



Democratization of Modeling & Simulation in Biomechanics Our Experience with Open Knee(s)

Ahmet Erdemir

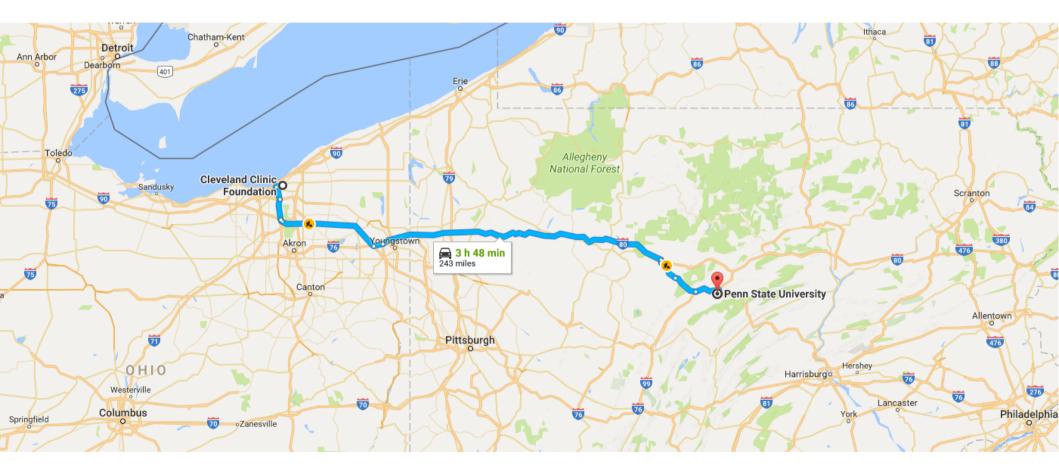
Computational Biomodeling Core Department of Biomedical Engineering Lerner Research Institute Cleveland Clinic

October 26, 2017 Kinesiology Colloquium Seminar Pennsylvania State University



fair use

CLEVELAND CLINIC



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Open Knee(s) Enabled by ...

Craig Bennetts





Snehal

Chokhandre

Tara Bonner





Robb Colbrunn

4/65



Open Knee(s) Enabled by ...

OPEN KNEE - GENERATION 1

Modeling

Craig Bennetts Ahmet Erdemir Randy Heydon Scott Sibole

Data

Bhushan Borotikar Antonie J. van den Bogert

Simulation Software

Ben Ellis Steve Maas David Rawlins Jeff Weiss

NIH/NIBIB R01EB009643 NIH/NIGMS R01GM083925 NIH/NIAMS R01AR049735 Simbios

OPEN KNEE(S) – GENERATION 2

Cleveland Clinic

Craig Bennetts Tara Bonner Snehal Chokhandre Robb Colbrunn Ahmet Erdemir Benjamin Landis

CWRU Chris Flask Shannon Donnola

Stanford University Scott Delp Joy Ku Henry Kwong

University of Utah

Ben Ellis Steve Maas Jeff Weiss

OLAN MONTHES

Community

Dvlan Beckler David Brigati Flvis Danso Sam Doerle Omar Gad Callan Gillespie Nicholas Haas **Connor Lough** Raghav Malik **Ervn Merico** Nicole Nassif Jason Halloran Katie Stemmer Diana Suciu Cara Sullivan Will Zaylor

Advisory Board

Jack Andrish Yasin Dhaher Trent Guess Morgan Jones Rami Korhonen Paul Saluan Carl Winalski



NIH/NIGMS R01GM104139



https://simtk.org/projects/openknee

M&S in Healthcare

Utility of computational modeling & simulation

For scientific discovery

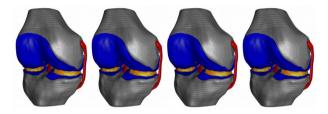
structure-function relationships in health & disease

mechanistic foundations of data associations

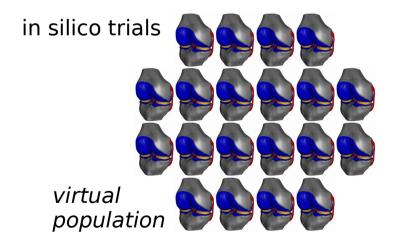
- For engineering innovation intervention design & evaluation
- For clinical care

diagnosis/prognosis intervention safety & performance medical training individualized medicine

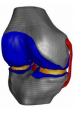
virtual experiments



virtual specimen(s) / subject(s)



virtual patient



Promise of M&S



Computational models can reduce

- Physical prototyping
- Animal studies
- Human subjects testing

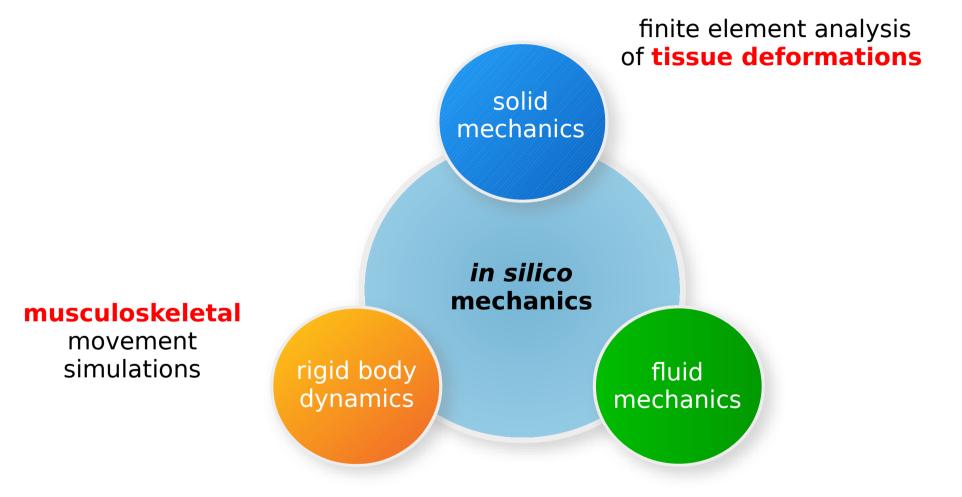
Cadaver experiments



Stimulate Innovation in Clinical Evaluations & Personalized Medicine to Improve Product **Development and Patient Outcomes**

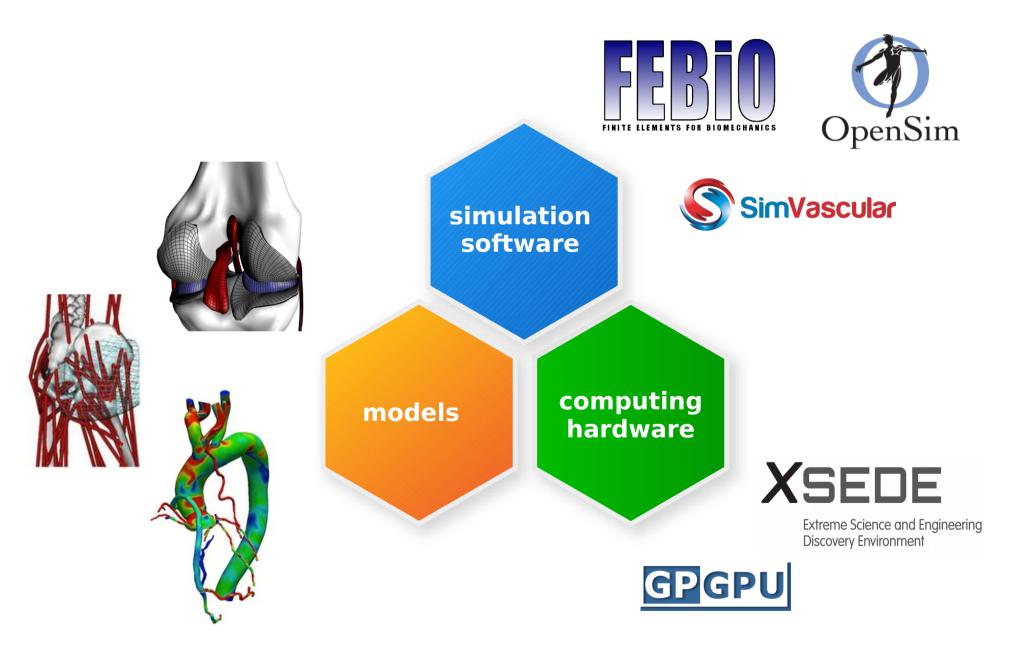
- 5. Develop a virtual physiologic patient: a) Encourage the development of computer models that incorporate radiological imaging data of healthy and diseased anatomy from a range of relevant diseases;
- b) Ensure the integration of these models with genomic and other physiological data to promote development of complete physiological models and simulations that can be used in the development and testing of medical devices and other medical products; and
- c) Create a library of models so that models validated by FDA are easily accessible to researchers.

