Multiscale Modeling in Computational Biomechanics

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Outline

1. Tissue Mechanics Working Group
2. Multiscale modeling in biomechanics
    1. Musculoskeletal system
        1. Intro
        2. Research examples (Guess)
        3. Research examples (Erdemir)
    2. Respiratory system
        1. Intro
        2. Research examples (Tawhai)

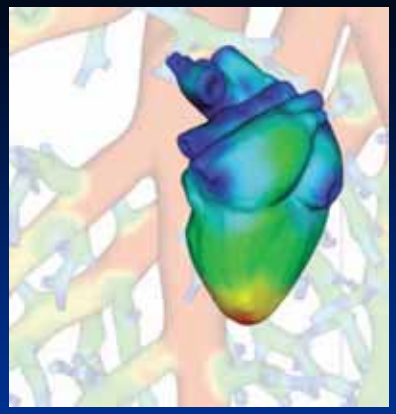
WG 6
Tissue Mechanics

- Participants
  - Jeff Bischoff
  - Daniel Einstein
  - Ahmet Erdemir
  - Trent Guess (lead)
  - Jeff Reinbolt
  - Merryn Tawhai

http://www.imagwiki.org/mediawiki/index.php?title=Working_Group_6

WG 6
Tissue Mechanics

- Goals and Objectives
  1. determine computational priorities and challenges related to multi-scale modeling (MSM), specifically MSM of tissue mechanics and biomechanics,
  2. explore solutions for model sharing, and
  3. provide a forum for discussion of issues related to MSM and biomechanics

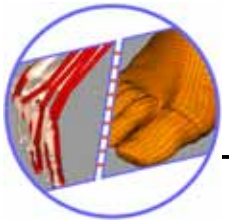


Multiscale Modeling in Computational Biomechanics

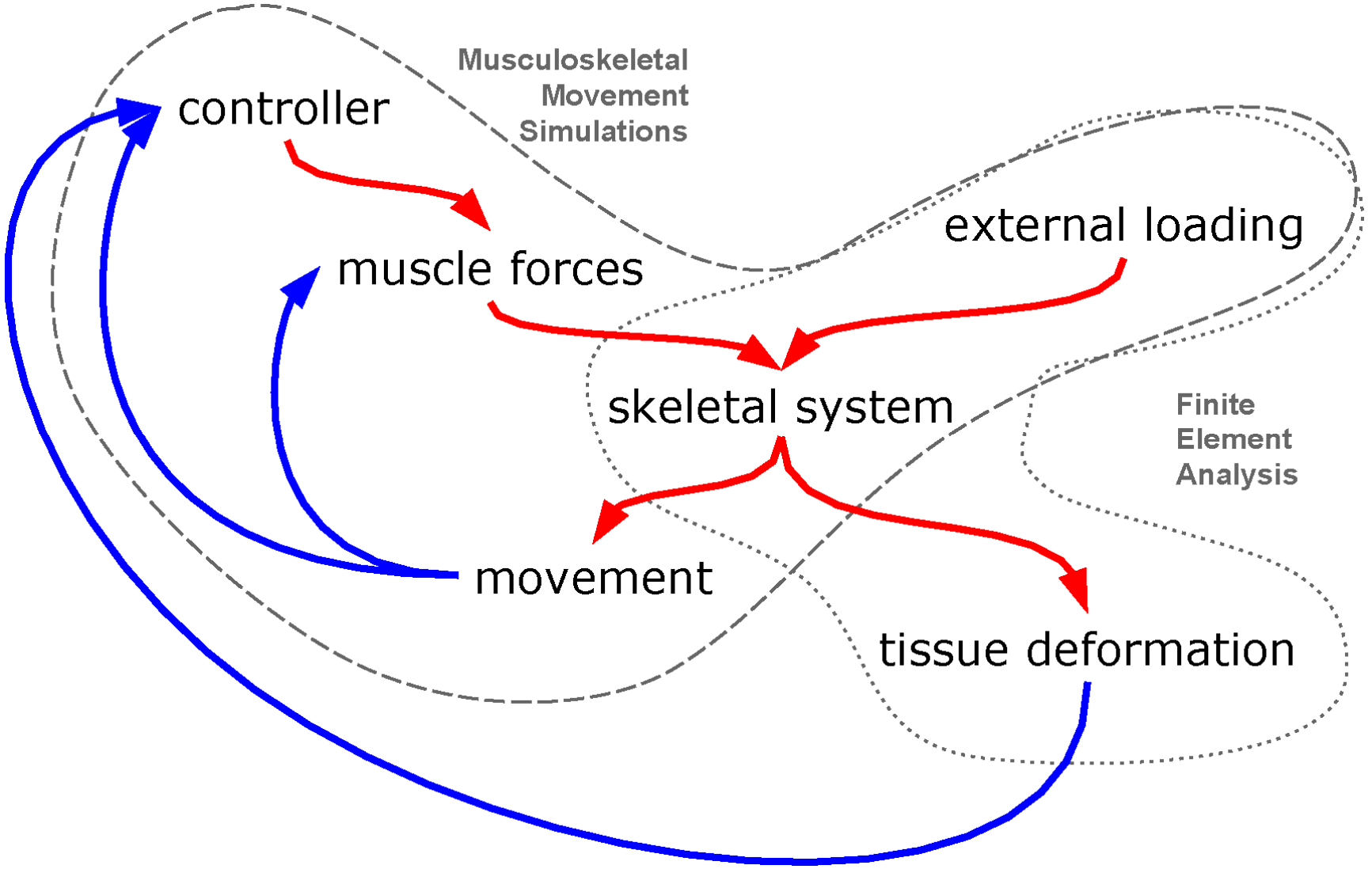
Determining Computational Priorities and Addressing Current Challenges

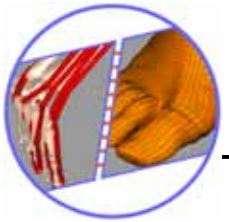
Tawhai M, Bischoff J, Einstein D, Erdemir A, Guess T and Reinbolt J. 2009. Multiscale modeling in computational biomechanics. *IEEE Eng Med Biol Mag*, **28**:41-49.

- Collaborative effort of WG members
  - Overview of current state in multiscale modeling in biomechanics
  - Members met the goals and objectives of the working group through the process of writing article



BACKGROUND


Musculoskeletal
Movement
Simulations
controller
muscle forces
external loading
skeletal system
Finite
Element
Analysis
movement
tissue deformation



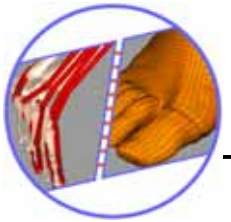
BACKGROUND

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



MOTIVATION

Why multidomain coupling?

to incorporate the influence of localized tissue mechanics on movement control

Imagine

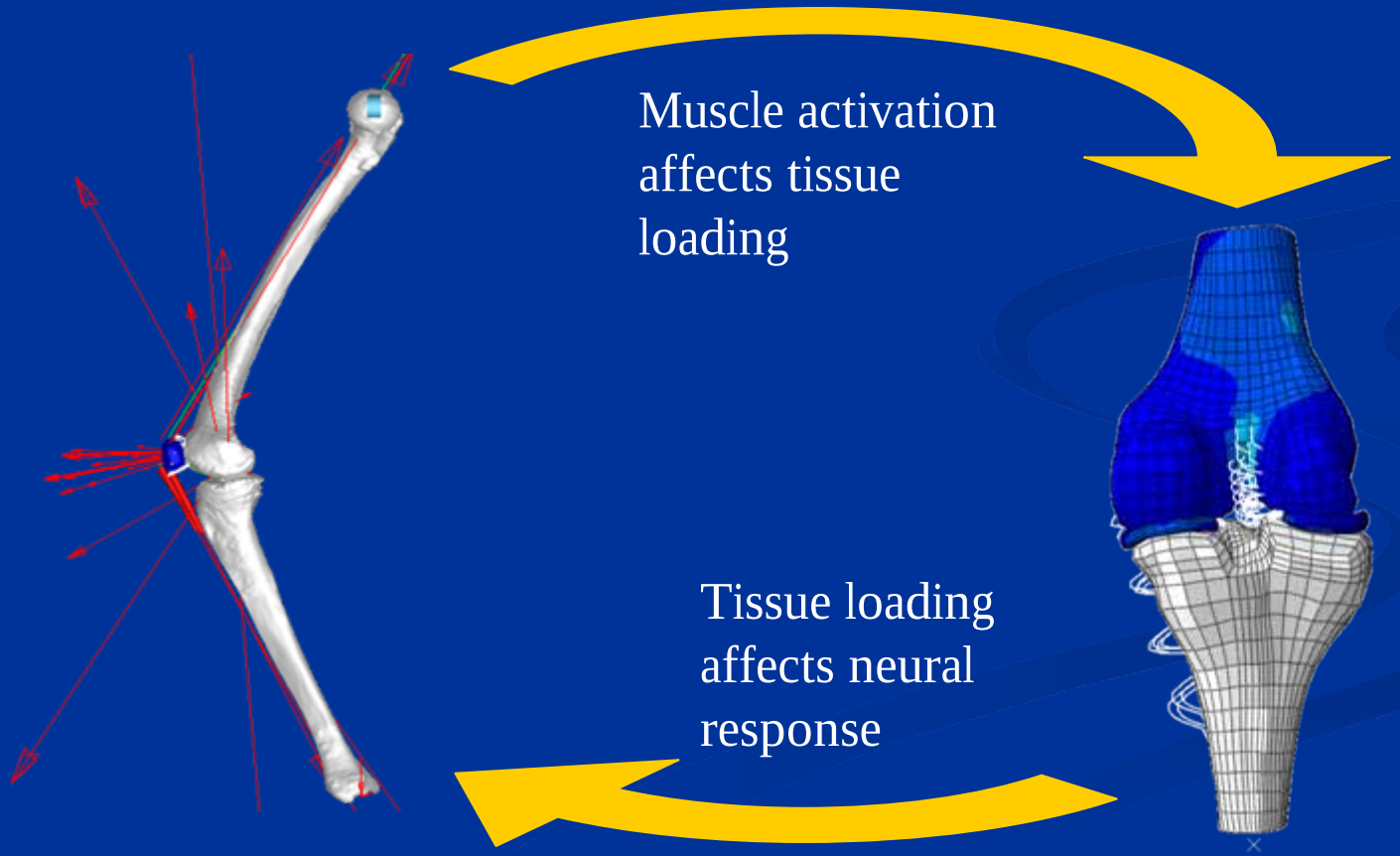
addressing compensatory movement strategies to accommodate tissue deficiencies
- quadriceps avoidance gait in anterior excruciate ligament deficiency

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

Musculoskeletal Interdependency

- In many scenarios, the interdependency of muscle force and tissue response justifies a concurrent multi-scale/multi-domain modeling approach



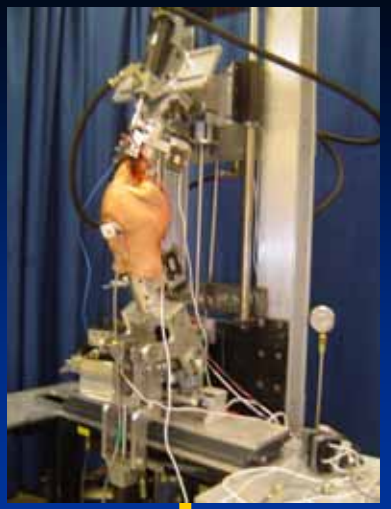
Musculoskeletal Interdependency (multidomain coupling) (concurrent simulation)

- Goal: develop computationally efficient, mechanically biofidelic, musculoskeletal joint models within forward dynamics movement simulations
  - interdependency of muscle force and tissue response
  - more realistic loading applied to organ and tissue level models
  - more realistic muscle activation patterns

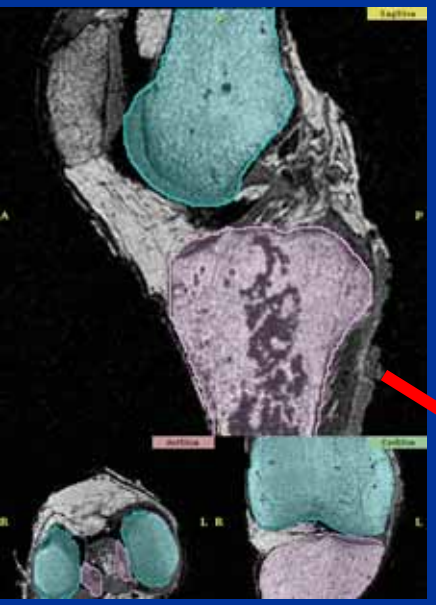
Modeling Platform

Cadaver knees (6)

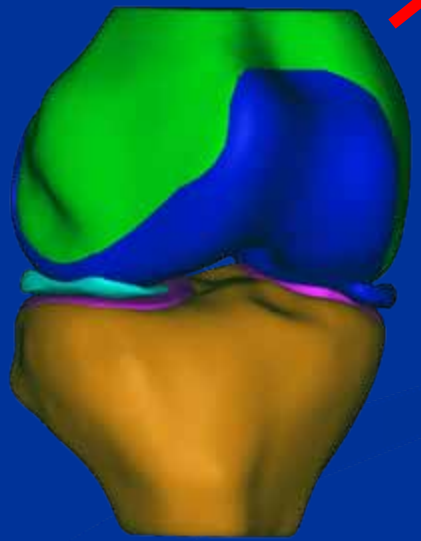
Kansas Knee Simulator (KKS)

