Stochastic Modeling of Biological Systems – Ranking the Model Parameters of the Human Vocal Folds

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Introduction

Computational models of biological systems are becoming more and more common in medical research areas. Evidence of this can be found by examining the number of articles containing the term "finite element" in the expansive National Institutes of Health (NIH) digital research archive PubMed. Between the years 1985 and 2005, the number of research studies that referenced the finite element method increased 29-fold from 206 in 1985 to nearly 6000 in 2005. Numerical modeling of biological systems allows the execution of "computational experiments" that are impossible to duplicate in reality, and provides many unique insights for biological research questions. However, unlike typical engineering systems, biological systems are characterized by extremely high levels of uncertainty. In biological modeling, many geometric and material parameters which are required for the solution of finite element models are either poorly understood, or have often never been measured experimentally. One way to circumvent this challenge is to use methods of stochastic modeling to create a "sample set" of numerical models in much the same way that medical researchers use a sample when conducting traditional medical research. This paper presents the use of COMSOL Multiphysics to generate a random sample of computational vocal fold models. Statistical analysis of these models was then used to rank the model parameters according to their influence on the model behavior, thus reducing the number of parameters that must be considered in future experimental and computational research studies.

The system of interest in this study was the human vocal folds (vocal cords). While the geometry of the human vocal folds is relatively well understood, less than half of the vocal fold material properties have been measured experimentally. The vocal fold geometry is shown in Figure 1. In this study, all model parameters were assumed to behave as random variables. A probability density function (pdf) was defined for each parameter, and individual vocal folds were formed by randomly sampling each model parameter from its respective pdf.

Use of COMSOL Multiphysics

COMSOL Multiphysics with MATLAB was used to create thousands of finite element models of the human vocal folds using the random sampling scheme mentioned above. Each model possessed a unique set of geometric and material parameters. Custom subroutines created each model geometry, defined material parameters and applied the same topologic mesh to all finite element models. The model described in this study is an improvement over previous models in that the geometry and boundary conditions have been updated to more accurately represent the physiology of the human vocal folds. Transitional boundary regions were also added to represent the gradual increase in stiffness that is observed near the boundary between the vocal folds and attachment cartilage. The structural mechanics module was used to perform eigenvalue/eigenvector analysis on each vocal fold model. The resulting data were then used to rank the model parameters according to their influence on modal frequencies.

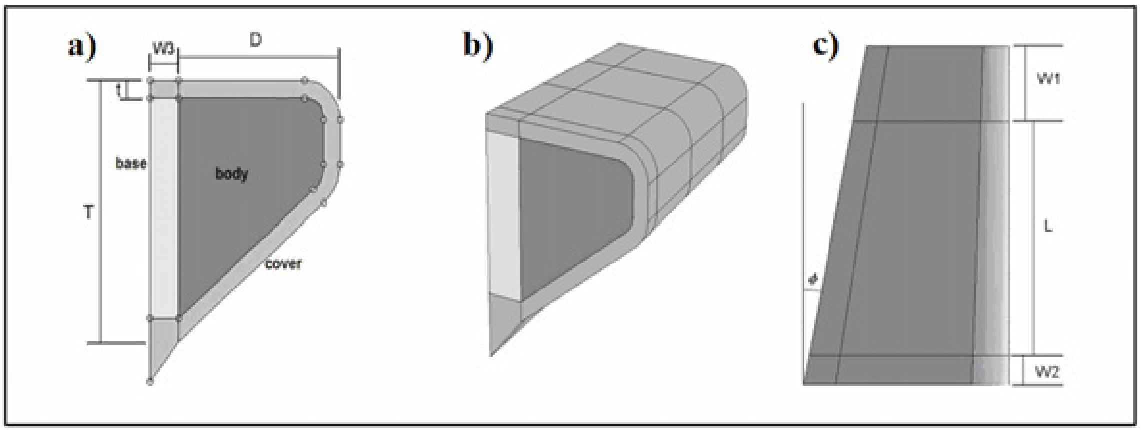

Figure 1: Idealized Geometry of the Human Vocal Folds

Results

Three distinct statistical methodologies were applied to this problem. First, Cotter's method (Cotter, 1979) of screening for influential parameters was used. Second, Monte Carlo sampling was used to generate a sample of 100 random vocal fold models. The correlation between modal frequencies and model parameters were examined using Pearson correlation. Finally, local sensitivity analysis was performed and the results were tabulated. The results of these three methods were in general agreement, identifying a set of five parameters as most influential in determining the modal frequencies of the vocal folds. Normalized rankings of all 14 model parameters are shown in Figure 2 below.

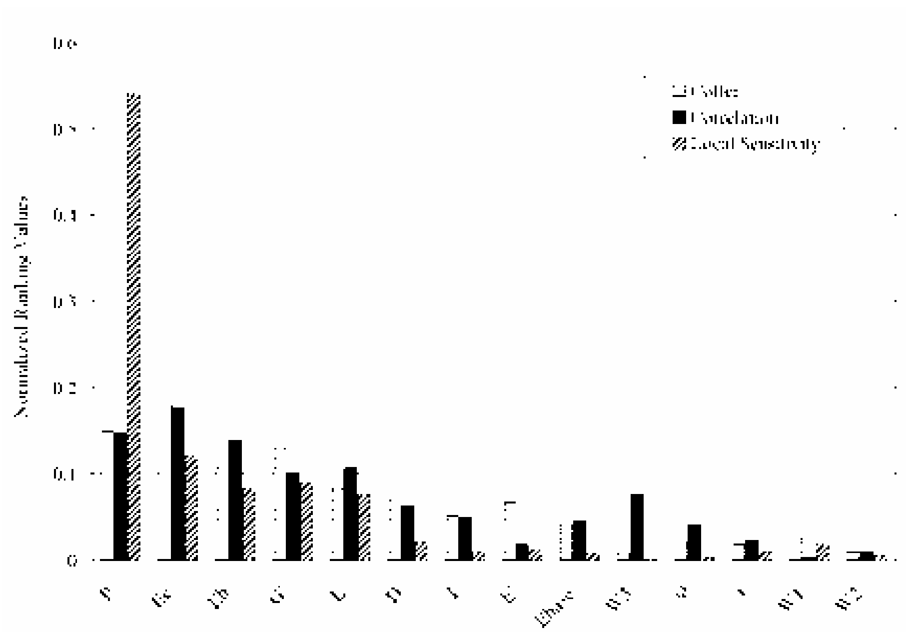

Figure 2: Comparisons of parameter ranking results

Conclusion

The above results have several interrelated applications. First, these results can be used to guide the experimental measurement of vocal fold tissues since more influential tissues should clearly be measured before less influential tissues. Second, the identification of the most and least sensitive model parameters has great importance for computational models of phonation. Highly sensitive parameters should either be based on experimental data or varied parametrically to account for uncertainty until more such data is available. Less sensitive parameters may be estimated with the assurance that erroneous estimations will not have serious adverse affects. Finally, the identification of several highly influential parameters may suggest new approaches for treating certain voice disorders.

Reference *(Optional)*

1. Cotter, S.C. (1979) “A screening design for factorial experiments with interactions” Biometrika, **66**(2) pp. 317-320.

2. Cook, D.D. (2009) “Systematic Structural Analysis of Human Vocal Fold Models” Ph.D. Dissertation, Purdue University.