M&S Enterprise in Biomechanics



computational fluid dynamics of cardiovascular systems

M&S Enterprise in Biomechanics



Emerging Need

- Simulation **software** free and open source
 - Simulation hardware cost-effective and/or public

Models

anatomical and physiological properties to support subject/specimen-specific authenticity

biomechanical response to support subject/specimen-specific evaluation

subject-to-subject variety to support population diversity

accessibility to promote wide-spread use

Goals

- To recognize desirable properties of democratization in modeling & simulation in biomechanics
- To identify challenges to achieve desirable properties
- To demonstrate strategies to tackle the challenges



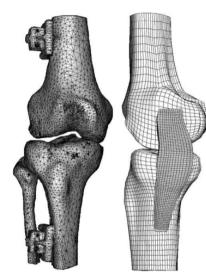
Open Knee(s), modeling & simulation for knee mechanics, as a **case study**

M&S in Knee Biomechanics

- How would this patellar alignment stabilize the movement of the patellofemoral joint? Will it cause increased cartilage contact pressures?
- Should I change the implant design? Will it reproduce natural knee movements? Will it fail? Will the host tissue be safe?
- Will this routing of ACL reconstruction benefit my patient? Will it work for all patients?

fair use **M&S in Knee Biomechanics**

Joint and tissue functions

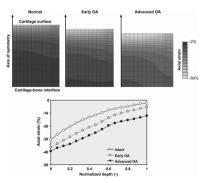


MCL function

Gardiner and Weiss, J Orthop Res, 21: 1098-106,2003.

Pathological impacts





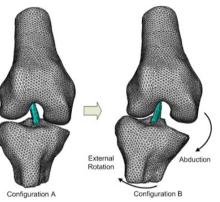
Osteoarthritis

Kalahari et al., Osteoarthritis and Cartilage, 18: 73-81, 2010.

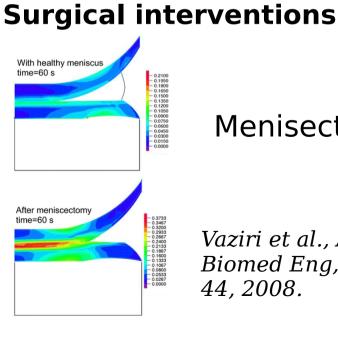
Injury mechanisms



Park et al., J Biomech, 43: 2039-42, 2010.



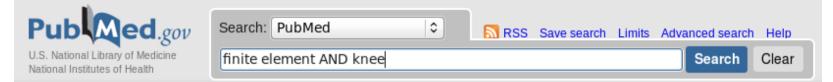
ACL impingement



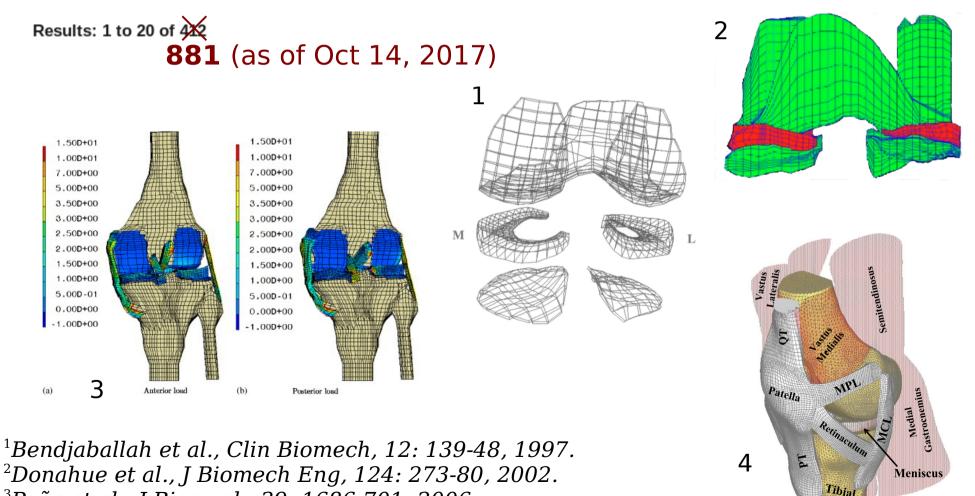
Menisectomy

Vaziri et al., Annals of Biomed Eng, 36: 1335-44,2008.

M&S in Knee Biomechanics



Display Settings: Summary, 20 per page, Sorted by Recently Added



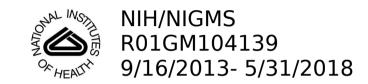
³Peña et al., J Biomech, 39: 1686-701, 2006. ⁴Dhaher et al., J Biomech, , 43: 3118-25, 2010.

Need for Progress

- How representative are the models?
- Are the models credible?
- Are the models accessible?
- Are the models usable?

