Estimation of the Orthotropic Elastic Properties of the Rat Eardrum

Ehsan Salamati1  Sumit K. Agrawal2  Abbas Samani1,3  Hanif M. Ladak1,2,3,*

1Department of Electrical and Computer Engineering, Western University, London, Ontario, N6A 3K7, Canada
2Department of Otolaryngology-Head and Neck Surgery, London Health Sciences Centre, London, Ontario, N6A 5W9, Canada
3Department of Medical Biophysics, Western University, London, Ontario, N6A 3K7, Canada

Received 31 Aug 2011; Accepted 16 Jan 2012; doi: 10.5405/jmbe.1005

Abstract

Finite-element models of the eardrum are developed to understand its function. Accurate models can potentially be used to optimize diagnostic tests and surgical procedures. However, modeling accuracy depends on the elastic properties specified when constructing the models. Although the eardrum is an orthotropic elastic structure whose stiffness varies in the radial and circumferential directions, for simplicity, many investigators have measured the eardrum’s elastic properties (specifically Young’s modulus) under the assumption of isotropy, thus limiting the applicability of these measurements. Whether the eardrum is assumed to be isotropic or orthotropic, most measurements of its properties are made using strips cut from the pars tensa. However, cutting can potentially cause damage to soft tissue. In this work, existing indentation-based and pressurization-based methods were extended for estimating the orthotropic elastic properties of the eardrum in situ. The two methods are initially tested using synthetic data with controlled amounts of noise. The results indicate that for the pressurization-based method, estimated elastic parameter values are within 10% of the known values used to generate synthetic data when the signal-to-noise ratio (SNR) is 2 or greater. An SNR of 200 or greater is required when using the indentation-based method to achieve error of less than 10%. The indentation-based method is applied to the rat eardrum for which experimental measurements of load-displacement curves are available in the literature, yielding average elastic orthotropic moduli values of $E_C = 23.4 \pm 1.6$ MPa (circumferential direction), $E_R = 58.7 \pm 4.2$ MPa (radial direction), and $G_{CR} = 35.6 \pm 3.3$ MPa using an average uniform pars-tensa thickness of 12 $\mu$m.

Keywords: Eardrum, Orthotropic elastic properties, Optimization, Finite-element modeling, Indentation testing, Pressurization testing

1. Introduction

Accurate finite-element (FE) models of the eardrum and middle ear can potentially be used for testing new surgical procedures and for refining audiological tests [1]. However, the accuracy of these models depends critically on a number of modeling parameters, including the shape of the individual eardrum, its thickness, and its mechanical properties [2]. Subject-specific shapes have been accurately measured using moiré profilometry [3], a non-contact optical technique, and micro-computed tomography [4]. The thickness has been measured using confocal microscopy for gerbils [5], cats [6], and humans [7].

A number of investigators have refined the measurements of the mechanical properties of the eardrum. Pioneering work in this area was conducted by Békésy [8], Kirikae [9], and Decraemer et al. [10]. Békésy [8] conducted a static beam-bending test on tissue strips cut from human eardrums. Kirikae [9] performed longitudinal vibration testing of strips of the human eardrum at 890 Hz. Decraemer et al. [10] did uniaxial tensile testing of human eardrum strips at frequencies up to 300 Hz. Particular focus in these studies and more recent ones has been on the estimation of the properties of the pars tensa of the eardrum because it is the main determinant of the impedance-matching function of the middle ear. Several studies have modeled the pars tensa as a homogeneous linearly elastic isotropic thin shell. Such a material can be characterized by its Young’s modulus and Poisson’s ratio. Typically, a Poisson’s ratio of 0.3 is assumed in modeling studies [2], and effort has focused on estimating the Young’s modulus of the pars tensa [8-16]. Note that although a Poisson’s ratio of 0.3 is typically used, some recent studies have used a value of approximately 0.5 to represent the incompressibility of soft tissues (e.g., [12]).

Fay et al. [17] found that when the pars tensa was assumed to be isotropic in their model of the eardrum, they could only...
simulate the mechanical behavior of the eardrum over a limited range of frequencies. For example, if a Young’s modulus of 30 MPa was used in their model, simulated frequency responses only matched measured responses up to about 1.5 kHz. Above that frequency, the mismatch between simulation and measurement results was significant. If a Young’s modulus of 100 MPa was used in their model, simulations better matched measurements at high frequencies (above 1.5 kHz), but with a mismatch at low frequencies. A single Young’s modulus could not be found for their isotropic model that allowed modeling results to match experimental data at all frequencies. If the pars tensa was assumed to be orthotropic in their model, then simulation results better matched measurements at all frequencies using a single set of orthotropic elastic parameter values. There was no need to adjust the values based on frequency [17]. They justified an orthotropic material model based on the fibrous ultrastructure of the eardrum.

The same group attempted to estimate the Young’s modulus of the eardrum in the radial and circumferential directions by using three methods: (1) constitutive modeling using experimental observations of radial and circumferential fiber densities, (2) re-examining previously published tensile testing and beam-bending experiments, and (3) performing their own dynamic measurements and adjusting the parameters of a fibrous composite shell model of the eardrum to make the simulations match measurements [18]. Using these approaches, bounds were determined for the elastic moduli. Luo et al. [19] refined these bounds by tensile testing strips cut along the radial and circumferential directions, respectively. However, tensile testing has a number of technical challenges. Apart from the issue of compromising the tissue’s structural integrity, to minimize the effects of boundary conditions on the measurement’s accuracy, tensile tests typically require a significant volume of homogeneous tissue [20]. However, both the fiber density [21,22] and thickness [5-7] of the eardrum can vary over a distance of a few millimeters. Furthermore, the eardrum is remarkably delicate, has a complex geometry, and is relatively difficult to extract. All of these factors contribute to the difficulty of conducting a uniaxial tension test, hence impacting its accuracy.

