IS THE OUTER HAIR CELL WALL VISCOELASTIC?

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1 Introduction

A growing body of evidence suggests that the cochlear outer hair cell (OHC) contributes to the active feedback process in the mammalian cochlea. The OHC is a hydrostat [1]: its lateral wall is both elastic and mechanically reinforced and its shape is maintained by a pressurized fluid core. Mechanical properties of the OHC wall have been both modeled and measured [2–5]. In particular, Brundin and Russell [6] subjected isolated OHCs to mechanical stimuli and found that OHC deformations could be described in terms of a damped mechanical oscillator. Our goal is to determine whether the damping results from either (i) the viscosity of the cytoplasm and the surrounding fluid as suggested by Tolomeo [7] or (ii) the cell wall which may possess the characteristics of a viscoelastic material or (iii) both.

2 Theory

The Brundin and Russell [6] experiment is difficult to model because the mechanical stimuli is an oscillating water jet aimed at the lateral wall. We, thus, consider an isolated OHC as cylindrical viscoelastic membrane of length, l_0, and radius, r_0, with one fixed closed end and an applied sinusoidal force at the other closed end. This model can be adapted to analyse the experiments described in this book by Hemmert *et al.* [8] The viscoelastic OHC wall incorporates the effects of membrane viscosity [9] together with a model of a cylindrical elastic membrane [2]. The longitudinal membrane tension is balanced by the fluid stresses from inside and outside the OHC. Our analysis differs from the approach taken by Jen and Steele [10]. A slender body perturbation approximation [11] based on the OHC aspect ratio, $\epsilon = r_0/l_0$, is used to determine equations for the longitudinal tension and pressure difference across the membrane.

2.1 *Fluid analysis*

The fluid inside and outside the OHC is modeled by the normalized unsteady axisymmetric Stokes equations:

$$St\frac{\partial u_z}{\partial t} = -\epsilon\frac{\partial p}{\partial z} + \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u_z}{\partial r}\right) + \epsilon^2\frac{\partial^2 u_z}{\partial z^2}$$

$$St\frac{\partial u_r}{\partial t} = -\frac{1}{\epsilon}\frac{\partial p}{\partial r} + \frac{\partial}{\partial r}\left(\frac{1}{r}\frac{\partial(ru_r)}{\partial r}\right) + \epsilon^2\frac{\partial^2 u_r}{\partial z^2}$$

$$\frac{1}{r}\frac{\partial(ru_r)}{\partial r} + \frac{\partial u_z}{\partial z} = 0$$

where $St = \omega {r_0}^2/\nu$ is the Stokes number; ω is the frequency of the disturbance; $\nu = \tilde{\mu}/\rho$ is the kinematic viscosity of the fluid. The fluid boundary conditions are related to the displacement of the membrane:

$$u_z = 0 \text{ at } z = 0; u_z = \frac{\partial \delta_z}{\partial t} \text{ at } z = 1; u_r = \frac{\partial \delta_r}{\partial t} \text{ at } r = 1; u_z = \frac{\partial \delta_z}{\partial t} \text{ at } r = 1$$

where δ_z and δ_r are the normalized longitudinal and radial displacement of the elastic cylinder respectively. The symmetry boundary condition is applied at $r = 0$ inside the cell and at $r = a$ outside the cell. At $r = 1$, the normalized fluid stress is:

$$\tau = \pm\left(\frac{\partial u_z}{\partial r} + \epsilon^2\frac{\partial u_r}{\partial z}\right)$$

where the sign indicates whether the fluid is inside or outside the cell.

Since we are modelling the response of the OHC to a sinusoidal force applied at $z = 1$, we consider harmonic oscillations:

$$u_r = U_r e^{\imath t}; u_z = U_z e^{\imath t}; p = P e^{\imath t}; \delta_z = \Delta_z e^{\imath t}; \delta_r = \Delta_r e^{\imath t}$$

