Chondrocyte Deformation as a Function of Tibiofemoral Joint Loading

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Role of Cell Deformations

Cellular deformation plays a role in:

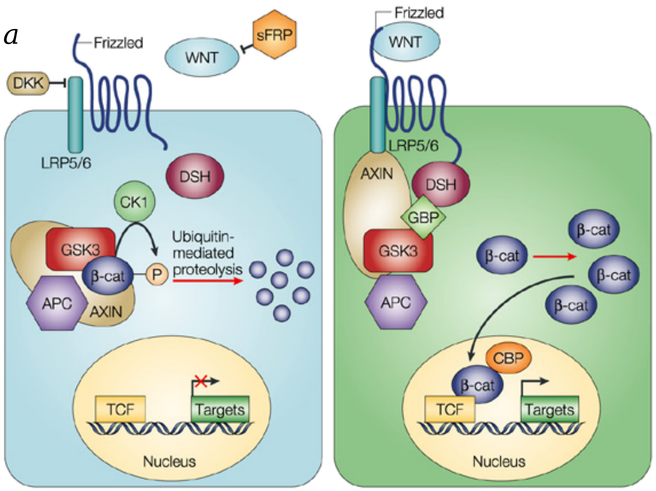
Cell activity[a]
- Matrix remodelling
- Chemical signaling
- Profileration
- Gene expression

Cell differentiation[b]

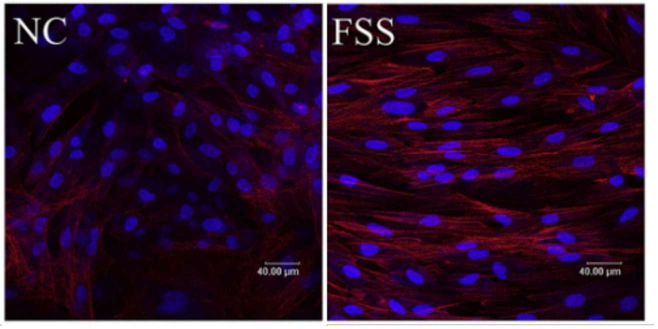
Cell vitality[c]

In musculoskeletal biomechanics, **joint loading** results in **chondrocyte deformations** in cartilage.

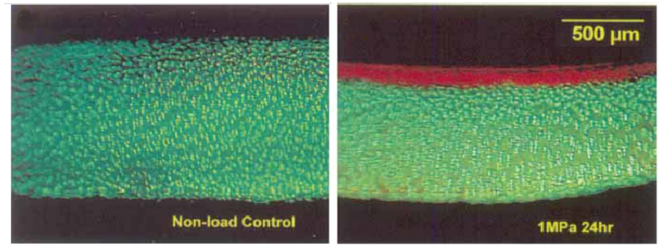
a



b



c



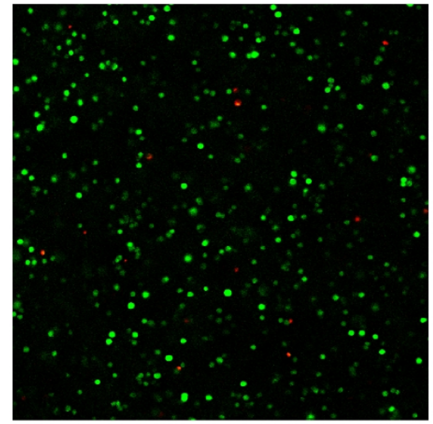
[a]*adapted from Moon et al., Nat Rev Genet 5: 691-701, 2004.*
[b]*adapted from Huang et al., Arch Med Res 41: 497-505, 2010.*
[c]*adapted from Chen et al., J Orthop Res 21: 888-898. 2003.*

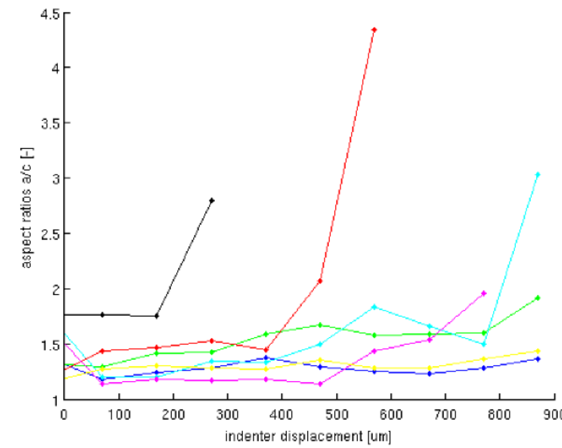
Quantifying Cell Deformations

Experiments with

in situ tissue explants,
cell seeded constructs

help understand load transfer to cells.



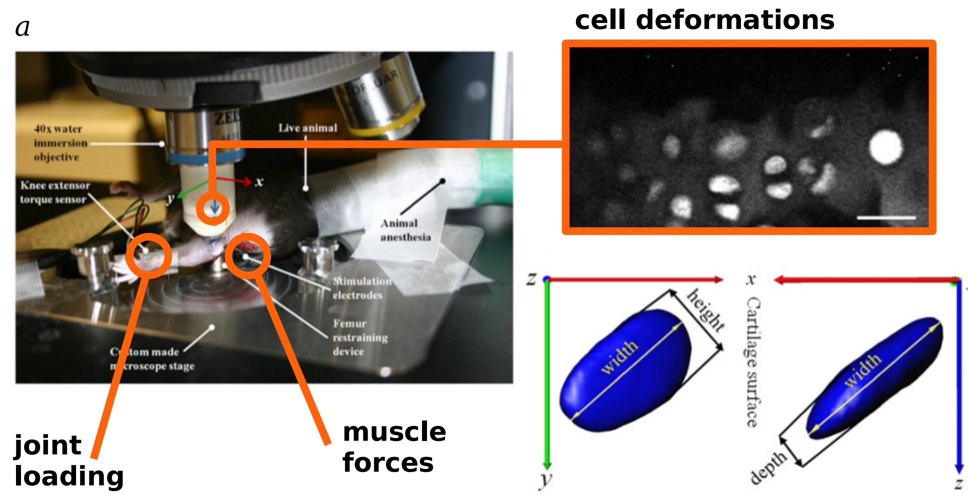


Animal studies[a] can relate simplified musculoskeletal loading to chondrocyte deformations.

