DEMOCRATIZATION OF MODELING AND SIMULATION IN BIOMECHANICS
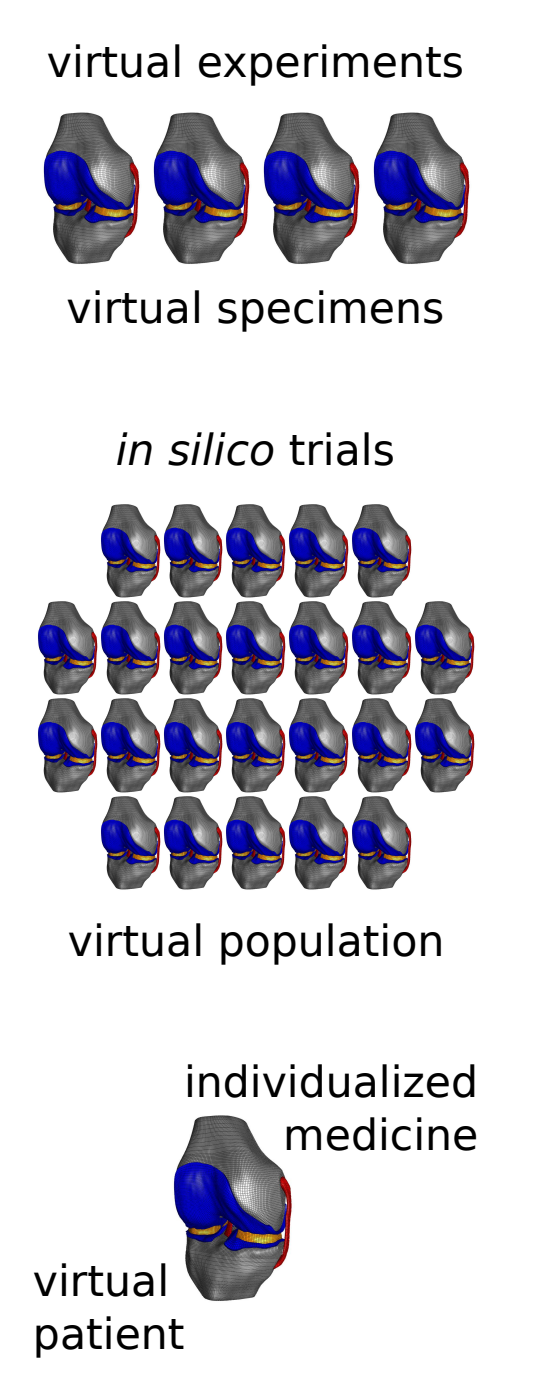
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CoBi Core

MOTIVATION

Modeling & simulation (M&S) has significant utility in:

- **scientific discovery**
  structure-function relationships in health & disease
  mechanistic foundations of data associations
- **engineering innovation**
  intervention design & evaluation
- **clinical care**
  diagnosis/prognosis
  intervention safety & performance
  medical training
  individualized medicine

virtual experiments
virtual specimens
in silico trials
virtual population
individualized medicine
virtual patient

Advancing Regulatory Science at FDA

Computational models can reduce:

- physical prototyping
- animal studies
- human subjects testing
- cadaver experiments

Utmost leverage of M&S will be possible by democratization of M&S enterprise:

- High performance computing hardware is accessible.
- Simulation software evolved dramatically for analysis of nonlinear biological structures.
- However, limited access to usable, comprehensible, and credible models with desired specificity and efficiency impedes progress.

simulation software
models
computing hardware
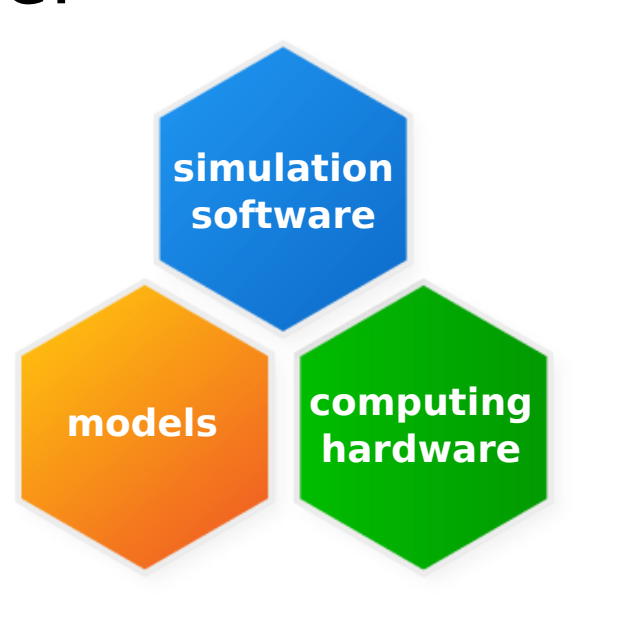
GOALS

Using biomechanics as the application domain, the goals of this study are:

- to recognize desirable properties for democratization of M&S
- to identify challenges to achieve the desirable properties
- to demonstrate strategies to tackle the challenges
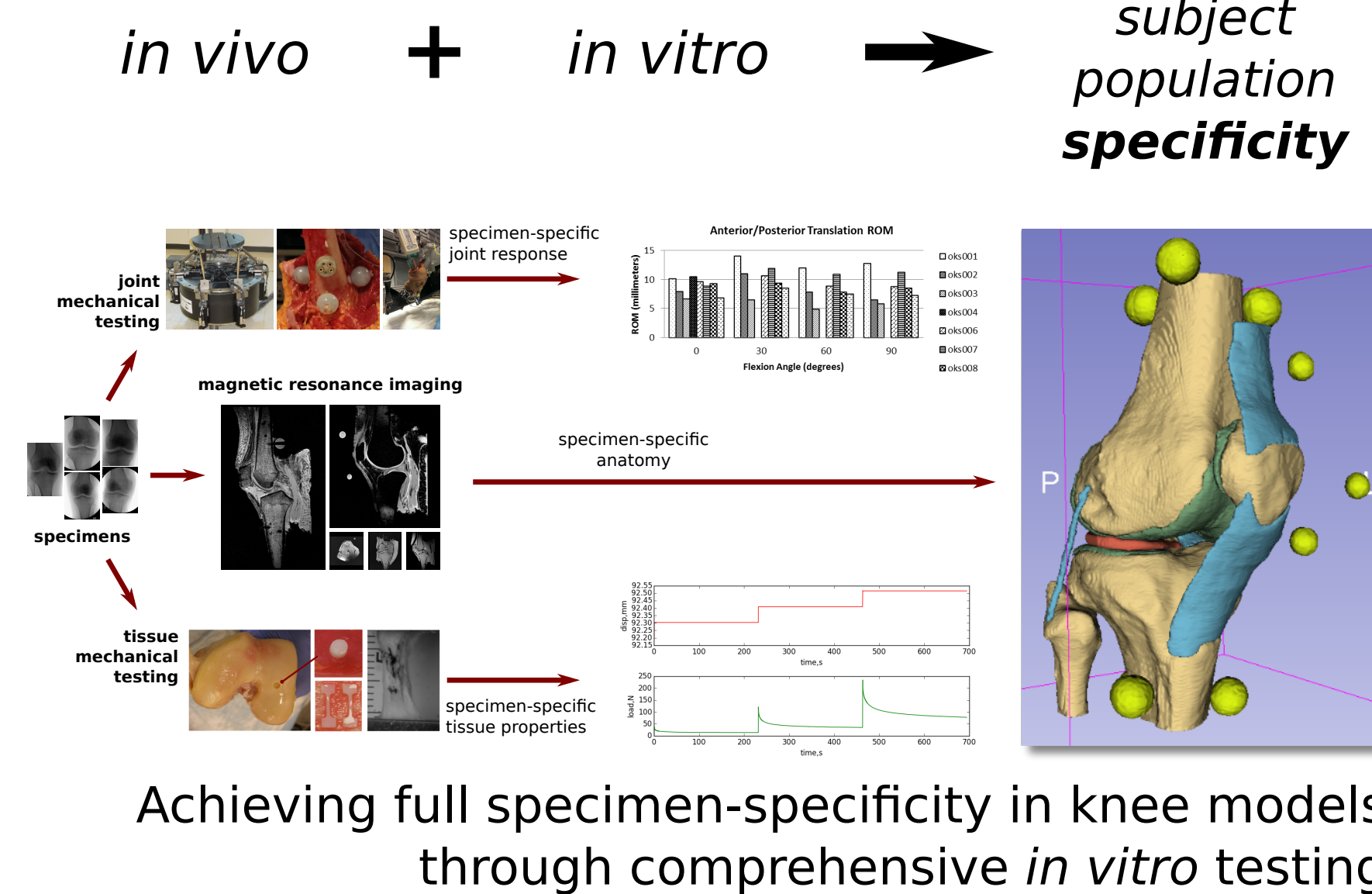
Sample projects are:

oks — to develop *in silico* biomechanical models of healthy and diseased knee joints of different genders and ages

OPERATION MULTiS — to provide knowledge, data and models for mechanics of multi-layer tissue structures of limbs

SPECIFICITY

Goal To increase the quality of relating to a particular subject

Challenges lack of comprehensive specimen-specificity ● limited availability of sample variations ● logistics of data collection

Strategies

in vivo + *in vitro* → specimen subject population **specificity**

joint mechanical testing → specimen-specific joint response
magnetic resonance imaging → specimen-specific anatomy
tissue mechanical testing → specimen-specific tissue properties

Achieving full specimen-specificity in knee models through comprehensive *in vitro* testing

Building a large database of multi-layer tissue properties with practical *in vivo* testing