The OHC aspect ratio, ϵ, is chosen as the perturbation parameter so that variables, U_r, U_z and P can be expanded in a power series in ϵ: $Y = Y_0 + \epsilon Y_1 + \epsilon^2 Y_2 + \ldots$. The superscripts I and E pertain to variables inside and outside the OHC respectively. Then in the limit as $a \to \infty$, the leading order expressions up to and including $O(\epsilon)$ for the fluid pressure and stress at $r = 1$ inside and outside the cell are:

$$\frac{d^2 {P_0}^I}{dz^2} = \frac{\imath {\beta^I}^2}{\epsilon} \frac{\left(Q^I \frac{d\Delta_z}{dz} + \Delta_r \right)}{\left(\frac{1}{2} - Q^I\right)}; \qquad \tau^I = -Q^I \left[\epsilon \frac{d{P_0}^I}{dz} + \imath {\beta^I}^2 \Delta_z \right]$$

$$\frac{d^2 {P_0}^E}{dz^2} = \frac{\imath {\beta^E}^2}{\epsilon} \frac{\left(Q^E \frac{d\Delta_z}{dz} - \Delta_r \right)}{\left(\frac{a^2-1}{2} - Q^E\right)}; \quad \tau^E = -\frac{\tilde{\mu}^E}{\tilde{\mu}} Q^E \left[\epsilon \frac{d{P_0}^E}{dz} + \imath {\beta^E}^2 \Delta_z \right] \tag{1}$$

where

$$Q^I = \frac{I_1(\beta^I)}{\beta^I I_0(\beta^I)}; \quad Q^E = \frac{K_1(\beta^E)}{\beta^E K_0(\beta^E)}; \quad \beta^I = e^{\imath\pi/4}\sqrt{St^I}; \quad \beta^E = e^{\imath\pi/4}\sqrt{St^E}$$

where I_n and K_n are the nth order modified Bessel functions of first and second kind respectively.

2.2 Membrane analysis

The normalized tensions, T_θ and T_z, are related to the fluid pressure and wall shear stress from inside and outside the OHC:

$$T_\theta = ({P_0}^I - {P_0}^E); \quad \frac{dT_z}{dz} = -\frac{1}{\epsilon}\left(\tau^I + \tau^E\right) \tag{2}$$

The membrane undergoes strains given by $e_\theta = \delta_r$ and $e_z = d\delta_z/dz$ which are related to the membrane tensions by a viscoelastic model[9]:

$$\begin{bmatrix} \Delta_r \\ \frac{d\Delta_z}{dz} \end{bmatrix} = \frac{\mathcal{T}}{\mathcal{D}} \begin{bmatrix} \mathcal{A} & -\mathcal{B} \\ -\mathcal{B} & \mathcal{A} \end{bmatrix} \begin{bmatrix} T_\theta \\ T_z \end{bmatrix} \tag{3}$$

where $\mathcal{A} = K + \mu + \imath\omega(\kappa + \eta)$; $\mathcal{B} = K - \mu + \imath\omega(\kappa - \eta)$; $\mathcal{D} = 4(K + \imath\omega\kappa)(\mu + \imath\omega\eta)$; $\mathcal{T} = \tilde{\mu}\omega l_0$; K and μ are the elastic area and shear moduli respectively; κ and η are the wall area and shear viscosities respectively.

2.3 Solution

If $P_0 = {P_0}^I - {P_0}^E$ then eqs. (1) through (3) are combined to describe the fluid-membrane interaction problem:

$$\frac{d^2}{dz^2} \begin{bmatrix} T_z \\ P_0 \end{bmatrix} = M \begin{bmatrix} T_z \\ P_0 \end{bmatrix} \tag{4}$$

The boundary conditions at $z = 0$ and $z = 1$ are:

$$\left.\frac{dP_0}{dz}\right|_{z=0} = \left.\frac{dT_z}{dz}\right|_{z=0} = 0; \left.\frac{dP_0}{dz}\right|_{z=1} = -\frac{\imath\gamma{\beta^I}^2 \left.\Delta_z\right|_{z=1}}{\epsilon}; \left.P_0\right|_{z=1} - 2\left.T_z\right|_{z=1} = F \tag{5}$$

where $\gamma = 1 + \frac{{\beta^E}^2}{{\beta^I}^2}\frac{(2Q^E+1)}{(a^2-1-2Q^E)}$; $\left.\Delta_z\right|_{z=1}$ is obtained from eq. (3); F is the normalized sinusoidal force applied at $z = 1$. If ${\lambda_1}^2$ and ${\lambda_2}^2$ are the eigenvalues of M and

