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Elastic properties of organ of Corti tissues from point-stiffness measurement and inverse analysis

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Abstract

We describe a method to use point-stiffness (PtSt) measurements, i.e., indentation measurements, to obtain elastic moduli of different organ of Corti (OC) tissues. A detailed finite element (FE) model of the OC is used to account for geometric effects in the indentation measurements. We also present a sensitivity analysis, performed within a Bayesian estimation framework, that can be used to improve experimental design. The sensitivity analysis shows that the basilar membrane (BM) PtSt is most sensitive to changes in the BM properties and to changes in the pillar cells (PC) properties. This result suggests that the BM and the PC dominate the macromechanics of the OC. The most likely values of the Young's modulus predicted for the middle turn for the BM arcuate, BM pectinate, and the PC are found to be 935 KPa (range 640 kPa – 1360 KPa), 300 KPa (range 190 KPa – 460 KPa), and 3 GPa (range 1 GPa – 9 GPa), respectively.

Keywords

gerbil; cochlea; finite element; sensitivity analysis; Bayesian perspective

1. Introduction

Our understanding of the micromechanics of the organ of Corti (OC) is impeded by our ignorance of the mechanical properties of its constituents. Measuring those properties directly is challenging due to both the small size scales involved and their inaccessibility.

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Conflict of interest statement

None.

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One approach to circumvent this difficulty is to measure point-stiffness (PtSt) at accessible locations such as the basilar membrane (BM) or the reticular lamina (RL) in presence of the supporting cells of the OC. The PtSt measurement technique can be traced back to the experimental work of Von Bekesy (Bekesy, 1960), which was improved upon in (Gummer et al., 1981; Miller, 1985) for their work on guinea pig to determine BM stiffness profiles as a function of the deflection depth. This technique was used more recently in (Olson and Mountain, 1991; Naidu and Mountain, 2001) to determine PtSt of gerbil's BM. Their results showed a good correspondence between in situ and excised cochlea PtSt measurements exists. This indicates that excised cochlear PtSt measurements reflect the micromechanical properties of an intact cochlea.

A PtSt measurement can be interpreted as an indentation test to measure elastic properties. Mechanical properties of biological tissues are commonly determined by indentation methods. The method consists of using a force probe with specified tip geometry to create indentation in the tissue while measuring the displacement of the probe tip and the force exerted on the probe. The force-displacement data measured by indentation is related to the elastic properties of the tissue. Calibrating the force-displacement slope to extract Young's modulus (E) requires a reference mathematical solution. In most situations, the calibration constant is derived from the solution representing indentation of a homogeneous, linear elastic, isotropic, semi-infinite medium. In more complicated situations detailed finite element (FE) models can be used to calibrate force-displacement measurements that account for non-idealized geometries (Samani et al., 2001) and/or non-ideal material behavior (Zhang et al., 2008), or both (Cristofolini et al., 2010).

In the work described here, we use a geometrically detailed 3D FE solution of a piecewise homogeneous model of the gerbil cochlea. Our FE model represents several components with different elastic properties. Hence our model is complicated by the fact that we have several tissue types, each with its own set of material constants, interacting within the indentation region. Each indentation measurement, therefore, depends upon the (possibly distinct) elastic properties of several different tissues. In our "calibration," therefore, we must account for all these different tissue types, and must use several distinct indentation measurements simultaneously to relate the PtSt measurements to the tissue elastic moduli. This task is akin to solving an elastic inverse problem (cf. (Samani et al., 2001)), and we approach it in a Bayesian framework (Tarantola, 2005; Stuart, 2010). In the Bayesian framework, a posterior belief is updated based on prior beliefs and new evidence. In the current context, prior knowledge of the distributions of the moduli is used to obtain updated distributions based on new PtSt data.

2. Methods

The experimental measurements of the OC's PtSt performed in (Naidu and Mountain, 1998a) was simulated here using a 3D linear elastic isotropic FE model to determine the elastic properties of each individual structural component within the OC. The geometry of the model was based on direct measurements of anatomical features within the OC. The middle turn section of the gerbil cochlea around the 4 kHz place was modeled.