Computational modeling can relate

muscle forces
joint kinematics/kinetics
cartilage stress/strain
chondrocyte deformations

for complex geometries and lifelike loading.



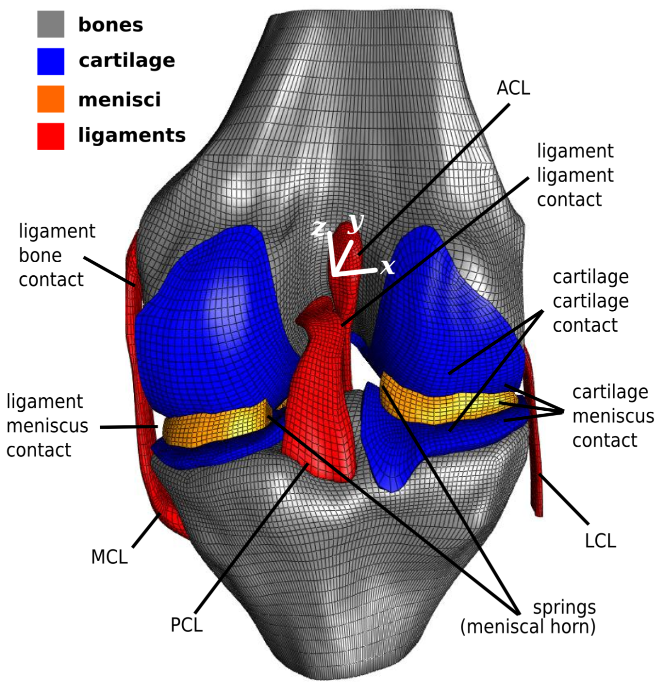
[a]*adapted from Abusara et al., J Biomech 44: 930-934, 2011.*

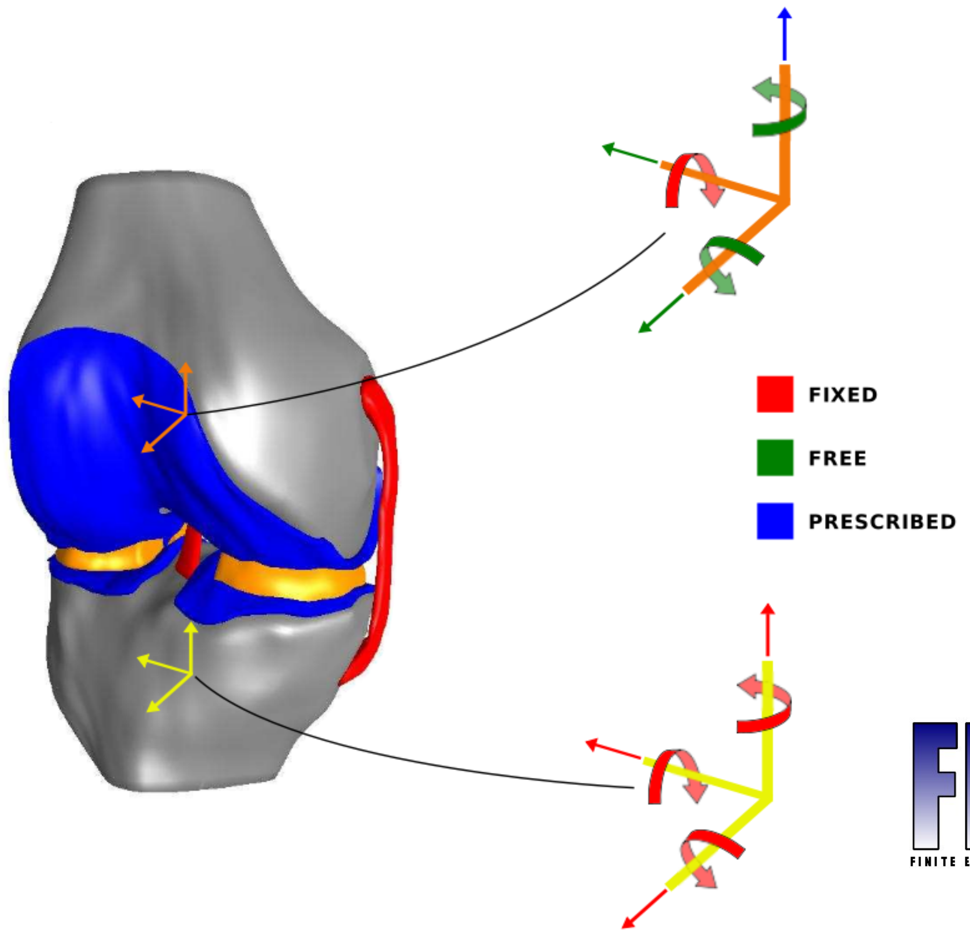
Objectives

- Establish a **post-processing platform** to analyze macroscopic tissue deformations for calculation of cell deformations
- For a given **tibiofemoral joint loading**, estimate regional **chondrocyte deformations** in tibial and femoral cartilage
- Explore the **relationship** between macroscopic **cartilage strains** and **chondrocyte deformations**
- Investigate the role of **single vs multiple cell** representations on prediction of chondrocyte deformations

