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Subject-Specific Computational Modeling of Evoked Rabbit Phonation

When developing high-fidelity computational model of vocal fold vibration for voice production of individuals, one would run into typical issues of unknown model parameters and model validation of individual-specific characteristics of phonation. In the current study, the evoked rabbit phonation is adopted to explore some of these issues. In particular, the mechanical properties of the rabbit's vocal fold tissue are unknown for individual subjects. In the model, we couple a 3D vocal fold model that is based on the magnetic resonance (MR) scan of the rabbit larynx and a simple one-dimensional (1D) model for the glottal airflow to perform fast simulations of the vocal fold dynamics. This hybrid three-dimensional (3D)/1D model is then used along with the experimental measurement of each individual subject for determination of the vocal fold properties. The vibration frequency and deformation amplitude from the final model are matched reasonably well for individual subjects. The modeling and validation approaches adopted here could be useful for future development of subject-specific computational models of vocal fold vibration. [DOI: 10.1115/1.4032057]

Keywords: vocal fold vibration, computational modeling, individual-specific models, fluid–structure interaction, magnetic resonance imaging

1 Introduction

Vocal fold vibration during voice production is a result of bio-mechanical fluid–structure interaction (FSI) between the glottal airflow and the elastic tissue of a pair of vocal folds. Computational modeling of this interaction is useful for understanding the physics of voice, studying vocal fold pathology (e.g., nodules and polyps), and developing computer-based tools for clinical

management of voice disorders [1,2]. In recent years, there have been significant efforts in developing advanced computational models of the vocal folds, which are driven by the rapid growth of computing power and also by the need for higher realism when one is trying to capture the features of the vocal fold dynamics for individual patients. For a comprehensive review of progress in vocal fold modeling, readers are referred to a recent article by Mittal et al. [1].

In general, a computational model for FSI of the vocal folds includes a flow model based on the viscous Navier–Stokes equation for the unsteady glottal aerodynamics and a solid mechanics model for dynamic deformation of the soft tissue. Previously,

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both 1D and two-dimensional (2D) models have been extensively used in the literature [3–5]. More expensive 3D models are also being increasingly adopted, and they may include 3D characteristics of the airflow, the tissue, or both [6–10] and can thus provide more details of the phonation process, e.g., the impact stress on the medial surface.

With assistance from modern medical imaging technology, such as computerized tomography (CT), the information on the 3D anatomy of the larynx can be obtained and incorporated into these computational models [11]. For example, Xue et al. [12] developed a subject-specific model of human phonation based on CT scans and discussed the influence of the anterior–posterior asymmetry on the phonation characteristics along with some interesting 3D flow features. Because the CT scan did not provide morphology of the interior tissue, the internal structure of the vocal fold in their study was based on histological data, and detailed comparison between simulation and subject-specific experimental results was not provided.

In terms of cost, the 3D models are usually computationally intensive and may require days of simulation or even longer on high-performance computers. Therefore, there are rare attempts for using such models for extensive exploration in large parameter spaces. Such exploration may be needed for design optimization and for determining unknown model parameters by solving an inverse problem. As one specific example, in the computational models that are based on medical images, one typically has to assume population-averaged material properties for the tissue, even if the individual 3D morphological features can be incorporated into the model. The unavailability of individual material characteristics thus limits realism of a subject-specific model. Generally speaking, how to incorporate specific tissue properties, validation of individual-specific vibratory characteristics, and reducing the computational cost will be three of the major challenges for subject-specific models.

In this work, we investigate the feasibility of developing subject-specific models based on MR images of the rabbit's larynx and explore the use of a low-dimensional flow model to assist with identifying the elastic properties of the vocal fold tissues, by matching the simulated vibratory characteristics, with those obtained from individuals during the phonation experiment. We expect that both the method of parameter identification and the method of validation will be instrumental for future development of 3D high-fidelity computational models with validated subject-specific characteristics.