In situ methods have been developed that allow one to estimate the properties of the eardrum while it is intact and attached to the ear canal. Hesabgar et al. [23] presented one such method in which the Young’s modulus of an FE model of the rat eardrum with subject-specific geometry is numerically optimized to produce a match between experimentally acquired force-displacement data obtained from indentation testing and the corresponding simulated data. The optimal value is then taken to be the actual Young’s modulus of the pars tensa under test. A similar indentation-based method was developed by Aernouts et al. [12]. Recognizing the challenges of indentation testing and modeling of indentation experiments, Jahromi [24] developed a pressurization-based method in which the acquired data consisted of measurements of the deformed shape of the eardrum after a sequence of static pressures had been applied. As with Hesabgar et al. [23], the Young’s modulus was estimated by optimizing its value in the model until simulated responses matched experimental measurements.

In the indentation-based method of Hesabgar et al. [23] and the pressurization-based method of Jahromi [24], the pars tensa is modeled as a linearly elastic homogeneous isotropic material and can thus be characterized by a single Young’s modulus (E) and a single Poisson’s ratio (ν). The primary objective of the present study is to extend this indentation-based method [23] by modeling the eardrum as a homogeneous linearly elastic orthotropic material and estimating the orthotropic elastic properties of the eardrum by numerical optimization of an FE model of the eardrum. A secondary objective is to determine whether extending the pressurization-based method [24] might offer some advantages over the modified indentation-based method. Four independent in-plane elastic parameters need to be determined for modeling thin orthotropic materials such as the pars tensa: the circumferential (Ec) and radial (Er) Young’s moduli, the in-plane shear modulus (Gcr), and the Poisson’s ratio. By using the commonly accepted value of 0.3 for the Poisson’s ratio, the problem reduces to estimating Ec, Er, and Gcr for the pars tensa. The feasibility of the two estimation techniques was first tested on synthetic computer-generated data with known ground truth values and with various levels of added noise. The synthetic data was used to verify that both algorithms work under ideal conditions before being applied to real data. Subsequently, the modified indentation-based approach was applied to measurements made by Hesabgar et al. [23] as these data are readily available.

2. Materials and methods

2.1 Overview

Two algorithms were developed and implemented to estimate the orthotropic elastic parameters, namely an indentation-based algorithm and a pressurization-based algorithm. As both algorithms share several common features, a single flowchart (Fig. 1) is used to describe them. The input to both estimation algorithms consists of a subject-specific three-dimensional (3D) FE mesh of the eardrum under test and its corresponding experimental response data. Response data are force-displacement curves for the indentation-based algorithm and pressurized shape measurements for the pressurization-based algorithm. The method for constructing the 3D FE mesh is the same for both algorithms and is described in Section 2.2.

The optimization framework described by Fig. 1 requires experimental data to which simulation results are matched. To test the fidelity of the proposed optimization-based data inversion algorithms, the two methods were first tested on synthetic computer-generated data for which orthotropic parameter values are known. For the indentation-based algorithm, these consisted of force-displacement curves, whereas for the pressurization-based algorithm, these consisted of the deformed shape of the eardrum at specific pressures. The approach used for generating synthetic response data for the two methods is described in Section 2.3.
In order to find the eardrum’s orthotropic parameters using either the indentation-based method or the pressurization-based method, a cost function is optimized such that the response simulated using these parameter values matches the synthetic response data. The cost function for each data inversion algorithm and the optimization algorithm are described in Section 2.4.

Finally, the indentation-based method is applied to estimate the orthotropic elastic properties of the rat eardrum using indentation data from Hesabgar et al. [23]. Although the acquisition of experimental force-displacement data is not part of this work, the methodology is briefly described in Section 2.5 for completeness.

2.2 FE model construction

FE models were constructed for the rat eardrum because experimental indentation data are available for the rat [23]. In order to construct an FE model of a rat eardrum, the 3D shape of the eardrum is required because the shape of the eardrum greatly impacts its mechanical function [2,17]. Shape data from the study of Hesabgar et al. were used [23]. In that study, healthy eardrums from adult Sprague Dawley rats were used. The rats were euthanized in accordance with Western University’s Animal Use Subcommittee. For each rat, the temporal bone was removed 30 min post mortem. The ear canal was dissected to within 0.5 mm of the eardrum in order to obtain a good view of the eardrum for shape measurement. To measure the mechanical response of the eardrum without the confounding effects of the ossicular and cochlear loads, the malleus was immobilized by gluing the mallear head to the middle ear wall as described elsewhere [25]. The eardrum was left intact; i.e., the eardrum was not dissected from its attachments to the ear canal or the manubrium of the malleus.

The 3D shape of each eardrum was measured using Fourier transform profilometry (FTP), which is a non-contact optical measurement method [26]. In FTP, a light pattern consisting of a set of parallel vertical lines is projected onto a diffusely reflecting surface. The surface modulates this pattern, resulting in a slightly deformed pattern of lines appearing on the surface. The deformed pattern is acquired using a CCD camera built into the FTP system and then processed by a computer to reconstruct the 3D shape of the surface. A commercially available Fourier transform profilometer was used in this work (MM-25D, Opton Company Limited, Seto, Aichi, Japan). This profilometer has a spatial measurement accuracy of 10 µm. Since FTP requires a diffusely reflecting surface with good contrast and the eardrum is transparent, a thin white spray-on coating (Spotcheck SKD-S2 Developer, Magnaflux, Glenview, IL) was applied to the eardrum. The effects of similar coatings on shape measurements have been shown to be negligible [27]. The output of the profilometer is a point cloud representing the surface being measured.