Joint Level Modeling

Open
Knee





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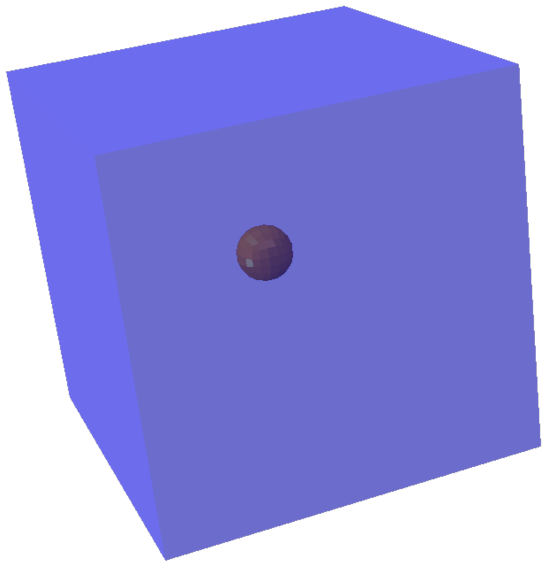
Ligaments	transversely isotropic hyperelastic
Cartilage[a]	Mooney-Rivlin: E = 10 MPa, ν = 0.48
Meniscus	transversely isotropic hyperelastic
Bones	rigid body

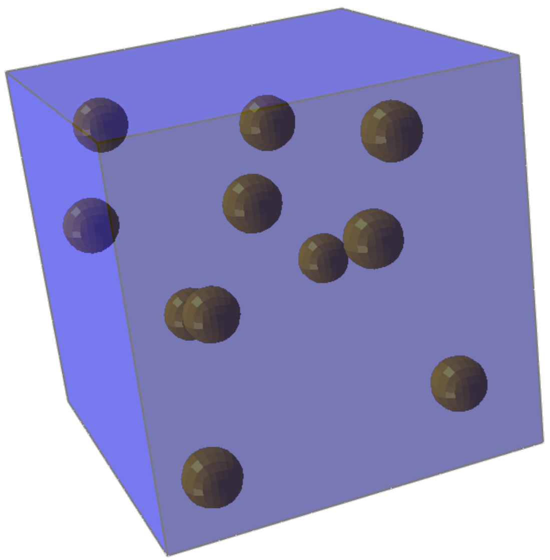
Implicit dynamics

Compression up to 780 N
(1 body weight)

[a] *adapted from Shepher and Seedhom, Rheumatology 38: 124-132, 1999.*

Cell Level Modeling





Single[a] vs 11-cell[b] RVEs

Extracellular Matrix

100x100x100 µm
Mooney-Rivlin: E = 10 MPa, ν = 0.48

Pericellular Matrix[c]

2.5 µm thickness
Mooney-Rivlin: E = 2.8665 MPa, ν = 0.048

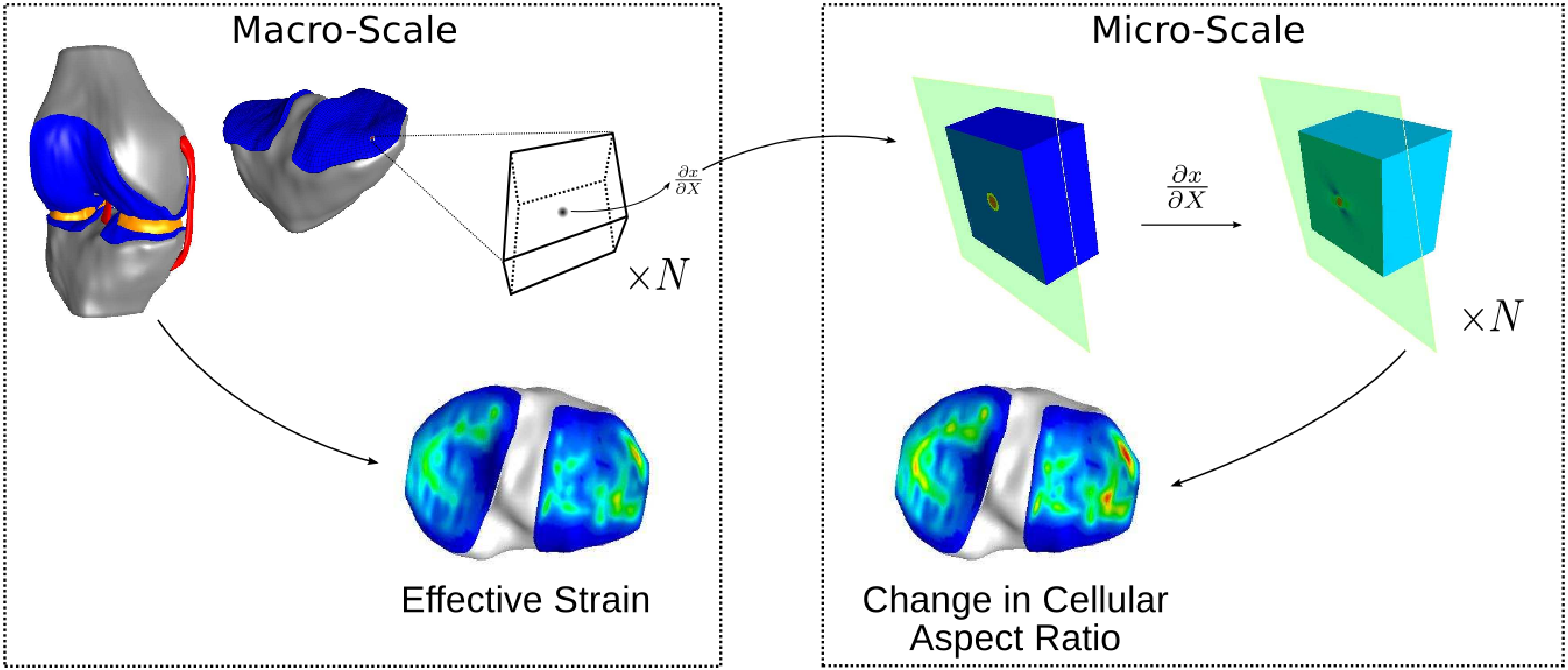
Cell[c]

5.0 µm radius
Mooney-Rivlin: E = 0.2398 MPa, ν = 0.48

[a] *adapted from Guilak and Mow, J Biomech 33: 1663-1673, 2000.*
[b] *adapted from Hunziker et al., Osteoarthritis Cartilage 10: 564-572, 2002.*
[c] *adapted from Michalek and Iatridis, J Biomech 40: 1405-1409. 2007.*

Coupling & Simulation Strategy

Post-processing approach



Deformation gradient of macro-model drives micro-scale simulations.

