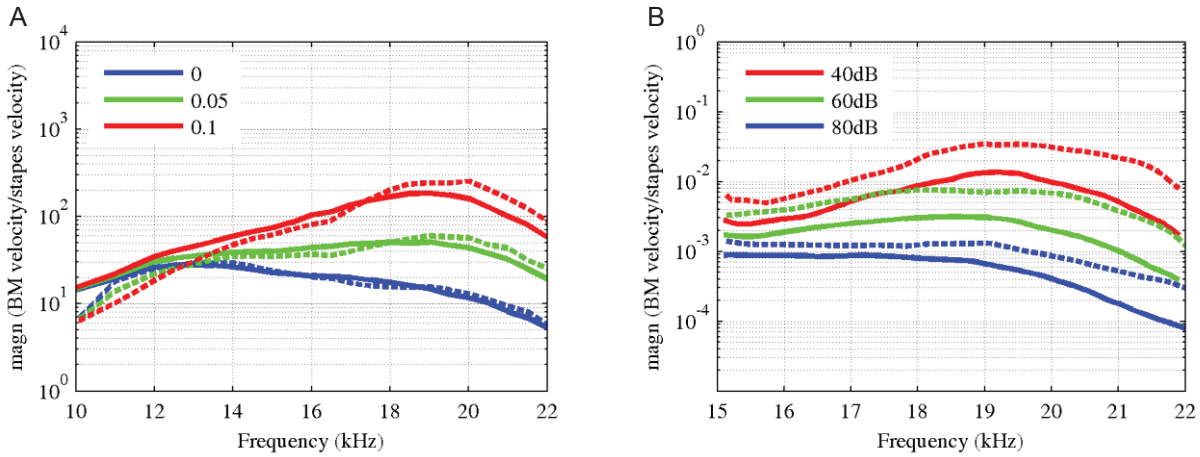

FIGURE 2. [Color version of figure available online] Velocity gain of (A) model and (B) experiments [2] for BM (solid line) and RL (dashed line). Important features for BM when going from passive to the active case include the amplification (20dB in model, 23dB in experiment), smaller peak at higher amplification and the shift to higher frequencies of the best frequency (BF) (BF = 13kHz → 19kHz in mouse model, BF = 16kHz → 19.3 kHz in GP experiment). At first sight, RL curves look similar to BM curves, but a close comparison of the RL magnitude to the BM, Chen et al. (2011) [2] (B) show a higher amplification in the active model (1.7 to 3 times, 5-10 dB) and a shift to higher frequencies of approximately 500 Hz. This amplification (1.4, 2.8dB) and shift (1000Hz) are also found in our model (A).

Novel in the present modeling approach is the possibility to calculate RL motion. At first sight, RL curves look similar to BM curves, but small and interesting differences are observed in Figs. 2 and 4. Important features, described by Chen et al. (2011) [2], are the larger RL magnitude compared to BM and the higher BF for RL than for BM. Interestingly, our simple modeling approach also allows us to describe similar differences. . Chen et al. (2011) [2] hypothesized that an important factor for this enhanced reticular lamina motion generated may be the interaction between the TM and OHC stereocilia and resonant motion that enhances these stereociliary deflections. The amplification in our model does not include these interactions between TM and stereocilia or any additional TM or OHC tuning (e.g. in [4, 5] the stereocilia of the OHC are tuned about an octave lower than the BM). The present more physicaly based model is able to describe BM and RL displacement quite well by only including the (Y-shaped) cellular structure and a simple OHC expansion force.

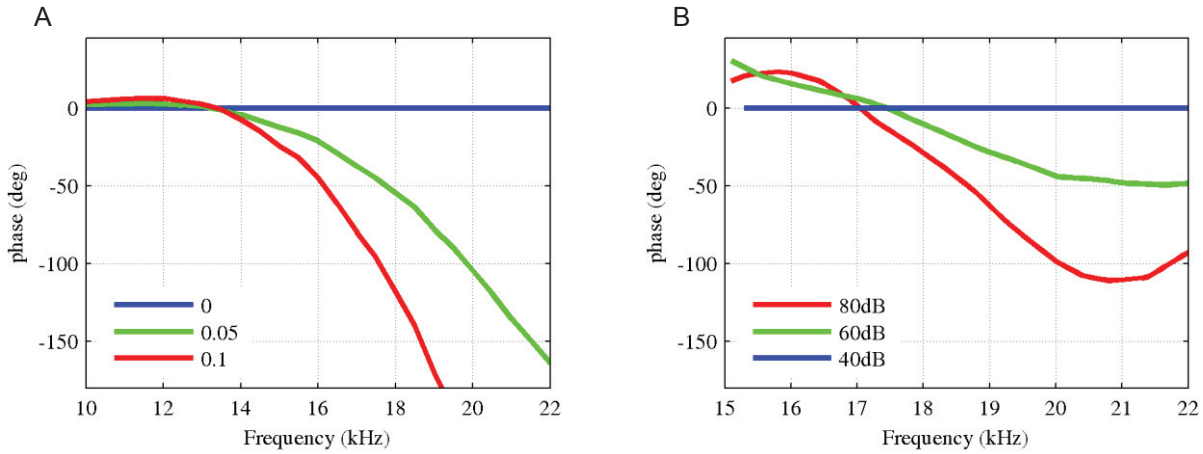

FIGURE 3. [Color version of figure available online] (A) Model and (B) experimental [2] results for BM velocity phase versus passive BM velocity. A trivial consequence is the zero line for the 'no amplification' case. In both model and experiment, phase of amplified model leads versus the passive model for frequencies lower than BF (~13 kHz for mouse, ~17 kHz for GP), and a lag is observed for higher frequencies. The travelling wave in our model is slower, resulting in more phase accumulation after BF.