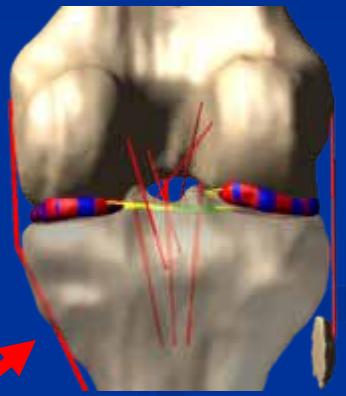


MRI



Geometries





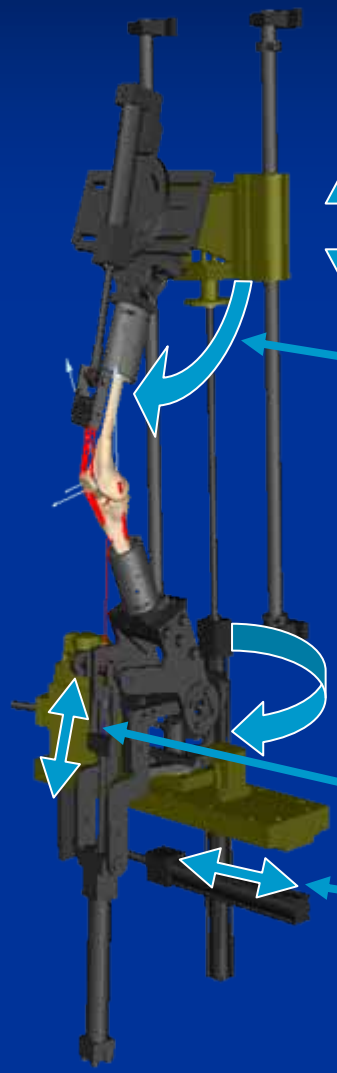
Multi-body knee model

Compare Kinematics

Knee model placed in model of KKS

Simulations: walking, squats, laxity tests

Kansas Knee Simulator, University of Kansas, Lawrence

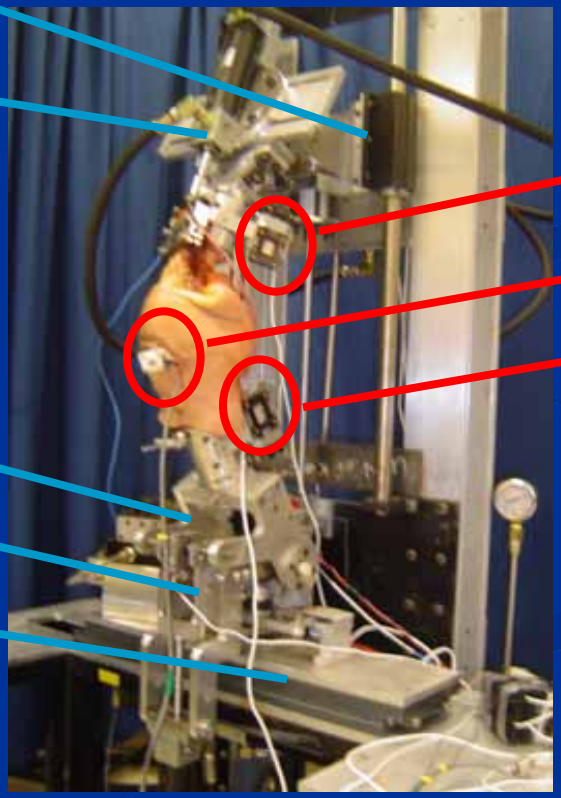


Loading is known

Hip Position,
Hip Load

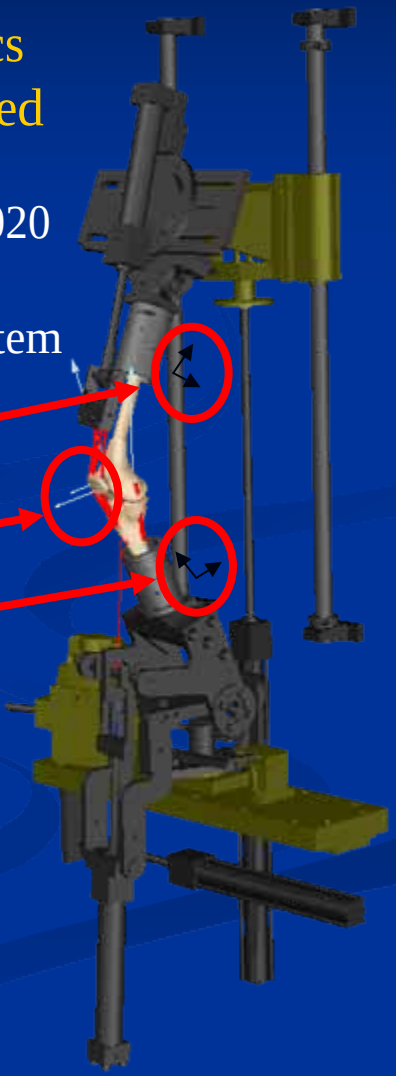
Hip Angle,
Quad Force

Ankle Loads

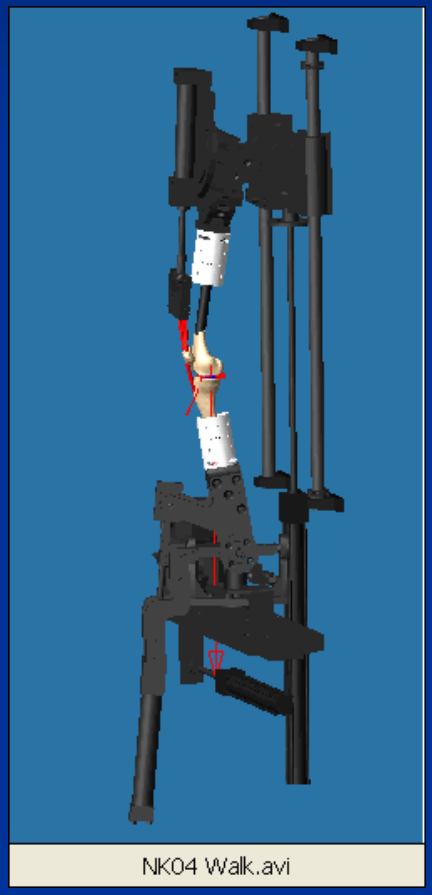


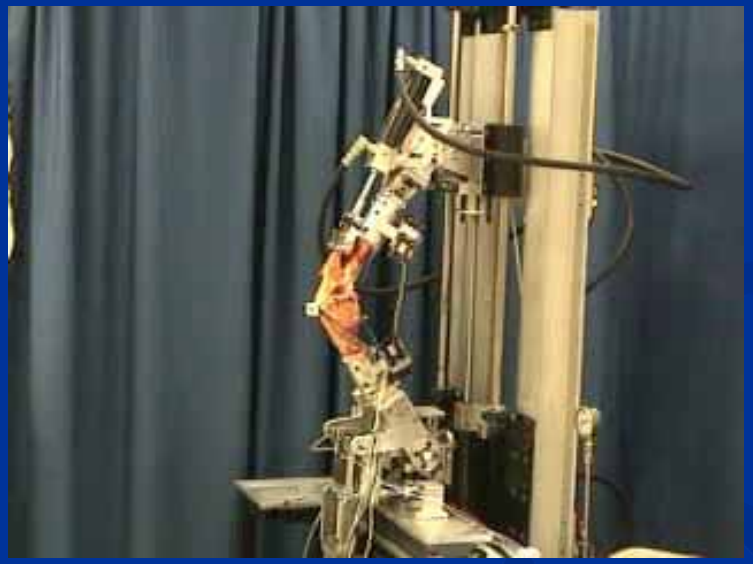
Bone kinematics
directly measured

Optotrak 3020
3D motion
tracking system

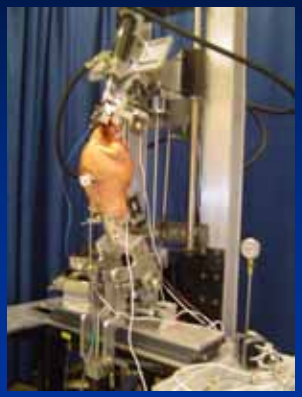


5 second Walk Cycle





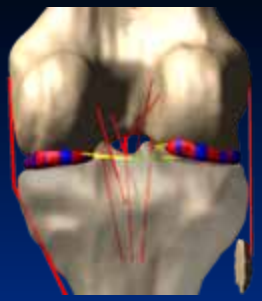
Modeling Platform



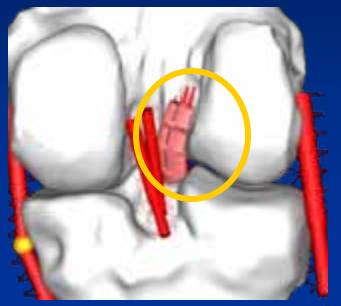
Compare Kinematics

Model Parameters

Katie Weimer, Paul Wilson



Bone wrapping
Zero-load lengths
Insertion / origin

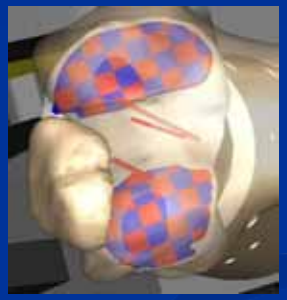


Ligaments

Katherine Bloemker

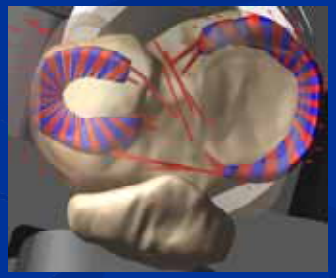
Cartilage

Dr. Hongzeng Liu



Meniscus

Mohammad Kia. Meenakshi Mishra, Dr. Ganesh Thiagarajan

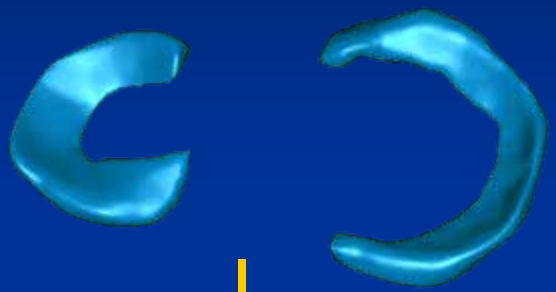


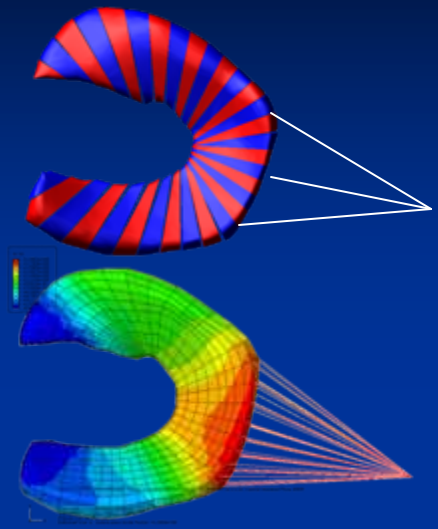
Tibio-femoral Neural Network

Gavin Paiva, Meenakshi Mishra, Dr. Reza Derahkhashani

Multibody Menisci

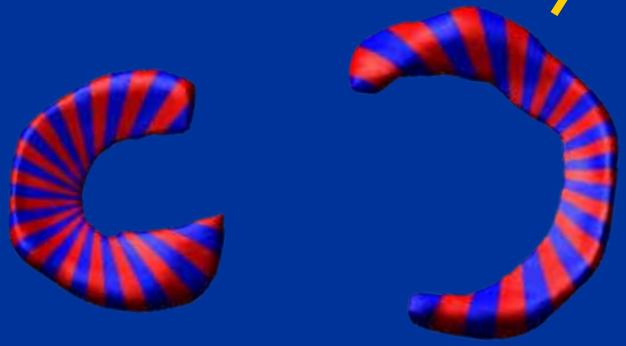
Meniscus geometry from MRI



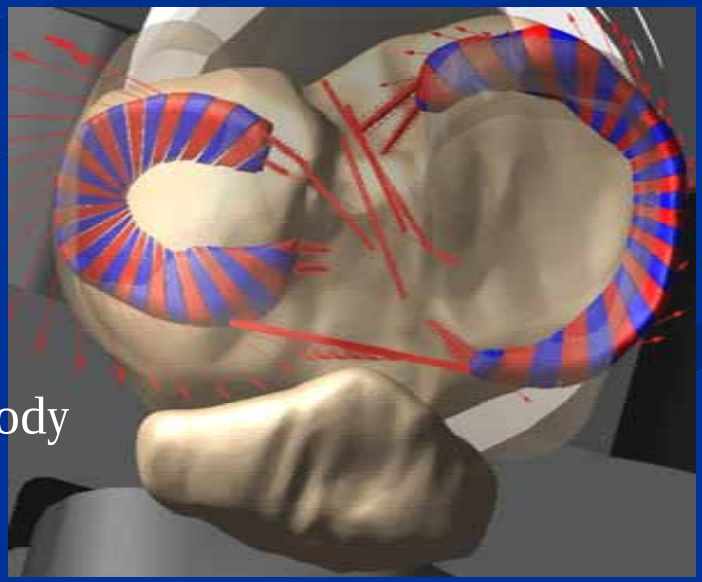


Stiffness matrix parameters optimized to minimize position error of an identically loaded FE model

Macro divides geometries and connects w/ 6x6 stiffness matrix



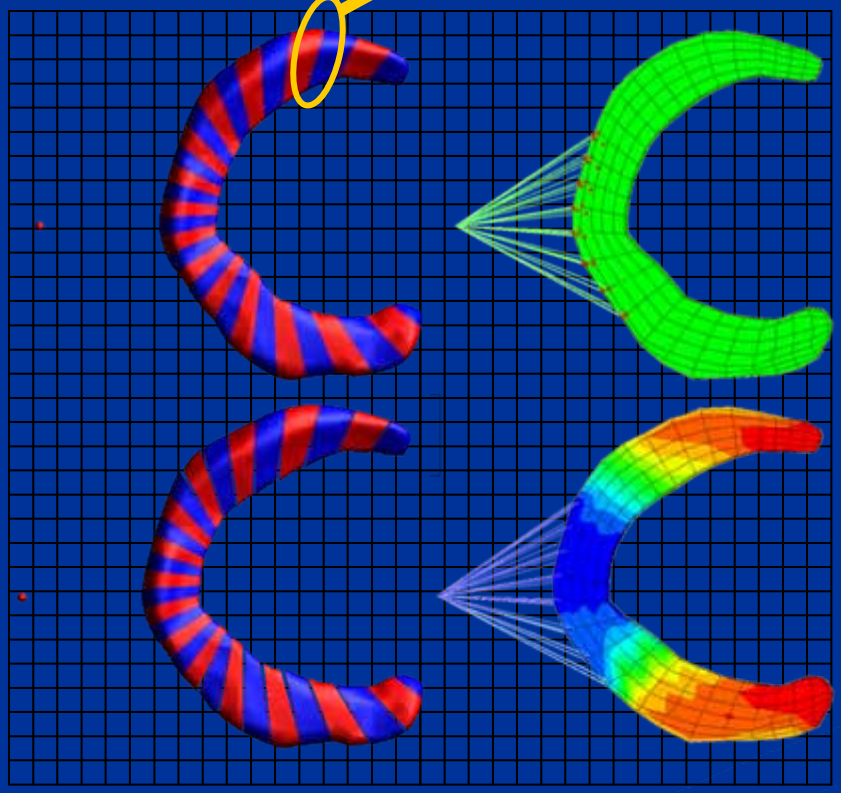
Meniscus model placed in multibody knee model



Multibody Menisci

Stiffness matrix located between discrete elements

$$[K] = \begin{bmatrix} K_\theta & K_{\theta r} & K_{\theta z} & 0 & 0 & 0 \\ K_{\theta r} & K_r & K_{rz} & 0 & 0 & 0 \\ K_{\theta z} & K_{rz} & K_z & 0 & 0 & 0 \\ 0 & 0 & 0 & T_\theta & 0 & 0 \\ 0 & 0 & 0 & 0 & T_r & 0 \\ 0 & 0 & 0 & 0 & 0 & T_z \end{bmatrix}$$



Response Surface Method Optimization

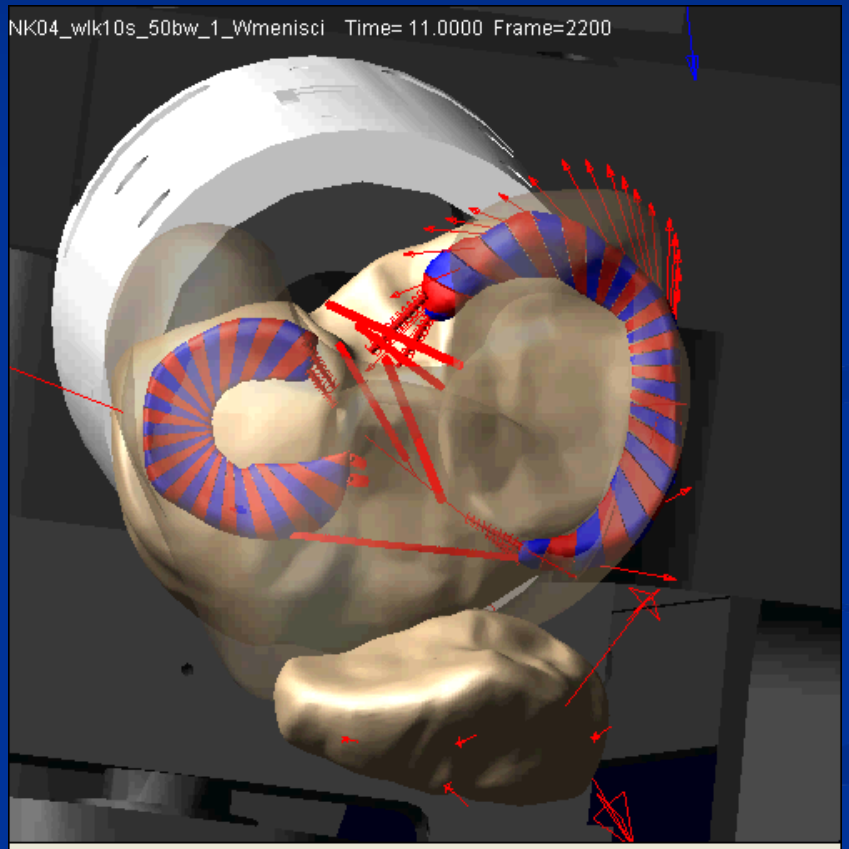
$$[K] = \begin{bmatrix} 320 & 83 & 83 & 0 & 0 & 0 \\ 83 & 270 & 25 & 0 & 0 & 0 \\ 83 & 25 & 330 & 0 & 0 & 0 \\ 0 & 0 & 0 & 25 & 0 & 0 \\ 0 & 0 & 0 & 0 & 25 & 0 \\ 0 & 0 & 0 & 0 & 0 & 23 \end{bmatrix}$$

N/mm N-mm/(rad)