USABILITY
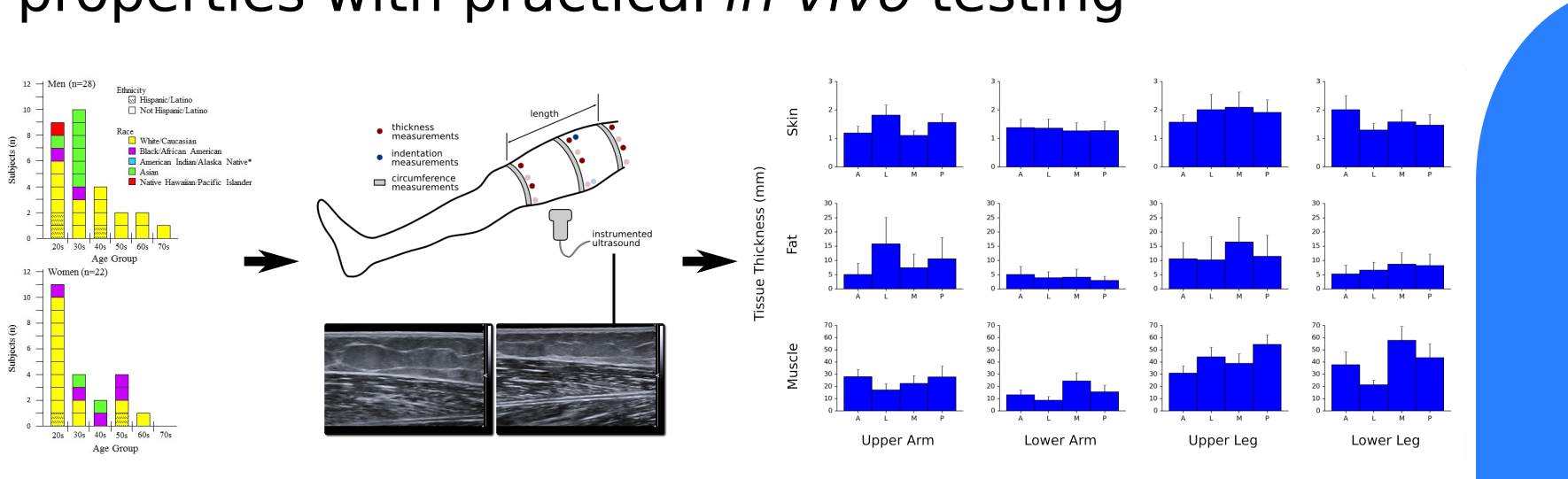
Goal To increase the quality of being easy to use

Challenges model robustness ● lack of tools for utilization ● customization for reuse ● translation to clinical practice

Strategies

Demonstrations with clinically relevant use cases

Open Knee: Open Source Modeling and Simulation in Knee Biomechanics
Ahmet Erdemir, PhD

ACL 1st Principal Stress vs Anterior Tibial Load

Cloud computing to evaluate models with ease
femur-ACL-tibia model

Providing various formats
FEBio
Sofa
Abaqus

EFFICIENCY

Goal To increase the quality of achieving maximum productivity with minimum wasted effort

Challenges manual workflows ● balancing cost and accuracy ● heterogeneous formats ● need for high-throughput analysis

Strategies

automation → data analysis / model development / simulation / post-processing

Python scripting for unsupervised mesh assembly, model generation, multi-format output with support for object replacement

connected to femur
connected to ACL
tibia
PCL
connected to PCL
connected to cartilage
connected to MCL

COMPREHENSIBILITY

Goal To increase the quality of being easy to understand

Challenges consistency of terminology ● specificity of information ● correspondence of documentation to reproduction

Strategies

Detailed and transparent documentation of specifications for experimentation and modeling

All Specifications Pages

~80 reporting parameters
model identification
model/simulation structure
verification & validation

ACCESSIBILITY

Goal To increase the quality of being easy to obtain

Challenges heterogeneous data management ● discoverability ● completeness of information ● tracking origin ● licensing

Strategies

Utilizing biomedical repositories for open development, and dissemination of raw and derivative data, models, and simulation results

Open Knee(s): Virtual Biomechanical Representations of the Knee Joint
Downloads

Free and open source licensing to promote modification, reuse, and redistribution

OPERATION MULTiS — Reference Models for Multi-Layer Tissue Structures
Search and Download Data

Web-based interfaces for organization, tracking, and query of large databases

CREDIBILITY

Goal To increase the quality of being trusted

Challenges lack of unified guidance ● uncertainty of reproducibility potential ● accountability throughout M&S lifecycle

Strategies

Informing and learning from community initiatives

Data integrity is supported by activities related to **Accessibility**.

Uncertainty estimation, sensitivity analysis, and verification & validation are supported by activities related to **Specificity**.

Rule 1 – Define context clearly.
Rule 2 – Use appropriate data.
Rule 3 – Evaluate within context.
Rule 4 – List limitations explicitly.
Rule 5 – Use version control.
Rule 6 – Document adequately.
Rule 7 – Disseminate broadly.
Rule 8 – Get independent reviews.
Rule 9 – Test competing implementations.
Rule 10 – Conform to standards.

CFMS

Ten "Not So" Simple Rules
by Committee on Credible Practice of M&S in Healthcare

Data reproducibility

Analysis reproducibility
vs

ACTIVITIES TO ACHIEVE DESIRABLE PROPERTIES FOR DEMOCRATIZATION

OPERATION MULTiS

OpenKneeS