$$\begin{aligned}
R_{11} &= \sinh\lambda_1 \left[\frac{\mathcal{T}\imath{\beta^I}^2\gamma(\mathcal{A}(M_{22}-{\lambda_1}^2)+\mathcal{B}M_{21})/\mathcal{D} - \epsilon M_{21}{\lambda_1}^2}{\lambda_1}\right] \\
R_{12} &= \sinh\lambda_2 \left[\frac{\mathcal{T}\imath{\beta^I}^2\gamma(\mathcal{A}(M_{22}-{\lambda_2}^2)+\mathcal{B}M_{21})/\mathcal{D} - \epsilon M_{21}{\lambda_2}^2}{\lambda_2}\right] \\
R_{21} &= 2\cosh\lambda_1\left(2(M_{22}-{\lambda_1}^2)+M_{21}\right) \\
R_{22} &= 2\cosh\lambda_2\left(2(M_{22}-{\lambda_2}^2)+M_{21}\right)
\end{aligned}$$

then, with a pressure of n Nm^{-2} at $z = 1$, we obtain the dimensional OHC displacement, ${\delta_z}^* = l_0\delta_z$:

$$\left.{\delta_z}^*\right|_{z^*=l_0} = \frac{2n{r_0}^2 M_{21}\sinh\lambda_1\sinh\lambda_2({\lambda_1}^2-{\lambda_2}^2)(\mathcal{A}M_{22}+\mathcal{B}M_{21})}{\mathcal{D}\lambda_1\lambda_2\det(R)} \tag{6}$$

3 Results

In our simulations, $r_0 = 5\mu$m which is a typical OHC radius; $\mu = 0.007$ Nm^{-1} and $K = 0.07$ Nm^{-1} are the OHC elastic moduli [2]; $\tilde{\mu}^E = 10^{-3}$ kgm^{-1}s^{-1} and $\rho^E = 10^3$ kgm^{-3} by assuming that the external fluid is similar to water; $\tilde{\mu} = 3\tilde{\mu}^E$ and $\rho^I = 1.06\rho^E$ by assuming that the cytoplasm is more viscous and denser than the surrounding fluid. Figure 1 shows the displacement of the OHC for lengths in the range $20-80\mu$m for a purely elastic wall; the OHC response is similar to the simulations of Tolomeo [7] in which the mechanical stimulus was applied uniformly on the lateral wall. The flat low frequency asymptote is numerically equal to the static displacement value of $2nr_0l_0/(9\mu+K)$. Figure 2a shows the effect of wall shear viscosity on the displacement of a 60μm long OHC for values of $\eta = 0, 10^{-8}, 10^{-7}$ and 10^{-6} Nsm^{-1}. Evidently as η increases, the OHC peak displacement becomes diminished leading to a band pass filter behavior. Figure 2b shows the effect of η on the mechanical impedance, $Z = n\pi{r_0}^2/(\imath\omega\left.{\delta_z}^*\right|_{z^*=l_0})$, for a 60μm long OHC. The high frequency asymptote for $\eta = 0$ behaves like $\omega^{-1/4}$.

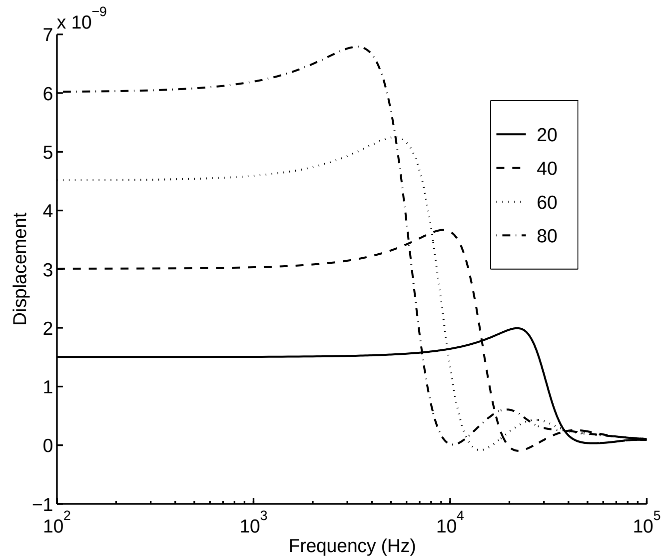

Figure 1: Displacement against frequency of applied pressure of magnitude 1 Nm^{-2} for purely elastic OHCs of length between 20μm (bottom) and 100μm (top).