Python scripting allows streamlined processing of macro/micro simulations.

Tackling Computational Cost

Ohio Supercomputer Center
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Problem Size

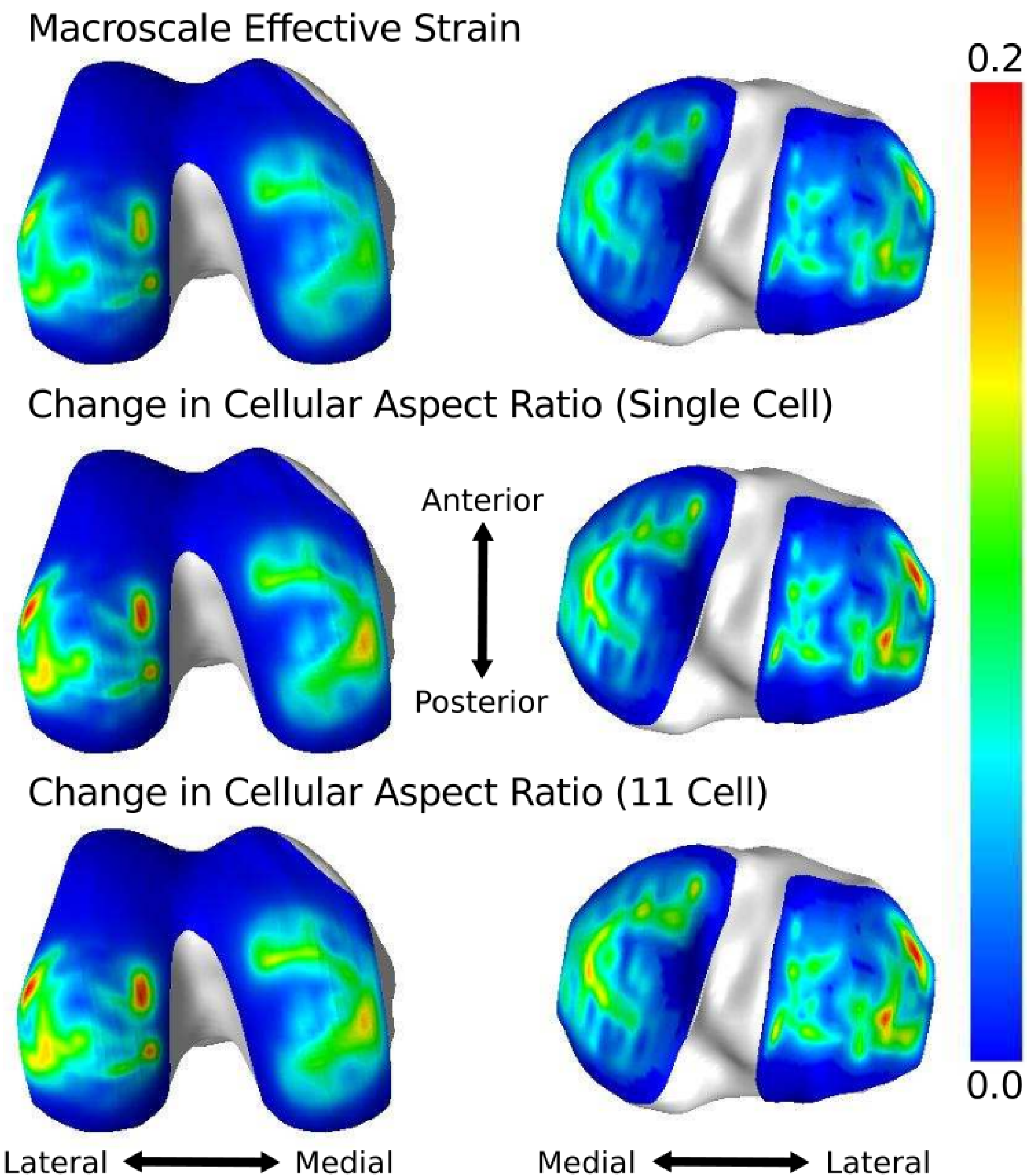
11 cell model: 249834 equations
7882 models

Parallelization

100 threads on Glenn Cluster @ OSC
Wall-clock time (slowest thread) **~ 19 hours**
Total CPU time **~ 1735.1 hours (72.3 days)**

Post-processing approach is also suitable for grid computing.