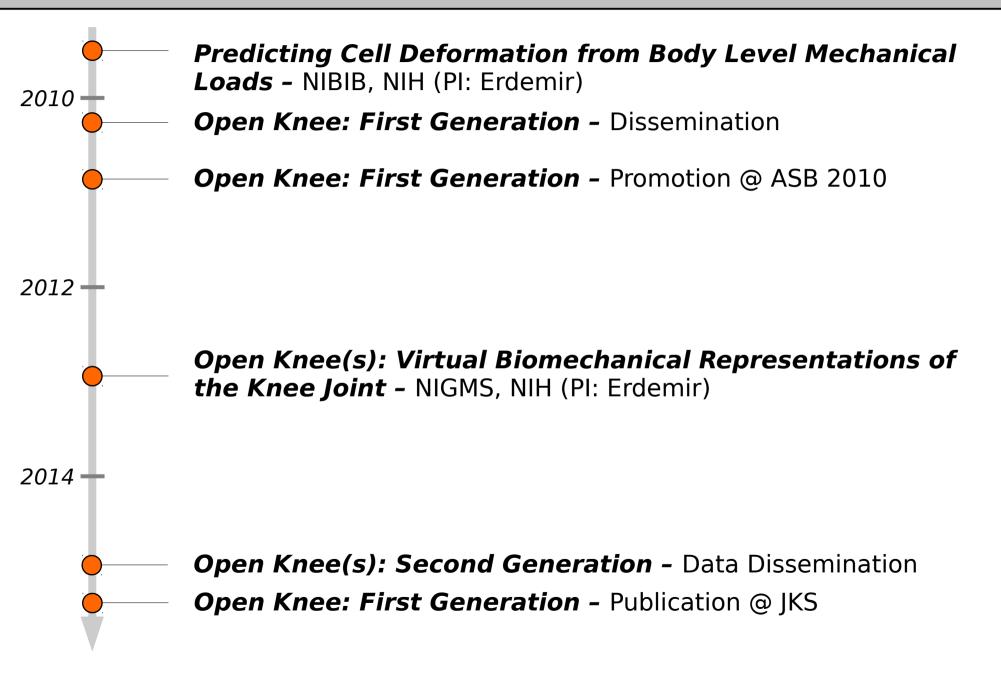
Open Knee(s) Goals



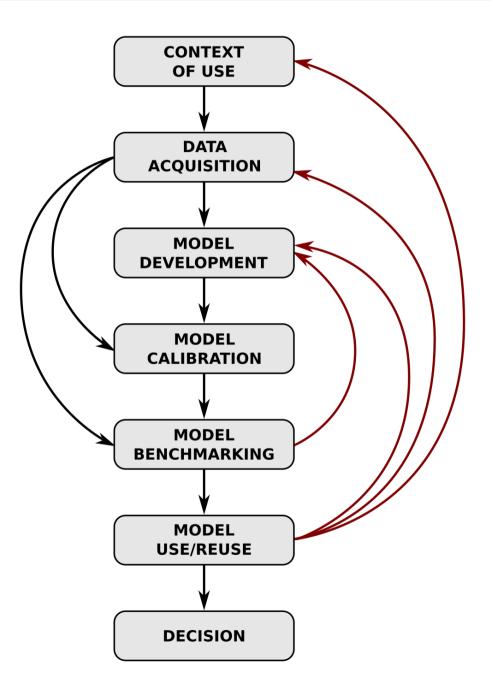


- To provide an open, freely available, and collaborative development, testing, simulation and dissemination platform for in silico exploration of the biomechanics of healthy and diseased knees.
- To develop in silico biomechanical models of healthy and diseased knee joints of different genders and ages, supported by specimenspecific joint and tissue level experimental mechanics.

Open Knee(s) Brief History

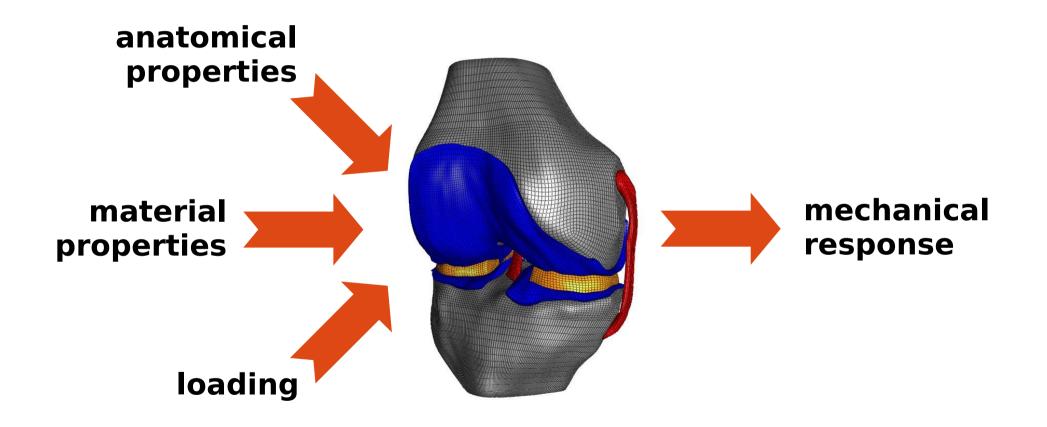


Open Knee(s) Lifecycle

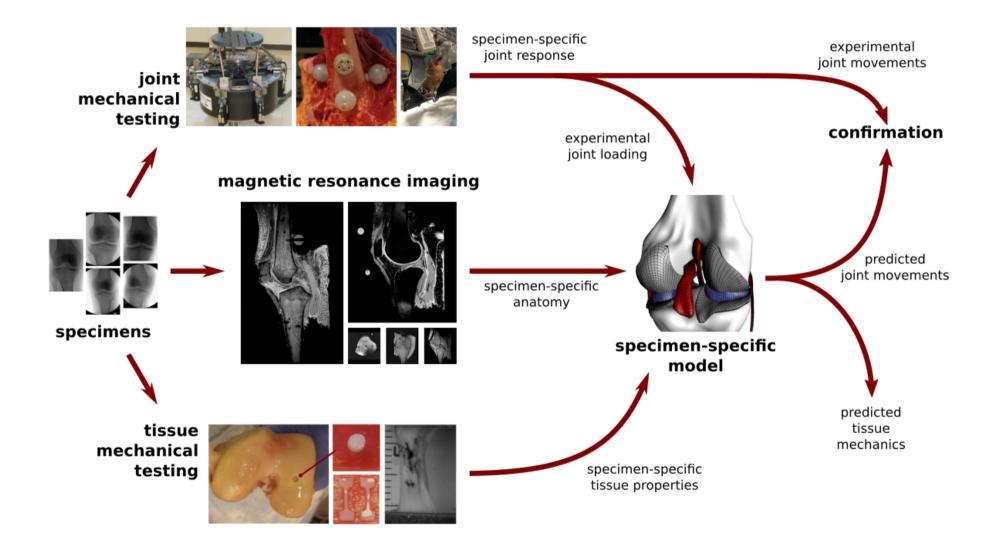


- Context of use targeted for prediction of joint and tissue mechanics of the knee in health and disease, and after intervention
- Iterations are anticipated to establish credibility and to customize for reuse

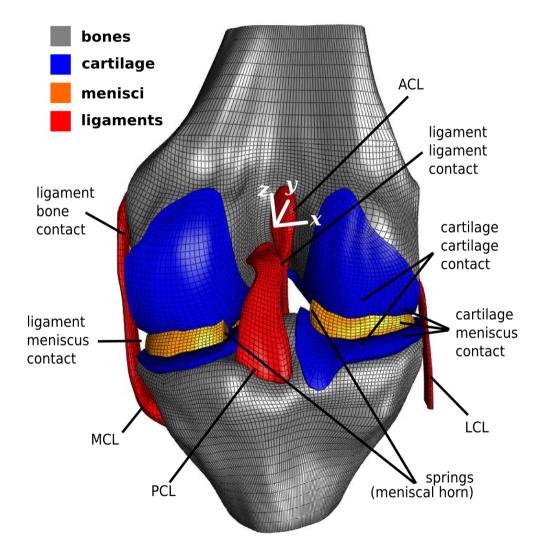
Building Open Knee(s)



Building Open Knee(s)



Building Open Knee(s)



Bones rigid body

Cartilage

nearly incompressible Neo-Hookean

Menisci

Fung orthotropic hyperelastic horn attachments as springs

Ligaments

transversely isotropic hyperelastic

Activities for Democratization

To meet desirable properties of modeling & simulation

- Specificity relating to a particular subject
- *Efficiency* achieving maximum productivity
- Accessibility easy to obtain
- Usability easy to use
- Comprehensibility easy to understand
- Credibility being trusted

Specificity

Goal to increase the quality of relating to a particular subject

Challenges

lack of comprehensive specimenspecificity

limited availability of sample variations

logistics of data collection

Integration of diverse data collection strategies to overcome *logistical*, *scientific*, and *technical challenges*

SPECIMEN-SPECIFIC ANATOMICAL & MECHANICAL DATA



RESEARCH ARTICLE

A Comprehensive Specimen-Specific Multiscale Data Set for Anatomical and Mechanical Characterization of the Tibiofemoral Joint

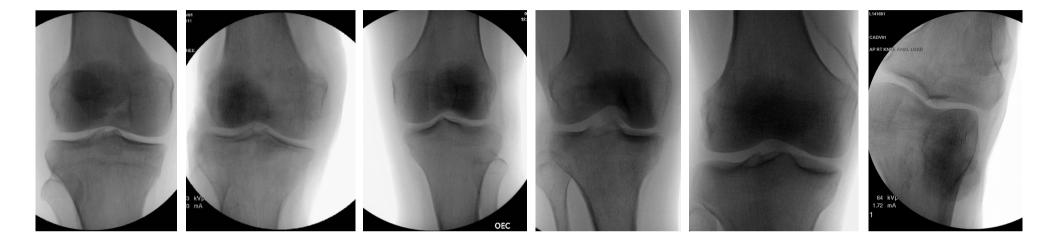
Snehal Chokhandre^{1,2}, Robb Colbrunn^{2,3}, Craig Bennetts^{1,2}, Ahmet Erdemir^{1,2}*