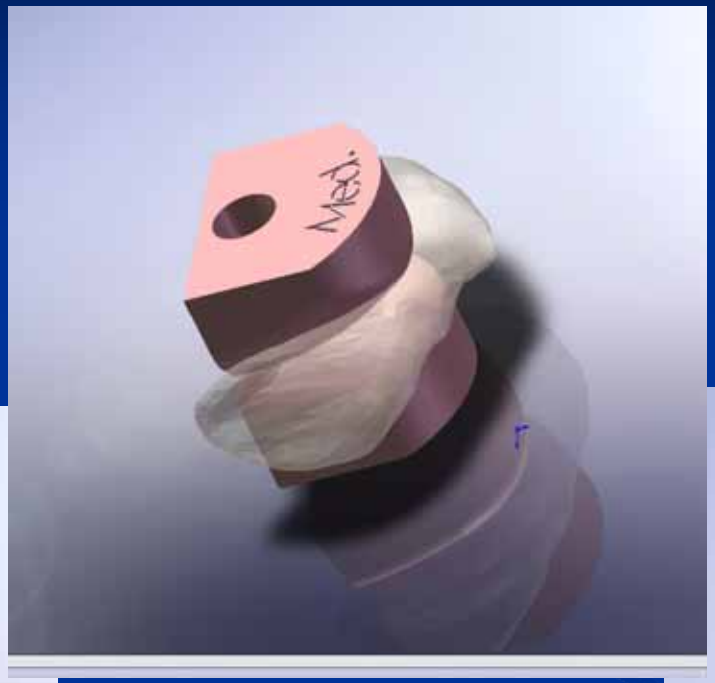
Objective Function: Displacement Error

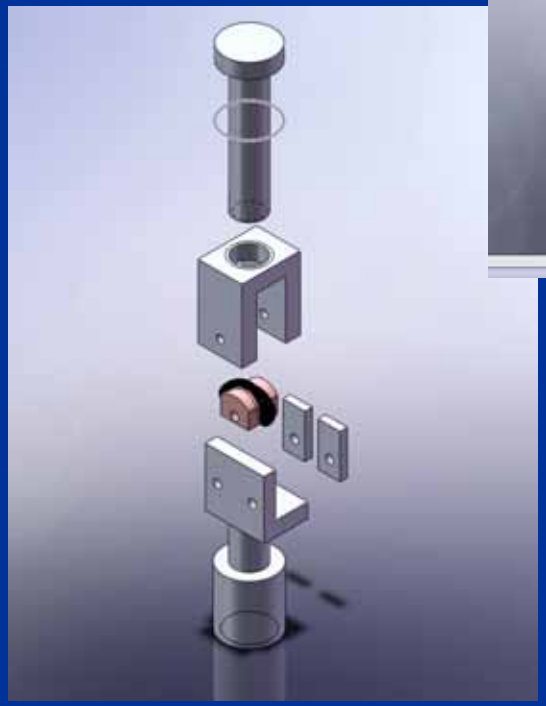
Walking

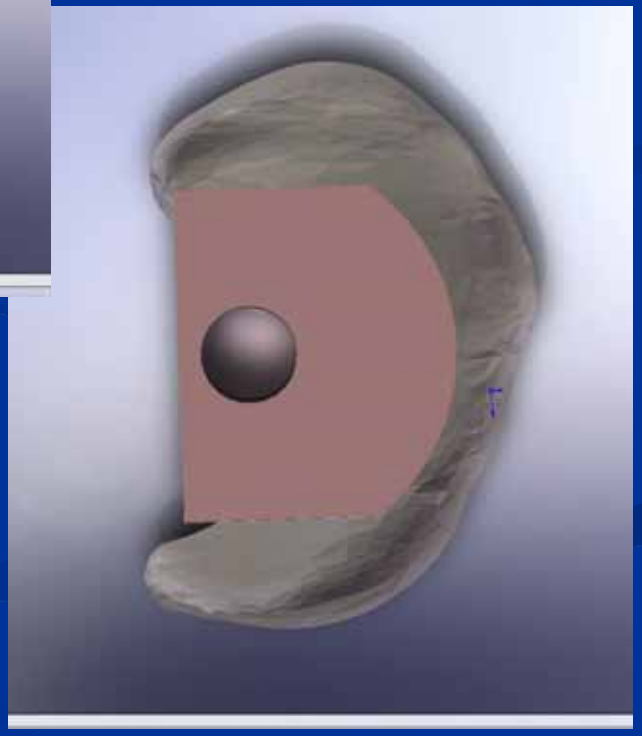
ISO 14243-1, right knee



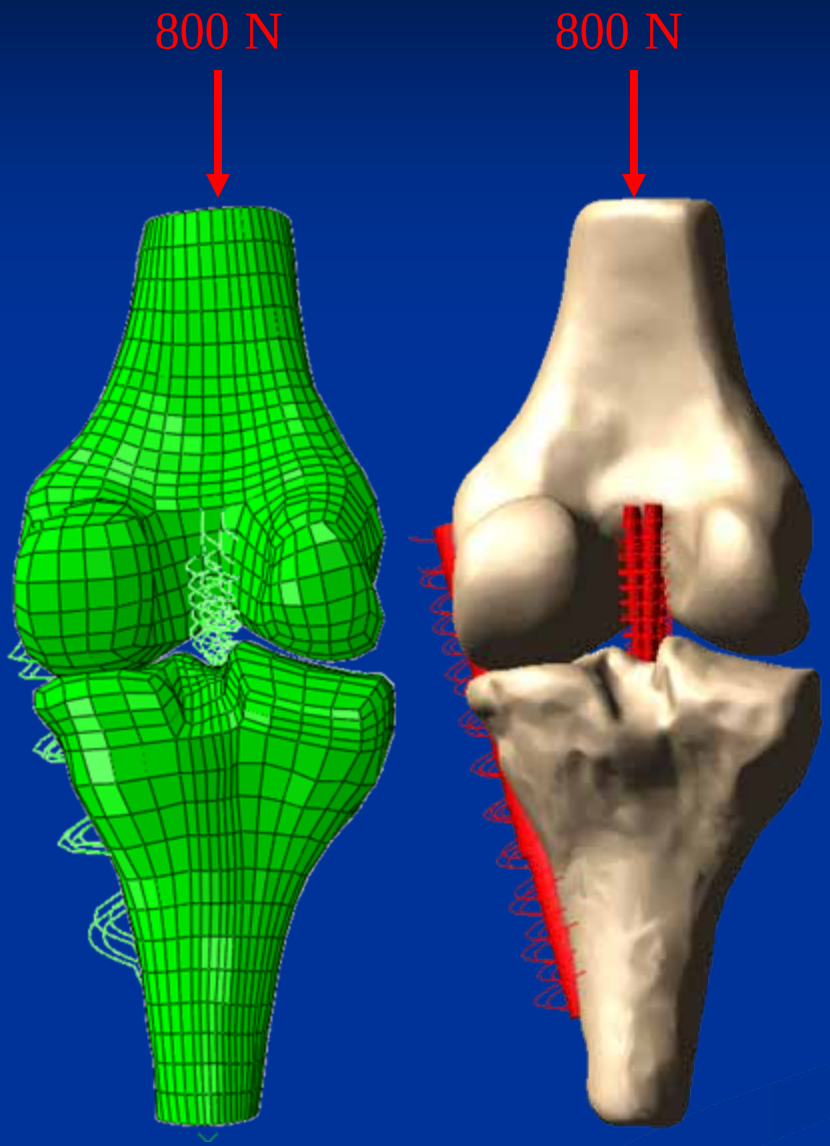
Experimental Testing on Canine Menisci







Tibio-femoral cartilage contact



FE model

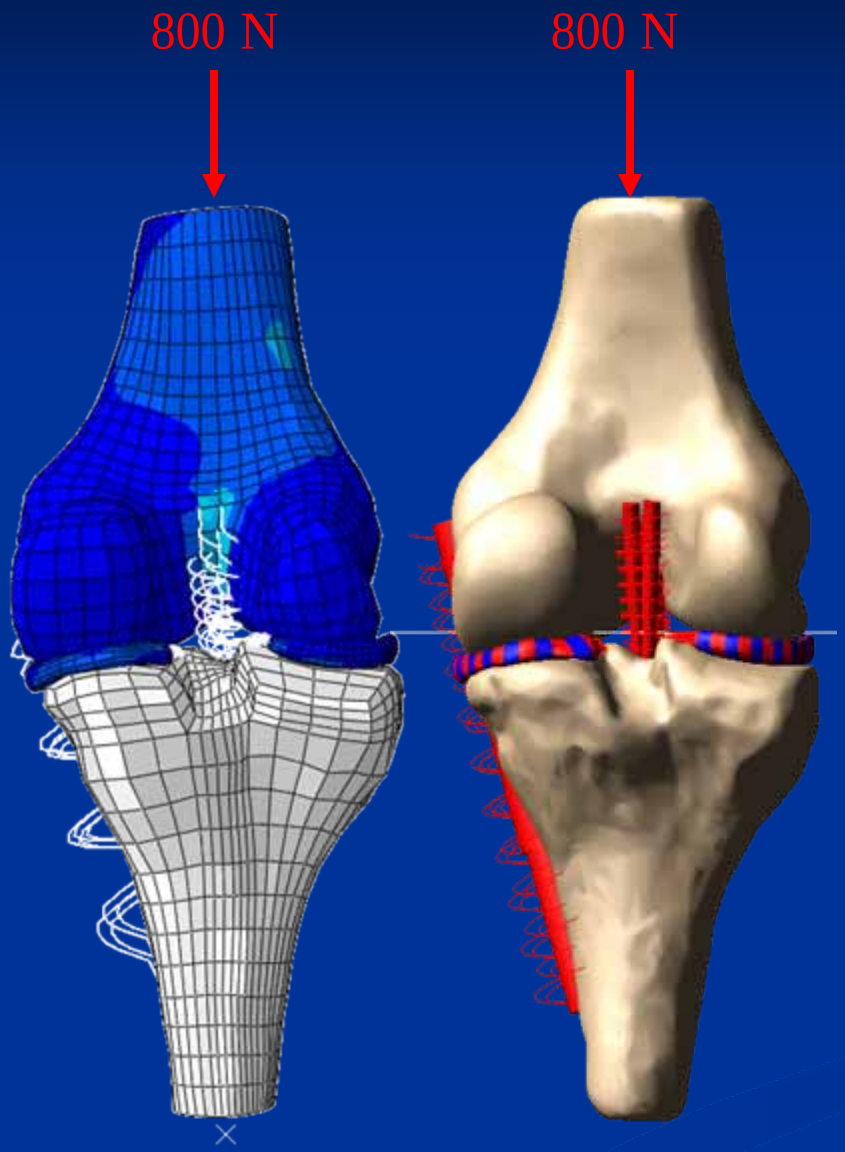
Multibody model

Compliant contact model

$$F_c = k\delta^{\exp} + B(\delta)\dot{\delta}$$

Parameters optimized such that displacement error under identical loading is minimized

Tibio-menisco-femoral contact



FE model

Multibody model

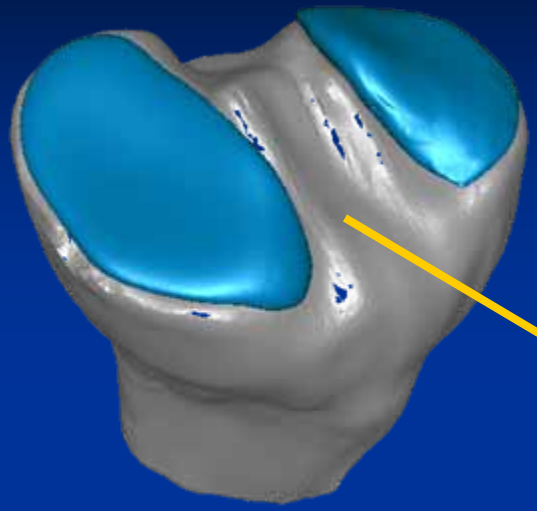
Compliant contact model

$$F_c = k\delta^{\exp} + B(\delta)\dot{\delta}$$

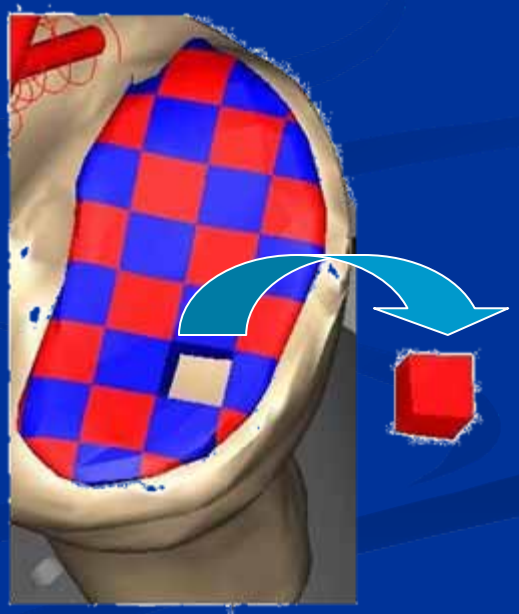
Parameters optimized such that displacement error under identical loading is minimized

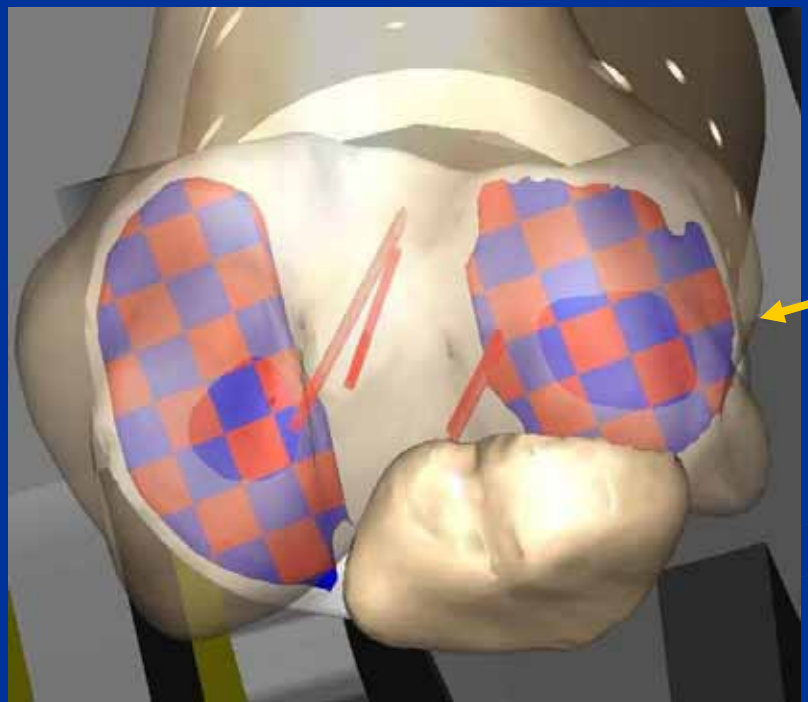
Multibody Cartilage

Geometry from MRI

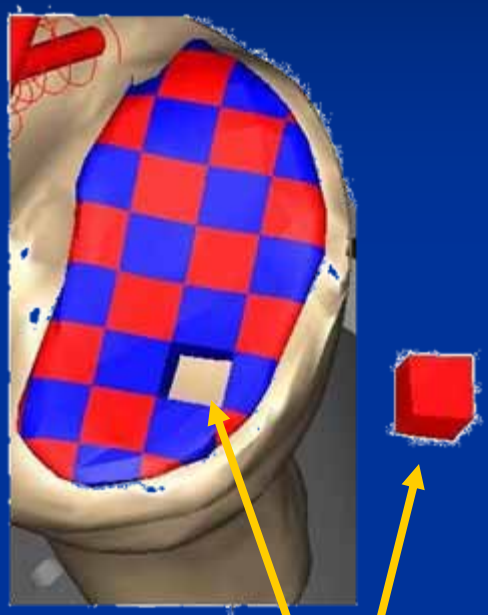


- Macro
  - Divides geometries into discrete elements
  - Attaches each to the tibia
  - Defines a compliant contact w/ femur cartilage