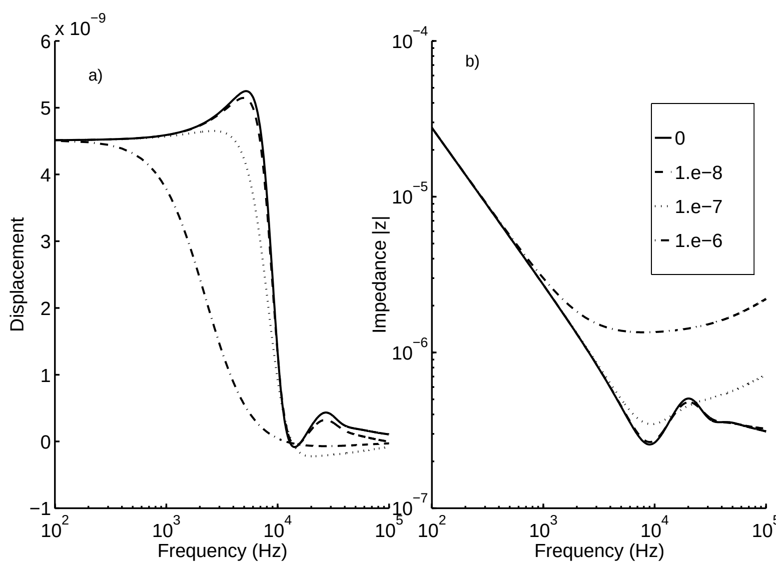

Figure 2: Effect of wall viscosity with $\eta = 0, 10^{-8}, 10^{-7}, 10^{-6}$ Nsm^{-1} on a) displacement and b) mechanical impedance for OHC of length 60μm.

4 Discussion

A model of the OHC viscoelastic wall has been developed to determine the nature of viscous damping in OHC motility. Results for a purely elastic wall suggest that when a mechanical stimulus is applied at one end of the OHC, a peak displacement is attained at a length-dependent frequency location. This location can be influenced by the choice of the membrane model. For example, a reduction in K and μ leads to a corresponding reduction in the break frequency location, which may explain why the break frequency data is an order of magnitude larger than that reported by Hemmert *at al.* [8] The highly organized structure of the OHC wall [5] suggests that the analysis may be improved if the isotropic model in eq. (3) is replaced by an orthotropic model. Results for a viscoelastic wall indicate that the peak displacement at the break frequency decreases with increasing wall shear viscosity resulting in a band pass filter for $\eta = 10^{-7}$ Nsm^{-1} which incidentally is an order of magnitude smaller than the value of red blood cell wall shear viscosity [9]. But if the OHC is to be mechanically tuned as suggested by Brundin and Russell [6], then the OHC wall shear viscosity has to be significantly smaller than that for the red blood cell (RBC). This suggests that the characteristic time, $t_c = \eta/\mu$, for the OHC is less than 10^{-4}s in contrast with 0.1s for the RBC [9]. Such a low value of t_c would allow the OHC wall to deform rapidly at acoustic frequencies. Also, η affects the behavior of the OHC mechanical impedance at high frequencies. However, when $\eta = 0$ the high frequency asymptote behaves like $\omega^{-1/4}$ in contrast with the $\omega^{1/2}$ behavior for the impedance on the wall of an infinite solid cylinder oscillating along its axis in an infinite fluid. This discrepancy may be attributed to the existence of the boundary layers of thickness $O(\epsilon)$ at $z = 0$ and $z = 1$; in these boundary layers, which become smaller for longer OHCs, the second order streamwise derivatives in the Stokes' equations become significant. It is, however, interesting to note that Hemmert *at al.* [8] encountered difficulties in measuring the impedance at frequencies above 5000 Hz probably due to both the vibration modes and the impedance of the atomic force cantilever which was applied at $z = 1$. In the present framework of our model, we conclude that viscoelastic effects may be significant at high frequencies.

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