Proceedings of the ASME 2011 Summer Bioengineering Conference
SBC2011
June 22-25, 2011, Farmington, Pennsylvania, USA

SBC2011-53749

A PIPELINE FOR HIGH THROUGHPUT POST-PROCESSING OF JOINT AND TISSUE SIMULATIONS FOR ESTIMATION OF CELL LEVEL DEFORMATIONS

Scott Sibole and Ahmet Erdemir

Computational Biomodeling (CoBi) Core and Department of Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, 44195

INTRODUCTION

In biomechanics, the search for a better understanding of multiscale spatial interactions has become an increasingly desirable objective, in order to establish the causal mechanical relationships between the loading of joints, tissues, and cells. Experimental acquisition of mechanical data, while attainable [1], becomes more difficult to obtain as the spatial scale decreases. If one attempts to gather data at different spatial scales simultaneously, also under lifelike loading scenarios, the present technology is limited. Computational modeling, particularly when conducted in a multiscale fashion, may provide solutions and has often been employed to span spatial scales.

Most multiscale modeling methodologies can be divided into two categories: concurrent or autonomous. Concurrent methods are symbiotic, requiring communication between models at different scales as the solution progresses. A common approach is computational homogenization [2], in which the macro scale constitutive behavior of a model is derived from on-the-fly simulation of a microstructural model. This methodology has been employed in many applications ranging from modeling of fibrous tissue [3] to structural analysis of cellular constructs [4]. Computational cost is a limitation, usually requiring utilization of high performance computing facilities. The advantage is that the macroscopic response is a direct function of microscopic behavior. Autonomous methods rely on post-processing and are unidirectional and have lower computational cost, because the macroscopic model is solved independently and micro level simulations utilize these results only for the final solution. Micro-level simulations are independent and can be conducted asynchronously. It should be noted that this process relies on the assumption that macroscopic constitutive behavior and the average response of the microscopic model are mechanically consistent [5]. Similar analysis has only been conducted for a few points in simplified tissue level macroscopic models for a limited number of loading cases [6].

The goal of this study is two fold: (i) to establish a pipeline to post-process macro-level finite element analysis results to estimate micro-level cell deformations for desired macroscopic regions at a desired time point of the loading, ii) to illustrate its utility through estimation of chondrocyte deformations in tibial cartilage for compressive loading of the knee undergoing passive flexion.

METHOD

Our approach involved a series of stages beginning with the solution of a single macroscopic model at the joint scale and ending with the post-processing of many microscopic model simulations at the cellular scale (Figure 1).

MACROSCOPIC MODEL: A free and open access finite element representation of the tibia-femoral joint was used to obtain a solution at the macroscopic scale (https://simtk.org/home/openknee). The tibia, femur, collateral and cruciate ligaments, menisci, and femoral and tibial cartilage were represented. All soft tissue were assigned hyperelastic material properties based on literature values, while the bones were assumed to be rigid. Frictionless contact was defined between all soft tissue structures which may interface. Loads and boundary conditions were prescribed to simulate passive flexion. Specifically, the tibia was fixed in space for the entire solution time, while the femur was prescribed a distal (compressive) load of 100N linearly ramped from time=0-1sec and then held constant; followed by a 45 degree flexion linearly ramped from time=1-2.5sec. All other

femoral degrees of freedom were free. Implicit dynamic analysis was conducted using FEBio [7]. The deformed nodal positions (at 0.1sec intervals) were written to a text file as the solution progressed.

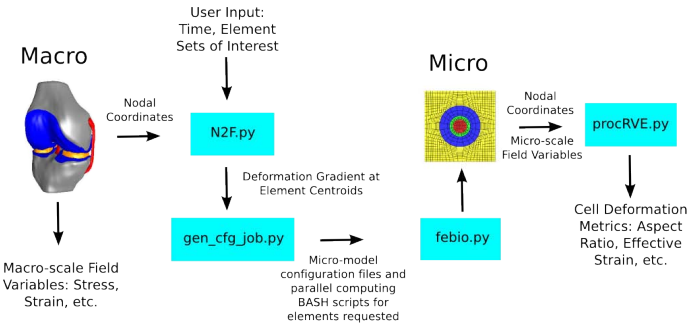

Figure 1: Pathway for determining cell scale deformations from a joint scale model autonomously. Finite element analysis was conducted using FEBio and Python was used for automation of model generation and post-processing.

MACROSCOPIC ELEMENT DEFORMATION GRADIENTS: The reference and deformed nodal positions from the macroscopic model were used to calculate the deformation gradients occurring at element centroids for user-specified element sets at user-specified simulation times. For the current study, the results reported are for the top layer of tibial cartilage at a simulation time of 1sec.