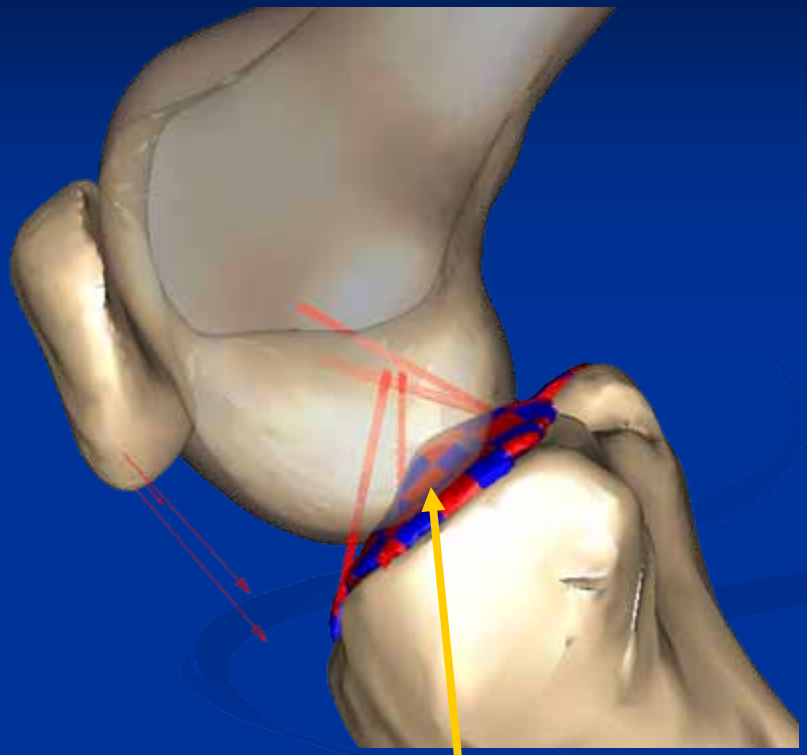




Multibody Cartilage



Fixed joint attaches each cartilage element to the tibia

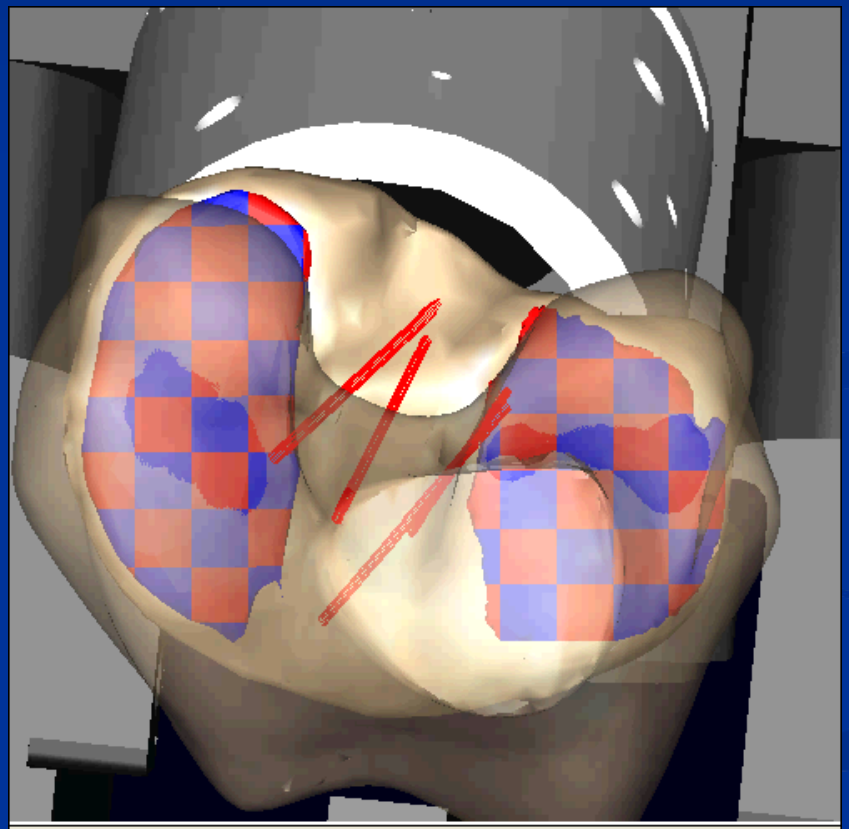


Compliant contact defined between each element and femur cartilage geometry

$$F_c = k\delta^{\exp} + B(\delta)\dot{\delta}$$

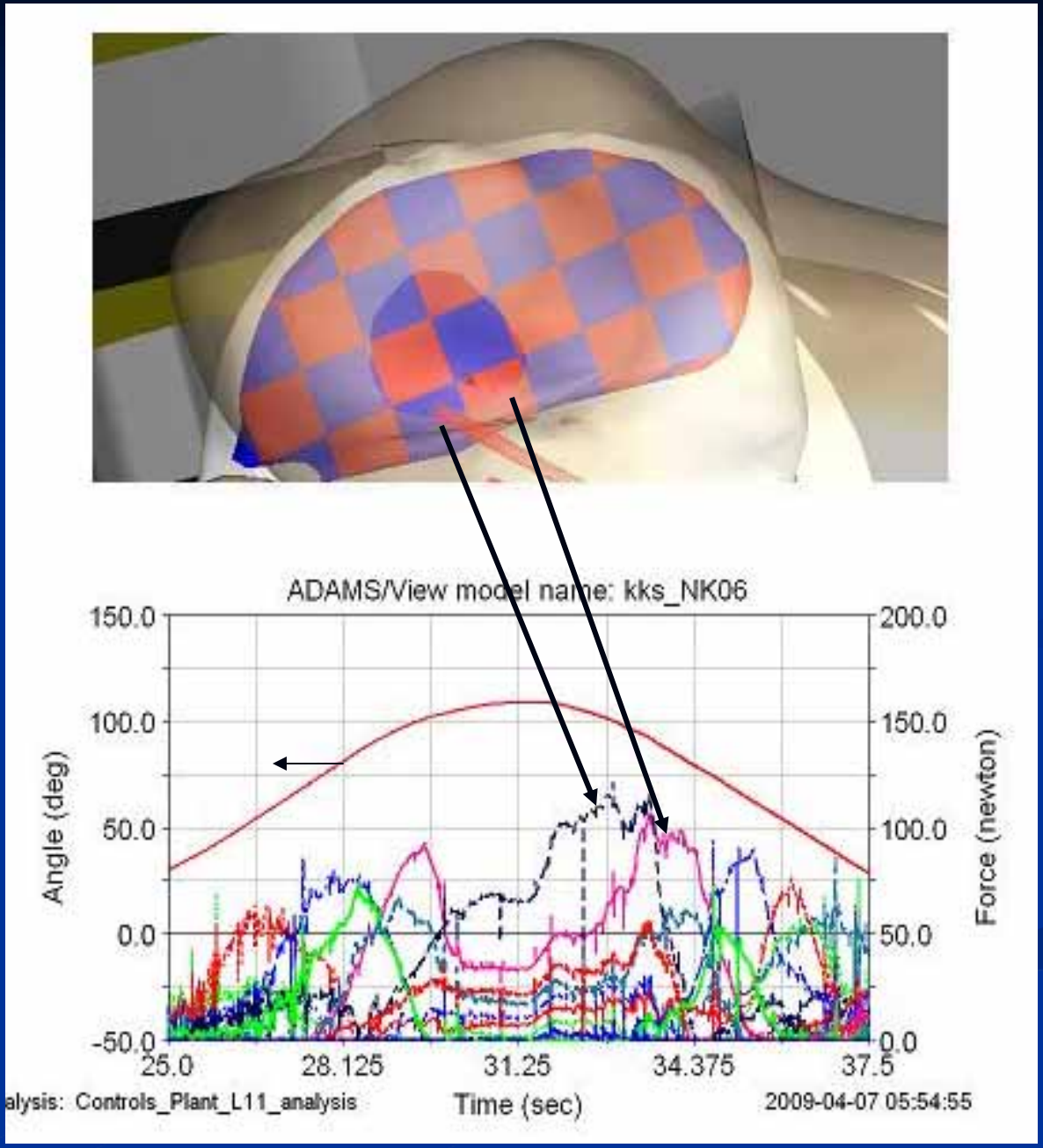
Squat

110 deg knee flexion, left knee

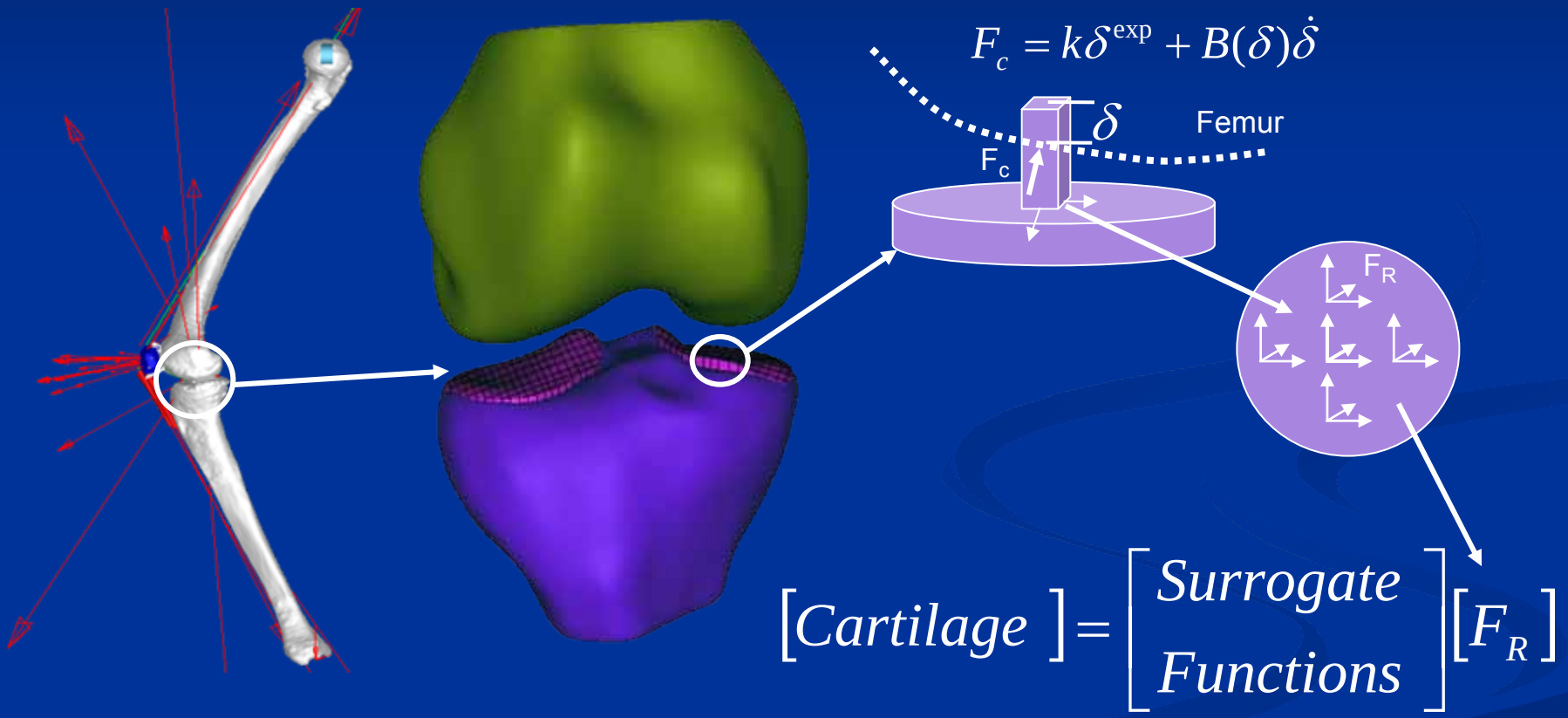


NK06_Squat.avi

- Contact forces during a squat
  - medial tibial plateau
  - 32 elements

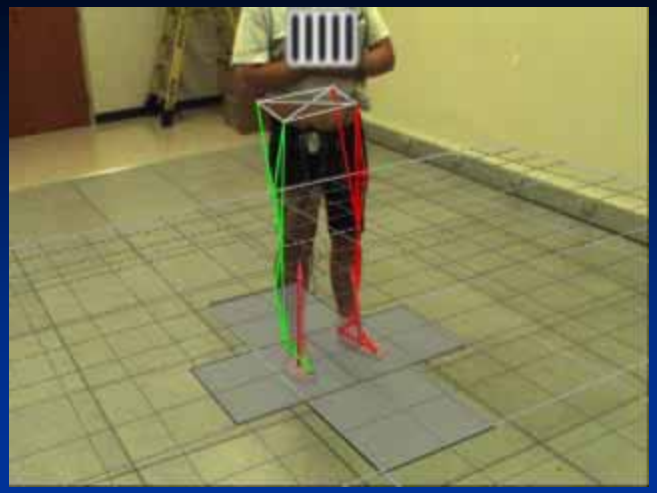


Cartilage Surrogate



Modeling approach for a multiscale multi-organ model to predict tissue level mechanical parameters

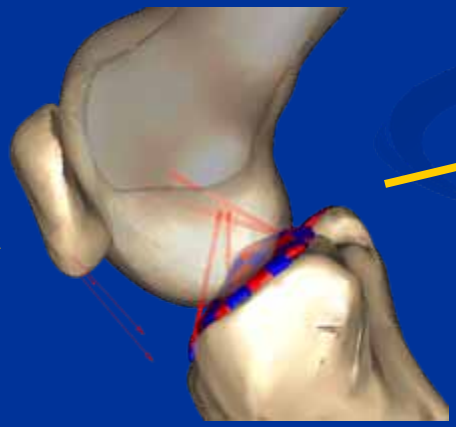
Musculoskeletal Interdependency (concurrent simulation)