2.1. Representing the cochlear section geometry

In the present middle turn model the geometry is very detailed. It includes most of the known details of the OC and the interstitial space that are usually ignored in cochlear models. Figure 1 shows the dominant cochlear components in the cross section, all of which are represented in the FE model. In Fig. 2, a 3D view of the model shows the complete cluster of the structural components. More precisely, $N = 11$ components are modeled as described in Fig. 1 and Fig. 2.

All of the different tissues are represented as 3D isotropic elastic solids. In the cochlea, the basilar and tectorial membranes are fibrous with fibers arranged to give orthotropic properties. This fibrous feature is more pronounced in the basal part of the cochlear spiral, and diminishes in density as it progresses apically (Iurato, 1962). Naidu and Mountain (1998b) have studied the pattern of deflection of the BM and shown that the BM is nearly isotropic in the apex. Hence, the BM may be treated as isotropic in the apical turns. To a first approximation, the BM is modeled as an isotropic elastic solid for the present middle turn model of the cochlea.

The dimensions for the middle turn of the gerbil cochlea are listed in Table 1 with the data source. Several dimensions are estimated from stacks of images described in (Karavitaki and Mountain, 2007). The resolution of the image measurement is estimated to be 230 nm/pixel. Some parameters were derived from geometric constraints and are listed at the bottom of Table 1. The short section comprises 5 OHC and 5 PC in each row.

The actual volumes of the various components of the OC were matched in the FE-model using combinations of Boolean operations on primitive body shapes represented within ADINA (Bathe, 1986).

2.2. Experimental conditions and modeling assumptions

A sketch of the PtSt measurements in Fig. 3 shows the locations where stiffnesses were measured. Experimental PtSt data are available at two and three radial locations, respectively, when the OC is surgically removed from the BM (see Fig. 3 A) and when the OC lies on the BM (Fig. 3 B). They correspond to PtSt measurement location 1, under the BMAZ, location 2, under the HC, i.e., under the BMPZ, and location 3, under the PC when the OC is present, as shown in Fig. 3 B. A fourth location between location 2 and 3, under the DC/OHC, is used to validate the OC model. The PtSt values are summarized in Table 2. Measurements on the isolated BM were obtained for the middle turn and used to provide initial estimates of the E_s for the BM components.

Because of the small deflection and the low frequency (quasi-static) probe drive used in the experiment (Naidu and Mountain, 1998a), a linear and a quasi-static deflection of the drained OC can be used to simulate the stiffness experiment. A Poisson's ratio of 0.49 is chosen for the practically incompressible cellular component of the OC.

Because the probe deflection at a given point affects the surrounding region, the length of the model must be chosen to include this spread of the deformation. This non-locally reactive deflection is characterized by the space constant defined as the extent of the

deformation from its center. The short section length of $45.0 \mu\text{m}$ is greater than the experimental space constant of $32.8 \mu\text{m}$ measured in (Naidu and Mountain, 2001). Symmetric boundary conditions are used, thus doubling the effective length of the model. Hence, there are about three space constants within the total length of the model. This assures that the section is longitudinally coupled, as it is in the experiment.

Here, the force probe is not physically modeled. It is represented as a pressure load over an area with dimension equal to the probe tip, which was $10 \mu\text{m}$ in diameter.

2.3. Estimating Es from PtSt measurements

2.3.1. Bayesian description—The FE model of the middle turn of the cochlea requires as input the E-values of each constituent. By identifying the E-values that most closely predict the measured data, we thus infer the properties of the individual components. In order to quantify both the modulus estimate and confidence in those estimates, we chose to formulate this inverse problem in a Bayesian context (Tarantola, 2005; Stuart, 2010).

To that end, we assume that the errors in the measured PtSt values are independent, identically normally distributed with a standard deviation of $\mathbf{k} = [k_1, k_2, k_3]$ for the three stiffness measurements. Then we may write the likelihood function for the observed stiffness values $\mathbf{k} = [k_1, k_2, k_3]$ ($M = 3$) given the vector of individual moduli $\mathbf{E} = [E_1, E_2, \dots, E_{11}]$:

$$P(\mathbf{k}|\mathbf{E}) \propto \exp \left(-\frac{1}{2} \sum_{i=1}^M \left(\frac{1}{\Delta k_i} \right)^2 (k_i^{\text{target}} - k_i(\mathbf{E}))^2 \right). \quad (1)$$

Here, $k_i(\mathbf{E})$ is the function representing the predicted PtSt given the Es.

