**Stochastic Simulation of Functional Knee Mechanics Enabled via Statistical Shape Modeling and High Throughput Computing**1 Colin R Smith, 2Yasin Dhaher, 1Darryl G Thelen

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Articular cartilage loading is determined by complex mechanics across multiple scales resulting from interactions between cartilage contact, ligament tension, limb dynamics, and neuromuscular coordination. Simulating the contributions of these factors to knee behavior can enhance our understanding of knee pathologies, e.g. osteoarthritis, and enable improvements in clinical treatments. In this abstract, we present a multiscale knee model and simulation framework that leverage recent advancements in musculoskeletal simulation, statistical shape modeling, and high throughput computing (HTC). The framework is used to stochastically simulate muscle, ligament and cartilage loading during complex movements such as gait.

A multibody knee model with six degree-of-freedom tibiofemoral and patellofemoral joints was integrated into a lower extremity musculoskeletal model. Fourteen ligaments are represented by bundles of nonlinear springs. An elastic foundation model is used to compute cartilage contact pressure. The ligament attachment and articular geometries can be constructed from medical images [1] or generated from a statistical shape model to investigate population variability. A novel simulation routine, Concurrent Optimization of Muscle Activations and Kinematics (COMAK), simultaneously predicts muscle forces, ligament loads and cartilage contact pressures that are consistent with measured movement dynamics [1]. We have performed Monte Carlo analyses to assess the influence of parametric uncertainty on simulated knee mechanics by representing the constitutive properties, neuromuscular coordination patterns, and knee geometries as population distributions and leveraging HTC to run thousands of simulations in parallel.

COMAK can simulate internal knee mechanics over a gait cycle in under 30 minutes on a standard desktop computer. When deployed in parallel on a HTC grid, several thousand stochastic gait simulations can be performed in a few hours [1]. The framework has been used to investigate the influence of ligament properties on cartilage contact pressures during walking [1]. Furthermore, we are using the framework to simulate the influence of surgical factors on knee behavior following anterior cruciate ligament (ACL) reconstruction and patellar tendon advancement (PTA) procedures. The knee model and COMAK simulation routine are now being implemented into OpenSim 4.0. A webinar demonstrating the use of OpenSim with the freely available HTC resources of the Open Science Grid is available online [2].

 We aim to improve the fidelity of the articular cartilage model to investigate the subtle alterations in internal cartilage loading that likely are an important factor in the initiation of osteoarthritis. We developed a finite element model of the knee that incorporates the structural hierarchies of the cartilage tissue enabling detailed investigation of the microstructure mechanics [3]. In the future, we intend to apply the COMAK predicted joint mechanics as boundary conditions to this finite element model to investigate the influence of macroscale interventions such as gait retraining and orthopedic surgeries on the loading of the cartilage microstructure.

Funded by NIH EB015410, HD084213, HD065690.

1. Smith CR, et al., *J Knee Surg* **29**(02):99-106, 2016.

2. Smith CR, et al., <https://web.stanford.edu/group/opensim/support/event_details.html?id=169>

3. Adouni A, et al., J Biomech 49:2891-2898, 2016