Predicting the Mechanical Environment of the Human Body

Ahmet Erdemir
Computational Biomodeling Core
Department of Biomedical Engineering
Cleveland Clinic

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Lerner Research Institute, Cleveland Clinic
Musculoskeletal and tissue loading on the human body: overview of work on isolated scales

Efficient methods for multidomain simulations

Predicting cell deformation from body level mechanical loads

Potential of multiscale modeling & simulation in medicine: mechanics of osteoarthritis
Role of Mechanics on Function

Mobility
- locomotion
- neuromuscular control

Injury Prevention
- cushioning

Damage Mechanisms
- trauma
- chronic degradation

Biological Response
- mechanical adaptation
- growth
- healing

Sensation
- tactile feedback
- pain
- proprioception

* adapted from Hannan et al., Osteoporos Int 15: 918-926, 2004.
Identification of Loading Conditions

Experimentation

_In vivo_
- Gait analysis (body level)
- MRI (tissue level)
- Buckle transducers (tissue level)
- Endoscopic cellular microscopy (cell level)

_In vitro_
- Robotics testing (organ level)
- Standard mechanical testing (tissue level)
- Confocal laser scanning microscopy (cell level)
- Two photon excitation microscopy (cell level)

Modeling & Simulation

Commonly required to analyze experimental data

Predictive capacity

1. adapted from Erdemir et al., J Biomech 36 (3): 449-455, 2003
3. adapted from Han et al., J R Soc Interface, EPub, 2009
Simulation-based approaches would give the practice of medicine the tools of modern engineering.

“... For example, doctors will be able to use simulations – initialized with patient specific anatomic and physiologic data – to predict the outcomes of procedures and thereby design optimal treatments for individual patients. ...”

“... manufacturers could use SBES methods to predict the performance of their medical devices in virtual patients. ...”

“... simulation-based methods could be used to model the transport of drugs through the circulatory or respiratory systems and to determine the local concentrations to use in pharmacokinetic models of drug metabolism. ...”
BODY & ORGAN REPRESENTATION

Abstraction of
- muscles
- joints
- passive structures
- external loading
- neuromuscular control

Significant for investigating
- motor control strategies
- muscle function
- interactions with the environment
- management of mobility disorders
- movement related rehabilitation
- surgical corrections of skeletal system
- sports performance
Inverse Dynamics

Solve algebraic equations to obtain joint torques
Optimization required to solve for muscle load sharing

**Erdemir et al., Clin Biomech 22 (2): 131-154, 2007**
Forward Dynamics

Solve ODEs to obtain joint movements
Optimal control required to solve for muscle excitations
Plantar Fasciotomy

Raising on toes pre- and post-surgery

JOINT & TISSUE REPRESENTATION

Abstraction of

- joint & organs
- tissue components
- interaction between tissue structures
- joint & organ loading

Significant for investigating

- load sharing between tissues
- injury mechanisms
- joint replacement
- tissue reconstruction
- surgical corrections on joints
- joint & tissue related dysfunction

* adapted from Borotikar, Doctoral Dissertation, CSU, 2009
Finite Element Analysis

Physical Problem

Mathematical Model
PDEs
Geometry
Material law
Loading
BCs, etc.

FE Representation
Mesh
Element defs.
Loading
BCs
Material properties

Refine FE representation

Accuracy of FE model

Interpretation of results

Validation

Improve mathematical model

adapted from Bathe, Finite Element Procedures, 1996
Insole design utilizing 2D and 3D finite element analysis to provide design guidelines

funded by NICHD/NIH, in collaboration with Peter Cavanagh, PhD, DSc, Univ. of Washington
Outcome of Trochlear Osteotomy

pre-surgery with dislocated patella
after patella realignment
after patella realignment and trochlear osteotomy

funded by Shalom Foundation, in collaboration with Jack Andrish, MD, Cleveland Clinic
TISSUE & CELL REPRESENTATION

Abstraction of

- cells
- pericellular matrix
- extracellular matrix (EM) architecture
- cell & EM interactions
- tissue loading

Significant for investigating

- mechanical role of EM
- mechanobiological response of cells
- cell & EM damage
- tissue engineering
- mechanobiological dysfunction

* adapted from Chahine et al., Eur Cell Mater 31 (13): 100-111, 2007
Finite Element Analysis

Physical Problem

Mathematical Model
- PDEs
- Geometry
- Material law
- Loading
- BCs, etc.

