SHIFTING TO POPULATION-BASED MODELS AND INFERRING MODEL STRUCTURE FROM DATA ARE TWO DIRECTIONS THAT WILL ENHANCE THE CLINICAL USEFULNESS OF MODELING

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INTRODUCTION

The clinical promise of biomechanical models lies in their ability to explain, illustrate and predict the functional consequences of injury, disease and treatment on the basis of first principles. Many advances in computational methods, computer hardware and computer graphics have greatly facilitated the creation and use of ever more complex models. We propose, however, that continuing on this path does not guarantee that modeling will revolutionize clinical care. We argue that the conceptual framework for modeling is, in general, limited because it is largely an exercise in parameter estimation that does not consider population variability. We underscore the need to adopt a population-based strategy where the structure of the model is inferred from data.

POPULATION-BASED MODELS

A model is generally taken to be a single instantiation of a biological process that results in specific predictions. This frequentist approach applies well when simulating the behavior of either a single individual or the representative (i.e., mean) behavior of a group. It is less informative of the general trend of behavior in the general population, or of how the unavoidable variability in a population produces variable performance across the population. Bayesian inference techniques like Monte Carlo simulations [1-3] are well suited to approach these questions. In this Bayesian approach, model parameters are variables that, like people, are best described as randomly drawn values from statistical distributions (called "prior distributions") instead of specific constant values. This approach produces "posterior distributions" describing the likely performance across the population. For example, the multimodal distributions of thumb kinematics arising from bone variability (Fig 1) enables the exploration of biomechanical explanations for the clinical reality that a same diagnosis leads to distinct groupings in the rate and amount of impairment and recovery after treatment. If there are truly several "types" of people, modeling can then explain why some are more/less susceptible to disease and more/less responsive to treatment.

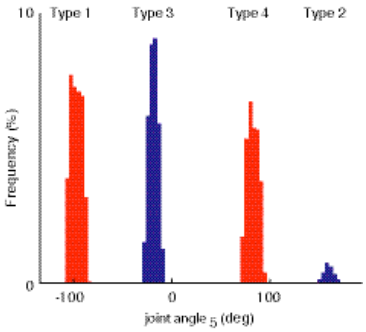

Figure 1: Monte Carlo simulations suggest there are 4 "Types" of thumb kinematics, distinguished by the angle at joint #5 needed to reach a reference configuration [1].

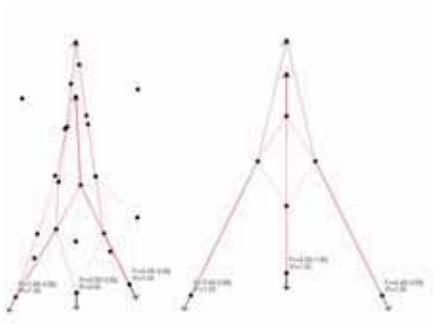

Figure 2: The tendon network at left arose from the unsupervised inference of the hidden network at right via random loading of a uniform mesh at three nodes.

INFERRING MODEL STRUCTURE FROM DATA

For complex anatomical structures such as the hand, it is necessary to explicitly distinguish between model structure (i.e., the preconceived morphology) and parameter values (i.e., the particulars of that structure). The inevitable discrepancies between predicted and measured data can be attributed to unsatisfactory parameter values, inadequate model structure or both. In contrast, today's biomechanical models consist of manually assembled structures where only the parameter values are systematically adjusted to explain and/or reproduce experimental data. Thus, improving current models necessitates that we explicitly investigate how the assumed model structure fundamentally determines and limits model behavior. Extending prior work [4], we now have unsupervised algorithms that simultaneously infer both the model structure and parameter values to best explain data (Fig 2). In this way, models can begin to clarify how disease and treatment affect the type, connectivity, properties, parameters and interactions of available "building blocks" such as bones, tissues, tendons, muscles, neural circuits, etc.

CONCLUSIONS

Population-based models with data-driven structures will enable new and powerful clinical applications of modeling.

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