1 Computational Biomodeling (CoBi) Core, Lemer Research Institute, Cleveland Clinic, Cleveland, Ohio, 44195, United States of America, 2 Department of Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, 44195, United States of America, 3 BioRobotics and Mechanical Testing Core, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, 44195, United States of America

* erdemira@ccf.org

adapted from Chokhandre et al. (2015)



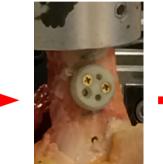


oks001	oks002	oks003	oks004	oks006	oks007
Right knee	Right knee	Left knee	Right knee	Right knee	Right knee
Gender: Male Age: 71 years Race: White Height: 1.83 m Weight: 77.1 kg BMI: 23.1	Gender: Female Age: 67 years Race: White Height: 1.55 m Weight: 45.3 kg BMI: 18.9	Gender: Female Age: 25 years Race: White Height: 1.73 m Weight: 68 kg BMI: 22.8	Gender: Female Age: 46 years Race: White Height: 1.58 m Weight: 54.4 kg BMI: 21.9	Gender: Female Age: 71 years Race: White Height: 1.52 m Weight: 49.4 kg BMI: 21.3	Gender: Male Age: 71 years Race: White Height: 1.7 m Weight: 65.8 kg BMI: 22.7

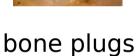
2 more tested; more on the way...

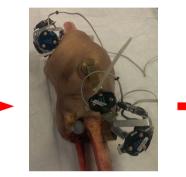
Preparation





dissection





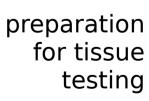
motion capture markers

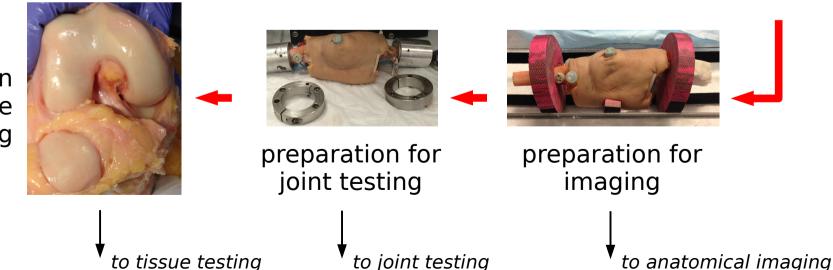


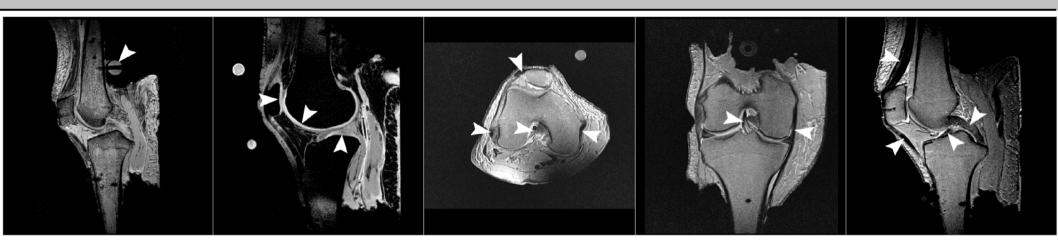
registration markers



anatomical landmarks







General Purpose

3D T1-weighted w/o fat suppression $0.5 \times 0.5 \times 0.5$ mm TE = 6.01 ms TR = 20 ms 3D T1-weighted w/ fat suppression 0.35 x 0.35 x 0.7 mm TE = 5.34 ms TR = 29 ms

Cartilage

Ligaments

Proton density Turbo spin echo $0.35 \times 0.35 \times 2.8 \text{ mm}$ TE = 9.7 ms TR = 10,000 ms

same 8 knee specimens

Х

Magnetic Resonance Imaging

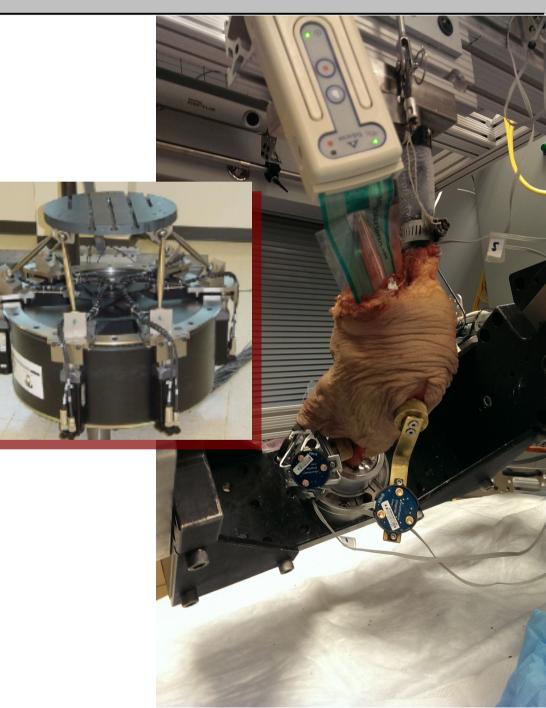
same 8 knee specimens

Х

1 tibiofemoral joint 1 patellofemoral joint

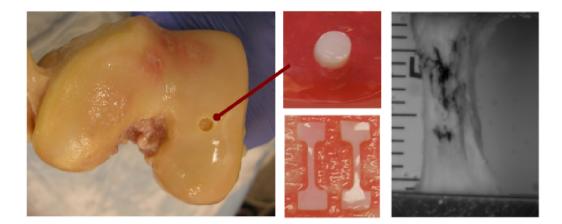
Х

Robotics Joint Testing Kinematics - Kinetics



same 8 knee specimens

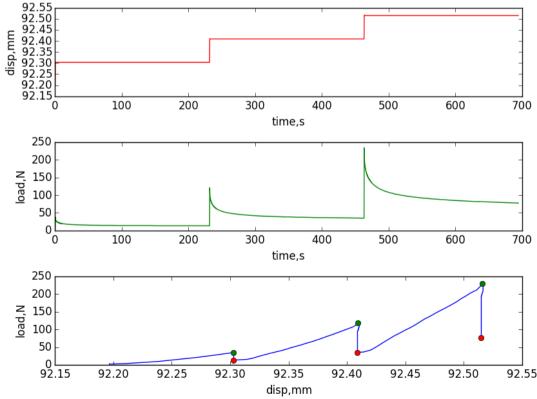
Χ



12 cartilage samples4 menisci samples6 ligament samples



X



Efficiency

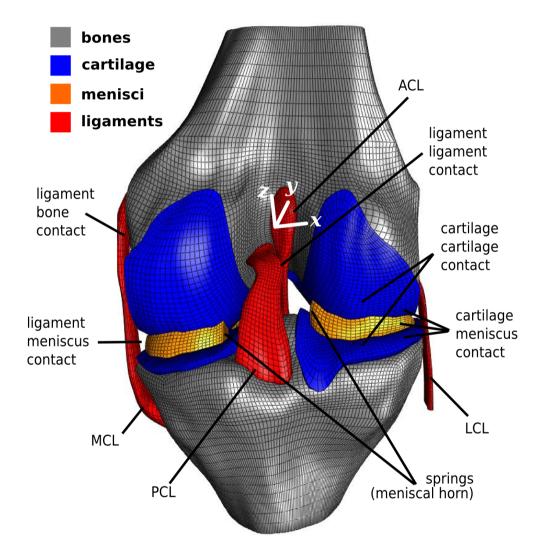
Goal to increase the quality of achieving maximum productivity with minimum wasted effort