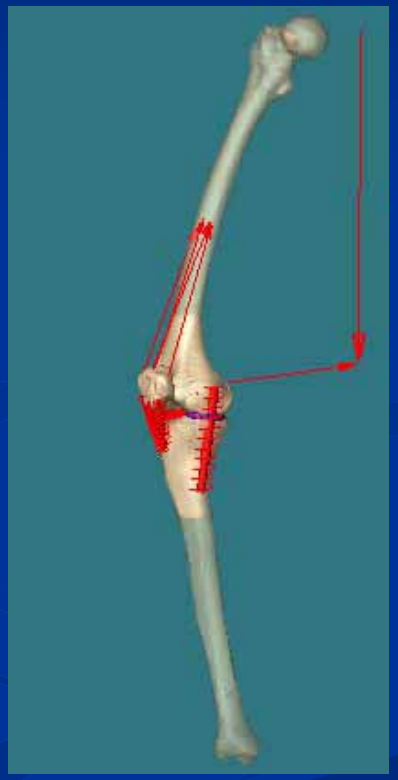
Gait lab measurements

UMKC Human Motion Lab

Forward dynamics

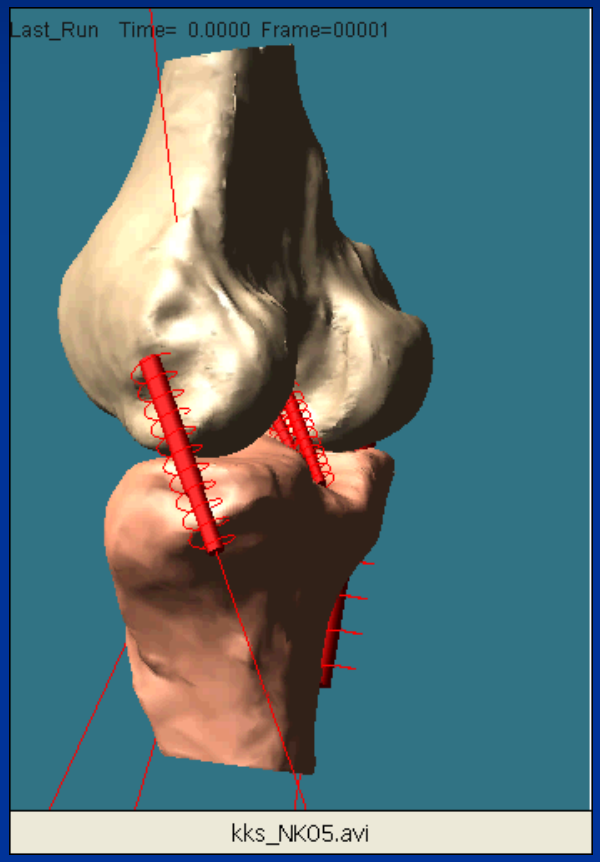


Multi-body Knee Models

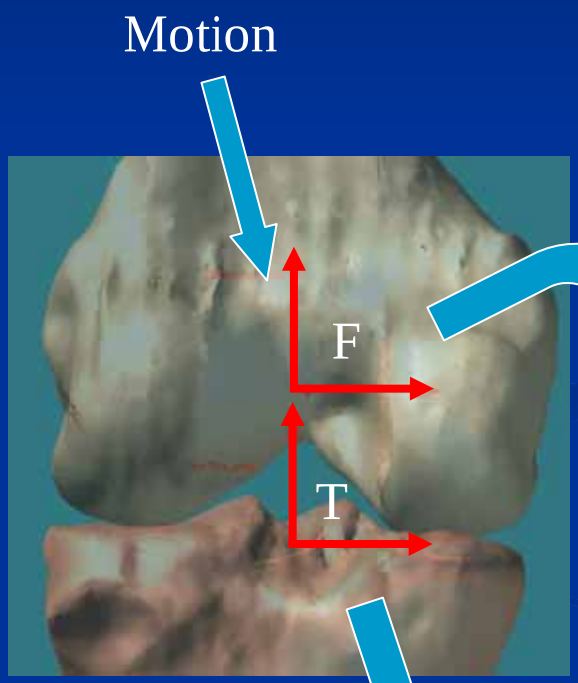


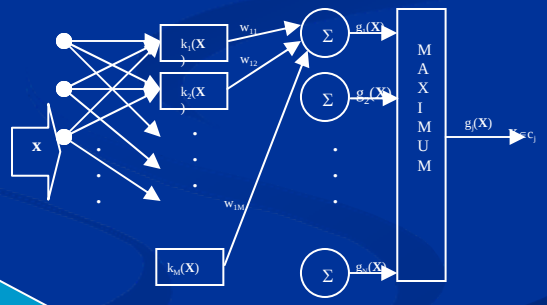
Neuromusculoskeletal Model

Neural Network Surrogate of Tibio-femoral Joint



Validated model of TF Joint

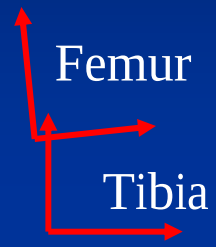


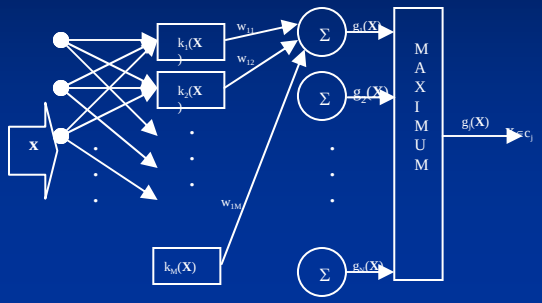


Surrogate
Training

Neural Network Surrogate of Tibio-femoral Joint

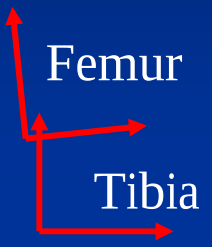
Relative motion

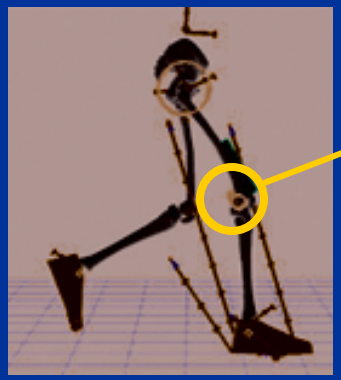




Hammerstein-Weiner black box model

Reaction Forces





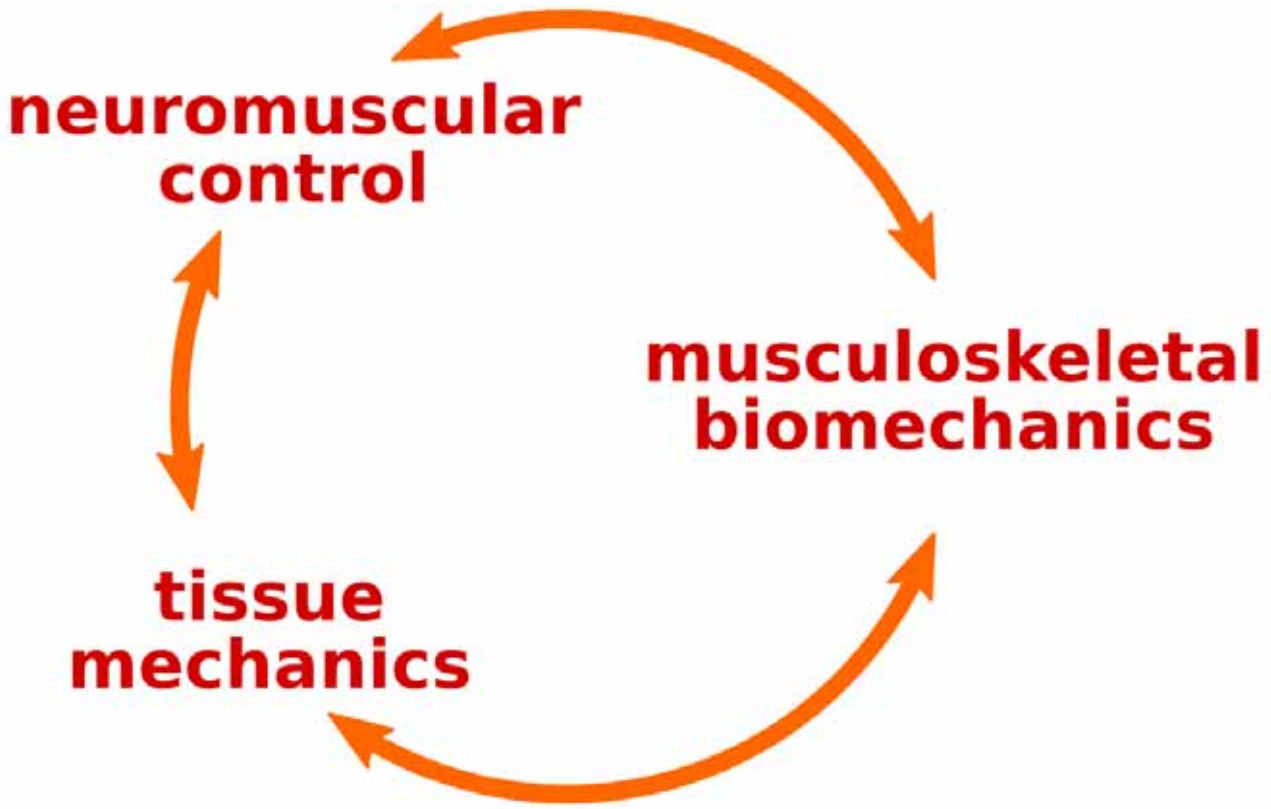
https://simtk.org/xml/neuromuscular-biomechanic.xml

Tibio-femoral surrogate

Replaces revolute joint

Acknowledgements

- Funding
  - National Science Foundation, Award Number CMS-0506297 under the IMAG program for Multiscale Modeling (PI: Guess)
  - National Science Foundation, Award Number CBET-0821459 (PI: Guess)
  - Missouri Life Sciences Research Board, Award Number 09-1078 (PI: Guess)



COLLABORATIONS

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University of Utah
Jeff Weiss
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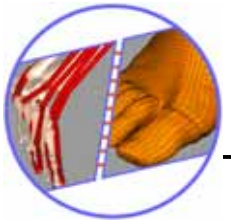
FUNDING

Efficient Methods for Multidomain Biomechanical Simulations
PI: van den Bogert
NIH/NIBIB 1R01EB006735



CHALLENGE

Coupling musculoskeletal dynamics with tissue mechanics is straight forward:

forward dynamics

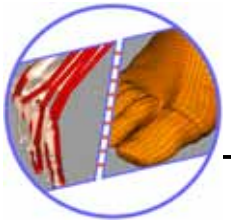
$$M(q)\ddot{q} + C(q,\dot{q}) + G(q) + R(q)F_{MT}(q,\dot{q}) + E + Q_{FEA}(q_{FEA}(q)) = 0$$

finite element analysis

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



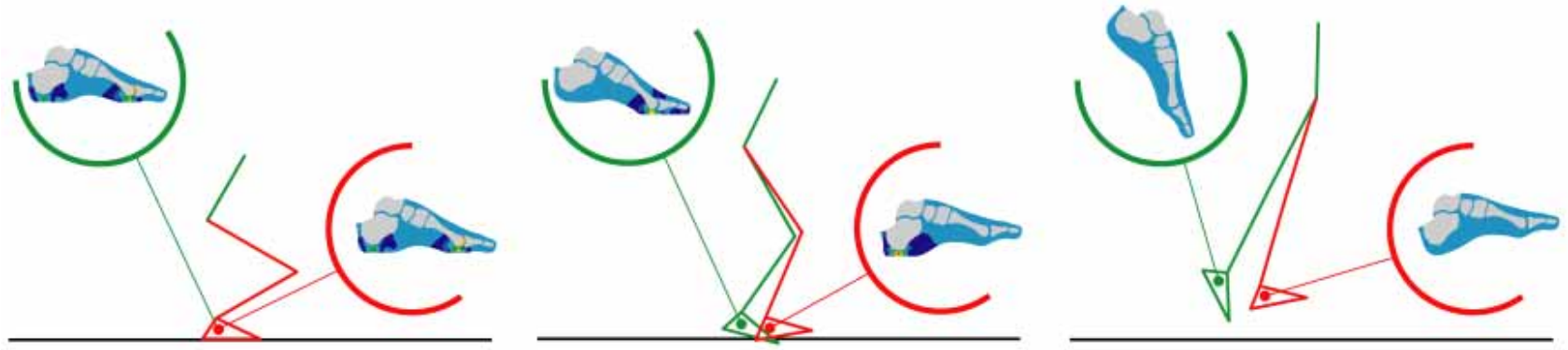
PROGRESS

Direct Coupling

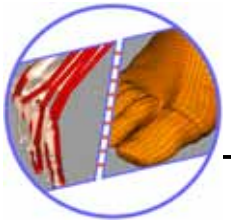
FEA performed each time step of musculoskeletal dynamics

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



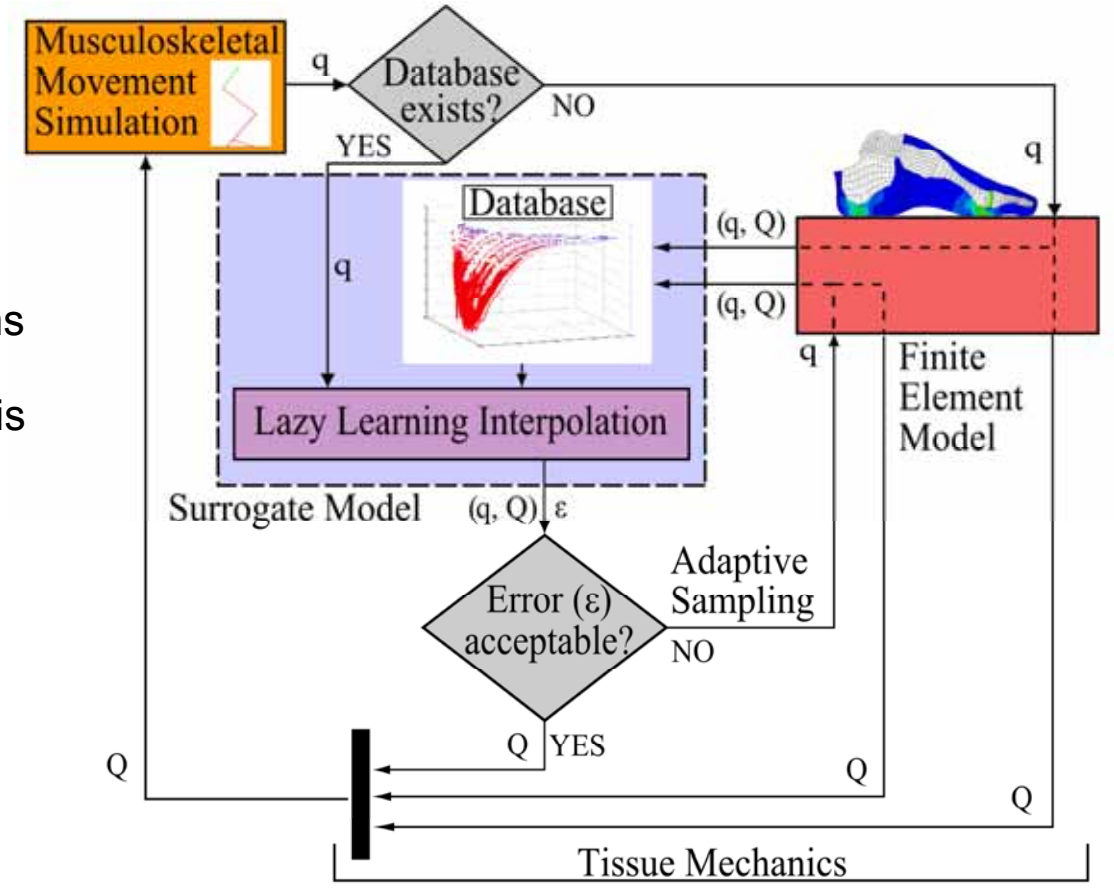
PROGRESS

Adaptive Surrogate Modeling

Relies on a database of previous tissue mechanics simulations

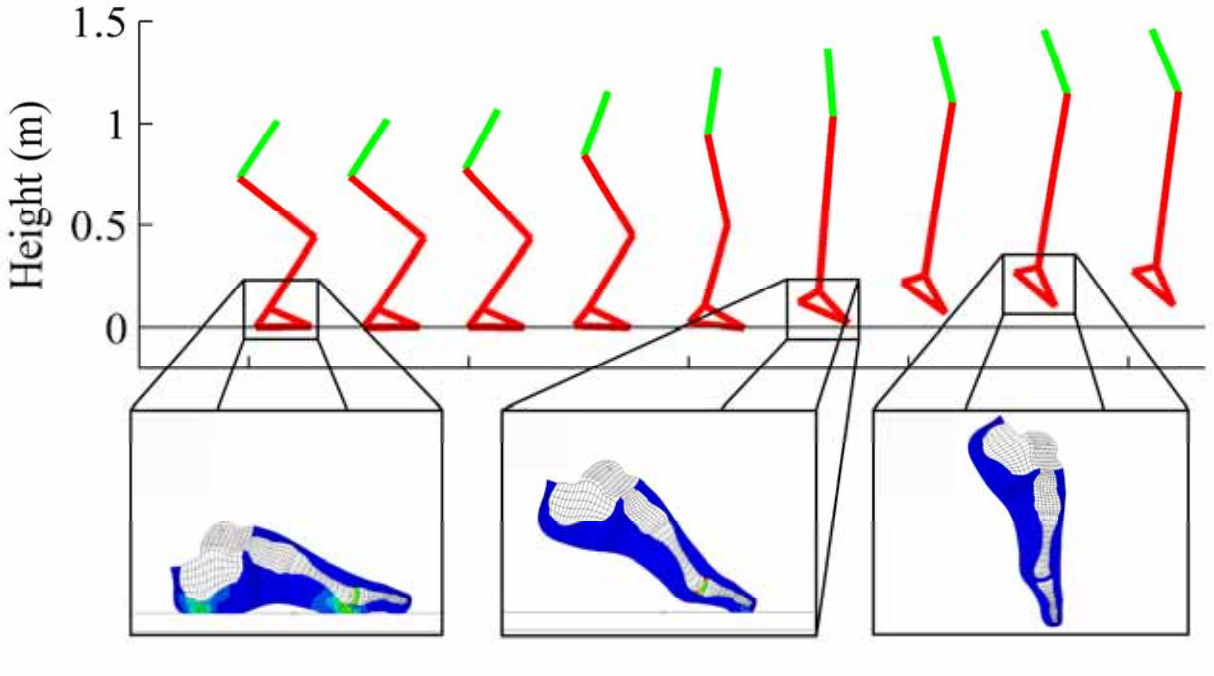
Conducts FEA on a need basis

Ensures mechanically consistent tissue response based on error prediction

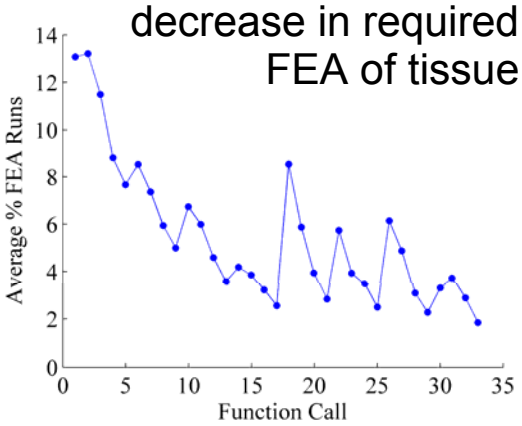


Halloran et al., J Biomech Eng 131 (1): 011014, 2009

PROGRESS



maximum height jumping predictions



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

PROGRESS

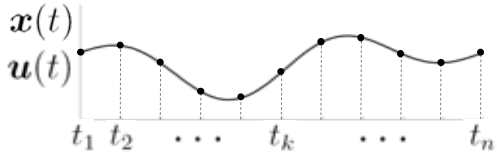
Direct Collocation

Converts optimal control & forward dynamics to full parameter optimization

Find

$$\boldsymbol{u}(t)\ \boldsymbol{x}(t)\ T$$

$\Longrightarrow$



$$\boldsymbol{x}_k = \boldsymbol{x}(t_k)\ \ \boldsymbol{u}_k = \boldsymbol{u}(t_k)\ \ T$$

that satisfy dynamics

$$\dot{x} = f(x, u, f_{gr})$$

Euler $\Longrightarrow$

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

and constraints

$$\boldsymbol{c}(\boldsymbol{x}, \boldsymbol{u}, t) \leq 0$$
$$\boldsymbol{c}_e(\boldsymbol{x}, \boldsymbol{u}, t) = 0$$

$\Longrightarrow$

$$\boldsymbol{c}(\boldsymbol{x}_k, \boldsymbol{u}_k, t_k) = 0$$
$$\boldsymbol{c}_e(\boldsymbol{x}_k, \boldsymbol{u}_k, t_k) \leq 0$$

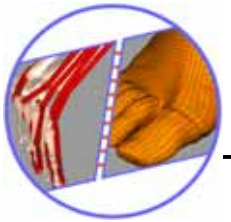
and minimize

$$J = \int_0^T L(\boldsymbol{x}(t), \boldsymbol{u}(t))\, dt$$

$\Longrightarrow$

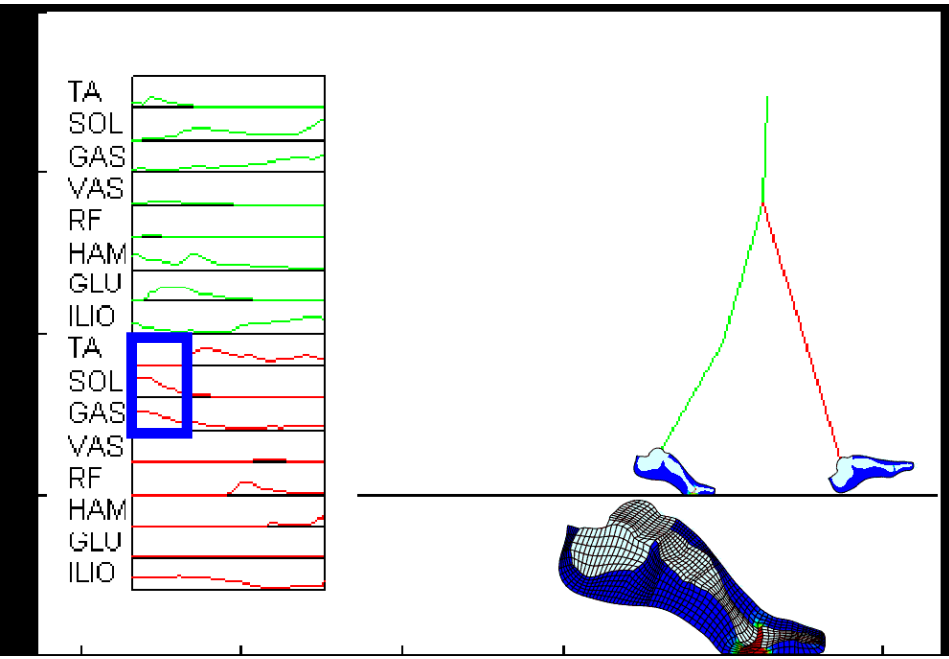
$$J = \sum_{k=1}^{n-1} L(\boldsymbol{x}_k, \boldsymbol{u}_k)$$