In order to form an FE mesh from the obtained point cloud, the trans-finite interpolation (TFI) technique was used [28]. In its simplest form, TFI warps a unit square with a mesh of quadrilateral elements, as shown in Fig. 2, into an arbitrary shape, thus producing a quadrilateral mesh for the arbitrary shape [29]. The eardrum has a complex shape with several sub-surfaces (pars tensa, pars flaccida, and manubrium), so the simple TFI method described in Fig. 2 cannot be used directly to produce its mesh. Instead, the TFI method was applied to simpler zones defined on the eardrum, as described below.

When applying TFI to the eardrum, a two-dimensional (2D) line drawing of the specific eardrum needs to be created in which the following boundaries are demarcated: the tympanic ring, the pars tensa, the pars flaccida, the ligament separating the pars tensa from the pars flaccida, and the manubrium. These boundaries were traced manually from a high-resolution digital image of the surface of the eardrum under test. This step of mesh construction is shown in Fig. 3(a). Although the ligament separating the pars tensa from the pars flaccida is included in the FE models, the only evidence for such a ligament is our own visual observation of a possible local thickening at the boundary between the two surfaces. However, this thickening is difficult to discern. With regard to FE models of the cat eardrum, although earlier models included such a ligament (e.g., [2]), later models (e.g., [30]) did not include it as there was no evidence for it. The effect of ignoring this ligament in our models is reported in Section 3.3.

227

Figure 1. Estimation flowchart describing both the indentation-based and pressurization-based methods for estimating the eardrum’s orthotropic elastic parameters. “e” refers to a specified tolerance.

Figure 2. Illustration of basic TFI meshing algorithm. A one-to-one transformation from a unit square with a quadrilateral mesh to an arbitrary shape is shown. $X_a$, $X_b$, $X_c$, and $X_d$ denote the left, right, top, and bottom boundaries of a shape, respectively. This figure is a reproduction from a figure by Courtis [29] with some changes.

Next, the 2D line drawing was decomposed into fourteen zones. This step is shown in Fig. 3(b). Each zone can be described as a quadrilateral with possibly curved sides. This meshing scheme is highly advantageous for modeling the pars
tensa as an orthotropic material as it contains zones with two sides directed along the radial direction with the remaining two sides being approximately in the circumferential direction. The radial direction refers to lines emanating from the manubrium and extending towards the tympanic ring. The circumferential direction is locally perpendicular to the radial direction and follows the contour of the tympanic ring. With this meshing scheme, the sides of the generated quadrilateral elements representing the pars tensa are approximately aligned with the radial and circumferential directions, which is necessary for specifying orthotropic material properties. For each zone, a unit square that is decomposed into a quadrilateral mesh (see Fig. 2) was mapped using the TFI method so that the quadrilateral mesh for the unit square was made to conform to the particular zone being considered on the eardrum. The implementation of the TFI method of O’Hagan and Samani was used [31]. Figure 3(c) shows the mesh for one zone. Note that the zonal mesh is 2D because each node on the mesh has a zero z-coordinate. Once the TFI method was applied to all zones, the z-coordinates of each node of the mesh was assigned to reflect the measured z-coordinate in the 3D point cloud produced by the profilometer. This resulted in a 3D FE mesh of quadrilateral elements, as shown in Fig. 4. Abaqus FE software (Simulia Inc., RI, USA) was used to model the eardrum with four-noded S4 quadrilateral thin shell elements. Each node of this element has six degrees of freedom (three translations and three rotations).

Figure 3. Three basic steps for generating an FE mesh of the eardrum using the TFI technique. (a) Boundaries of the tympanic ring, the pars tensa, the pars flaccida, the ligament separating the pars tensa from the pars flaccida, and the manubrium were traced manually in 2D from a high-resolution digital image of the eardrum. (b) 2D line sketch of the eardrum was decomposed into fourteen zones. (c) Each zone was meshed using the basic TFI algorithm. Only the mesh for one of the fourteen zones is shown.

Figure 4. Typical FE mesh for a rat eardrum. (a) View of FE mesh as seen from the ear canal (i.e., lateral side). The position of the indenter is indicated by a dot. (b) View normal to view in (a). The anterior (A), posterior (P), superior (S), and inferior (I) directions are indicated in view (a).

Note that when using the TFI method, the number of nodes on the left boundary of a zone must be the same as that on the right boundary. Similarly, the number of nodes on the top boundary must be equal to that on the bottom boundary. The left, right, top, and bottom boundaries of a zone are shown in Fig. 2(b). In order to achieve geometrically well-formed elements with aspect ratios close to unity, the pars flaccida is divided into 5 zones. If the tip of the manubrium is not divided as shown, elements on the manubrium become skewed. The division as shown, achieves aspect ratios of between 1.0 and 1.5.

The TFI method ensures that boundary nodes of one zone match the boundary nodes of an adjacent zone if the two boundaries are shared. These boundary points are initialized by the user and remain in the same position throughout the TFI meshing process. Using mixing functions, these boundary points are propagated inside each zone to determine the position of internal zone points.

Progressively increasing the resolution of the mesh shown in Fig. 4 did not affect estimates of $E_C$, $E_R$, and $G_{CR}$ by more than 5%. Moreover, as the mesh resolution was increased, the estimated values of $E_C$, $E_R$, and $G_{CR}$ converged. The mesh shown in Fig. 4 was thus used as a compromise between the accuracy of these estimates and computational demands.