Challenges manual workflows

balancing cost and accuracy

heterogeneous formats

need for high-throughput analysis



Bones rigid body

Cartilage

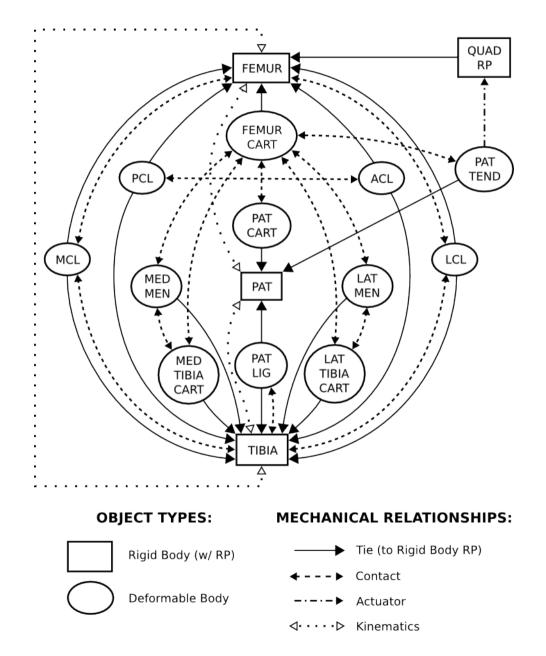
nearly incompressible Neo-Hookean

Menisci

Fung orthotropic hyperelastic horn attachments as springs

Ligaments

transversely isotropic hyperelastic



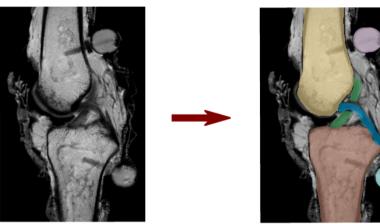
Modularity

Swap components based on

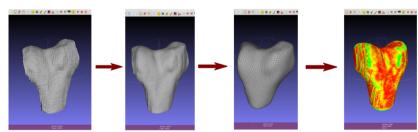
> fidelity of representation intervention

Compartmental modeling, e.g., cruciate complex patellofemoral joint

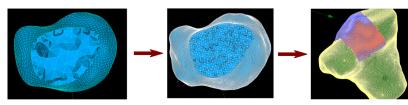
SEGMENTATION



GEOMETRY GENERATION

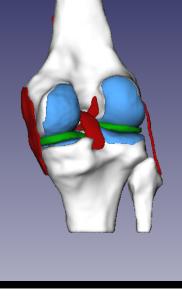


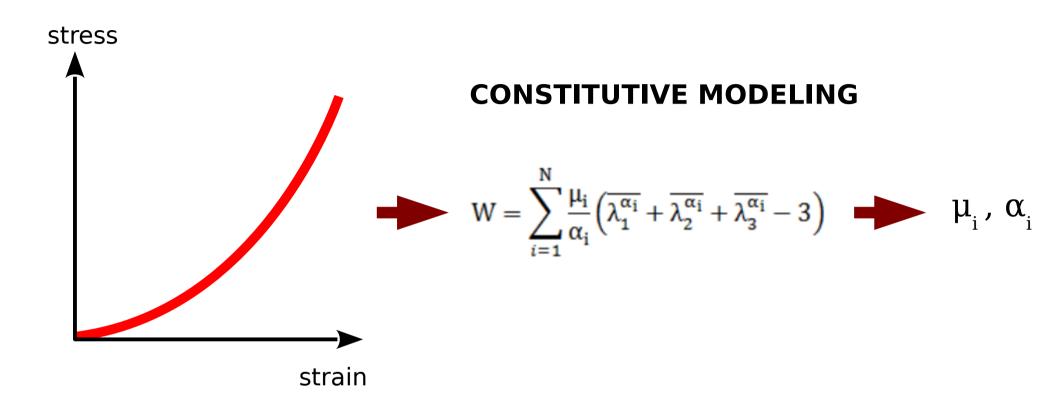
MESH GENERATION



specimen-specific joint anatomy

D

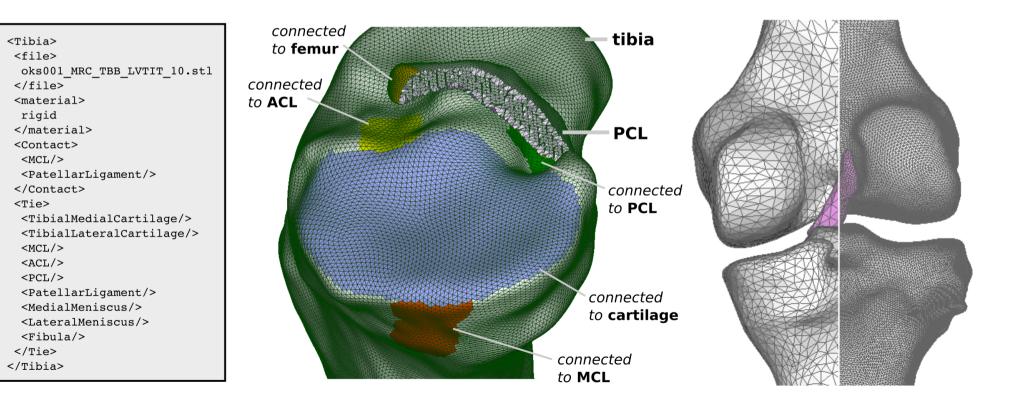




specimen-specific material properties for cartilage – ligaments - menisci



Scripting for **unsupervised** mesh assembly, model generation, multi-format output with support for object replacement



Accessibility

Goal to increase the quality of being easy to obtain

Challenges heterogeneous data management

discoverability

completeness of information

tracking origin

licensing

Accessibility

ACCESSIBILITY PROBLEM

Вюмсн-L

Sponsored by the International Society of Biomechanics

12-18-1997, 07:39 PM

Ahmet Erdemir Guest

Knee kinematics

Dear Subscribers,

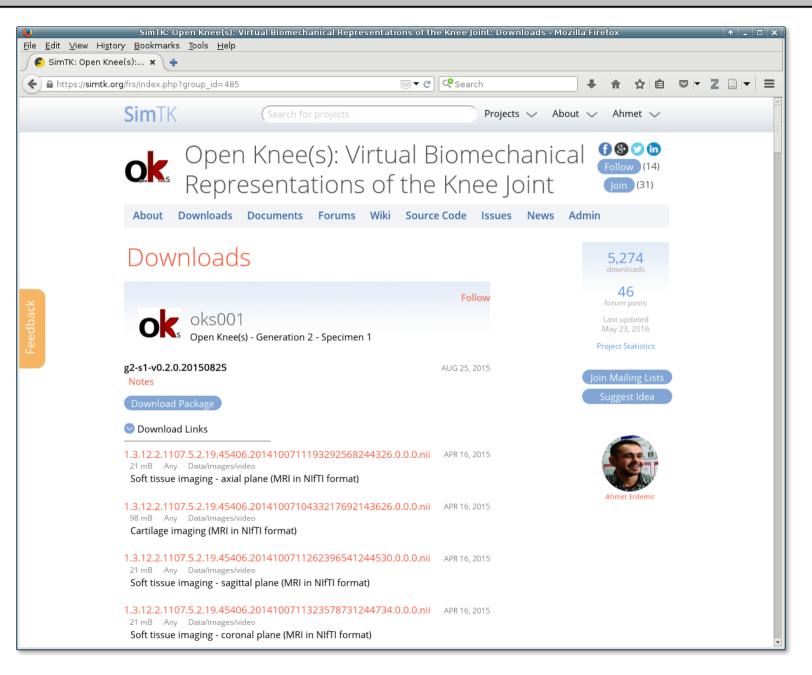
Does any of you know references describing the 3D knee kinematics and change in ligament lengths obtained from in vitro experiments, for full range of flexion?