FE Representation
- Mesh
- Element defs.
- Loading
- BCs
- Material properties

FE solution of mathematical model

Refine FE representation

Accuracy of FE model

Interpretation of results

Validation

Improve mathematical model

adapted from Bathe, Finite Element Procedures, 1996
Chondrocyte Stresses under Uniform Tissue Loading

uniaxial compression

simple shear

influence of single and three-cell representations on stress distribution

\[ \times 10^4 \text{MPa} \quad \max (\sigma_V) \quad \max (P) \quad \max (\tau) \]

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\[ \times 10^4 \text{MPa} \quad \max (\sigma_V) \quad \max (P) \quad \max (\tau) \]

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Bennetts et al., Annual Meeting of the ASB, 2009
To understand the influence of macroscopic loading on microstructural function

“... A multiscale modeling approach is likely to identify the pathways to cell damage from organ level mechanical loading to cell level deformations. ...” from Tawhai et al., IEEE Eng Med Biol Mag 28 (3):41-49, 2009

To establish the effect of microscopic changes on body level function

“... the microscopic interactions of cells are the underlying cause of the order and complex patterns in the macroscopic world. ...” from Schnell et al., American Scientist 95 (2):134, 2007

To relate clinical practice with scientific developments in individual spatial scales
neuromuscular control

musculoskeletal biomechanics

tissue mechanics

COLLABORATIONS

Cleveland Clinic
Ton van den Bogert
Craig Bennetts
Ahmet Erdemir
Marko Ackermann
Jason Halloran
Xuemei Huang
Snehal Chokhandre
Pavana Srimamilla
Anna Fernandez
Kristen Thomas

Stanford University
Scott Delp
Joshua Webb

University of Utah
Jeff Weiss
Ben Ellis
Steve Maas

FUNDING

Efficient Methods for Multidomain Biomechanical Simulations
PI: van den Bogert
NIH/NIBIB 1R01EB006735
https://simtk.org/home/multidomain
BACKGROUND

controller

muscle forces

skeletal system

movement

tissue deformation

Musculoskeletal Movement Simulations

external loading

Finite Element Analysis
Multibody dynamics

- Discrete force producing elements (muscles, tendons, etc.)
- Idealized joints (hinge, etc.)
- Fast, therefore convenient for movement optimizations
- Simplification may affect movement predictions
- No feedback from localized tissue response

Finite element analysis (FEA)

- Tissue level mechanics
- Whole structure/joint behavior
- Assumed or measured boundary conditions
- Computationally intensive, therefore not suitable for movement simulations
Why multidomain coupling?

to incorporate the influence of localized tissue mechanics on movement control

Imagine

addressing compensatory movement strategies to accommodate tissue deficiencies
quadriiceps avoidance gait in anterior cruciate ligament deficiency

establishing the link between somatosensory system and motion
proprioception
movement alterations to relieve pain

designing musculoskeletal rehabilitation programs for tissue relief
prevention and management of lower back pain
Coupling musculoskeletal dynamics with tissue mechanics is straightforward:

\[ M(q)\ddot{q} + C(q, \dot{q}) + G(q) + R(q)F_{MT}(q, \dot{q}) + E + Q_{FEA}(q_{FEA}(q)) = 0 \]

What if multiple forward dynamics solutions are needed, e.g. optimal controls?