Macroscopic Map of Cartilage

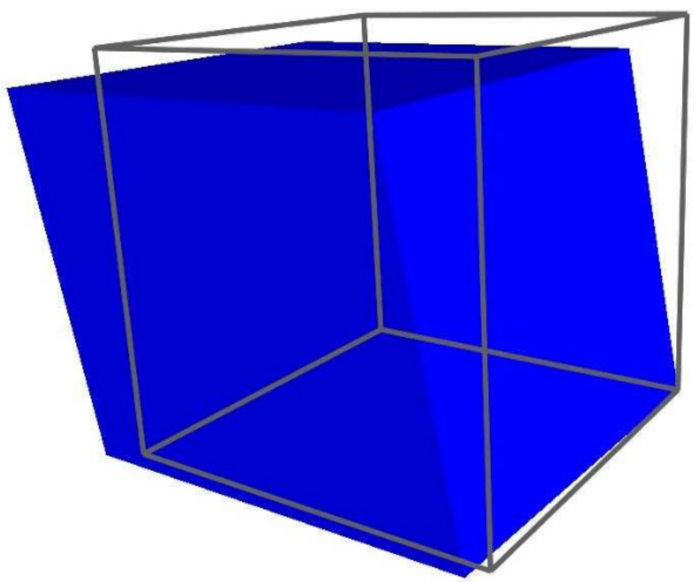


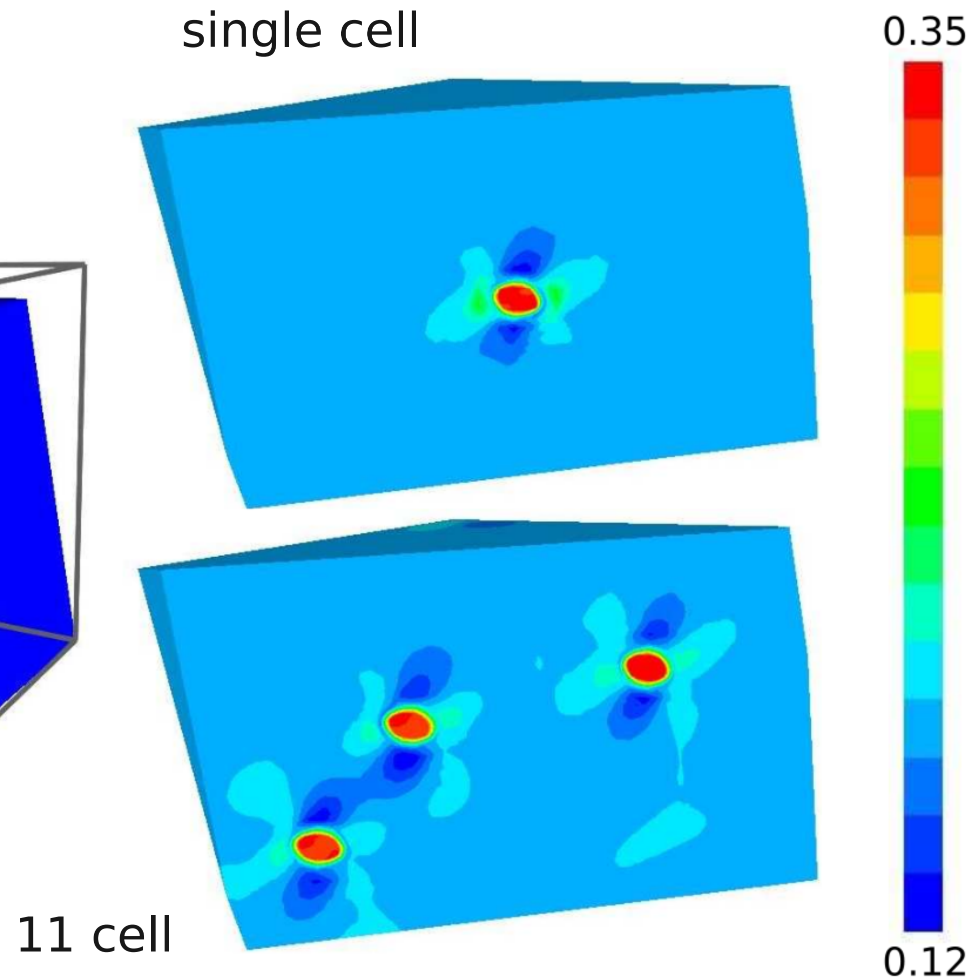
Macroscopic and microscopic deformations for the transitional zone