My aim is to introduce these kinematic results in my three dimensional anatomical model of the human knee to optimize the ligament parameters such as reference strains, stiffness.

The loading conditions and well-defined coordinate systems at these experiments are needed as input to my knee model.

Ahmet ERDEMIR ODTU, ICHMT Mak. Muh. Bol., 06531 Ankara, TURKEY tel: +90 312 210 2541 fax: +90 312 210 1331 e-mail: erdemir@fiesta.me.metu.edu.tr

Accessibility: Data & Models



Adapted from Open Knee(s), refer to https://simtk.org/frs/index.php?group_id=485.

Accessibility: Impact

January 30, 2012

Open Knee S	tatistics (January 30, 2012)		
Project site	https://simtk.org/home/openknee		
Project launch date	February 18, 2010		
Page hits	19525 (past 180 days)		
Unique visitors	902 (past 180 days)		
Team members	8 total 3 active 2 original, 1 from community		
Documentation	1 user's guide 3 conference abstracts		
Development	248 repository commits		
Releases	v.1.0.0.199 (major) December 17, 2010 v.1.0.1.202 (minor)		
Release downloads	207 total 162 unique		
Expected use of downloads (feedback provided by users)	56 research 54 training 24 reference for other models 14 evaluation 9 anterior cruciate ligament 9 instrumentation/implants/ orthotics/prosthetics 6 cartilage/osteoarthritis 5 potential contributions 4 impact biomechanics 4 knee loads 2 knee movements 2 knee geometry 1 meniscal injury 1 femur biomechanics Rest unspecified/unsure		

October 15, 2017

- 9 download packages
- >10,000 total downloads
- >35 enabled studies

Visitor demographics sample



Accessibility: Impact

ACKNOWLED GEMENTS

The authors would like to express their sincerest gratitude to Dr. Ahmet Erdemir for his generosity in developing the freely-available OpenKnee project (available from https://simtk.org/home/openknee). Finite element model development is a laborious process, often prohibitively so. OpenKnee was a potent springboard for this investigation, greatly facilitating initial model development. The authors would also like to thank Dr.

adapted from Westerman et al. (2013)

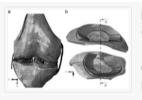
ization method and material model^{14–18}. To calculate knee articular osteochondral tissue property, we have to segment meniscus layer and cartilage layer; however it is extremely difficult to segment these two layers from clinical CT data. Fortunately, there is a template of meniscus which can be obtained from the Open Knee(s)¹⁹ at NIH. Thus we can calculate the volume of cartilage layer by subtracting the volume of a template of meniscus from the whole

adapted from Zhang et al. (2016)

Journal of Biomechanics

June 2015

Biomechanics and Mechanobiology of the Meniscus



Influence of meniscus shape in the cross sectional plane on the knee contact mechanics

Piotr Łuczkiewicz, Karol Daszkiewicz, Wojciech Witkowski, Jacek Chróścielewski, Witold Zarzycki p1356–1363

Published online: March 18 2015

Preview Abstract Full-Text HTML PDF



The sensitivity of cartilage contact pressures in the knee joint to the size and shape of an anatomically shaped meniscal implant M. Khoshgoftar, A.C.T. Vrancken, T.G. van Tienen, P. Buma, D. Janssen, N.

Verdonschot p1427–1435 Published online: February 26 2015

Open Access

Preview Abstract Full-Text HTML PDF

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

Usability: Cloud Computing

a 1	nttps:// simtk.org /simulati	ons/viewJobs.php	?group_id=485	C Searc	h	
	SimTK	Se	earch for Pr	rojects 🗸	Projects 🗸 A	About 🗸 Ahmet 🗸
	ok Op Rej	en Kne preser	ee(s): Virtua Itations of t	al Biom he Kn	nechani ee Joint	ical follow (19)
	About Downloa	ids Documen	ts Forums Wiki Sou	irce Code	Server:	openknee-aws ~
	Simulations: View My Jobs			5	Software: Model:	FEBio 2.5.0 ~ model.feb ~
	Job Name	Status	Job details		Modify model:	● Yes ◯ No
	2017-02-15 13:05:3 2017-02-11 16:43:2 2017-02-11 16:43:0	6 Completed	Model: model.feb Config File: Software: FEBio Version: 2.5.0 Server: openknee-aws Duration: 118 secs Last updated: 02/16/2017 Model: model.feb Config File: Software: FEBio Version: 2.5.0 Server: openknee-aws Duration: 123 secs Last updated: 02/11/2017 Model: model.feb Config File: Software: FEBio Version: 2.5.0		Model Configuration File: Notification email: Job name:	modify_model.cfg ~ Change the numerical values below to modify the model to be simulated with the simulation (mm) *AP ** anterior (+) / posterior (-) translation (mm) -2.0 *ML ** medial (+) / lateral (-) translation (mm) 3.0 *DC ** distraction (+) / compression (-) (mm) 10.0 *FE erdemira@ccf.org 2017-03-11 12:13:47

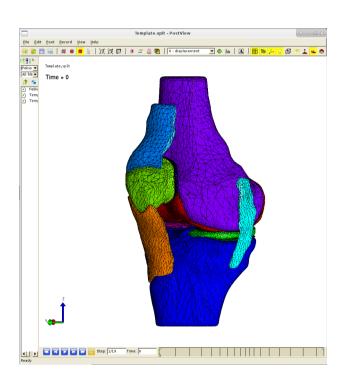
Adapted from Open Knee(s), refer to https://simtk.org/simulations/viewJobs.php?group_id=485.

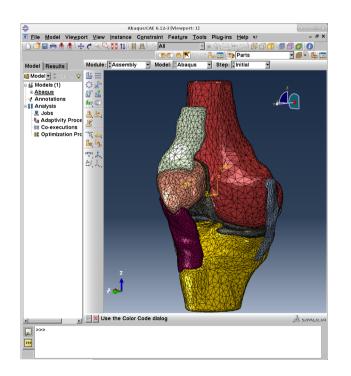
Usability: Different Formats

Capability to push same mesh with template material properties, contact definitions, and constraints to different simulation software

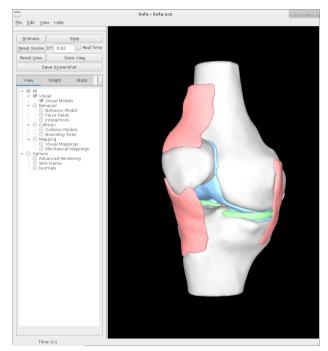
Abaqus

FEBio





SOFA

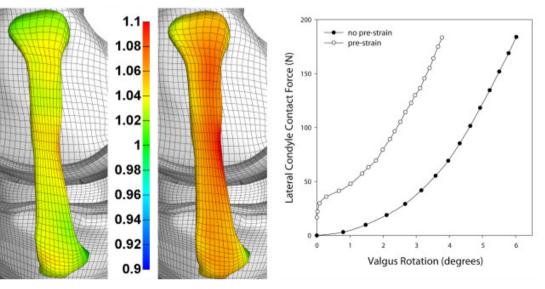


Usability: Simulation Features

Open Knee(s) is a **driving project** for simulation software development

- 🔹 In situ strain
- Element, node, surface sets
- Coordinate systems
- Kinematic joints
- Wrapping springs
- Modular file input