The quadrilateral elements used in this work have straight sides; however, the radial and circumferential coordinate system required for specifying the orthotropic elastic moduli represent a curved system. As the mesh resolution is increased, this curved coordinate system is better represented. Based on analysis using a progressively increasing mesh resolution, it is estimated that less than 5% error is induced in estimates of the moduli caused by approximating the curvature.

To enable simulation, all parameters of the FE model were set to values from the literature except for the orthotropic elastic parameters of the pars tensa ($E_C$, $E_R$, and $G_{CR}$) which needed to be optimized. The optimization algorithm sets $E_C$, $E_R$, and $G_{CR}$ to some arbitrary initial values and then refines them. These values are selected from a range of values determined a priori. This helps reduce the search space over which optimization is conducted, leading to convergence to similar values. The thickness of the pars tensa was measured from a micro-CT image and an average value of 12 µm was assigned to the model by averaging 10 sample points along 5 slices of the micro-CT image [23]. Voxels were isotropic and had an edge length of 8 µm. Furthermore, the pars flaccida was assumed to be isotropic and more compliant than the pars tensa.
Its Young’s modulus was constrained to be equal to one-fourth of the sum of the longitudinal and the transverse Young’s moduli of the pars tensa. Furthermore, the thickness of the pars flaccida was taken to be the same as that of the pars tensa. The pars-flaccida thickness and Young’s modulus values were arbitrarily chosen to make the pars-flaccida model more compliant than the pars-tensa model. Note that numerical simulations conducted by Hesabgar et al. [23] indicated that the measured elastic modulus of the pars tensa is not significantly sensitive to the selected thickness and Young’s modulus values of the pars flaccida. Note that although no measurements have been made of the Young’s modulus of the rat pars flaccida, measurements have been made on the gerbil, yielding an average value of 41.0 kPa [32]. The value used in the current work is higher to test what, if any, effect the stiffness of the pars flaccida has on the estimated orthotropic parameters for the rat eardrum. In Section 3.3, the effects of varying the Young’s modulus and thickness of the pars flaccida are reported.

The ligament separating the pars tensa from the pars flaccida corresponds to the extreme row of elements of the pars flaccida and was modeled as having a thickness of 12 µm. Its Young’s modulus was taken to be 100 MPa, which is the same as that of other ligaments [33]. The manubrium was modeled as consisting of dense cortical bone, as done by Funnell et al. [34]. As stated in their work, this provides an upper limit on the Young’s modulus value of the manubrium. The Young’s modulus was assumed to be 15 GPa, which is the same as that of typical cortical bone [35]. The manubrial thickness was set to 100 µm based on a micro-CT scan [23]. All tissues were assumed to have a Poisson’s ratio equal to 0.3. The tympanic ring was assumed to be fully clamped as was the superior boundary of the manubrium. However, the rest of the manubrium was tightly coupled to the eardrum and was free to move with it. This condition approximately simulates the experimental condition of immobilizing the malleus head as in indentation and pressurization testing. The superior end of the manubrium is not in the same place as the malleus head, so fully clamping the superior end approximately simulates malleus head fixation.

### 2.3 Generating synthetic data

The FE mesh described in Section 2.2 was used in generating synthetic data to test both the indentation-based and pressurization-based estimation methods. Specifically, ground truth values of $E_C = 20$ MPa, $E_R = 34$ MPa, and $G_{CR}$ = 12 MPa were assumed. The $E_C$ and $E_R$ values were selected based on the circumferential and radial Young’s moduli reported by Gan et al. [36]. The value of $G_{CR}$ was arbitrarily set at 12 MPa. Henceforth, this model with ground truth parameter values is referred to as the ground truth model. Another model generated from the same shape data but with different arbitrary initial parameter values was then optimized using the techniques described in Section 2.4.

In the indentation experiment of Hesabgar et al. [23], a point on the anterior pars tensa (indicated by the dot in Fig. 4) was indented with a spherical-ended indenter with a diameter of 0.5 mm. To simulate the experiment, the indenter was modeled as a rigid body and using small-slipping contact modeling. The small-slipping contact model was developed using Abaqus by defining a contact pair consisting of the eardrum as a deformable body and the indenter as a rigid surface. In this model, the “SMALL SLIDING” parameter in the “CONTACT PAIR” option of Abaqus, which invokes contact formulation with small sliding within Abaqus, was used. The indenter was used to indent the eardrum to a depth of up to 90 µm in steps of 10 µm. At each step, the reaction force was computed using Abaqus FE software. Furthermore, because the amount of displacement in the indentation experiment was significant compared to the eardrum’s thickness, the FE model incorporated geometric nonlinearity. Material nonlinearity was not included.

To generate synthetic data for the pressurization-based method of Jahromi [24], pressures were applied to the model eardrum in steps of 0.5 kPa to a maximum of 4 kPa. At each pressurization step, the deformed shape of the eardrum was calculated using Abaqus with the inclusion of geometric nonlinearity to account for the large deformations. Displacements generated for the synthetic pressurization experiment were larger than those used with indentation. For instance, at 1 kPa of pressure, the maximum computed displacement was 245 µm compared to 90 µm for indentation.

Additionally, zero-mean Gaussian noise was added to each synthetic data set. Various levels of noise were used to achieve signal-to-noise ratio (SNR) values of 2, 10, 100, and 200, respectively. For the indentation-based approach, noise was added to the simulated reaction forces. For the pressurization-based approach, noise was added to the simulated deformed shape.