femoral and tibial cartilage

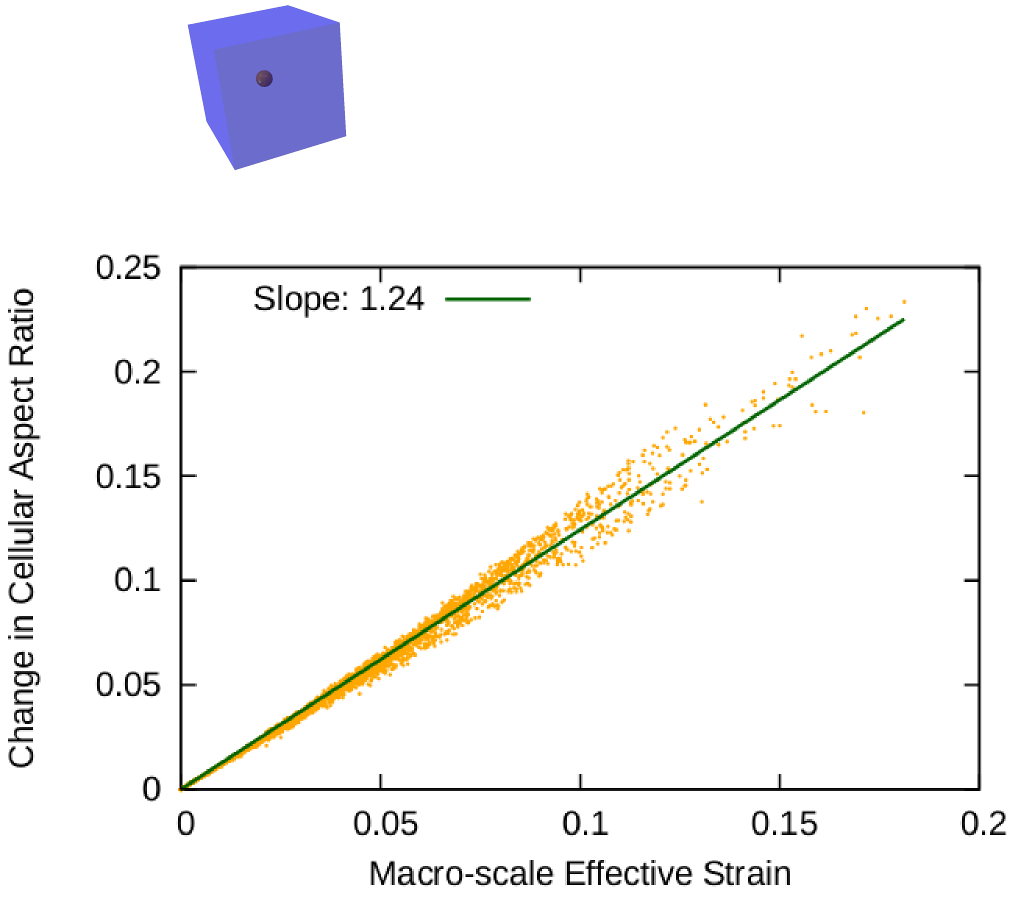
Microscopic Map of Individual Cells

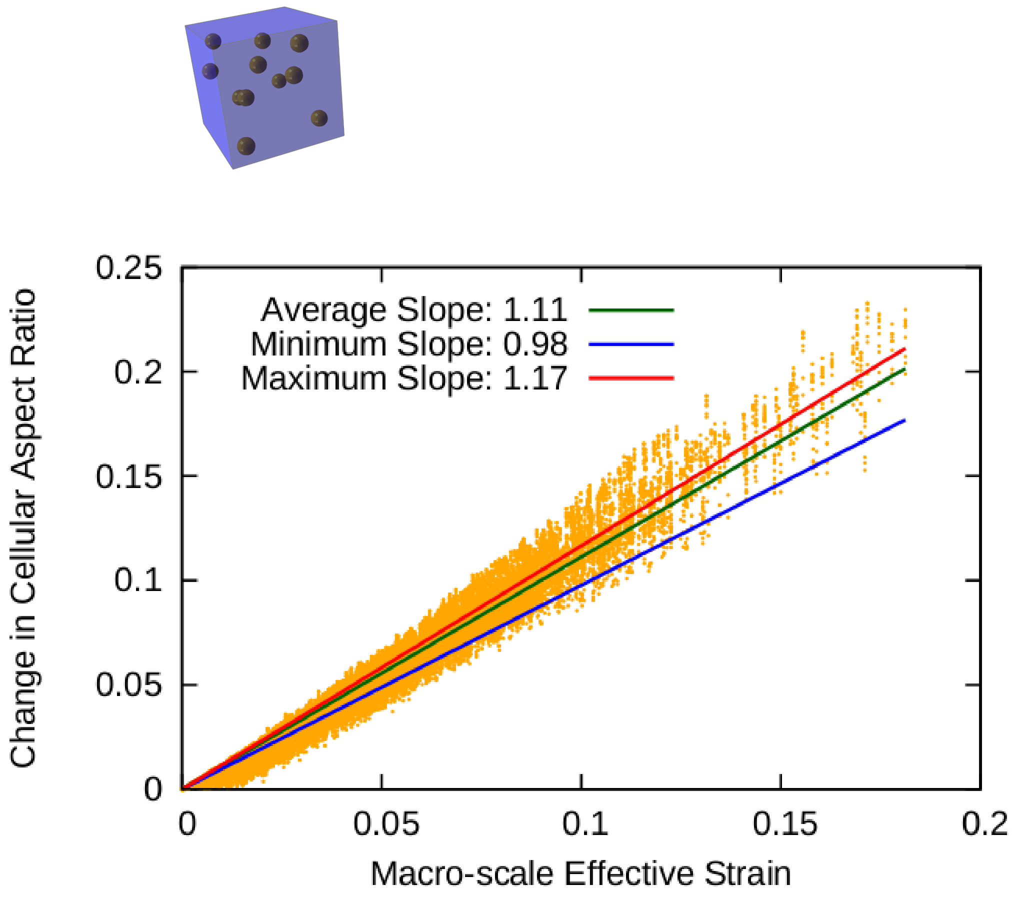
Deformation gradient from a combined loading case





Macro-Micro Relationships





effective macroscopic cartilage strain ~ change in chondrocyte aspect ratio

Discussion

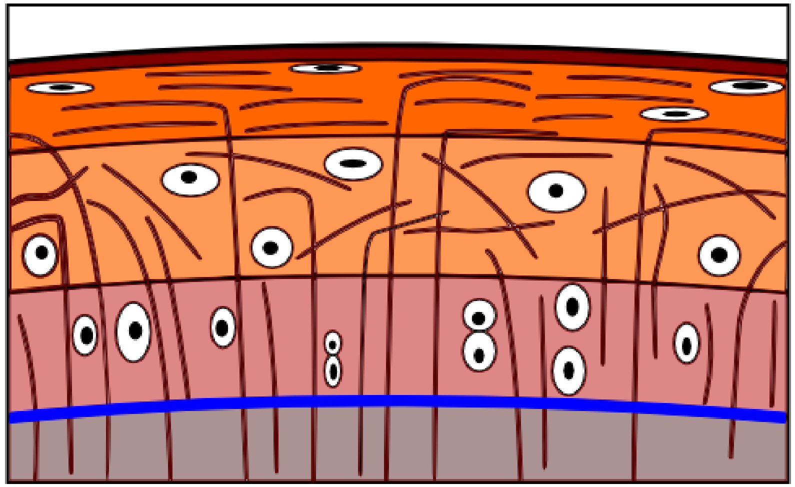
- Establish a **post-processing platform** to analyze macroscopic tissue deformations for calculation of cell deformations
  - Hypothesis generation platform to provide insight into how cells may be deforming under lifelike loading
  - Highly scalable parallelized processing
  - Generalizable for different macro/micro models
  - Weak coupling (assumption of mechanical consistency)
  - Cell deformation metrics at a snapshot (no mechanical history)
- For a given **tibiofemoral joint loading**, estimate regional **chondrocyte deformations** in tibial and femoral cartilage
  - A step towards the realization of relating knee joint mechanics to the mechanics of chondrocytes
  - Full spatial analysis of cartilage rather than a handful of limited spatial locations
  - No verification & validation