- Speed-up tissue mechanics calculations
  - Adaptive Surrogate Modeling
- Implement efficient optimal control approaches
  - Direct Collocation
Direct Coupling

- FEA performed each time step of musculoskeletal dynamics
- Muscle controls from previous optimal control solutions with simple foot model
- Predicted time history of foot stresses during jumping

van den Bogert and Erdemir, ASME Summer Bioengineering Conference, 2007
Adaptive Surrogate Modeling

Relies on a database of previous tissue mechanics simulations

Conducts FEA on a need basis

Ensures mechanically consistent tissue response based on error prediction
Adaptive Surrogate Modeling

Facilitates nested tissue mechanics simulations in optimal control iterations

Considerably decreases computational cost

Provides tissue related variables to incorporate into movement predictions

Halloran et al., J Biomech Eng 131 (1): 011014, 2009
Direct Collocation

Converts optimal control & forward dynamics to full parameter optimization

Find
\[ u(t) \ x(t) \ T \]
that satisfy dynamics
\[ \dot{x} = f(x, u, f_{gr}) \]
and constraints
\[ c(x, u, t) \leq 0 \]
\[ c_e(x, u, t) = 0 \]
and minimize
\[ J = \int_0^T L(x(t), u(t)) \, dt \]

\[ \begin{align*}
x(t) \\
u(t)
\end{align*} \quad \Rightarrow \quad \begin{align*}
x_k = x(t_k) \\
u_k = u(t_k) \ T
\end{align*} \]

Euler
\[ \frac{x_k - x_{k-1}}{\Delta t} = f(x_k, u_k, f_{gr,k}) \]

\[ \begin{align*}
c(x_k, u_k, t_k) &= 0 \\
c_e(x_k, u_k, t_k) &\leq 0
\end{align*} \]

\[ J = \sum_{k=1}^{n-1} L(x_k, u_k) \]

Ackermann and van den Bogert, J Biomech, in review
prediction of neuromuscular control, movement and foot deformations during gait

Direct Collocation also decreases computational cost of predictive movement simulations

Halloran et al., J Biomech, in review
Concurrent Simulations illustrate that tissue level variables may alter movement predictions.

Adaptive Surrogate modeling may further decrease the computational demand when used with Direct Collocation.
tool trajectory in image volume

**ROBOTICS TESTING & IMAGING**

*Erdemir et al., J Biomech Eng 131 (9): 094502, 2009*
FUTURE

Dissemination

Foot Testing Data
Erdemir et al., J Biomech Eng 131 (9): 094502, 2009

Jump Optimization
Halloran et al., J Biomech Eng 131 (1): 011014, 2009

Continue following us on https://simtk.org/home/multidomain

Research

Generalization of adaptive surrogate modeling
coupling of mechanical simulations of tissue and cell structures
Physiologically detailed modeling of muscles

Clinical

Rehabilitation programs targeted at reducing or inducing tissue stress
e.g. pain relief, healing
Anterior cruciate ligament injury mechanisms
from neuromuscular control to tissue stress
Predicting Cell Deformation from Body Level Mechanical Loads

PI: Erdemir
NIH/NIBIB 1R01EB009643
https://simtk.org/home/j2c
Cell deformations are dictated by **body level loads** transferred to cells through complex joint anatomy, tissue structure and **extracellular & cellular interactions**.
Why multiscale coupling?

to establish the relationship between mechanical variables at the joint level and those at microscopic levels triggering cellular processes

Imagine

identifying potentially harmful movements/loads that can cause cell damage
traumatic wounds
ulcer formation (pressure or diabetic)
osteoarthritis

establishing the mechanical link between body loads and biological cell processes
bone loss in space
tissue degradation due to immobilization
adaptation and tissue growth

designing interventions applied at musculoskeletal joints but targeting cells
Autonomous Simulations

Post process

Simple joint models for joint movement/loads

FEA of joints (macro level) with continuum tissue models for tissue strain/stress

FEA of cell and extracellular matrix (micro level) for cell strain/stress

straightforward
cost effective
descriptive

but

macro models should be mechanically consistent with micro models

limited potential to explore predictive macro-micro level interactions (no feedback from micro levels)
Concurrent Simulations

Given joint movement/loads nested simulations of

- **anatomically detailed joint models** and
- **microscopic models of cell and extracellular matrix**

provide cell deformations

response of macro level is a direct function of microscopic models

full functionality to explore bidirectional dependencies between spatial levels

but high computational cost & need for reliable micro level models
Potential Pathways for Accurate & Cost Effective

**Autonomous Simulations**
- Continuum models of tissue representative of underlying microstructure
- A-priori simulations with microstructural models for surrogate modeling