### 2.4 Optimization

For each of the methods (indentation or pressurization), a specific cost function with $E_C$, $E_R$, and $G_{CR}$ as the independent variables was formulated such that minimizing this cost function resulted in a match between simulation results and the experimental or synthetic response data. The optimal values of $E_C$, $E_R$, and $G_{CR}$ were taken to estimate the actual parameter values for the eardrum under test. For validation, only synthetic data generated using the ground truth model were used. For the indentation-based method, orthotropic elastic parameters that produced the best match between the simulated force-displacement curve and corresponding synthetic response data were sought. The cost function $C_o$ for the indentation method is defined as the sum of squared reaction force differences between simulated and response data, leading to the following constrained optimization problem:

$$C_o(E_C, E_R, G_{CR}) = \sum_{i=1}^{n} (f_{i}^{sim} - f_{i}^{exp}(E_C, E_R, G_{CR}))^2$$

Minimize $C_o(E_C, E_R, G_{CR})$

Subject to

\[
\begin{align*}
E_{C_{\min}} & \leq E_C \leq E_{C_{\max}} \\
E_{R_{\min}} & \leq E_R \leq E_{R_{\max}} \\
G_{CR_{\min}} & \leq G_{CR} \leq G_{CR_{\max}}
\end{align*}
\]
where \( f^{\text{exp}} \) and \( f^{\text{sim}} \) denote the ground truth (or experimental) reaction force and simulated reaction force, respectively, for point \( i \) along the force-displacement curve. Note that \( f^{\text{sim}} \) is a function of the variables to be optimized \((E_c, E_R, \text{and } G_{CR})\), and is calculated at each iteration of the optimization algorithm using the FE model and the current values of \( E_c, E_R, \text{and } G_{CR} \). The number of points along the force-displacement curve is specified by \( n_i \). \( E_{cs} \) and \( E_{cv} \) are lower and upper bounds of the longitudinal Young’s modulus \((E_c)\), respectively. \( E_{as} \) and \( E_{av} \) are the lower and upper bounds of the transverse Young’s modulus \((E_R)\), respectively. \( G_{cas} \) and \( G_{cav} \) are the lower and upper bounds of the in-plane shear modulus \((G_{CR})\), respectively.

In the pressurization-based method, the cost function was designed so it was minimum when the values of \( E_c, E_R, \text{and } G_{CR} \) were such that the match between the simulated pressurized shape and the corresponding synthetic reaction data was best. The pressurization-based cost function \( C_c \) is defined at a particular pressure as the sum of squared nodal \( z \)-coordinate differences between simulated and response data, leading to the following constrained optimization problem:

\[
C_c(E, E_x, G_{c,x}) = \sum_{i=1}^{n_i} (z^{c,x}_{i} - z^{\text{exp}}_{i})^2 \]

Minimize \( C_c(E, E_x, G_{c,x}) \)

Subject to:

\[
\begin{align*}
E_{ax} & \leq E_x \leq E_{ax} \\
E_{ax} & \leq E_x \leq E_{ax} \\
G_{cas} & \leq G_{cx} \leq G_{cav}
\end{align*}
\]

where \( z^{c,x}_{i} \) and \( z^{\text{exp}}_{i} \) are the ground truth and simulated surface shape \( z \)-coordinates, respectively. The number of points on the surface is specified by \( n_i \).

For both the indentation-based cost function and the pressurization-based cost function, the upper and lower limits were set to: \( E_c = 72 \text{ MPa}, E_R = 88 \text{ MPa}, G_{CR} = 48 \text{ MPa}, E_c = 7 \text{ MPa}, E_R = 7 \text{ MPa}, \text{ and } G_{CR} = 4 \text{ MPa}. Based on the available literature, the search space defined by these limits is very large.

Each cost function was minimized to find the optimal orthotropic elastic parameters using a variant of the Nelder-Mead simplex method [37]. For the pressurization-based method, the minimization was done for each pressure, and the optimal values at each pressure were averaged to get the final result. The optimization process starts by using initial guesses for the orthotropic parameters and then systematically changes them until the minimum of the cost function is reached. The optimization process is terminated when the cost function values and orthotropic parameter values are below the given tolerances. For the synthetic data, the tolerances were set to 10 Pa for \( E_c, E_R, \text{and } G_{CR} \) and \( 10^{-6} \) for the cost function. For the experimental indentation data (see next section), the tolerances were set to 100 Pa for \( E_c, E_R, \text{and } G_{CR} \) and \( 10^{-8} \) for the cost function. Tighter tolerances can be set for the synthetic data than for the experimental data because the synthetic data were generated using a model that exactly matched the model used for the estimation of orthotropic parameter values. With the experimental data, modeling assumptions described in Section 2.2 are simplifications of the experimental situation.

2.5 Experimental indentation data

As mentioned previously, the indentation data of Hesabgar et al. [23] were used to estimate \( E_c, E_R, \text{and } G_{CR} \) for actual rat eardrums. In their experiment, indentation testing was done prior to applying a coating and making a shape measurement. Measurements were made in this order to prevent the coating from affecting the mechanical behavior of the eardrum.

A spherical-ended indenter with a diameter of 0.5 mm was used. A spherical-ended indenter does not have sharp edges and does not result in tearing of the eardrum, which would occur with a plane-ended indenter. However, the contact area of a spherical-ended indenter grows gradually as the indenter moves further down on the eardrum. The contact area growth characteristics depend on the geometry of the eardrum and the indenter in addition to their stiffnesses. To obtain the contact area incrementally throughout the indentation process, which is necessary for indentation force calculation, contact problem modeling is necessary.