2 Materials and Methods

2.1 In Vivo Rabbit Phonation Procedure. The animal protocol was approved by the Vanderbilt University Institutional Animal Care and Use Committee. Five male New Zealand white breeder rabbits were used. As previously described [13,14], rabbit phonation was elicited by performing a bilateral Isshiki type IV thyroplasty. The procedure entailed suturing the thyroid and cricoid cartilages, thus bringing together the vocal folds, while delivering continuous humidified airflow to the glottis. In setting the sutured adduction, suture tension was adjusted for each animal

until audible phonation was produced [15]. This technique promotes the maintenance of the vocal folds in the adducted phonatory position for later microimaging. In vivo phonation was captured using a high-speed camera (KayPENTAX, Montvale, NJ) filming at 10,000 frames per second, and the acoustic and aerodynamic measurements were performed, including measurements of the subglottal pressure, the volume flow rate, and acoustic intensity. Details of the experimental setup and data collection can be found in Novaleski et al. [15] and Ge et al. [13], which provide methodological details and schematics of the experimental setup. The subglottal pressure will later serve as an input parameter for the computer model.

To minimize the degree of vocal fold tissue change, phonation trials were elicited for only brief periods (i.e., 10–20 s per trial). These short durations were interspersed with rest periods in between each trial, until all data were collected, to control for the influence of external factors, such as changes in hydration, humidity, and other environmental effects. Presented in detail elsewhere [15], the data collected from trial to trial were fairly consistent.

2.2 Scanning Procedure. After the phonation procedure, the larynx was excised and high-resolution MR imaging was performed to obtain details of the morphology of the vocal folds in the adducted phonatory position. These subject-specific scans were then used to accurately replicate the individual rabbit's laryngeal anatomy. Excised laryngeal specimens were secured in a 12 mL syringe with Fomblin 06/6 perfluoropolyether (Solvay Solexis, Thorofare, NJ) and placed in a 38-mm inner diameter radiofrequency coil. The specimen was not doped in contrast agent and was scanned within several minutes after harvest. A magnetization-prepared and rapid gradient-echo imaging sequence was used with T2-weighted-prep with echo train length of 40, repetition time of 550 ms, and a field of view of $32 \times 17 \times 17 \text{ mm}^3$. The matrix size was $512 \times 256 \times 256$. Total scanning time was 12 hrs. A Varian 9.4 T horizontal bore imaging system (Varian Inc., Palo Alto, CA) was used in the sequence to obtain multislice scout images in the axial, coronal, and sagittal imaging planes. Acquired data were reconstructed in MATLAB 2012a (MathWorks Inc., Natick, MA) using an inverse Fourier transform. We have not yet performed scanning of the in vivo sutured geometry.

2.3 Model Reconstruction. The laryngeal architecture was reconstructed using manual segmentation. Based on the reconstructed larynx, a 3D computer model was generated to simulate the flow-induced vibration of the vocal folds. Figure 1 shows the workflow of reconstructing the laryngeal model from the MR images. The rabbit larynx was extracted from the MR scans as a surface mesh using the open-source software ITK-SNAP. The larynx included the true vocal folds, the false vocal folds, and a short segment of the trachea and supraglottal area. Manual segmentation was used here to ensure accuracy of the reconstructed geometry. The segmentation procedure was repeated by a second experimenter to ensure its reliability. The extracted surface mesh originally had a stair-step shape but was smoothed in ITK-SNAP with Gaussian image smoothing using standard deviation of 2.0

Fig. 1 Workflow of model reconstruction: (a) segmentation, (b) surface mesh extraction, (c) mesh smoothing, and (d) the finite-element mesh

and approximate max error of 0.02. Then, a tetrahedral mesh for finite-element analysis was generated using commercial software (ANSYS ICEM, version 13.0). The reconstructed laryngeal geometry was approximately 1.0 cm long, 1.0 cm wide, and 1.0 cm high and contained around 10,000 vertex nodes and 40,000 elements. Figure 2 shows the reconstructed larynx from the posterior and superior views. In the finite-element model, all the exterior surfaces are fixed except that the lumen surface is free. Because the cover layer of the vocal fold is very thin (two elements at some locations), its geometric specification could be mesh-sensitive. Thus, we manually made the larynx model and its meshing symmetric. This treatment did not create any significant problems, since the actual vocal fold vibration was fairly symmetric, as observed in the high-speed video recordings.

The vocal fold tissue was assumed to be isotropic and governed by the Saint Venant–Kirchhoff model with the density $\rho_s = 1000 \text{ kg/m}^3$ and Poisson's ratio of 0.3. The Saint Venant–Kirchhoff is a simplified nonlinear model which assumes a linear relationship between the stress and the strain but the finite strain takes into account the nonlinear effects due to large displacements and large rotation, i.e., geometric nonlinearity as previously discussed for vocal fold modeling [9,16].