Prescribing ligament *in situ strain*



adapted from Maas et al. (2016)





fair use

Usability: Insights



Physicians

Jack Andrish, MD

Morgan Jones, MD

D Paul Saluan, MD

Carl Winalski, MD

Trent Guess, PhD Yasin Dhaher, PhD Rami Korhonen, PhD



Engineers/Scientists

Open Knee(s) Advisory Board

Usability: Use Cases

Demonstration of utility through *clinically relevant* simulations



ADAPTATION IN SCIENTIFIC AND CLINICAL DOMAINS

Open Knee: Open Source Modeling and Simulation in Knee Biomechanics

Ahmet Erdemir, PhD¹

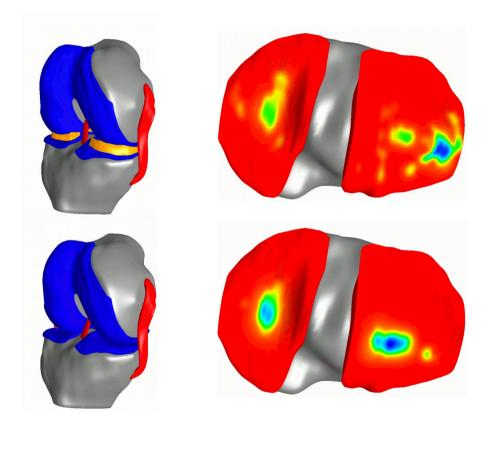
¹ Computational Biomodeling (CoBi) Core and Department of Biomedical Engineering, Cleveland Clinic, Cleveland, Ohio

J Knee Surg 2016;29:107-116.

Address for correspondence Ahmet Erdemir, PhD, Computational Biomodeling (CoBi) Core and Department of Biomedical Engineering, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195 (e-mail: erdemira@ccf.org).

adapted from Erdemir (2016)

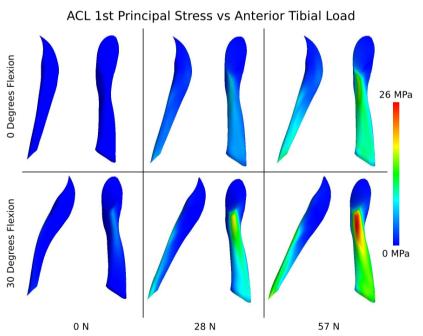
Usability: Use Cases



Influence of **menisectomy** on cartilage loading



ACL mechanics during laxity testing



Open Knee(s) – Generation 1 predictions; adapted from Erdemir (2016)

Comprehensibility

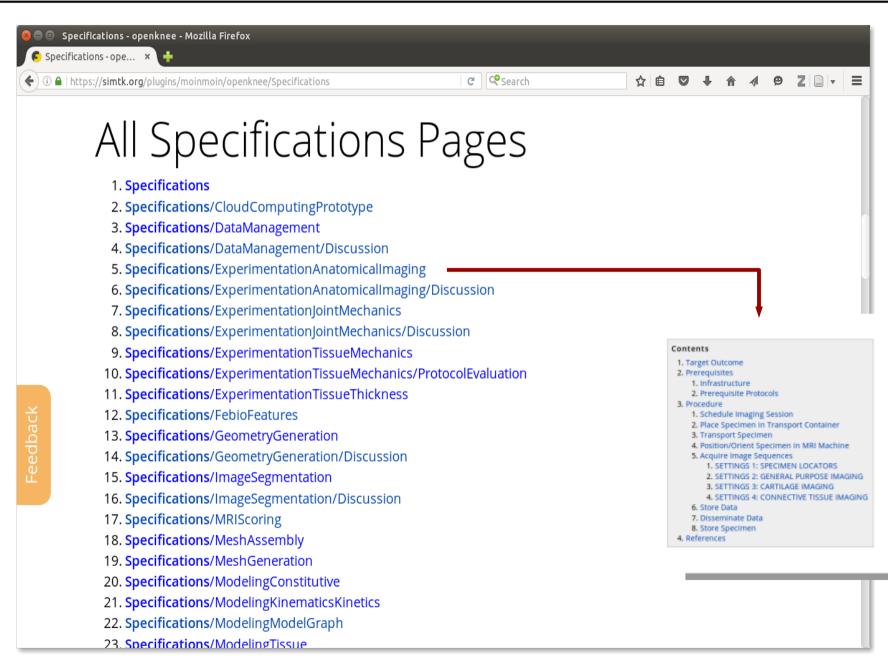
Goal to increase the quality of being easy to understand

Challenges consistency of terminology

specificity of information

correspondence of documentation to reproduction

Comprehensibility: Know-How



Adapted from Open Knee(s), refer to https://simtk.org/plugins/moinmoin/openknee/Specifications.

Comprehensibility: Reporting

Good reporting practice

clarifies uncertainty of **reproducibility**, promotes **reusability**, and establishes **accountability**.

CONFIDENCE IN MODELING & SIMULATION

Journal of Biomechanics 45 (2012) 625-633



Perspective article

Considerations for reporting finite element analysis studies in biomechanics

Ahmet Erdemir^{a,b,*}, Trent M. Guess^c, Jason Halloran^{a,b}, Srinivas C. Tadepalli^d, Tina M. Morrison^e

^a Computational Biomodeling (CoBi) Core, Lerner Research Institute, Cleveland Clinic, Cleveland, OH 44195, USA

^b Department of Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, Cleveland, OH 44195, USA

^c Department of Civil and Mechanical Engineering, University of Missouri – Kansas City, Kansas City, MO 64110, USA

^d Department of Orthopaedics and Sports Medicine, University of Washington, Seattle, WA 98195, USA

^e Center for Devices and Radiological Health, Food and Drug Administration, Silver Spring, MD 20933, USA

adapted from Erdemir et al. (2012)

Comprehensibility: Reporting

Documented ~80 reporting parameters classified under:

- Model identification (20)
- Model structure (7 main 27 subcategorized)
- Simulation structure (6)
- Verification (6)
- Validation (9)
- Availability (5)

Credibility

Goal to increase the quality of being trusted

Challenges lack of unified guidance

uncertainty of reproducibility potential

accountability throughout M&S lifecycle

Credibility: Data Quality

Anatomical imaging & geometry
Registration markers

Segmentation reproducibility

Joint mechanics

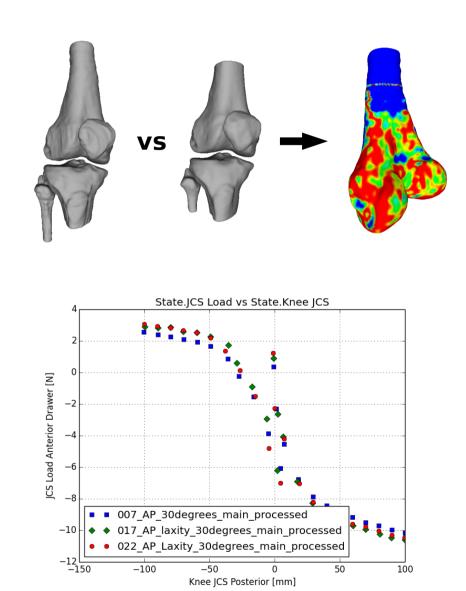
Registration markers

Surrounding tissue effects

Repeatability of anteriorposterior laxity response

Tissue mechanics

Reproducibility of uniaxial tissue stress-strain response

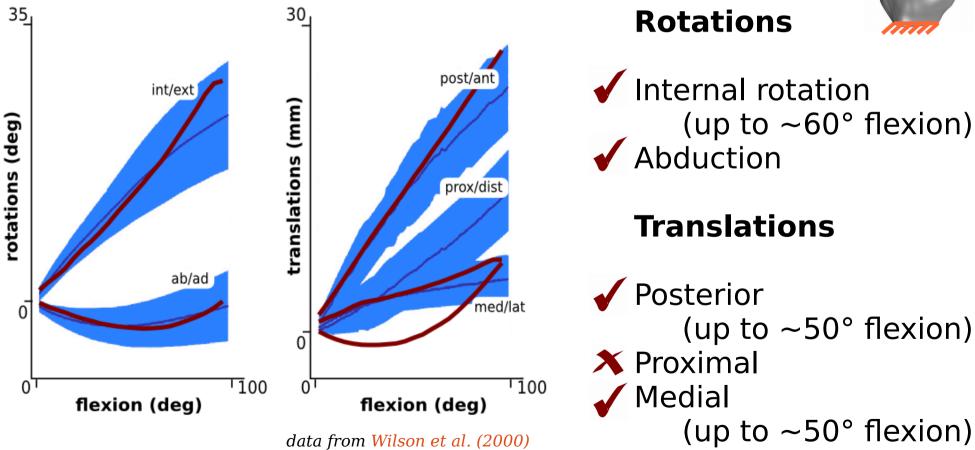


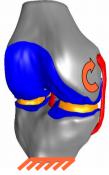
adapted from Erdemir (2016)