The indenter descended until it just touched the surface of the eardrum and was then stopped. To determine the point of contact initiation, the indentation machine was programmed such that the indenter moved down toward the eardrum very slowly until the load cell registered a force larger than a user-defined force threshold. At that point, the indenter was moved back up a few \( \mu \text{m} \) very slowly until the load cell registered insignificant force readings. That point is regarded as the point of contact initiation at which the indenter position and force data acquisition is started until the end of the indentation experiment. The point of contact was in the pars tensa, as shown in Fig. 4, for one eardrum. Furthermore, the orientation of the eardrum was chosen such that the indenter was normal to the surface at the point of contact in order to avoid slippage between the eardrum and indenter. This is consistent with the small-slipping contact condition used in the modeling of the eardrum (see Section 2.2).

After several sinusoidal indentation cycles of loading and unloading were applied for preconditioning, four similar cycles of sinusoidal indentation were applied to the specimen with a frequency of 0.5 Hz. The force-displacement curve corresponding to the four cycles were recorded. The purpose of applying four cycles was to have a number of cycles from which the best one could be chosen given that the quality of the force-displacement curve can be affected by random mechanical vibration or electrical noise.

For optimization, only the loading part of the best sinusoidal indentation cycle was used. The experimentally measured unloading part of the loading cycle was not used because of inaccuracy in the measured forces throughout the unloading phase of the cycle. As described in [20], this inaccuracy is due to the discontinuity of contact between the indenter and the tissue during unloading.
3. Results

3.1 Algorithm testing on synthetic data

The ground truth values were recovered with both estimation techniques without any error in the absence of noise. Values of the in-plane shear modulus ($G_{CR}$) recovered by the indentation-based and pressurization-based techniques are shown in Fig. 5 and Fig. 6, respectively, for various levels of zero-mean Gaussian noise. The optimization algorithm parameters and FE models are the same for both figures while the initialization values of $G_{CR}$ were chosen to be at the upper limit and lower limit for the indentation and pressurization methods, respectively. Of note, reversing the choice of initialization values at the lower and upper limits for the indentation and pressurization methods, respectively, led to the same curves. As expected, these figures show that the recovered values are closer to the ground truth values with smaller levels of noise. Graphs of $E_C$ versus SNR and $E_R$ versus SNR are not shown as the behavior is similar to that exhibited by the $G_{CR}$ versus SNR curve. When using the pressurization technique, estimated elastic parameter values were within 10% of the known values used to generate the synthetic data when the SNR was 2 or greater. For the indentation technique, an SNR greater than 200 was required to achieve estimates that are within 10% of the known values. The above estimation methods are valid over a wide range of initialization values used with the optimization algorithms (from half the ground truth values to twice the ground truth values); i.e., the starting values had little effect on the results. Note that for an SNR value of 2, the indentation-based technique did not produce estimates that were different from the initial estimates because of the relatively high level of noise. Therefore, the estimated value of $G_{CR}$ is not shown in Fig. 5.

![Figure 5. Ground truth and recovered values of in-plane shear modulus ($G_{CR}$) for the indentation-based method applied to synthetic response data with various levels of Gaussian noise.](image)

3.2 Estimates from actual indentation data

Table 1 lists the estimated values of $E_C$, $E_R$, and $G_{CR}$ for three of the rats used by Hesabgar et al. [23]. The indentation-based algorithm was used because these authors provide indentation data. The average orthotropic parameter values plus/minus one standard deviation across all three rats were $E_C = 23.4 \pm 1.6$ MPa, $E_R = 58.7 \pm 4.2$ MPa, and $G_{CR} = 35.6 \pm 3.3$ MPa using an average uniform pars-tensa thickness of 12 µm in the models.

![Figure 6. Ground truth and recovered values of in-plane shear modulus ($G_{CR}$) for the pressurization-based method applied to synthetic data with various levels of Gaussian noise.](image)

<table>
<thead>
<tr>
<th>Sample number</th>
<th>$E_C$ (MPa)</th>
<th>$E_R$ (MPa)</th>
<th>$G_{CR}$ (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24.0</td>
<td>54.0</td>
<td>38.5</td>
</tr>
<tr>
<td>2</td>
<td>24.5</td>
<td>62.0</td>
<td>36.2</td>
</tr>
<tr>
<td>3</td>
<td>21.6</td>
<td>60.0</td>
<td>32.0</td>
</tr>
</tbody>
</table>

The quality of the fit between experimental indentation data and simulation results using the optimal orthotropic parameters is shown in Fig. 7 for each of the three rats. Recall that only the loading phase of the experimental data was used. The fit is best for sample 3.

![Figure 7. Experimental and corresponding simulated force-displacement curves. Experimentally acquired loading part of one indentation cycle (dashed curve) in rat eardrums and corresponding simulated indentation response obtained from FE simulation (solid curve) with the corresponding optimal orthotropic elastic parameter values.](image)
3.3 Variation of model parameters

Although the shape of the eardrum was known exactly through measurement, several approximations had to be made in constructing the FE model of each eardrum. The thickness and Young’s modulus of the pars flaccida, of the ligament, and of the manubrium were not based on subject-specific measurements but were taken from the literature. In addition, the thickness of the pars tensa was based on micro-CT measurements on one animal [23], and represented the average thickness of the pars tensa since variations in thickness across the pars tensa could not be quantified due to the limited resolution of the micro-CT scanner. This value was used for all animals. Also, the Poisson’s ratio was assumed to be 0.3, although as noted in Section 1, some studies used a value that is close to 0.5. Thus, the above values were varied in the models to quantify their effects on the estimated optimal orthotropic parameters.