To build our prior expectations on the moduli, we choose the prior distribution of the moduli $P_0(\mathbf{E})$, to be log-normal, with prior standard deviation reflecting our confidence in their order of magnitude. Based on earlier measurements, we assume

$\ln(E_j/E_j^0) = \mathcal{N}(0, (1/\log_{10}(e))^2)$, giving an uncertainty of one order of magnitude in the prior E-values. Here, E_j^0 are our initial guesses/prior E-values for each tissue component.

Choosing our estimate as the maximizers of the posterior probability distribution of $\mathbf{E}$, $P(\mathbf{E}|\mathbf{k})$ (see Appendix A), leads to the following optimization problem in terms of $\mathbf{u}$ with components $u_j = \ln(E_j/E_j^0)$:

Find the state $\mathbf{u}$ which minimizes the function

$$\mathcal{O}(\mathbf{u}) = \sum_{i=1}^M \left(\frac{1}{\Delta k_i} \right)^2 (k_i(\mathbf{u}) - k_i^{\text{target}})^2 + \sum_{j=1}^N (\log_{10} e)^2 (u_j - u_j^0)^2 \quad (2)$$

The derivatives of $\mathcal{O}(\mathbf{u})$, $\nabla_{\mathbf{u}} \mathcal{O}$ where $\nabla_{\mathbf{u}}$ is the N-dimensional gradient operator with respect to the $\mathbf{u}$, must vanish. We solve for $\mathbf{u}$ by Gauss-Newton's method. Linearizing $\nabla_{\mathbf{u}} \mathcal{O}$ about $\mathbf{u}^0$ yields the following linear system of equations:

$$\sum_{j=1}^N (A_{pj} + (\log_{10} e)^2 \delta_{pj}) \delta u_j = b_p, \quad p=1, \dots, N \quad (3)$$

$$A_{pj} = \sum_{i=1}^M \left(\frac{1}{\Delta k_i} \right)^2 k_{i,p}^0 k_{i,j}^0 \quad (4)$$

$$b_p = - \sum_{i=1}^M \left(\frac{1}{\Delta k_i} \right)^2 (k_i^0 - k_i^{target}) k_{i,p}^0 \quad (5)$$

$$k_{i,p} = \frac{\partial k_i}{\partial u_p} = E_p \frac{\partial k_i}{\partial E_p} \quad (\text{no summation}) \quad (6)$$

δ_{pj} is the Kronecker delta representing the identity matrix components.

Note that the quantities $k_i^0 = k_i(\mathbf{u}^0)$ and $k_{i,p}^0 = k_{i,p}(\mathbf{u}^0)$, which appear in the linear system Eq. 3 are provided by the numerical sensitivity experiment which we describe later. This system is solved for the increment $\delta \mathbf{u}$. The resulting vector $\mathbf{u} = \mathbf{u}^0 + \delta \mathbf{u}$ provides a revised estimate of the distribution of Es within the OC. Hence, the solution to the problem of finding the Es distribution given the experiment PtSt is provided by the converged solution $\mathbf{u} = \mathbf{u}^*$.

Our posterior distribution of the Es is approximated by a log-normal distribution with statistics dependent on the prior and the experimental data. With this Gaussian approximation of the posterior distribution, the confidence interval in the result is estimated using the covariance matrix. These approximations are detailed in Appendix A.

2.3.2. Solution algorithm for PtSt mapping—The PtSt matching experiment proceeds as shown in the flowchart of Fig. 4. The optimization algorithm consists in performing the sensitivity analysis and solving the linear system to update E. The sensitivity is calculated by decreasing, one at a time, each component's E by 1%, the other moduli remaining constant, and performing the numerical stiffness experiment to calculate the change in PtSt. The optimization algorithm then uses these stiffness gradient values to adjust the Es to match the values of the experimental PtSt at the radial locations simultaneously. The model of the BM alone initializes the E-values for BM. The solution is found by using in model 2 of BM+OC these initial E-values for BM and the initial values of the OC components given in Table 3, and running the optimization until convergence is attained within predefined tolerances for the Es and the stiffness of $\varepsilon_E = 0.1$ and $\varepsilon_k = 0.01$, respectively.