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Credibility: Correspondence to Literature

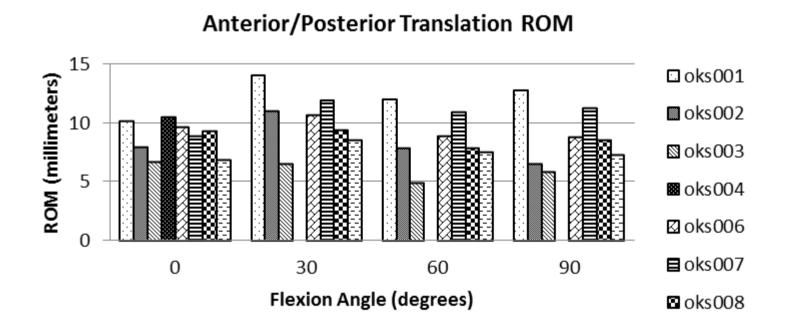
Tibiofemoral joint kinematics during passive flexion Open Knee(s) – Generation 1 vs data from a sample population





Credibility: Specimen-Specificity

Specimen-specific joint response can vary largely.



fair use

IARPA

MITACS

Credibility: Guidance

Credible Practice of M&S in Healthcare

To establish credible practice guidelines, consistent terminology and a model certification process, as well as to demonstrate workflows and identify new areas of research for reliable development and application of M&S in healthcare practice and research."





CFMS



Credibility: Guidance



Ten "Not So" Simple Rules for Credible Practice of Modeling & Simulation in Healthcare **Rule 1** – Define context clearly.

Plan and develop the M&S activity with clear definition of the intended purpose or context accommodating end-users' needs.

Rule 2 – Use appropriate data.

Use data relevant to the M&S activity, which can ideally be traced back to the source.

Rule 3 – Evaluate within context.

Evaluate the M&S activity through verification & validation, uncertainty quantification, and sensitivity analysis faithful to the context/purpose/scope of the M&S efforts, with clear and a-priori definition of evaluation metrics and including test cases.

Rule 4 – List limitations explicitly.

Provide an explicit disclaimer on the limitations of the M&S to indicate under what conditions or applications the M&S may or may not be relied on.

Rule 5 – Use version control.

Implement a version control system to trace the time history of the M&S activities, including delineation of contributors' efforts.

Rule 6 – Document adequately.

Document all M&S activities, including simulation code, model markup, scope and intended use of M&S activities, users' and developers' guides.

Rule 7 – Disseminate broadly.

Disseminate appropriate components of M&S activities, including simulation software, models, simulation scenarios and results.

Rule 8 – Get independent reviews.

Have the M&S activity reviewed by independent third-party users and developers, essentially by any interested member of the community.

Rule 9 – Test competing implementations.

Use competition of multiple implementations to check the conclusions of different implementations of the M&S processes against each other.

Rule 10 – Conform to standards.

Adopt and promote generally applicable and discipline specific operating procedures, guidelines, and standards accepted as best practices.

Open Knee(s) Summary

- We are building <u>general purpose</u>, <u>publicly accessible</u>, <u>reusable</u>, and <u>credible</u> virtual knees faithful to specimen-specific anatomy and mechanics.
- Ultimate goal is to enable virtual experimentation for cost-effective and prompt explorations in <u>knee</u> <u>biomechanics</u>.

VISIT http://wiki.simtk.org/openknee

What's Next for Open Knee(s)?

Build specimen-specific virtual knee(s)

Generate geometry and meshes Characterize tissue properties Assemble models

Make virtual knee(s) credible

Evaluate predictions against specimen-specific mechanical response

Make virtual knee(s) accessible

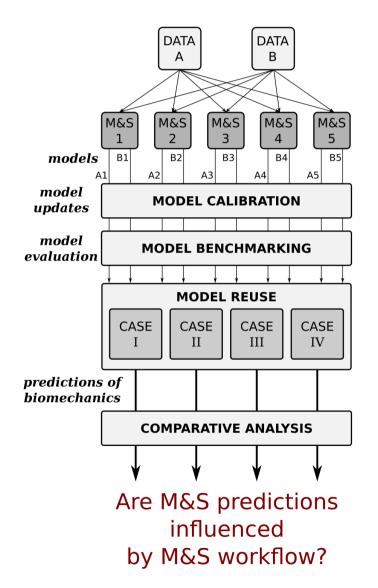
Continue public dissemination

Make virtual knee(s) usable

Expand cloud computing framework Launch clinically relevant use cases

What's Next for Open Knee(s)?

Emphasis on reproducibility and "art" of modeling



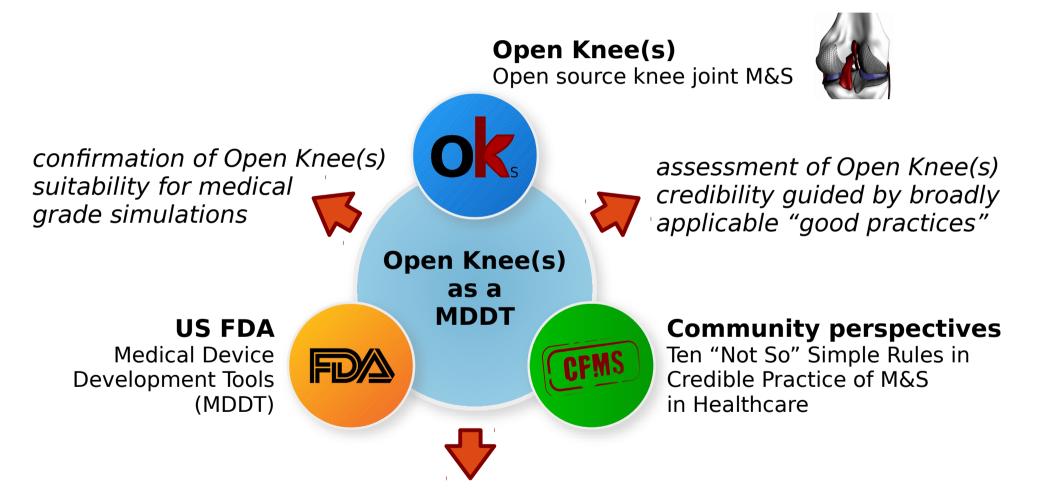
Do the predictions of natural knee biomechanics depend on modeling decisions of separate development teams when the target simulation scenarios and the source data to build models remain the same?



Funding by NIBIB, NIH; refer to https://simtk.org/projects/kneehub.

What's Next for Open Knee(s)?

Emphasis on credibility for translational use



correspondence between community recommendations for M&S practice and M&S considerations of regulatory agencies

What's Next for M&S in Biomechanics?

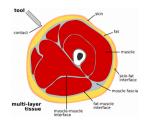
Promote principles of democratization in modeling & simulation in biomechanics

specificity - efficiency - accessibility comprehensibility - usability - credibility

 Apply principles of democratization in other areas of computational biomechanics



Reference Models for Multi-Layer Tissue Structures of Musculoskeletal Extremities



https://simtk.org/projects/multis

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LICENSING

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