Addressing Multiscale Challenges in Lower Extremity Musculoskeletal Simulation

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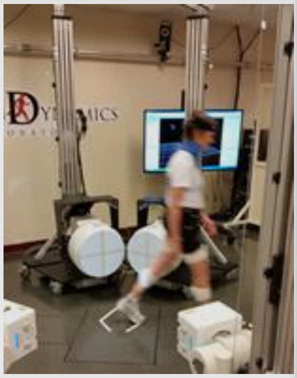
Our vision is to create data and models to describe the human musculoskeletal system with the realism needed to understand pathology and improve treatment. Understanding how musculoskeletal pathology interacts with human movement is a multiscale challenge. Diseases and injuries often affect tissues at the microstructural scale and small-scale pathology impacts biomechanics at larger scales, leading to whole-body movement compensations and oftentimes further injury or degeneration. Ultimately, a multiscale approach, describing the behavior of individual tissues, and the biomechanics of the whole body, is needed to elucidate the etiology of diseases, mechanisms of adaptation and best treatments.

A complete dynamic model of the human lower extremity capable of predictive simulation does not exist, nor does the multiscale patient-specific data for development and validation. The current state of the art has artificially separated scales to make the problem more manageable both conceptually and computationally. The gaps in this approach are the lack of consistency between representations and the inability to perform predictive simulations because of the lack of interaction between the tissue and whole-body scales. For these reasons, *our research team has pioneered development of deformable multiscale models of the human body that combine dynamic muscle modeling and detailed finite element analysis in a single simulation framework [1,2].* Our efforts are grounded in our use of in vivo and cadaveric testing to support development and validation, and our participation as co-investigators in Reproducibility in Simulation-Based Prediction of Natural Knee Mechanics (R01EB024573, Erdemir PI).

The overall goal is to create a comprehensive multiscale musculoskeletal model of the human lower extremity, which includes seamless connection between tissue and whole-body function during dynamic human activities and enables realistic investigations of musculoskeletal disease and treatment. While we will create and share models with broad applicability in biomechanics, our targets are understanding the effects of knee osteoarthritis on patient function and optimizing treatment through total knee arthroplasty (TKA).

Aim 1

Shared
Multiscale
Data of
Healthy, OA
and TKA
Patients



Aim 2

Multiscale
Deformable
Models of
Normal, OA,
and TKA
Lower
Extremity

Aim 3

Simulation
to Assess
and
Predict
Subject
Function

Aim 1: Measure and share multiscale biomechanical data linking tissue and body movement mechanics. The dataset will consist of knee stereo radiography, MRI and CT imaging, EMG, ground force, and whole-body motion captured for healthy subjects, patients with knee OA, and patients following TKA. Notably, we will collect patients with OA pre- and post-TKA, including obese patients. With NSF support, we acquired a novel high-speed stereo radiography system that enables in-vivo measurement of bone and implant motion with sub-millimeter resolution.

Aim 2: Develop subject-specific multiscale models of the lower extremity including deformable representations of the functional anatomy to improve realism and utility for dynamic simulation. Models are being developed with the geometry and properties to represent the major structural tissues, including bone, cartilage, ligament, muscle, tendon, and adipose tissue for the lower extremity. Improved 3D anatomical representations are critical to model obese patients who constitute nearly half of all recipients of TKA and interactions between tissues.

Aim 3: Create realistic dynamic simulations to assess and predict the effects of disease state, surgical, and other biomechanical variables on a patient's function. Using a combined model and experimental approach, we will explore functional differences between healthy and OA cohorts, and the changes that occur from OA to TKA. Efficient inverse and forward-dynamic simulations will be used to assess key variables such as limb alignment, ligament balance, implant geometry and alignment, muscle inhibition, and obesity during activities that are needed for high function.

[1] Navacchia et al. (2019) *A computationally efficient strategy to estimate muscle forces in a finite element musculoskeletal model of the lower limb*, J Biomechanics, in press. [2] Hume et al. (2019) *A lower extremity model for muscle-driven simulation of activity using explicit finite element modeling*, J Biomechanics, in press.