Discussion

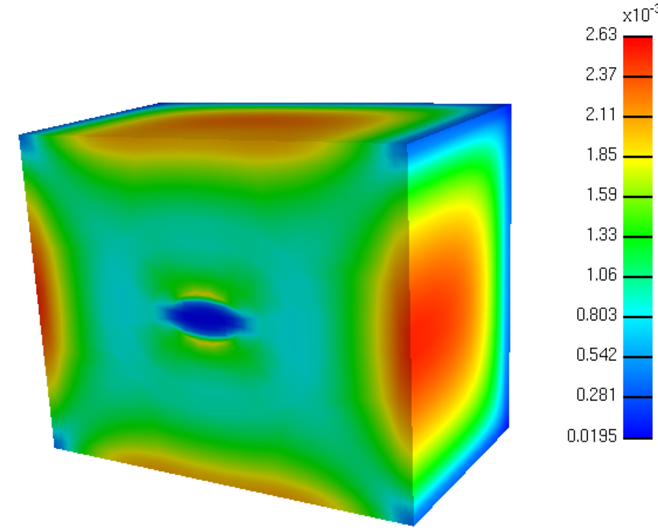
- Explore the **relationship** between macroscopic **cartilage strains** and **chondrocyte deformations**
  - Amplified transfer of macroscopic strains to cells
  - Linear relationship between macro/micro variables with some variability
  - Large database of cell deformations for functional tibiofemoral joint loading
- Investigate the role of **single vs multiple cell** representations on prediction of chondrocyte deformations
  - Indications of strain shielding for multiple cell distributions
  - Neighboring cells may not experience similar levels of deformations
  - Onset of mechanobiological function and damage may be spatially different
  - Cell-to-cell interactions

Future Work

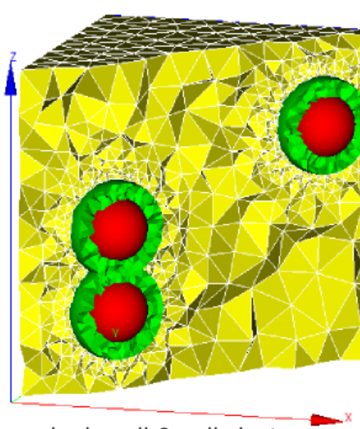
Anisotropic microstructure & cartilage zones



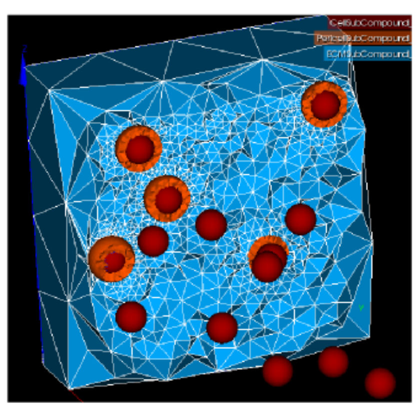
Biphasic analysis



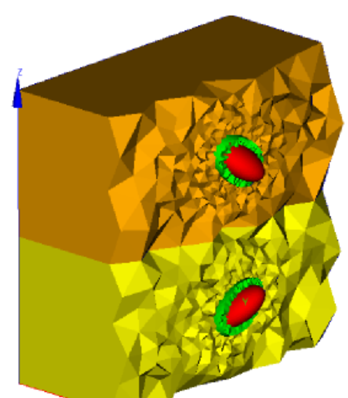
Complex cell shapes and distributions



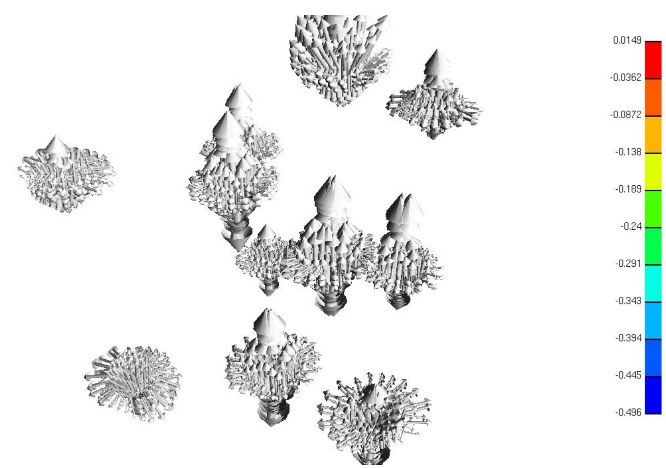
single cell & cell clusters



high density cell distribution



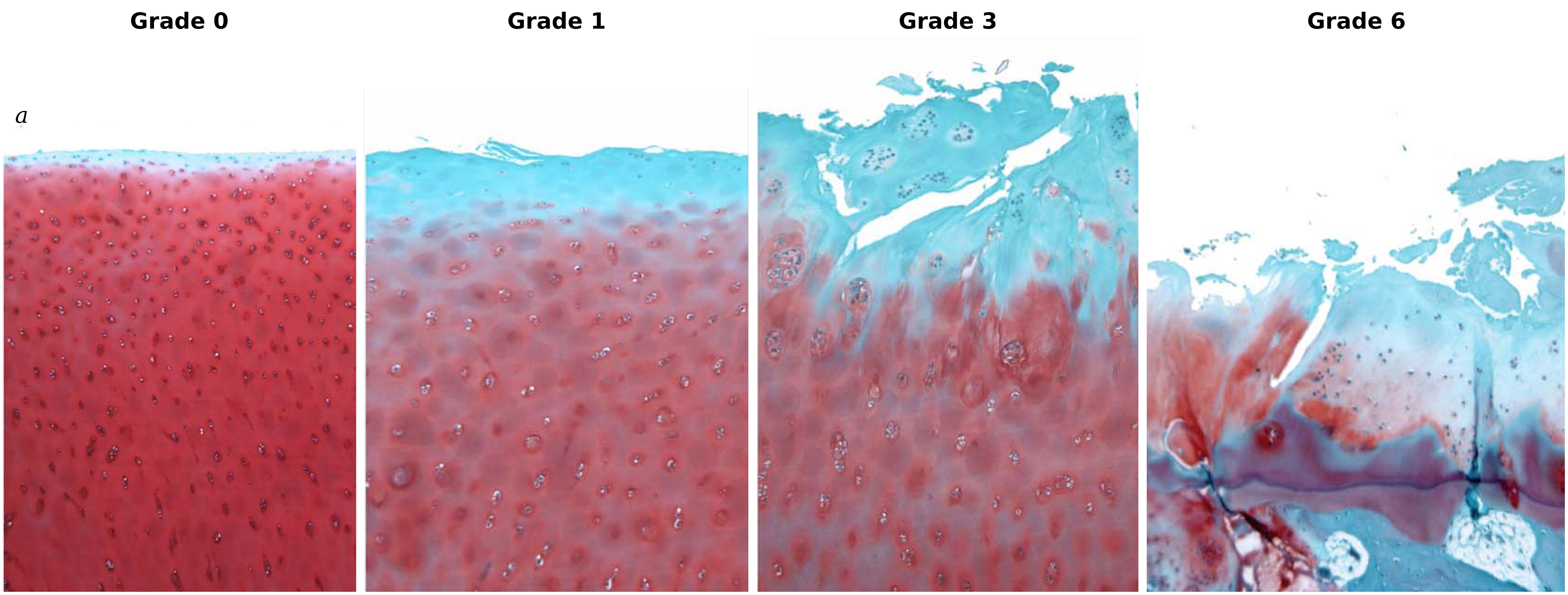
ellipsoidal cells oriented in multiple zones