Ackermann and van den Bogert,, J Biomech, in review

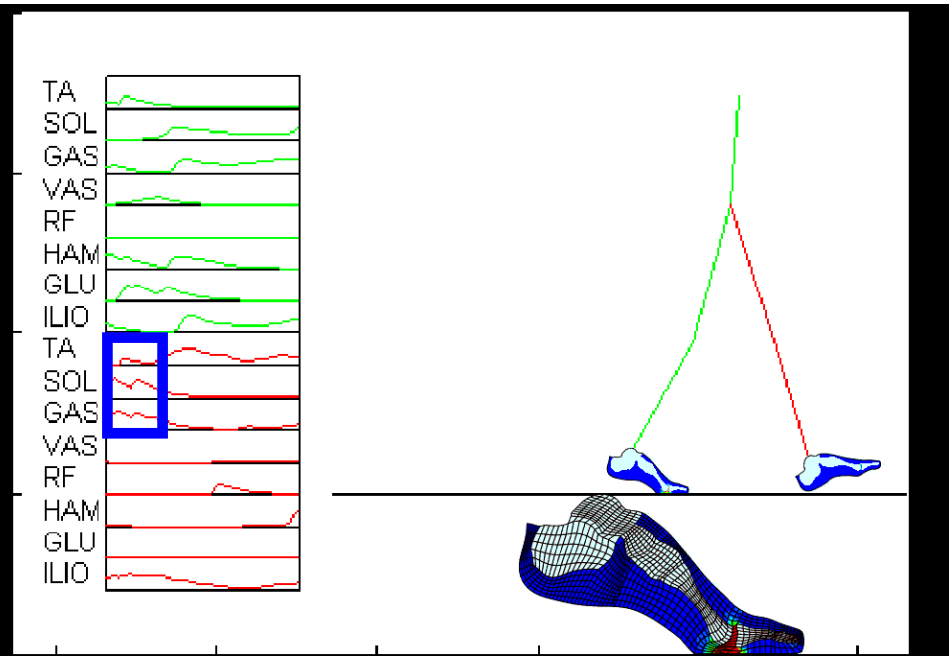


PROGRESS

prediction of neuromuscular control, movement and foot deformations during gait



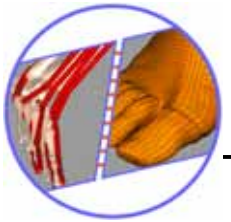
tracking + fatigue



tracking + fatigue + strain energy density

Direct Collocation also decreases computational cost of predictive movement simulations

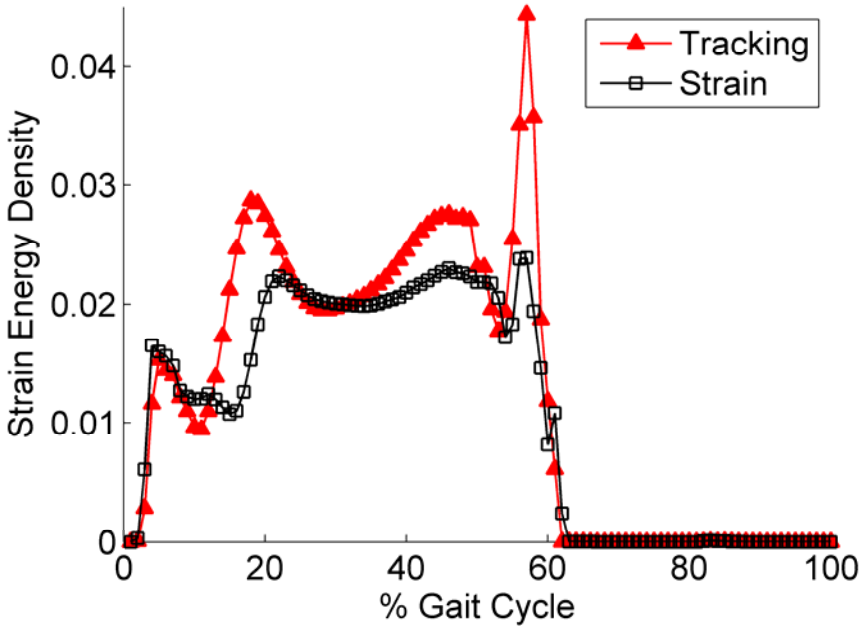
Halloran et al.,ASME Summer Bioengineering Conference, 2009

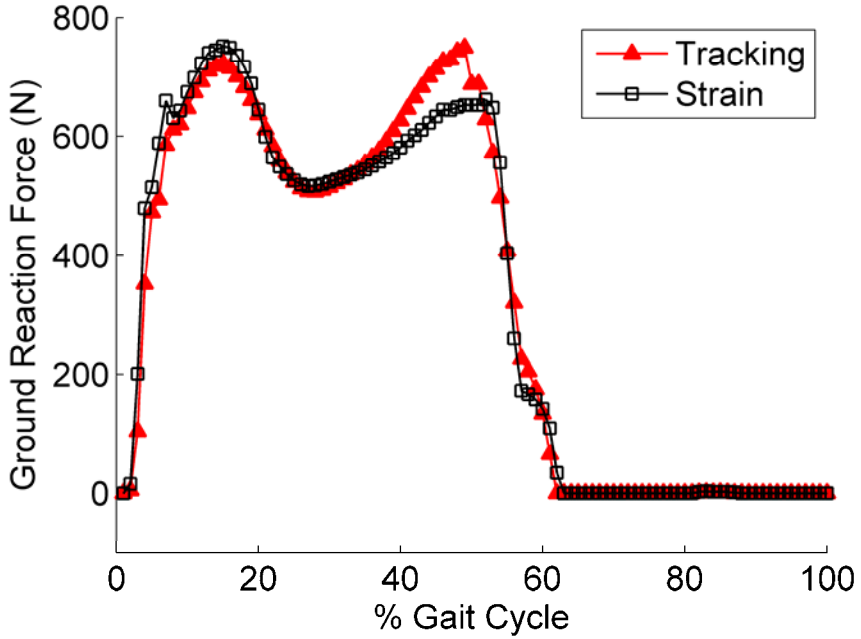


PROGRESS

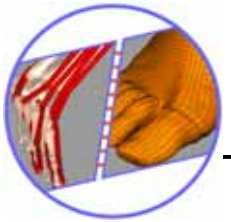
Concurrent Simulations illustrate that tissue level variables may alter movement predictions

Adaptive Surrogate modeling may further decrease the computational demand when used with **Direct Collocation**





Halloran et al.,ASME Summer Bioengineering Conference, 2009



FUTURE

Effective Glueing of Computational Tools

Matlab (The Mathworks, Inc., Natick, MA), for surrogate modeling, optimization
Abaqus (Simulia, Providence, RI), for finite element analysis
Python, for scripting of FEA
C/C++, musculoskeletal movement simulations, surrogate modeling

Dissemination

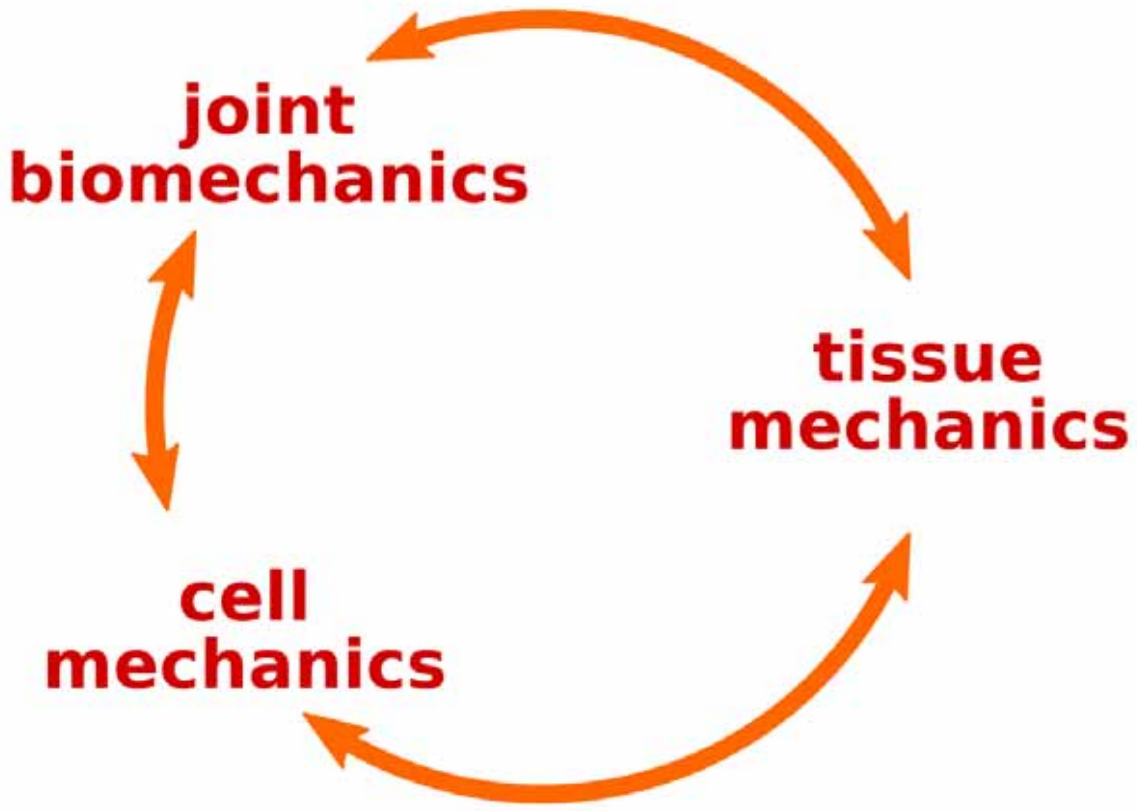
Simbios, NIH Center for Biomedical Computation at Stanford
project site: https://simtk.org/home/multidomain

General Use

Establish general rules for effective surrogate modeling and direct collocation

Novel Scientific and Clinical Problems

Physiologically detailed modeling of muscles
Identification of rehabilitation programs targeted for unloading of tissue
e.g. pain relief, healing



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University of Utah
Jeff Weiss

Duke University
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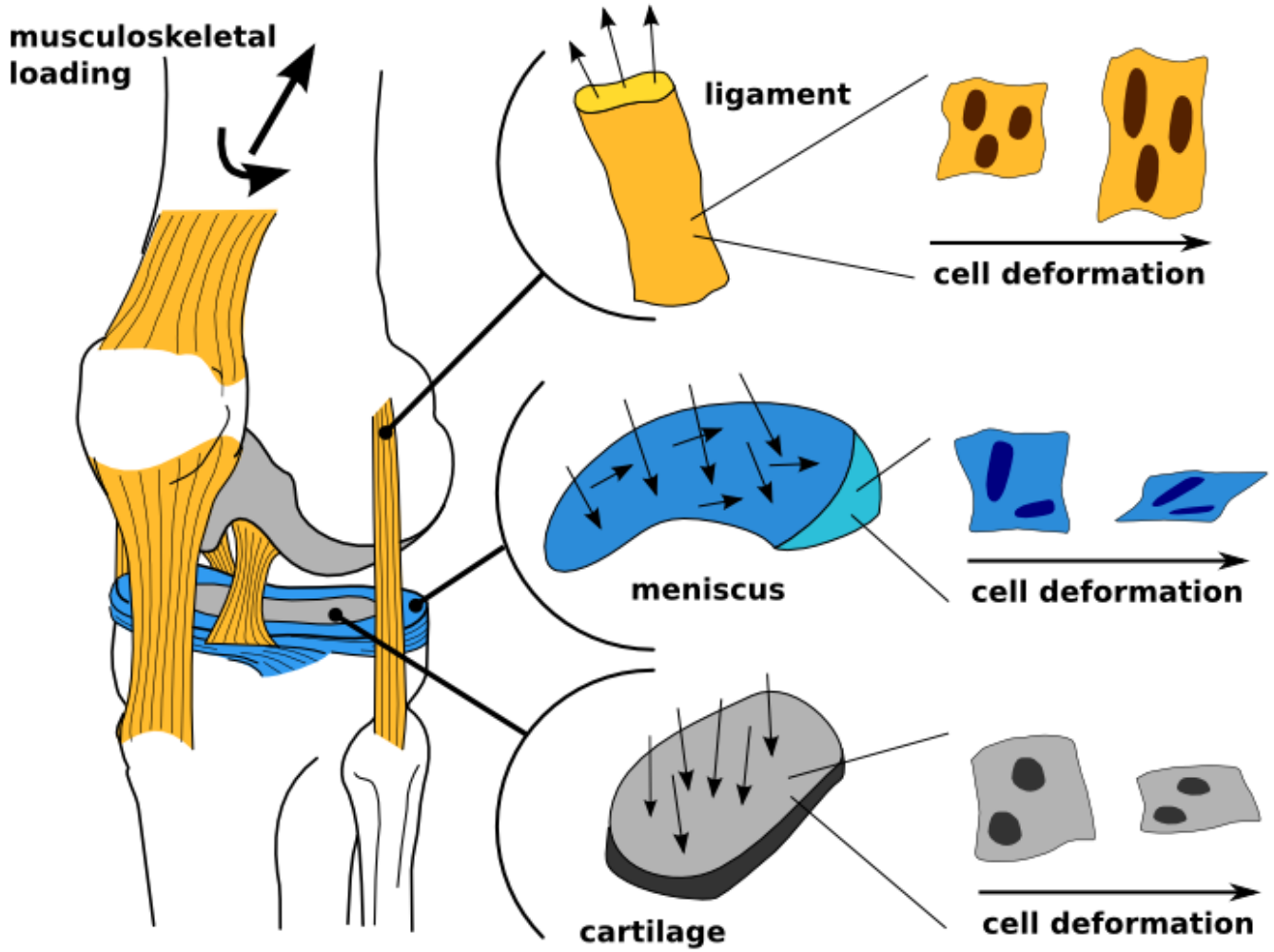
FUNDING

Predicting Cell Deformation from Body Level Mechanical Loads
PI: Erdemir
submitted to NIH/NIBIB, funding decision pending

BACKGROUND



Cell deformations are dictated by **body level loads** transferred to cells through complex **joint anatomy**, **tissue structure** and **extracellular and cellular interactions**

MOTIVATION

Why multiscale coupling?

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

Imagine

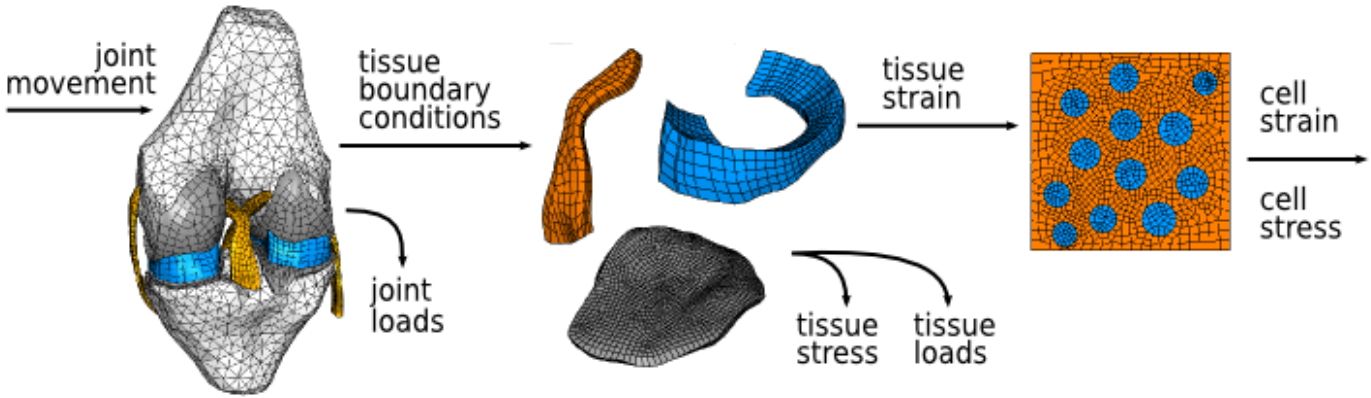
identifying potentially harmful movements/loads that can cause cell damage
- traumatic wounds
- ulcer formation (pressure or diabetic)
- osteoarthritis