Approximately two layers of the internal structure of the vocal fold tissues were observed as shown in Fig. 3(a), and thus the vocal folds were modeled to have a two-layered setup as shown in Fig. 3(b), i.e., the vocal fold cover in contact with the air and the body underneath the cover. Such a simplified structure has also been adopted in previously studied idealized vocal fold models [6,17]. Young's modulus of each layer was later determined from the simulations. From previous measurements of the tissue stiffness for the human vocal fold, the body layer is much stiffer than the cover layer. Furthermore, the effect of the body-cover stiffness ratio has been investigated previously [17]. From these results, the ratio was kept above five in the current simulations. The thickness of the cover layer, h_c , is around 1 mm. Note that in Fig. 3, the view is along the x -direction and the slice is not exactly parallel with the vocal fold (see Fig. 4 for the orientation of the vocal

Fig. 2 Reconstructed larynx geometry from (a) a posterior view and (b) a superior view, where the vocal fold remains in a closed position

Fig. 3 (a) An axial slice of the vocal fold from the MR scan, where the cover layer is marked out, and (b) assumption of the profile of the vocal fold cover and body in the model

Fig. 4 Three-dimensional flow simulation in the stationary domain with an open glottis, where the thick curved line indicates the streamline extracted for later 1D flow model and the thick straight line represents a cross section perpendicular to the streamline

fold). Therefore, the cover layer is not as posterior as it appears to be in Fig. 3.

2.4 Setup of the Hybrid FSI Model. The low-dimensional flow model in the current study is simply based on the Bernoulli principle of ideal flow. Nevertheless, when applying this principle, we will identify a proper streamline for the anatomical geometry through a 3D flow simulation of the stationary domain. Note that the Bernoulli principle has long been used as a simple tool by the voice community to study vocal fold function [18]. Previously, this 1D flow model was also combined with vocal fold models of higher dimensions (2D or 3D) to study the FSI of phonation and was shown to be capable of capturing the most basic characteristics of vocal fold vibration [19,20].

Extending the lumen surface of the reconstructed vocal fold in both subglottal and supraglottal directions as shown in Fig. 4, we obtain an approximate domain for the airflow, which is driven by the subglottal pressure at the inlet. To identify a proper streamline in the curved passage, the vocal fold deformation is first simulated in the absence of flow but under a constant pressure load on the tissue surface. Then, the stationary geometry with an open vocal fold was used to simulate the 3D flow through the glottis using an in-house code. Note that the magnitude of the vocal fold opening and the detailed variation in the glottal shape along the flow do not significantly affect the direction of the streamline before the glottal exit. A segment of the streamline was taken from the center of the glottis and was used for subsequent application of the Bernoulli equation. The equation and the continuity equation are

$$P_0 + \frac{1}{2} \rho u_0^2 = P_1 + \frac{1}{2} \rho u_1^2 = P_s + \frac{1}{2} \rho u_s^2 \quad (1)$$

$$u_0 A_0 = u_1 A_1 = u_s A_s$$

where P , u , and A represent the pressure, the velocity, and the area of the cross section, respectively, and the subscripts represent the location of evaluation, i.e., 0 for the start of the streamline, 1 for the end where the flow separation takes place, and s for an arbitrary point on the arc in between. P_0 is assumed to be the constant subglottal pressure measured from the phonation experiment, and $P_1 = 0$ is simply the ambient pressure. The area of the cross section at any given point s will be calculated in the hybrid FSI model, based on the time-dependent deformation of the vocal folds.

Decker and Thomson [19] reported that the influence of position of the flow separation point on the vibration frequency and displacements was small. In the current model, the separation point was consistently selected as the location with the minimum cross section area, $A_{\min}$. We have tested sensitivity of the model to the flow separation point. If this location is near the minimum cross section area, then the vocal fold vibration is not significantly affected. For example, we have moved the separation point further downstream at $A_1/A_{\min} = 1.1$, and the vibration amplitude only

changes by 3% and the frequency by 1%. However, if we fixed the location at any particular point rather than keeping it dynamically varying, the change in the vibration could become more evident (e.g., significantly reduced amplitude).