Pathways for Translation

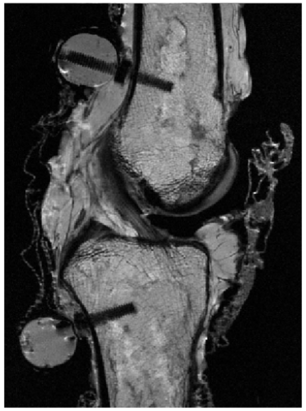
Musculoskeletal markers of age-related changes in cartilage and chondrocyte mechanics

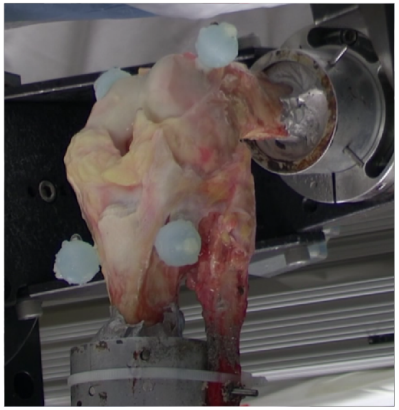
Macro/micromechanical environment of cartilage during progression of osteoarthritis



[a] *adapted from Pritzker et al., Osteoarthritis Cartilage 14: 13-29, 2006.*

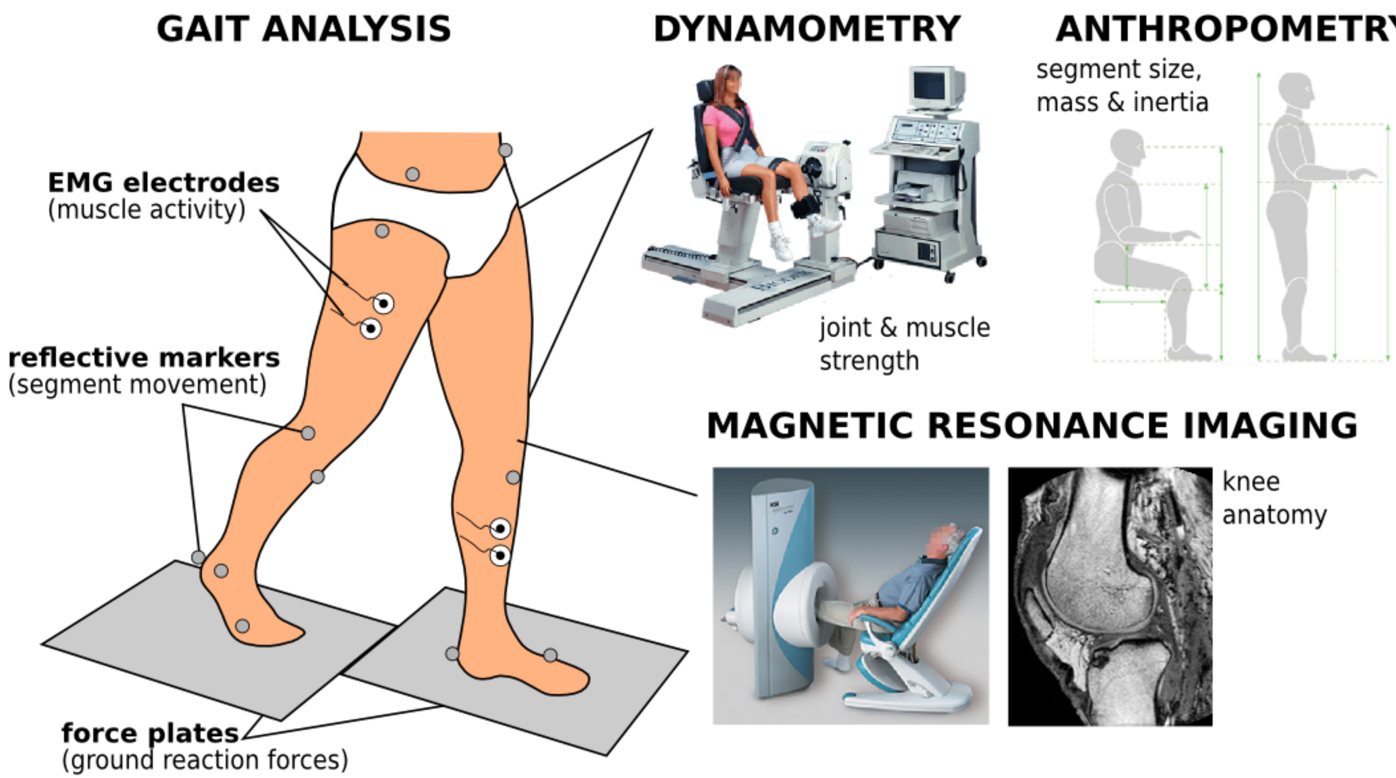
Bridging to Higher Scales





Relationship between joint loading and chondrocyte deformations

In vivo deformations of chondrocytes during locomotion



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