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

CHALLENGE

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

straight forward
cost effective
descriptive

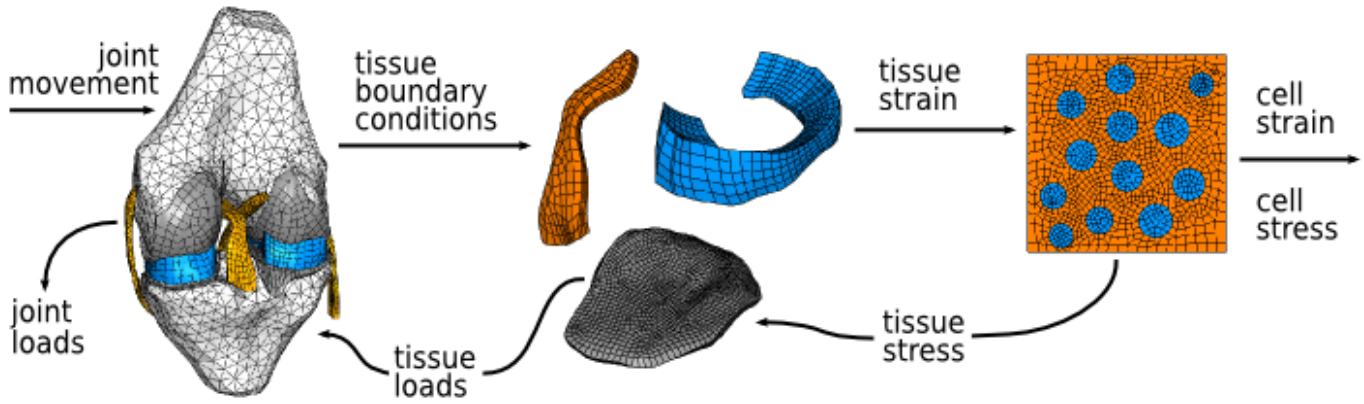
but

macro models should be mechanically consistent with micro models

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

CHALLENGE

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

CHALLENGE

Potential Pathways for Accurate & Cost Effective

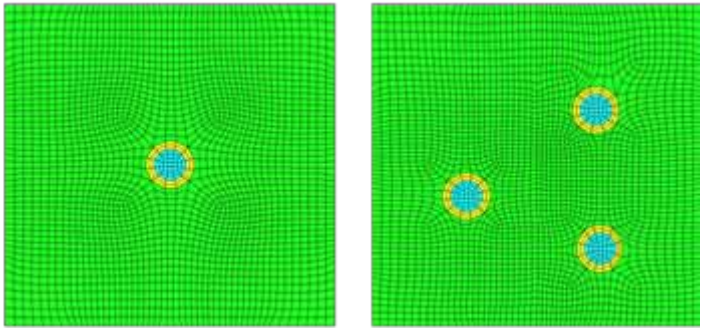
Autonomous Simulations

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

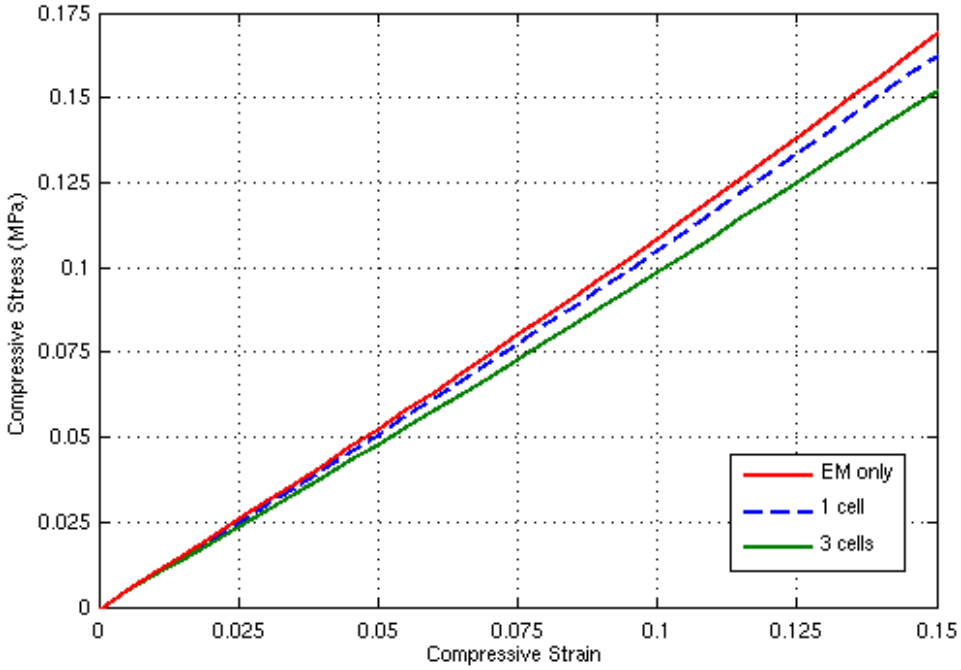
Concurrent Simulations

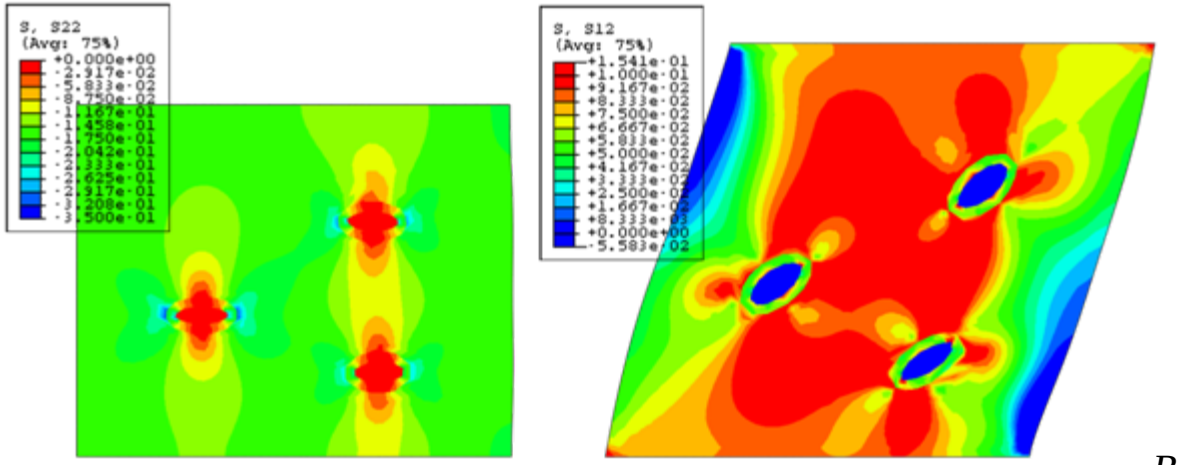
- Computational homogenization
- Adaptive surrogate modeling
- Parallel processing

PROGRESS



influence of cell distribution on the mechanics of representative volume element



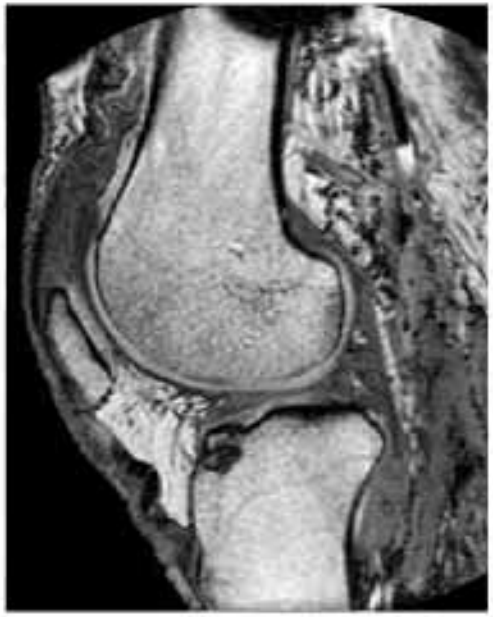


nonlinear distribution of cell level stresses under uniform loading of representative volume element

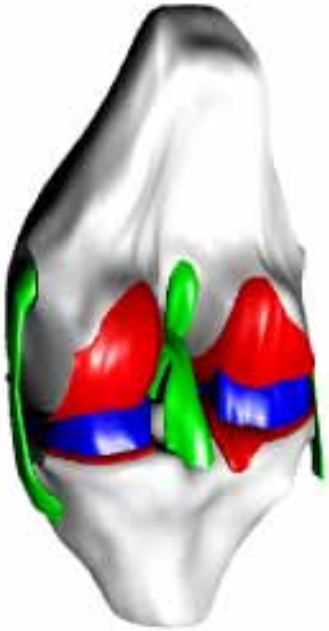
Bennetts et al.,ASB Annual Meeting, 2009

PROGRESS

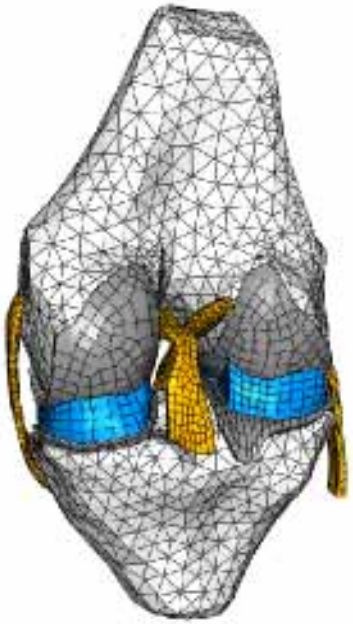
joint level modeling



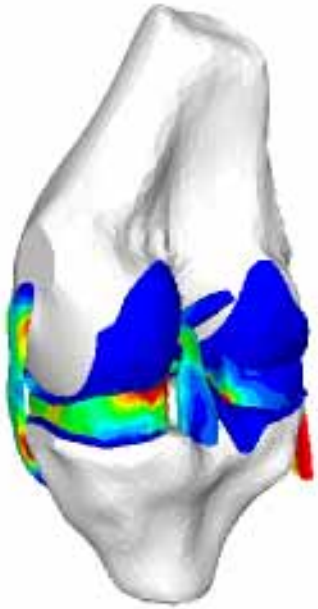
MRI



geometric reconstruction



mesh generation



FEA

FUTURE

Accessible Computational Tools

SciPy (http://www.scipy.org), for scientific computing with Python
FEBio (by Jeff Weiss, University of Utah), for finite element analysis
C/C++, for high performance computations

Research

Computational approaches
Experimentation at all levels, for model development and validation
Diseased conditions

Dissemination

Simbios, NIH Center for Biomedical Computation at Stanford
Data dissemination utilizing Hierarchical Data Format (http:/www.hdfgroup.org)

Multi-scale mechanics:
Airway hyper-responsiveness, from molecule to organ

NIH 1R33HL087789-01A1

Principal Investigators

MJ Sanderson (lead PI), University of Massachusetts

JHT Bates, University of Vermont

AM Lauzon, McGill University, Montreal, Canada

J Sneyd, University of Auckland, Auckland, New Zealand

MH Tawhai, University of Auckland, Auckland, New Zealand

Special acknowledgement to

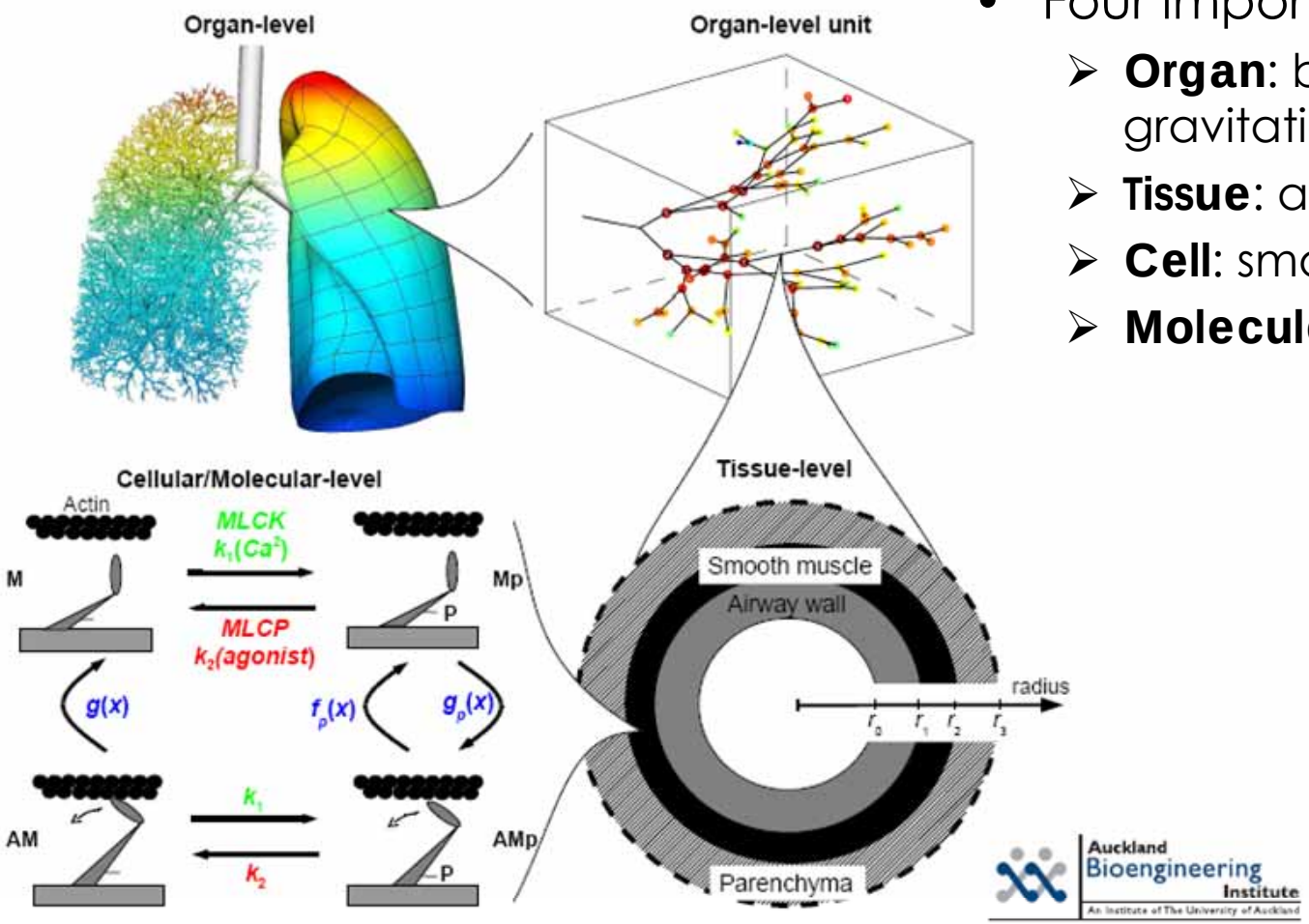
GM Donovan & AZ Politi, University of Auckland

Asthma & AHR

- Asthma is caused by airway constriction, characterised by twin emergent phenomena: **airway hyper-responsiveness** (AHR) and **airway hyper-sensitivity** (AHS)
  - AHR – airways contract too severely
  - AHS – airways contract too readily
- AHR is the primary factor in asthmatic mortality and morbidity.
- The causes of asthmatic AHR are not well understood.
  - Airway wall thickening
  - Smooth muscle functional or structural changes
  - Structural vs dynamic instabilities

- Multi-scale model is a tool to **test hypotheses**, to **embody experimental understanding**, to **predict emergent behaviour**.

Multi-scale model for AHR



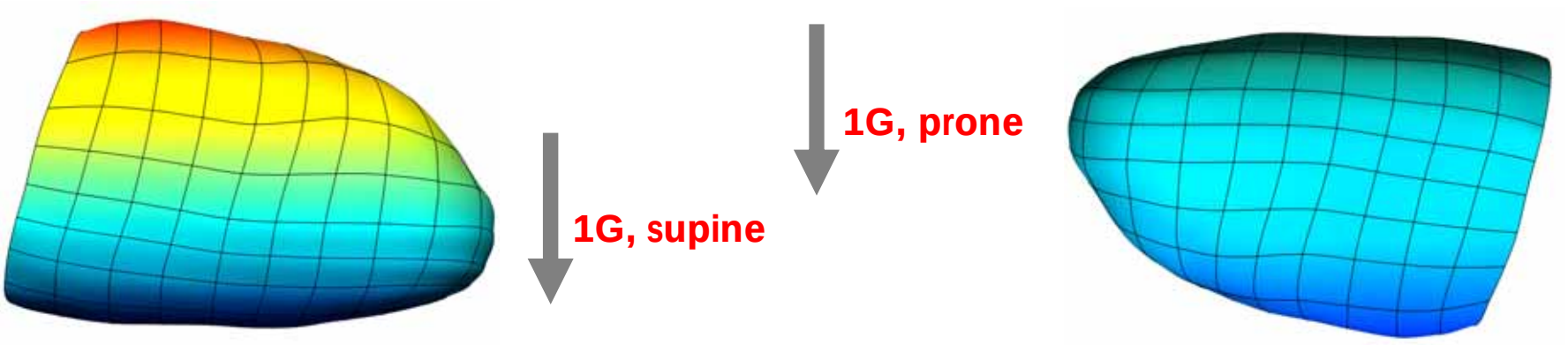
- Four important spatial scales:
  - **Organ**: breathing and gravitational mechanics
  - **Tissue**: airway wall mechanics
  - **Cell**: smooth muscle dynamics
  - **Molecule**: calcium dynamics

Auckland Bioengineering Institute
An Institute of The University of Auckland

Organ scale

Soft tissue mechanics for lung motion

- Parenchymal continuum: 3D, compressible, hyperelastic
- Finite deformation elasticity: $W = C/2 \exp (aJ_1^2 + bJ_2)$
- Patient-specific geometry
- Breathing & gravity deformations solved via finite element method
- Lung free to slide in a cavity, with frictionless contact constraints
- Embedded & tethered conducting airway tree