The FSI simulations are performed using an in-house finite-element code for soft tissue deformations [9]. The time step was 0.001 ms, and one vibration cycle took about 2000 time steps. A small gap of 0.05 mm was imposed between the two medial surfaces, at which the surfaces are assumed to be in contact. More than 20 vibration cycles were simulated after the vibration was well established, and from these cycles statistics were taken.

3 Results

3.1 Experimental Results. As mentioned earlier, in vivo phonation was captured using high-speed imaging and acoustic and aerodynamic measurements. Figure 5 displays images from the high-speed video recordings for one typical vibration cycle of sample 1. In this figure, we also illustrate the definition of the vocal fold length, L , which begins from the anterior commissure and ends at the vocal process. From the imaging sequences, sustained vibration was observed for all samples and the opening/closing motion was fairly consistent among the samples. The vocal folds move mostly in the lateral direction. However, the phase differences in the longitudinal direction and also in the inferior–superior direction can be observed.

The time-dependent vibration amplitude at the midportion of the glottis was extracted in MATLAB using its image processing toolbox, and its peak value averaged from multiple vibration cycles, $d_{\max}$, will be used later to compare with the simulation

Fig. 5 A typical vibration cycle in the evoked rabbit phonation via high-speed imaging, where the definition of vocal fold length, L , and the amplitude of opening, d , are shown

Table 1 Aerodynamic and acoustic measures with the subglottal pressure P_0 (kPa), the volume flow rate of air, Q (cm³/s), the fundamental frequency of vibration (Hz), the acoustic intensity (dB), and the ratio between the vibration amplitude and the vocal fold length, $d_{\max}/L$

Sample	P_0	Q	Frequency	Intensity	$d_{\max}/L$
1	1.05	33	564–618	59.22–62.6	0.088
2	0.78	40	553–563	56.7–58.6	0.081
3	0.72	40	419–432	56.1–57.9	0.098
4	1.00	40	613–683	63.2–65.9	0.076
5	0.98	50	539–728	64.8–68.5	0.081

results. Table 1 lists the in vivo aerodynamic and acoustic measurements for each sample. We point out that the phonation frequency and intensity values are similar to those obtained from experimentally induced phonation using neuromuscular stimulation (rather than suture) [14,15]. Such aerodynamic and acoustic assessment confirms that the current elicited phonations are consistent with previous modal intensity phonation and that the suture tension was appropriate.

3.2 Simulation Results. The hybrid FSI model was constructed from the reconstructed 3D vocal fold tissue structure and the simplified 1D flow model as described in Sec. 2.4. Since the elastic properties of specific tissue samples are a priori unknown, in this study we adopted a trial-and-error approach. Note that an automated approach by solving an optimization problem is also possible but is not adopted here since the number of samples and the parameter space are relatively small in this exploratory study. Young's modulus of each vocal fold layer was first chosen based on an eigenmode analysis of the vocal fold tissues, and a sequence of simulations of the hybrid model was then run with the goal of matching the normalized vibration amplitude, $d_{\max}/L$, and the fundamental frequency with the experimental data listed in Table 1. Between 10 and 50 simulations were usually enough for each sample. The final result from the simulations is listed in Table 2.

In the previous work of Thibeault et al. [21] and Rousseau et al. [22], the shear modulus of the rabbit vocal fold lamina propria (within the cover layer) is between 0.2 and 20 kPa. Latifi et al. [23] later did uniaxial tensile testing of rabbit vocal fold tissues in the longitudinal direction and determined that Young's modulus is up to 170 kPa, a result that needs to be further confirmed according to them. In the current study, the vocal fold is assumed to be isotropic; thus, the stiffness becomes higher when matching the frequency with that of the anisotropic tissue, which has greater stiffness in the longitudinal direction. Nevertheless, the Young's modulus we obtained, around 10 kPa for the cover layer, still has the same order of magnitude as measured in Thibeault et al. [21] and Rousseau et al. [22].

Comparison of the simulation and experimental results is shown in Fig. 6 for the vibration frequency and amplitude. It can be seen from these results that in general, the vibration frequency from the model falls within the range of measured frequency, even though the model frequency is slightly lower. In Decker and Thomson [19], the frequency obtained from a similar hybrid model (where the vocal fold geometry is idealized) is about 6% lower compared with the full 3D model. Therefore, we expect that the frequency match will be better in full 3D FSI models, developed later based on this work.

