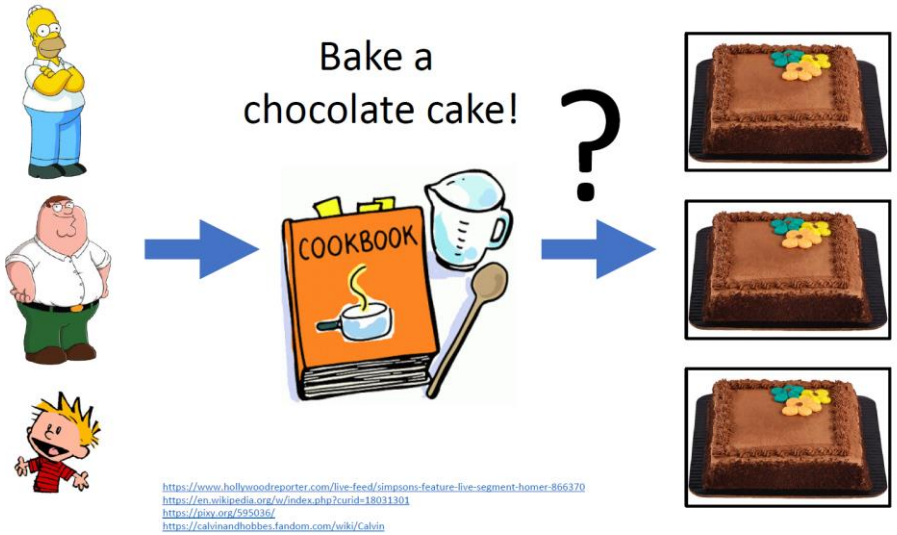
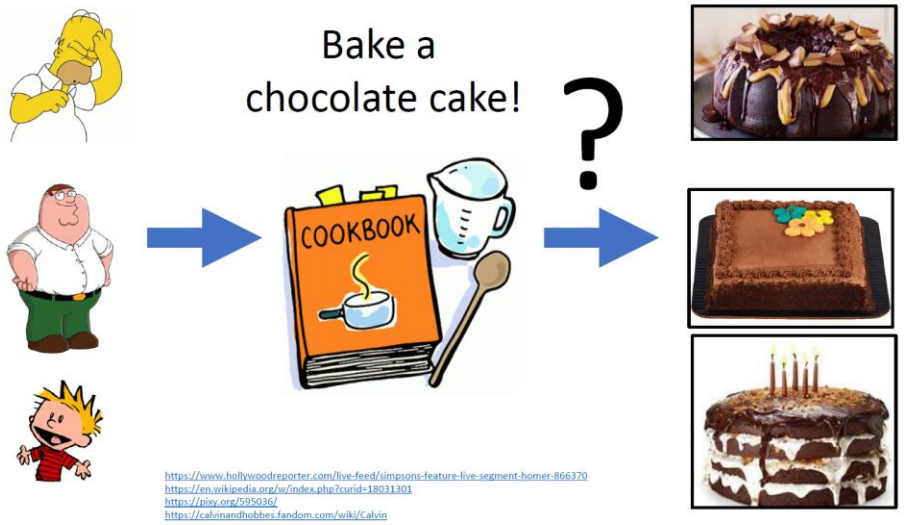
Research Use Case

Computable Biomedical Knowledge (CBK) may accelerate research by improving dissemination of best practices and reproducibility.

What is Reproducibility?

- **Computational Reproducibility** — obtaining consistent computational results using the same input data, computational steps, methods, and code, and conditions of analysis





- **Replicability** — obtaining consistent results across studies aimed at answering the same scientific question, each of which has obtained its own data

National Academies of Sciences, Engineering, and Medicine. 2019. Reproducibility and Replicability in Science. Washington, DC: The National Academies Press. doi: https://doi.org/10.17226/25303

From C. Imhauser, "Reproducibility in Modeling and Simulation of the Knee, Orthopedic Research Society Meeting, Feb 2019.

Reproducibility in biomedical research

Open access, freely available online

Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

OXFORD JOURNALS ILAR Journal

Accelerating Biomedical Discoveries through Rigor and Transparency

Judith A. Hewitt,[1] Liliana L. Brown,[1] Stephanie J. Murphy,[1] Franziska Grieder,[1] and Shai D. Silberberg[1]

ILAR J. 2017 Jul 1; 58(1): 115–128.

PERSPECTIVE

SCIENTIFIC INTEGRITY

What does research reproducibility mean?

Steven N. Goodman,* Daniele Fanelli, John P. A. Ioannidis

The language and conceptual framework of "research reproducibility" are nonstandard and unsettled across the sciences. In this Perspective, we review an array of explicit and implicit definitions of reproducibility and related terminology, and discuss how to avoid potential misunderstandings when these terms are used as a surrogate for "truth."