A few iterations of the process are required to bring the relative change in each individual OC component's E, defined as e_E , within ε_E . Similarly, the relative change in the PtSt with

respect to the target PtSt is defined e_k to indicate how closely the target is matched. These changes are taken as a measure of the convergence errors, and they are expressed as:

$$e_{E_j} = \exp(\delta_{u_j}) - 1 \leq \varepsilon_E \quad (7)$$

$$e_{k_i} = \frac{k_i^{target} - k_i}{k_i^{target}} \leq \varepsilon_k, \quad (8)$$

where E_j and k_i are updated at each iteration.

3. Results

3.1. Distribution of E within the cochlear section

The distribution of E within the cochlear short section is summarized in Table 4. For the insensitive components, the minimum and maximum values for each component's E are, respectively, one order of magnitude less and greater than the mean estimate. They are in the same proportion as for the prior standard deviation. For the sensitive components, the BM and the PC, the extreme values of the E are on the same order of magnitude as the estimate, and thus result in a more precise prediction.

Three iterations of the algorithm were performed. Starting Young's moduli vector $\mathbf{E}^0$ at the first iteration is also given in Table 4. After the third iteration, the error e_E on the E of each component was brought to below $\varepsilon_E = 10\%$. The stiffness converged quickly to the experimental PtSt and the error e_k was brought to less than 1% for each component in only three iterations.

3.2. Sensitivity of the PtSt under the BM to changes in the E of the OC's components

The sensitivity function $\mathcal{S}$ is defined as the ratio of the relative change in PtSt k to the relative change in Young's modulus E . The corresponding sensitivity matrix is expressed in formula 9:

$$\mathcal{S}_{ij} = (\delta k_i / k_i^0) / (\delta E_j / E_j^0) \quad i=1, \dots, M \quad j=1, \dots, N, \quad (9)$$

where, indices are as previously defined. This matrix is updated at each iteration of the algorithm. The sensitivity function is plotted in Fig. 6 when convergence is reached. As shown in this figure, the three PtSt are mostly sensitive to changes in the BM and PC Es, with sensitivity value, expressed in percent, between 2% and 100%. On the other extreme, the cilia, with zero sensitivity value, does not affect PtSt measurements from the BM side.

The HC contribute slightly to the stiffness under BMPZ ($\mathcal{S} = 3.2\%$), barely influence the stiffness under the OPC foot (0.4%), but have almost no effect on the stiffness under the BMAZ (0.05%).

The sensitivity of the PtSt to the DC, the RL, the Ph, and the TM is less than 0.2%. The measurements are, therefore, nearly insensitive to these structures.

The OHC/IHC E affects the stiffness under BMPZ and under the OPC foot with sensitivity values 0.6% and 0.3%, respectively, but, the OHC/IHC play a lesser role in defining the stiffness under BMAZ (0.06%).

The OSL E appears to affect the PtSt under the OPC foot (0.4%) 10 times more than the PtSt under BMAZ (0.03%) and BMPZ (0.05%).

The PtSt is in general most sensitive to the elastic properties of the structures directly in contact with the probe. Under the OPC foot, the stiffness is largely sensitive to both BMAZ and PC, but about twice as sensitive to BMAZ (59%) as to PC (34%).

3.3. Model validation

In order to provide a validation for the OC model, we assign the converged values of the OC components' E, and we predict the experimental PtSt under the DC/OHC as described in the experimental condition's section.

The PtSt thus obtained from the OC model is $k_{DC/OHC} = 0.69$ N/m. The corresponding experimental value is given as previously mentioned: $k_4^{target} \pm \Delta k_4 = 0.55$ N/m $\pm$ 0.30 N/m. The model estimate of the PtSt under DC/OHC differs from the experimental mean value by only 0.14 N/m, corresponding to an overestimate of $e_k = 25\%$. Most importantly, the model prediction of the PtSt, $k_{DC/OHC}$, is well within the experimental measurement range of 0.25 – 0.85 N/m for this location.