The figure also shows that the normalized vibration amplitude is generally in the range of experimental results, although for samples 1, 3 and 4, the simulation gives an overall smaller amplitude.

Self-sustained vibration is established in all final simulation cases. Figure 7 shows typical sequences of oscillations of the glottal gap width from the experimental and model simulation. The gap width has been normalized by its averaged peak magnitude so that we can focus on the waveform only. The time is also shifted

Table 2 Final result from the FSI simulation including Young's modulus of the vocal fold body, E_b (kPa), Young's modulus of the cover, E_c (kPa), the normalized vibration amplitude, and the vibration frequency (Hz)

Sample	E_b	E_c	$d_{\max}/L$	Frequency
1	60	12	0.0719	601
2	80	8	0.0851	545
3	80	8	0.0836	611
4	90	9	0.0675	589
5	90	9	0.0848	591

Fig. 6 Comparison between the simulation result and experimental measurement: (a) frequency and (b) amplitude-to-length ratio, $d_{\max}/L$

Fig. 7 Waveform of the normalized glottal gap width from the experiment and simulation

Fig. 8 A typical cycle of vibration obtained from the simulation for sample 1

by a constant offset for easier comparison. It can be seen that the waveform obtained by the simulation matches that from the experiment reasonably well.

In Fig. 8, one typical vibration cycle is shown for the superior view of the glottis. It can be seen that the narrow opening of the glottis generally is consistent to that observed in the high-speed video recordings. As observed in the experiment, the simulated glottis has greatest opening amplitude and greatest impact around the midportion of the medial surface.

4 Further Discussion

The current study only represents an exploratory step toward developing future subject-specific computational models of phonation, and we focus on identification of unknown model parameters, and comparison of individual-specific characteristics between the model and subject. Both the number of subjects and number of unknown parameters in the model are very small. However, the result has implications to broader and more extensive study in the same direction. For example, the current model could be extended in a straightforward manner to incorporate an

anisotropic tissue model [6] or hyperelastic materials [24]. Furthermore, a suite of well-established optimization packages could be adopted to automate the procedure. We emphasize that in this parameter identification process, reduced-order models such as in the current study will be useful tools for rapid model-based predictions and for complementary analyses along with full 3D models. We envision that the general methodology developed in this work could be extended to the study of individual human subjects, e.g., to determine the tissue properties of the vocal fold in vivo and to develop corresponding 3D FSI models. However, there are several challenges in performing similar studies for live human subjects. In particular, the suture method cannot be used. Thus, performing in vivo high-resolution MR scanning in humans would require the development of a subject-specific task (e.g., Valsalva) that can be accomplished during the imaging procedure to overcome these challenges. Alternative imaging modalities (e.g., CT) may also be explored in future studies and used to validate the computational models generated.

Due to the simple model adopted here, the current study is also subject to some limitations. First, an isotropic tissue representation has been used with a simple constitutive law (the Saint Venant–Kirchhoff model). Second, the flow model is based on the Bernoulli principle and thus does not provide any information on vortex formation or 3D flow pattern in the supraglottal region. This model will need to be refined for study of vibration asymmetry, where the flow may become skewed and the flow separation point will be different on the medial surfaces of the two vocal folds. Future studies using experimental and 3D computational approaches are planned to advance the accuracy of such reduced-order models.

Finally, another limitation of the current approach is that the criteria used for model validation are still limited to the most basic temporal and spatial variables. As the tissue model becomes more realistic and 3D flow is included in the full simulation, we plan to collect additional details of the vibratory characteristics and pursue higher levels of validation.

5 Conclusion

A combined experimental and numerical study has been performed for evoked rabbit phonation with the goal of exploring issues related to parameterization and validation of subject-specific computational models. In the present study, the laryngeal anatomy was successfully reconstructed using MR scans. An efficient hybrid model was then created to identify the unknown properties of the 3D vocal fold tissue, and the model validation was based on comparison of individual-specific characteristics of vocal fold vibration measured from the in vivo phonation experiment. The results show that the models with identified parameters were able to match the vibration frequency and magnitude of individual samples. These models will be used for future study of full 3D models.

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