MICROSCOPIC MODEL GENERATION: Microscopic model input decks for elements which experienced deformation gradients that varied from the identity tensor by more than 0.01 in any index were generated. The model consisted of a single spherical chondrocyte (of radius 10 μm) surrounded by a peri-cellular matrix (PCM) (of thickness 5 μm) and contained within a 100x100x100 μm block of extracellular matrix (ECM), similar to previous studies [8]. These were assigned elastic material properties valid for finite strain [9]. The nodes on the six faces of the ECM block were prescribed displacement boundary conditions derived from the application of the macroscopic element deformation gradients to their reference positions. This was done with a Python script executed repeatedly in serial.

MICROSCOPIC MODEL SOLUTION: The solutions to all microscopic finite element models were obtained in parallel using FEBio [7] on the Glenn Cluster of the Ohio Supercomputer Center (http://www.osc.edu). All stress and strain tensor components and deformed nodal positions were written to text files for each solution.

MICROSCOPIC MODEL DEFORMATION ANALYSIS: To quantify the deformation of cells in the microscopic models the volume averaged effective (von Mises) strain, effective stress, and maximum shear strain, as well as, the initial and deformed aspect ratios were calculated for the chondrocyte. These analyses were performed in parallel. The aspect ratios were obtained by calculating the moment of inertia tensor with the mass contribution of each element within the cell, assuming a unit density. The eigenvalues, λ_i, of this tensor correspond to the principal moments of inertia which can be related to the object shape [10].

RESULTS

The employed autonomous approach was capable of processing joint scale simulation results to estimate cellular scale deformations for a large number of points within the tibial cartilage volume (Figure 2: left). Cellular models, associated with element centroids experiencing the highest strains in the macroscopic model, exhibited the highest deformation metrics. Further, the cellular deformations were greater in magnitude than the deformations occurring at the joint scale (Figure 2: middle and right).

A wall-clock time of approximately 12 hours was needed to complete the entire process. The majority of this time, approximately 6 hours, was spent solving the macroscopic model. Microscopic model generation took approximately 4 hours as it was performed in serial at the current stage of the proposed pipeline. Microscopic model solutions and data processing were both performed in parallel taking less than an hour wall-clock time each. A total of 852 micro-level simulations were conducted.

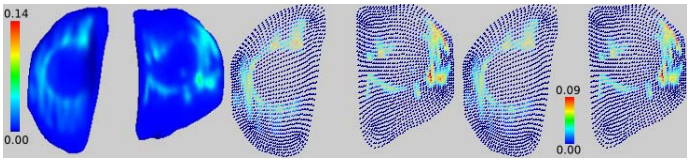

Figure 2: (left) Effective Green-Lagrange strain distribution in the macroscopic model. (middle) Volume averaged effective Green-Lagrange strain experienced by cells. (right) Change in cell aspect ratio (major to minor).

DISCUSSION

The pathway developed in this study was a preliminary step to relate the body level mechanics to cell scale deformations. To our knowledge, this is the first to study to provide an estimate of chondrocyte deformations for a large number of points within a tissue region of the knee, which was loaded at the joint level. As in previous modeling studies [11], macroscopic deformations were found to be transmitted to chondrocytes in an amplified manner.

The autonomous method employed in this study allows asynchronous simulations at the micro scale, indicating the suitability of the procedure for grid computing. With access to freely available finite element analysis software platforms [7] and volunteer grid computing resources (http://www.boinc.edu), prediction of cell deformations for a range of lifelike loading conditions throughout the whole tissue geometries may be possible.

Many fundamental multiscale issues such as mechanical consistency between scales and statistically, geometrically and mechanically appropriate representative volume element selection still need to be addressed. Nonetheless, these may be handled independently without modification of the described method. Data generated using this method may be employed to define constitutive relationships between tissue and cellular scales through correlation of macroscopic strain tensors and microscopic deformation metrics. This will provide a possible means to circumvent the need for concurrent simulations.

ACKNOWLEDGMENTS

Support from NIBIB, NIH grant R01EB009643 is greatly appreciated.

REFERENCES

(1) Z Abusara et al., *Journal of Biomech* (2010)
(2) Kouznetsova, et al., *Comp Meth Appl Mech and Eng* **193**,48 (2004)
(3) Sander et al., *Proc IEEE Eng in Med and Bio Society Conf* (2009)
(4) Breuls et al., *Journal of Biomech Eng* **124**, 2 (2002)
(5) Federico et al., *Journal of Biomech* **38**,10 (2005)
(6) Korhonen et al., *Molecular & Cellular Biomech: MCB* **7**,3 (2010)
(7) Maas et al., *SCI Technical Report* (2009)
(8) Guilak et al., *Journal of Biomech* **33**,12 (2000)
(9) Michalek et al., *Journal of Biomech* **40**,6 (2007)
(10) Peeters et al., *Annals of Biomedical Engineering* **32**,10 (2004)
(11) Wu et al., *Journal of Biomech* **39**,4 (2006)