Thus, based on the experimental PtSt measurements under the BM, we conclude that the OC model is valid.

4. Discussion

We have determined, based on experimental PtSt values measured across the BM, the distribution of Young's moduli within the middle turn section of the gerbil OC. This distribution displays the material heterogeneity within the OC associated with the spatial organization of cellular components. The mean value of E for the elastic materials ranges from 2.41 KPa to 10 GPa for the cochlea section studied. In particular, the E of the PC found using our sensitivity analysis method is 3 GPa (range 1 – 9 GPa). This value is comparable to the experimentally determined E value of 2 GPa from measurements of the PC microtubule bundles' stiffness in (Tolomeo et al., 1996).

The BM is considered to be the main mechanical component of the cochlea and has been studied in great detail. There is evidence that the BM microstructures comprise the ground substance and fibers and that the arrangements of the fibers in bundle and their density within the ground substance give structural rigidity (Iurato, 1962). Hence, it is worthwhile discussing the estimated E-values for the homogeneous BM model with respect to the microstructures.

Elastic modulus estimates for the fibers and ground substance from previous studies span a wide range of values dependent on the species and the type of model used. For example, the beam model of the BM used by Miller (1985) based on guinea pig BM stiffness data gives E

of ground substance and fiber filaments of 10 KPa and 10^6 KPa, respectively. Based on the gerbil's BM stiffness measurements, Naidu and Mountain (2007) found, using a reinforced plate model of the BM, E of ground substance to be one order of magnitude higher (140 KPa), while E for the fibers was two orders of magnitude lower (1.4×10^4 KPa) than found in (Miller, 1985). Based on Naidu and Mountain (2007) PtSt data from the BM pectinate, Liu and White (2008) used a nonlinear FE analysis of a composite orthotropic plate model of the BM to estimate E. For the BM section at 6.6 mm from the base (similar to the location in our study), the longitudinal and transverse E-values were $E_x = 88.5$ KPa and $E_y = 664$ KPa, respectively.

The estimated E value of 298 KPa found for the BMPZ is similar to the E for the ground substance found in (Naidu and Mountain, 2007; Steele, 1987). Compared with the values in Liu and White (2008), the estimate range (190 – 460 KPa) lies between E_x and E_y . The thick layer of BM ground substance, peculiar to the BM pectinate of the gerbil (Lay, 1972), and the low density of fibers (Iurato, 1962) contribute to the modest values of PtSt and E in BMPZ. The mean estimate is four orders of magnitude smaller than E for collagen fibers but 10 times greater than E for elastin.

The E-value of 935 KPa for the BMAZ lies between the values for the ground substance and the fibers found in (Naidu and Mountain, 2007). In the BM arcuate, as shown in (Iurato, 1962), the fibers are not arranged in bundles as in the pectinate zone but merely run through the ground substance as a single layer. The estimated E may be interpreted as the mean value of the ground substance and the traversing fibers. The resulting E is comparable to E for elastin.

Novel approaches to BM measurements were used in (Ketten et al., 2008) to obtain elastic values for the BM fibers for cat, guinea pig and gerbil. The E-values of the fibers were found to be in the hundreds of KPa range. These values are consistent with our estimates. Based on these comparisons, the estimated E-values from the isotropic model of the BM are similar to those from other models of the gerbil's BM that include its microstructures.

The estimated E for OHC are consistent with experimental values. The experiment in (Hallworth, 1995) provides OHC axial compliance in the range 0.04 – 1.2 Km/N for OHC 20–80 μm in length. For the length of 40 μm used in our model and with a cylindrical elastic rod model of the OHC, this compliance range is converted into Es in the range 0.7–20 KPa. The sensitivity analysis yielded values in the range 0.2–24 KPa for the OHC E, which covers well the experimental range.

The PtSt gradients computed in the process of obtaining the E distribution defines how small changes in the Young's modulus for each individual OC component affect the PtSt measurement. This information can be useful in the design of additional experiments. Knowing, for example, that a specific PtSt measurement is not particularly sensitive to certain cellular components could be used to verify the model if one or several of these cellular components were damaged and the stiffness measurement did not change. The TM could for example be removed and should not alter the PtSt measurement on the BM, or the DCs could be damaged to see if the BM stiffness changes. Conversely, potential PtSt

measurement sites could be explored to find locations that are more sensitive to specific cell types of interest than the locations used in the currently available data.