The effects of varying the thickness of the pars tensa from 6 µm (i.e., 50% of the nominal value of 12 µm) to 30 µm (i.e., 2.5 times the nominal value) are shown in Fig. 8. This particular range was chosen as it encompasses the range of thickness values seen in similar animals such as gerbils [5]. Increasing the thickness of the pars tensa causes a decrease in the estimated optimal values of $E_C$ and $E_R$. In contrast, $G_{CR}$ does not vary substantially. It is noteworthy that in Fig. 8, the lines corresponding to $E_C$ and $E_R$ were truncated at thickness values of 18 µm and 24 µm, respectively. This truncation was necessary as the optimization reached the default lower bound of 7 MPa and using lower bound values smaller than 7 MPa led to numerical FE instabilities; hence, no reliable data were available beyond these thickness values. Table 2 shows estimated orthotropic elastic parameter values for more realistic pars-tensa thickness values of 9 µm and 15 µm.

Regardless of the value of Poisson’s ratio used to model the pars tensa, the values of $E_C$, $G_R$, and $G_{CR}$ were estimated to within one decimal place of each other.

Varying the Young’s modulus or the thickness of the pars flaccida has negligible effects on the estimated optimal values as long as the pars flaccida is kept more compliant than the pars tensa. Changing the thickness or Young’s modulus of the ligament from half its value to twice its value does not appreciably affect the estimated optimal values of $E_C$, $E_R$, and $G_{CR}$. Removing the ligament completely results in only a 2% change in the estimated values. Similarly, changing the thickness or Young’s modulus of the manubrium from half its value to twice its value does not appreciably affect the estimated optimal values of $E_C$, $E_R$, and $G_{CR}$.

### 4. Discussion

#### 4.1 Algorithm testing on synthetic data

Applying both the indentation-based approach and the pressurization-based approach to noiseless synthetic data demonstrates that, under ideal conditions (i.e., all FE modeling assumptions are correct), both techniques are able to recover the ground truth values of $E_C$, $E_R$, and $G_{CR}$ exactly. Even with the addition of noise, the difference between estimated parameter values and known values is less than 10% when the SNR is greater than 200 for the indentation-based method and greater than 2 for the pressurization-based method. In practice, such SNR values are easy to achieve as the amount of force data averaging in indentation testing that occurs during data acquisition to obtain each force value can be easily adjusted to increase the SNR. In indentation testing, 1000 samples are averaged when acquiring a single point on the force-displacement curve [23]. In the FTP system used by Jahromi [24], up to 10 point clouds can be averaged to produce a single acquisition. For the profilometer, the worst-case SNR is 6.0 for points furthest away from the imaging plane. For the indentation device, considering that each force recorded for the orthotropic parameter calculation is obtained from averaging 1000 force samples, the SNR was estimated at 7.5 to 450 for minimum and maximum force readings of 0.01 gr to 1.8 gr, respectively.

In the indentation method, $G_{CR}$ is over-predicted for low SNR values, as shown in Fig. 5. For the pressurization method, $G_{CR}$ is under-predicted for low SNR values, as shown in Fig. 6. This could be attributed to the expected different topologies of the cost functions with the indentation and pressurization methods.

The pressurization-based method has some advantages over the indentation-based method. When acquiring experimental force-displacement curves in indentation testing, the indenter must remain perpendicular to the local eardrum surface in order to minimize slipping. If a spherical indenter is

<table>
<thead>
<tr>
<th>Sample</th>
<th>9 µm</th>
<th>15 µm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample 1</td>
<td>$E_C = 38.7$</td>
<td>$E_C = 10.2$</td>
</tr>
<tr>
<td></td>
<td>$E_R = 69.4$</td>
<td>$E_R = 51.8$</td>
</tr>
<tr>
<td></td>
<td>$G_{CR} = 34.3$</td>
<td>$G_{CR} = 39.5$</td>
</tr>
<tr>
<td></td>
<td>$E_C = 49.7$</td>
<td>$E_C = 15.0$</td>
</tr>
<tr>
<td>Sample 2</td>
<td>$E_C = 72.2$</td>
<td>$E_C = 56.8$</td>
</tr>
<tr>
<td></td>
<td>$G_{CR} = 29.2$</td>
<td>$G_{CR} = 38.8$</td>
</tr>
<tr>
<td></td>
<td>$E_C = 35.3$</td>
<td>$E_C = 11.6$</td>
</tr>
<tr>
<td>Sample 3</td>
<td>$E_C = 71.8$</td>
<td>$E_C = 52.8$</td>
</tr>
<tr>
<td></td>
<td>$G_{CR} = 32.0$</td>
<td>$G_{CR} = 39.2$</td>
</tr>
</tbody>
</table>

Figure 8. Variation in optimal orthotropic parameters of the pars tensa as functions of the pars tensa thickness. Reliable estimates of $E_C$ and $E_R$ could not be obtained for pars-tensa thicknesses above 18 µm and 24 µm, respectively, due to numerical instability.
used during the experiments to prevent damage to the eardrum, FE modeling becomes more complicated since the indentation test must be simulated as a contact problem. Using contact problem modeling is necessary because the area of contact between the indenter and eardrum grows as the indenter is pushed into the eardrum. The contact area’s continuous growth implies that the loading of the eardrum also changes continuously, hence conventional prescribed force or displacement boundary conditions become inappropriate in the corresponding FE model. The pressurization-based method has none of these complications.

