Predicting Cell Deformations from Body Level Mechanical Loads
Tackling the Hurdles

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The deformations of cells trigger a cascade of events, desirable or undesirable. Mechanobiological response, which helps maintain the integrity of extracellular matrix and stimulate growth and adaptation, is a result of cellular deformations. Mechanical loads exerted on the cells may also induce traumatic damage, which may or may not be recovered, or chronic conditions facilitating cell apoptosis in health and disease. If related to tissue and joint level mechanical response, quantification of cell deformations will further associate the mobility and musculoskeletal function of the body to cellular response and provide a path for multiscale evaluation of clinical interventions commonly prescribed at the joint and tissue levels. This task can be accomplished through modeling and simulation, which provide descriptive and/or predictive analysis of multiscale mechanics of joints, tissues, and cells[1]. Nonetheless many technical and scientific hurdles need to be tackled to reach the ultimate utility of simulation-based multiscale explorations. This document summarizes some of these hurdles along with our completed and ongoing work to tackle them.

Difficulties in multiscale mechanics simulations may appear at different stages including model development, simulation, and interpretation phases. Such difficulties motivate experimentation, software development, high performance computing, and adequate reporting and dissemination. Development of models require not only anatomically realistic geometries but also reliable material properties and our recent work has focused on collection of such data at joint, tissue, and cell scales[2,3]. In addition, expedited model development can be a necessity, particularly when multiple models, representative of different populations, regions of the tissues, etc., need to be constructed. Our software development efforts accommodate streamlined development of representative volume elements, incorporating any desirable cellular distribution, arrangement, and their ellipsoidal shapes[4]. When appropriate models at joint, tissue, and cell levels exist, simulations can yield cell deformations as a function of joint loading[5]. Multiscale coupling strategies can dictate the predictive capacity of these simulations as well as their feasibility. Even in a post-processing sense (simplest multiscale simulation scenario), identification of cell deformations for a single joint loading case may require high performance computing[5]. These simulations need to rely on robust and extensible solvers[6], and additional code development is necessary to automate the post-processing of cell level mechanical variables for interpretation[5]. Our recent experience with biphasic simulations of the cartilage has illustrated that the desire to simulate more realistic multiphysics nature of tissues may further complicate multiscale coupling approaches[7]. Our ongoing work aims to confirm the adequacy of information exchange among spatial scales when biphasic nature of tissues are being considered. Our additional efforts have focused on establishing recommendations for reporting of models[8] and promotion of public dissemination for utmost reproducibility and wide-spread utility. Regardless the technical details of multiscale analysis, the simulations need to be driven by scientifically and clinically relevant loading and boundary conditions under healthy and diseased conditions. Our efforts keep this long-term goal in mind and ongoing experiments not only provide such information but also data to confirm appropriateness of our simulation and model development procedures.

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