Previous experimental work, which mapped the cochlear partition PtSt to its cellular architecture can be found in (Naidu and Mountain, 2001; Olson and Mountain, 1994; Naidu, 2001; Emadi et al., 2004; Miller, 1985; Naidu and Mountain, 1998a). It was found in (Naidu and Mountain, 1998a) that the PtSt under the BM decreased when the OC cells were removed from the BM. Thus, the OC components contribute in stiffening the BM. It seems natural to attribute this stiffening to the component just above the measurement location. However, the sensitivity test performed here reveals that the increase in the PtSt under the BM is not the result, alone, of the stiffness of the OC component directly above the BM. This increase in stiffness is mainly due to the PC whose effect on the PtSt spreads across the BM. In (Miller, 1985) the rigid junctions of the heads of the PC were shown to couple the OC longitudinally. Here the PC are found to radially couple the OC components. The PC thus contribute to the stiffness of the OC in both directions. The sensitivity analysis shows that the BM and the PC dominate the indentation mechanics of the cochlear short section.

The accuracy of the result depends on accuracy of measurements, through sensitivity. The estimated range (see Table 4) of each component's E reflects our confidence in the value found. We note that the posterior distribution is similar to the prior for the insensitive components. The E s are known no more precisely than their prior values. Indeed, in this underdetermined inverse problem it is expected that the posterior measure depends strongly on the prior, and that uncertainty remains for these insensitive components. On the other hand, the predictions for the most sensitive components, the BM and the PC, are much more precise. We would expect that these components' E s could be determined without uncertainty in the limit of vanishing experimental error.

Fig. 5 shows significant bending of the PC. Bending of the OPC around the level of the DC and OHC connection was observed in the experiment by Karavitaki and Mountain (2007). To the extent that bending dominates this deformation, the relevant stiffness might be EI , the bending stiffness of the PC. In this figure, the OC deformation spans at least two OPC on each side of the probe; This is consistent with the experimentally observed space constant.

It is widely accepted that the components are interconnected, and supported by the OSL, which is often regarded as rigid. Here we tried to accommodate any flexibility in this supporting structure by meshing this region and solving for its E . We found that perturbation of this E -value does not affect the PtSt deflection under the BMAZ and BMPZ. Thus, for the gerbil cochlea, this shelf may be regarded as a rigid wall with clamped boundary condition at the BM junction.

It is possible that the Newton method may not yield a unique solution. However, with the initial guess based on experimentally known estimates for the internal components of the OC, the stiffness distribution converges quickly and most likely is the solution within the error bound. This rapid convergence supports the validity of the assumptions made in the formulation of the problem. Even so, it is impossible to accurately estimate 11 material parameters from only 3 stiffness measurements.

The posterior covariance matrix found is non-diagonal. The relationship between distinct OC components E can be assessed from the corresponding correlation matrix. We found that all off-diagonal entries of the correlation matrix are smaller than 0.03 except those corresponding to (BMAZ, PC), (BMPZ, HC) and (BMPZ, PC) whose values are 0.6, 0.2 and 0.1, respectively. This would suggest that there exist a higher degree of correlation between the Es of the sensitive components. These values seem consistent with the spatial distribution and connection between the corresponding OC components. As suggested by the large correlation coefficient, the BMAZ and the PC (arch of Corti) situated on top of BMAZ, have the most dependent Es. Similarly, BMPZ and HC have dependent Es, albeit to a lesser degree; whereas, the geometrically offset BMPZ and PC have the least dependent Es among the sensitive components.