4.2 Application to actual indentation data

This work represents the first attempt at estimating the orthotropic elastic properties of the rat pars tensa. The longitudinal modulus ($E_l$) corresponds to the circumferential fiber direction, whereas the transverse modulus ($E_t$) corresponds to the radial fiber direction. As listed in Table 1, $E_R$ is larger than $E_C$, which is consistent with the observation that the pars tensa is stiffer in the radial direction than in the circumferential direction [38].

Luo et al. [19] performed tensile testing on strips cut from the human eardrum, and they investigated the effects of the strain rate. For strips cut in the radial direction, they modeled the strip as an isotropic material and estimated that the Young’s modulus varies from 45.2 MPa to 58.9 MPa for strain rates of 300 to 2000 s$^{-1}$. Note that the Young’s modulus increases with increasing strain rate. The comparable value in the present work is $E_R$, which was estimated to be 58.7 ± 4.2 MPa across the three rats. For strips cut in the circumferential direction, Luo et al. [19] estimated that the Young’s modulus varies from 34.1 MPa to 56.8 MPa for strain rates of 300 to 2000 s$^{-1}$. The comparable value in the present work is $E_C$, which was estimated to be 23.4 ± 1.6 MPa across the three rats. Although the values presented here cannot directly be compared to those of Luo et al. [19] due to differences in species (rat vs. human), modeling assumptions (orthotropic vs. isotropic), and strain rates (0.5 s$^{-1}$ used in our work), it is interesting to note that the moduli are in similar ranges. Luo et al. [19] did not report an in-plane shear modulus ($G_{CR}$).

Despite the reassuring similarity in the values reported here and by Luo et al. [19], the fit between the simulated indentation curves with the optimal orthotropic elastic parameters and measured curves is not exact, as shown in Fig. 7. This is most likely due to only the geometric nonlinearity being taken into account in the FE models. Improvements could result if material intrinsic nonlinearities are also considered. The measured response curves for the three animals presumably differ from each other due to inter-specimen differences in local material properties, thickness, and local surface geometry [23].

Estimates of $E_C$, $E_R$, and $G_{CR}$ made using the indentation-based and pressurization-based approaches do not vary appreciably with modeling assumptions made about the thickness and Young’s modulus of the pars flaccida, ligament, or manubrium. The pars flaccida is much more compliant than the pars tensa and represents only a small fraction of the total eardrum surface area in comparison to the pars tensa. Its mechanical behavior is not tightly coupled to that of the pars tensa. Hence, changes in the properties of the model pars flaccida do not affect estimates of $E_C$, $E_R$, and $G_{CR}$ for the pars tensa as long as the pars flaccida is constrained to be more compliant than the pars tensa in the FE models. The ligament and manubrium are essentially rigid in comparison to the pars tensa, and variations in their properties would not be expected to affect $E_C$, $E_R$, and $G_{CR}$ as long as the model ligament and manubrium remain rigid despite these variations.

$E_C$ and $E_R$ do vary significantly with the thickness of the model pars tensa; however, $G_{CR}$ does not. As the thickness increases, estimates of $E_C$ and $E_R$ must decrease in order to maintain the overall structural stiffness. The upper thickness values were limited as estimates of $E_C$ and $E_R$ reach the set lower bound of the search space (7 MPa for both $E_C$ and $E_R$) at large thicknesses. The lower bound was not further decreased because it is unlikely that the rat eardrum is uniformly thicker across its surface and because of numerical instabilities. Hesabgar et al. [23] also observed that their estimate of the Young’s modulus in their isotropic model of the pars tensa decreases as the thickness of the model pars tensa increases. Micro-CT as used here cannot resolve the variations in pars tensa thickness over its surface. Confocal microscopy is suitable [5-7], but has not been applied to rats. This work highlights the need for the measurement of thickness variations in rats.

The pressurization-based method is simpler to use than the indentation-based approach for two primary reasons. First, when conducting indentation testing on an actual eardrum, care must be taken to ensure that the indenter remains perpendicular to the local eardrum surface to minimize the slipping of the indenter with respect to the eardrum. Second, simulating the indentation experiment involves contact modeling, which is complex. Despite its relative simplicity, the pressurization-based approach was not applied to actual rat eardrums as the effects of coating the eardrum on its mechanical behaviour need to be investigated for this particular coating. Recall that when using profilometry to measure shape, a coating is needed to ensure that the eardrum reflects light diffusely and has high contrast. The effects of the coating are currently being tested. The pressurization-based approach will be applied to actual eardrums in future studies.

5. Conclusion

Two techniques were developed to estimate the orthotropic elastic parameters of the rat eardrum, namely an indentation-based technique and a pressurization-based technique. Tests on synthetic data indicate that the pressurization-based technique is more robust to simulated noise than the indentation-based technique. With the pressurization-based method, estimated parameter values are within 10% of the known values used to generate synthetic data for an SNR of 2 or greater in the measurements. The indentation-based technique requires an SNR of 200 or greater to attain errors of less than 10%. Although in general the simplex optimization method requires initialization values that are not very different from the correct
parameter values, both the indentation and pressurization techniques as described here are robust to a wide range of initialization values. Using an average uniform pars-tensa thickness of 12 µm, estimates of $E_T = 23.4 \pm 1.6$ MPa, $E_P = 58.7 \pm 4.2$ MPa, and $G_{CR} = 35.6 \pm 3.3$ MPa were obtained for rat eardrums using the indentation-based technique for which prior data were available. These estimates are insensitive to all other modeling parameters except for pars tensa thickness.

Acknowledgements

Funding for this work was provided by the Natural Sciences and Engineering Research Council of Canada by Medtronic Canada. E. Salamati also received partial stipend support from Western University.

References