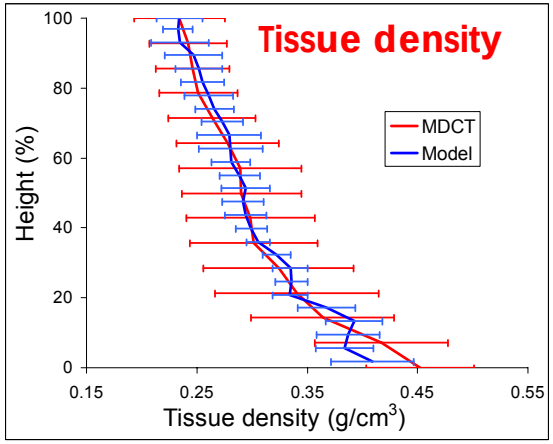


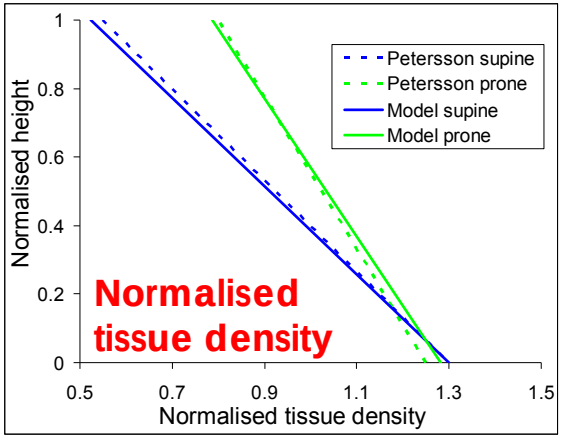
Tawhai et al. Acad Radiol 13(1):113-120, 2006; Tawhai et al. submitted to J Appl Physiol, 2009

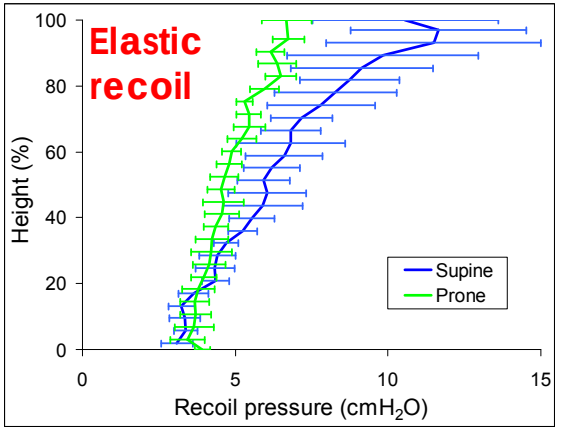
Organ scale

Soft tissue mechanics for lung motion

- Model tissue density compared with MDCT imaging supine at FRC
- Normalised tissue density compared with independent study supine and prone (Petersson et al. Resp Phys Neurobiol 156: 293 - 303, 2007)
- Regional elastic recoil pressure predicted in supine and prone model at FRC (note increased uniformity in prone model)



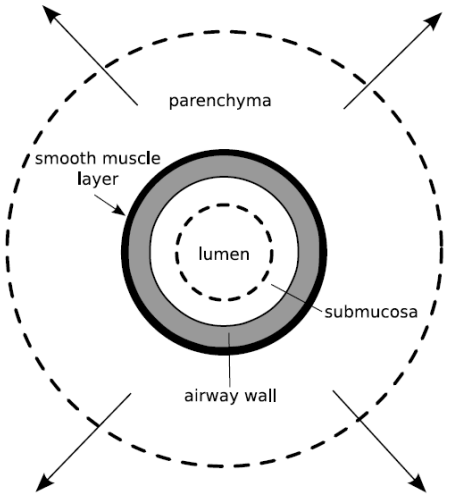


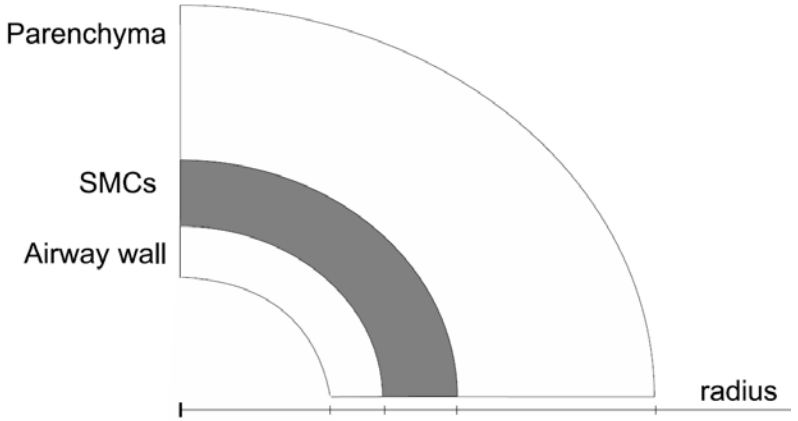


Tawhai et al. submitted to J Appl Physiol, 2009

Tissue scale

- Embedded airway segments radially-symmetric and longitudinally-stiff
- Airway radius determined from force balance across all layers
  - Internal pressure
  - Smooth muscle contractile force (cellular level)
  - Parenchymal tethering pressure
  - External pressure (organ level)





Donovan et al., ATS 2009; Politi et al., submitted to Royal Soc Interface, 2009.

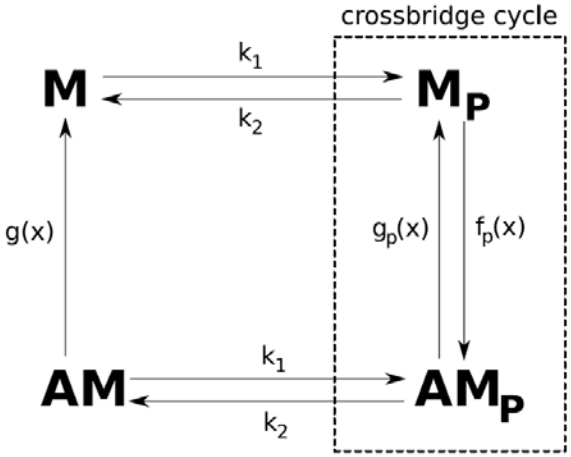
Parenchymal tethering

- Airway contraction results in a restoring force from the compressible parenchymal layer.
- Estimate local tethering pressure by linearising material state from the organ level model.
- Plane strain, radial symmetry
- Result is similar to widely-used quadratic heuristic, but coefficients depend on organ-level material state
  - $P_2 = 2\mu[\Delta R_2 + 1.5(\Delta R_2)^2] + P_3$

Donovan et al., ATS 2009; Politi et al., submitted to Royal Soc Interface, 2009.

Cellular scale

- Thin filament theory: **actin** and **myosin**
- Smooth muscle force generation and dynamics controlled by **crossbridge model** (Huxley, Hai-Murphy, Wang et al.)
- Crossbridge population states governed by a system of PDEs



Donovan et al., ATS 2009; Politi et al., submitted to Royal Soc Interface, 2009.

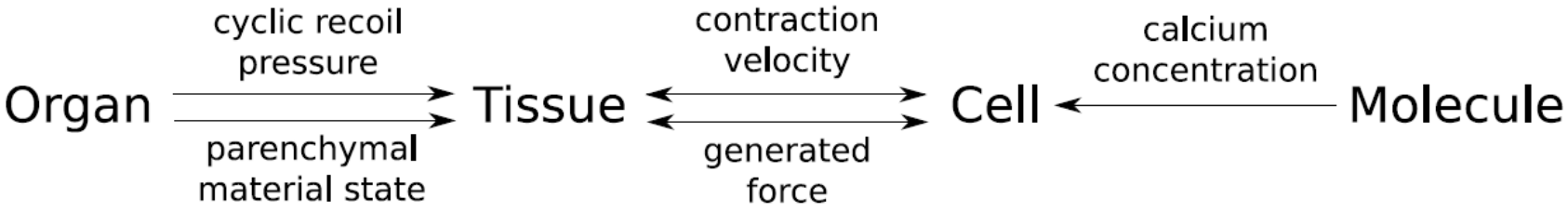
Molecular scale

- Cellular scale smooth muscle activation is controlled by **agonist** and **calcium** concentrations.
- Agonist (ie MCh) is introduced to the system at a specified time
- Mimic a bronchial challenge

- Agonist → calcium → smooth muscle contraction → airway constriction

Multi-scale connections

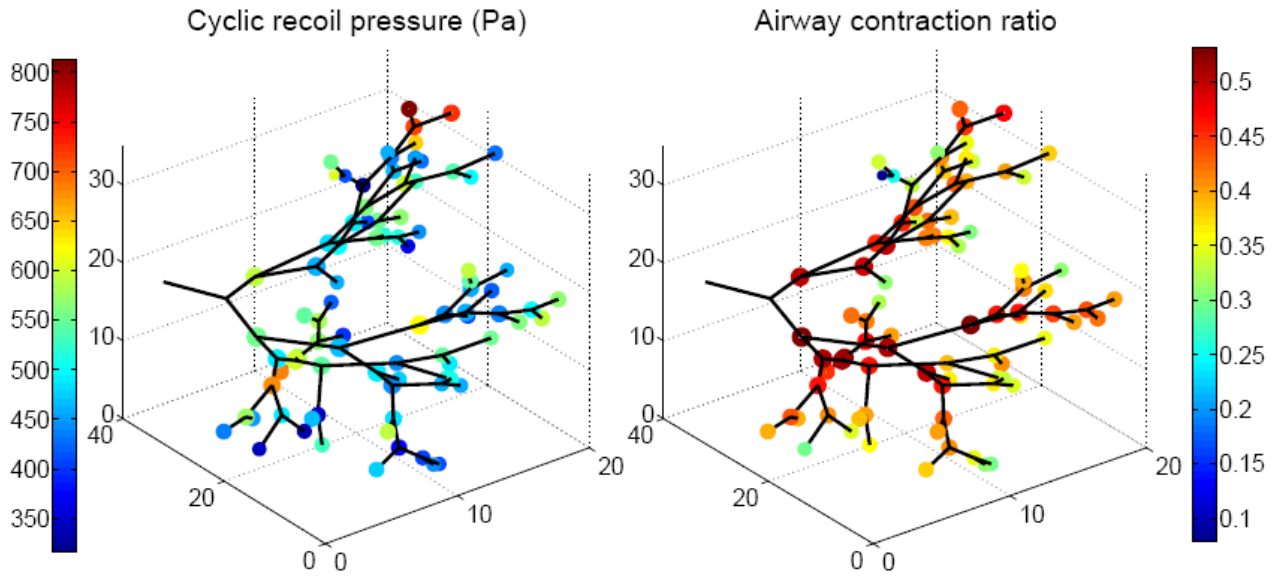
- Each scale interacts with its immediate spatial neighbours.



Donovan et al., ATS 2009; Politi et al., submitted to Royal Soc Interface, 2009.

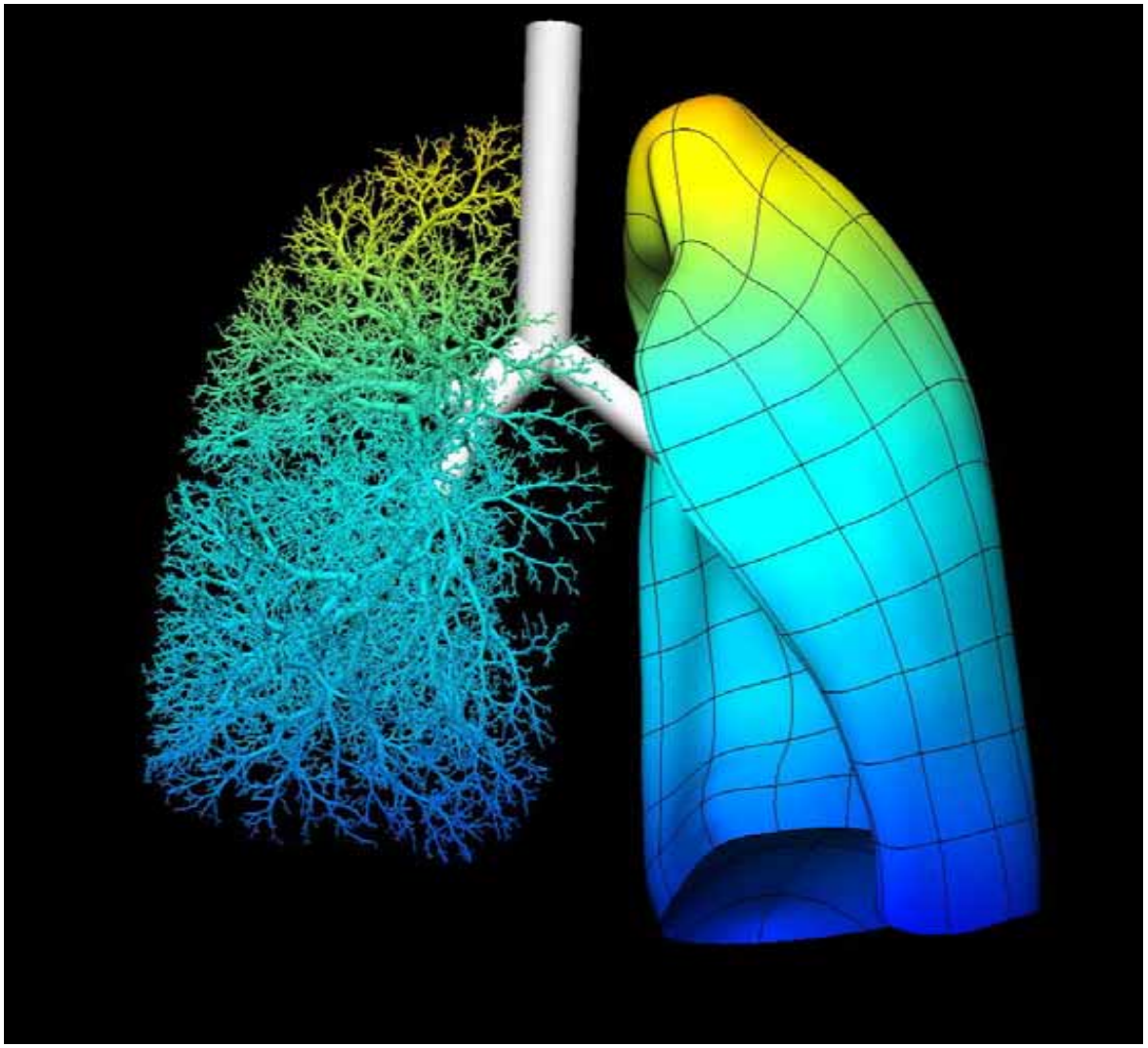
Simulated bronchial challenge

- 3 second tidal breathing
- Agonist introduced at 10 s
- Emerging spatial variation



Donovan et al., ATS 2009; Politi et al., submitted to Royal Soc Interface, 2009.

Simulated bronchial challenge



Donovan et al., ATS 2009; Politi et al., submitted to Royal Soc Interface, 2009.

Summary

- Initial multi-scale model through organ, tissue, cellular, & molecular scales
- Emerging behaviour
- Model development is paralleled by experimentation in collaborating groups, also multi-scale
  - Molecular & cellular: Lauzon
  - Tissue: Sanderson
  - Organ: Bates
- Current work is studying regional constriction & integrating with models for air flow

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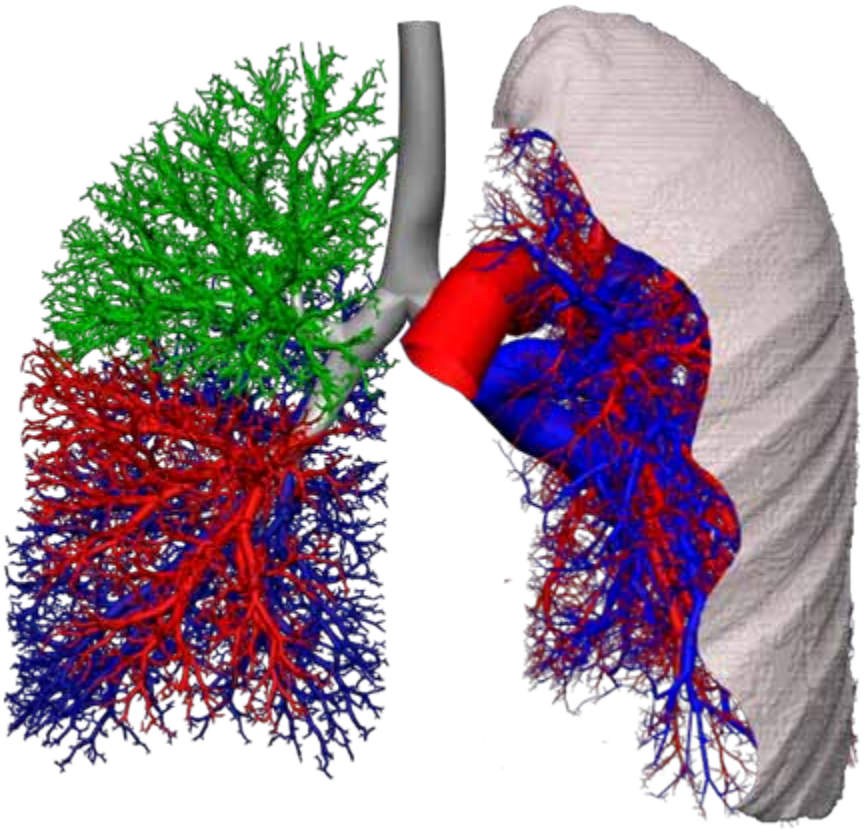
Dr AZ Politi

U. Auckland: Prof J Sneyd

U. Mass: Prof MJ Sanderson

U.Vermont: Prof JH Bates

McGill U. : Dr A-M Lauzon



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