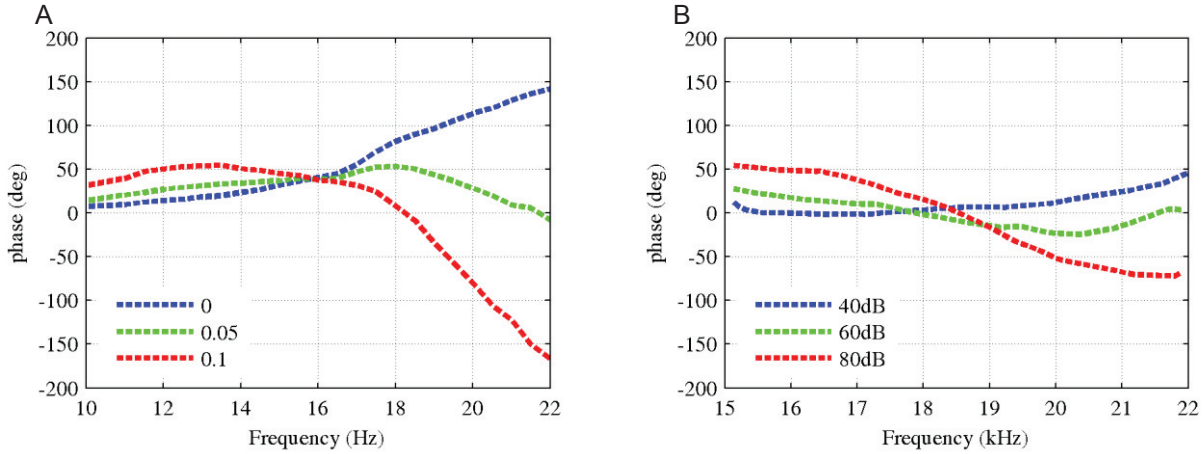

FIGURE 4. [Color version of figure available online] (A) Model and (B) experimental results for RL velocity phase versus passive BM velocity. In the passive case, RL phase always leads the BM phase. In both experiment and model the RL phase in the active case leads the RL phase before BF and a part after BF (in model till 16 kHz for a BF of 13 kHz; in experiment: till 18.5 kHz for a BF of 16 kHz;).

CONCLUSIONS AND FUTURE DIRECTIONS

Our multi-scale computer model of the cochlea based on realistic mechanical parameters and an explicitly solved and fully coupled OoC allows us to model the well-known BM displacements. Novel in this study is the possibility to calculate the recently measured RL motion [2]. A qualitative correspondence is obtained without assuming any OHC or TM tuning. This shows the possible importance of OoC cytoarchitecture in the function of the cochlear amplifier.

In future we plan to compare quantitatively our model with measurements in mice. Next, we want to add more detail into our cochlea, including a more realistic box model, a more realistic OoC with 3 rows of OHC (recently obtained in [6]), tunnel of Corti and TM mechanics. We also hope to reduce the excess phase accumulation observed in the current model.

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COMMENTS AND DISCUSSION

Lisa Olson: The paper is well written and it's been great to see the development of this model. I have a question about one of the model predictions. Figure 3 shows BM velocity phase for several SPLs in experiment (right) and for a range of OHC force constants in theory (left). The agreement is not good. In the experimental result (right), at the low-SPL best frequency of ~ 19 kHz, the phase has advanced about 60 degrees more at low than at high SPL. In contrast, in the theoretical curve, at the ~ 19 kHz BF the phase advance with increased OHC forcing is much greater: ~ 170 degrees. Thus, the level-dependence of the dispersion in the model is much greater than what is observed in the data. Is this an intrinsic and important property of the model — is this level-dependent dispersion at the heart of how the model is working?

Joris Soons [reply to Lisa Olson]: Thanks for your comment. In general the phase accumulation in our model is approximately double of this measured in experiments (both for the passive and active case, this is actually similar as for instance shown in Fig. 3 of Yoon et al. 2011, doi:10.1016/j.bpj.2010.11.039).

We think we can overcome this issue in future by including more realism by adding the tunnel of Corti and two zones for the basilar membrane (arcuate and pectinate). It is true that level-dependent dispersion have a lot of information in how the traveling wave in amplified. We that think if we could solve for this high phase accumulation in the model, model and experiment would compare much better (this is something we definitely have to test). Nevertheless, our simple model (1 row of Y-shaped structures) already shows some important correspondence with experiments (without assuming any additional OHC or TM tuning), for instance: magnitude of both BM and RL look qualitatively similar as in experiment; phase of the active BM leads passive BM before CF and lags behind CF. We also get a shift for the junction from 14 kHz for the BM to 16 kHz for the RL. We hope this adequately addresses your question. — Joris Soons et al.