**Concurrent Simulations**
- Computational homogenization
- Adaptive surrogate modeling
- Parallel processing
EXPERIMENTATION IN

JOINT SCALE

TISSUE SCALE

stress

strain

CELL SCALE
A 3D Small Specimen Testing Platform Compatible for Microimaging
Co-PIs: Kuban & Erdemir, NIH/NCRR 1R21RR031243 (pending IRG review)
MODELING IN

JOINT SCALE

TISSUE SCALE

\[ W(\lambda_1, \lambda_2, \lambda_3) = \sum_{i=1}^{\infty} \frac{\mu_i}{\alpha_i} \left( \lambda_1^{\alpha_i} + \lambda_2^{\alpha_i} + \lambda_3^{\alpha_i} - 3 \right) \]

CELL SCALE
Open Knee: A Three-Dimensional Finite Element Representation of the Knee Joint

https://simtk.org/home/openknee

effective strain in meniscus  > 10%
SOLVER DEVELOPMENT

Computational Homogenization
adapted from Kouznetsova, PhD Thesis, TU/e, 2002

http://mrl.sci.utah.edu/software/febio

in collaboration with Jeff Weiss, PhD, University of Utah
influence of heterogeneous microstructure on macroscopic deformations in beam bending
Dissemination

Follow us on https://simtk.org/home/j2c

Research

Why stop at cell scale?

adapted from Schnell et al., American Scientist 95 (2):134, 2007
Osteoarthritis influences ~26.5 million people only in the United States. Rate of osteoarthritis dramatically increases with age.

Aging influences the mechanical state and properties of the tissues at many spatial scales.

In long-term, understanding the multiscale coupling between mechanical risk factors of osteoarthritis is possible with computational modeling.

An experimentally driven, validated modeling and simulation platform can establish patient-specific risk assessment for cartilage damage.

Coupling with models of biological processes?
Effects of Aging: Joint <-> Cell

**changes in joint movement**  
adapted from Karamanidisd and Arampatzis (2009)

**alterations in chondrocyte and EM**  
adapted from Temple et al. (2007)

**changes in cartilage**  
adapted from Hudelmaier et al. (2001)
Effects of Aging: Joint <-> Cell

Multiscale Modeling of the Aging Cartilage
PL: Erdemir, NIH/NIA 1K02AG037570 (pending IRG review)
Effects of Aging: Body <-> Tissue

changes in neuromuscular control
adapted from Kang and Dingwell (2009)

changes in muscuoskeletal properties
adapted from Nonaka et al. (2002)
Effects of Aging: Body <-> Tissue

subject-specific in vivo experimentation

Mechanical Environment of the Cartilage during Gait: Effects of Aging
PI: Erdemir, NIH/NIA 1R01AG038517 (pending IRG review)
Effects of Aging: Body <-> Tissue

SUBJECT-SPECIFIC MODELING
- dynamometry (experimental)
- anthropometry (experimental)
- subject-specific skeletal parameters

MUSCULOSKELETAL MOVEMENT SIMULATIONS
- muscle activity (simulated)
- muscle forces
- tibiofemoral joint movements
- tibiofemoral joint loads

SIMULATION OF KNEE DEFORMATIONS
- magnetic resonance imaging (experimental)

finite element analysis

mechanical environment of cartilage during gait (stress & deformation)

vs (validation)

movements (simulated)

movements (experimental)

ground reaction forces (simulated)

vs (validation or tracking)
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Plantar Fasciotomy

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Xuemei Huang
Steve Maas
Pavana Srimamilla
Kristen Thomas
Ton van den Bogert
Joshua Webb
Jeff Weiss

Footwear Design

Donald Bly
Georgeanne Botek
Sachin Budhabhatti
Peter R. Cavanagh
Steve Goske
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Trochlear Osteotomy

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BME Administration
BME Cores

Cell Mechanics

Snehal Chokhandre

BME Support

LRI Support

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Jeanne Ineman
LRI Administration
Computing Services
LRI Cores

Cleveland Clinic

... and many more, who implicitly made my life easier.