5. Conclusion

We have developed a method to determine the elastic properties of the OC cellular components from experimental PtSt data. This method is particularly useful for modeling purposes. It can systematically be applied to any section along the cochlea to determine the properties of the individual components of the OC section, provided PtSt measurement data are available. The method can provide more accurate results if more measurements are provided at selected locations such as the top and inside of the OC. A more accurate interpretation can be obtained if the filaments of the BM structure are included and the orthotropy property is modeled. The sensitivity analysis within the method can be used to interpret experimental PtSt measurement results. Conversely, the method can serve to design the proper experiments for measuring properties of the internal components from peripheral deflection of the OC. The map of the properties provides information on the dominant features and can be used to infer their function. We have implemented the method based on a realistic model for the middle turn location tuned to 4 kHz. The material property results indicate that the structural elements within the partition that dominate its stiffness are the BM and the PC. This suggests that these two components control the passive cochlear mechanics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

The cochlea cross section is accurately represented in the FE model. (A) Histological section of the middle turn gerbil cochlear cross section enclosed in the temporal bone. The organ of Corti (OC) sits on the basilar membrane (BM) (*arrow*). The BM+OC complex is suspended between the spiral ligament (LIG) on the right and the osseous spiral lamina (OSL) on the left. The hammer like structure protruding from the OSL is the tectorial membrane (TM). Surrounding the suspended complex are the scalae fluids. (B) FE representation showing the parts of the cochlear cross section including the cochlear fluids.

Figure 2.

3D view of the structural components within the FE model of the OC including the BM, the TM and the OSL. The components are the BM pectinate zone (BMPZ), BM arcuate zone (BMAZ), pillar cells (PC) comprised of inner PC (IPC) and outer PC (OPC), Deiters' cells (DC), inner hair cells (IHC) and outer hair cells (OHC), stereocilia (cilia), TM, reticular lamina (RL), Hensen cells (HC), and the OSL. One cilium is visible and appears as a short dark line protruding from the OHC's head. The IHC (not shown) are embedded in the phalangeal supporting cells (Ph). The RL lies on the top of the OHC and PC and can be

identified on the figure as the thin plate just below the TM. The *inset* shows the RL and the visible cilium pointed by an *arrow*.

Figure 3.

Sketch of the PtSt measurement experiment showing the measurement locations where the force probe (*thick filled bar*) is applied. (A) PtSt is measured under the BM with the overlaid OC cells removed. Two measurements are performed under the BMAZ and BMPZ, one location at a time, and correspond to location 1 and 2, respectively. As shown on the sketch, the probe is positioned in the middle of the BMAZ at measurement location 1. (B) In the presence of the OC cells, PtSt measurements at three radial locations are performed. In addition to the previous two locations, when OC is removed, a third measurement is added under the foot of the OPC.

Figure 4.

Flowchart of the solution algorithm for OC PtSt mapping. E represents the Young's modulus of the OC components, and δk is the PtSt variation. e_k and e_E denote the convergence errors as defined in text, and ε_k and ε_E represents the preset tolerances.

Figure 5.

Static PtSt experiment simulation to determine the Young moduli of (A) BMAZ and BMPZ; (B) OC structural components. Shown are the deformation of the structures in response to a probe forced under BM at a particular radial location.

Figure 6.

Sensitivity of PtSt measurement under BM with respect to change in the elastic properties of the OC shows that OC stiffness is most sensitive to change in the properties of the BMAZ, BMPZ and PC. The other OC components have sensitivity less than 5%. The BM PtSt is insensitive to the cilia stiffness.

Table 1
Model dimensions for the middle turn of the gerbil organ of Corti

Data source not referenced are deduced parameters. d_r and d_l designate the center to center distance of two adjacent components in the radial and longitudinal direction, respectively.

Parameter description	Length (μm)	Angle ($^\circ$)	Data source
RL/BM angle		27.3	(Edge et al., 1998)
RM/BM		51.9	(Edge et al., 1998)
ToC height	64.0		(Karavitaki and Mountain, 2007)
IPC length	64.3		(Edge et al., 1998)
BMPZ width	192.0		(Edge et al., 1998)
BMAZ thickness	4.0		(Plassmann et al., 1987)
BMPZ thickness	36.0		(Plassmann et al., 1987)
OHC length	40.0		(Mountain and Hubbard, 2003)
IHC length	35.0		(Mountain and Hubbard, 2003)
TM width	182.0		(Edge et al., 1998)
TM thickness	49.3		(Edge et al., 1998)
OHC radius	4.0		From image
RL thickness	2.0		(Böhnke et al., 1999)
$d_l(\text{PC,PC})$	9.0		From image
$d_r(\text{OHC,OHC})$	13.6		From image
$d_l(\text{OHC,OHC})$	9.0		From image
PC radius	1.7		From image
Space of Nuel width	9.0		From image
Subtectorial space thickness	3.7		(Böhnke et al., 1999)
Stereocilia radius	0.2		(Böhnke et al., 1999)
OPC/BM angle		53.1	
IPC/BM angle		84.5	
BMAZ width	67.1		
Total BM width	259.1		
OPC length	81.2		
RL width	90.5		
RM thickness	10.0		
Outer cilium length	3.8		
Inner cilium length	2.2		
Short section length	45.0		

Table 2
PtSt data used to determine the distribution of Es

The standard deviations of the values of the PtSt (k) are provided for the experiment with BM+OC. Estimates of the experimental values of the PtSt for the BM when the OC is removed are obtained for two locations using an exponential extrapolation of the available stiffnesses from the basal turn and are used to set the initial values of Es for BM.

Experiment	Location 1 (under BMAZ) k (N/m)	Location 2 (under BMPZ) k (N/m)	Location 3 (under PC) k (N/m)	Location 4 (under DC/OHC) k (N/m)
BM+OC	0.62 ± 0.25	0.78 ± 0.29	1.63 ± 0.51	0.55 ± 0.30
BM alone	0.13	0.42	--	--

Table 3
Starting values of Young's modulus (E) of the organ of Corti's components

These values are assigned according to the strategy and sources listed in the right-most column. For guessed initial values, no source is mentioned. In the rod model k_{exp} is the experimental PtSt; L and R are the length and the radius, respectively of the cylindrical cells.

OC structure	E^{0start} (kPa)	Data source
BMAZ	225	Optimization with BM model
BMPZ	1×10^4	Optimization with BM model
PC	1.5×10^6	(de Boer, 1996)
HC	100	
OHC/IHC	2.39	(Hallworth, 1995; Tolomeo et al., 1996) Elastic rod model: $E = \frac{k_{exp} \times L}{\pi R^2}$
OSL	1×10^7	(Steele, 1987)
RL	2×10^4	$1/5^{th}$ of E_{BMPZ}^{0start}
DC	10.7×10^3	(Naidu and Mountain, 2001) Elastic rod model: $E = \frac{k_{exp} \times L}{\pi R^2}$
TM	60	(Ghaffari et al., 2007)
Ph	7.5	
Cilium	20×10^3	(Böhnke et al., 1999)

Table 4
Young's modulus (E) distribution within the middle turn of the Gerbil organ of Corti

E estimate, $\mathbf{E}_{\text{predicted}} = \mathbf{E}^{(3)}$ at iteration 3, is found within the confidence interval provided. The starting vector $\mathbf{E}^0$ at iteration 1 is motivated by the values reported in the literature, and adjusted by trial and error to be within basin of attraction of global minimum. The convergence error bounds for the PtSt, e_k , and for the Young's modulus, e_E , are also provided. The OC components are listed top to bottom in decreasing order of overall sensitivity to PtSt under the BM. An arbitrary number is assigned to each OC component (as described in the text) and is indicated in parenthesis.

OC structure (index)	$\mathbf{E}^0$ (kPa) $e_k < 31\%$	$\mathbf{E}_{\text{predicted}}$ (kPa) $e_k < 0.3\%, e_E < 3\%$	$\mathbf{E}_{\min} - \mathbf{E}_{\max}$ (kPa)
BMAZ (1)	960	935	640 – 1360
BMPZ (10)	400	298	190 – 460
PC (9)	1.1×10^6	3×10^6	$(1 - 9) \times 10^6$
HC (5)	3.50	3.52	0.35 – 35
OHC/IHC (2)	2.39	2.41	0.24 – 24
OSL (11)	1×10^7	1×10^7	$(0.1 - 10) \times 10^7$
RL (4)	246	247	25 – 2470
DC (3)	1.07×10^3	1.07×10^3	$(0.11 - 11) \times 10^3$
TM (8)	30	30	3 – 300
Ph (6)	3.50	3.52	0.35 – 35
Cilium (7)	2×10^4	2×10^4	$(0.2 - 20) \times 10^4$