NATURE | COMMENT

Policy: NIH plans to enhance reproducibility

Francis S. Collins & Lawrence A. Tabak

27 January 2014

Francis S. Collins and Lawrence A. Tabak discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

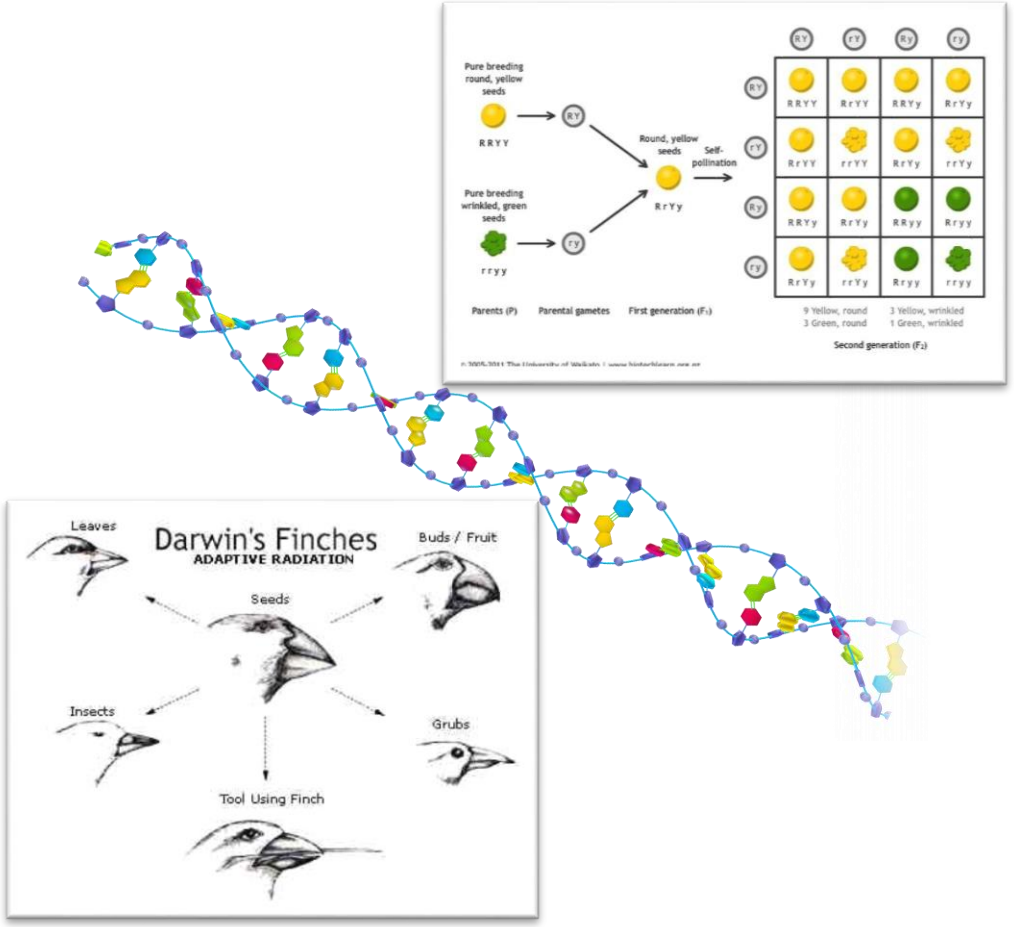
Reproducibility is a cornerstone of science

Art

Expression of personal vision.

Science

Seeks to identify independent truth of the natural world.

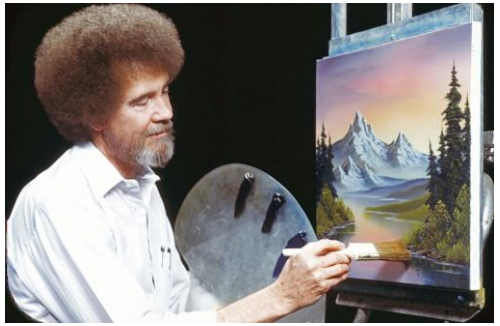


Art versus Science

Art

Expression of personal vision.

Artistic methods and skills can be taught.

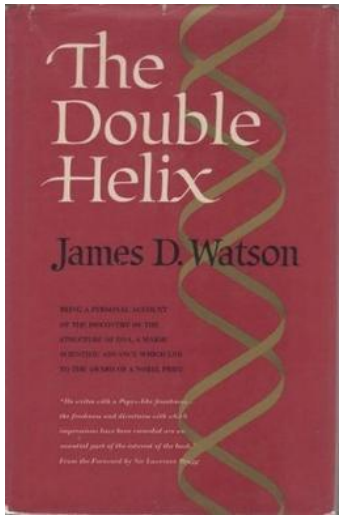


But replicas are not the equivalent of an original creation.

Science

Seeks to identify independent truth of the natural world.

Relies on effective communication of hypotheses, experimental methods, and analyses to establishing validity and support reproducibility.



bioRχiv

THE PREPRINT SERVER FOR BIOLOGY

Meet Ahmet, a bioengineer

Ahmet Erdemir
erdemira@ccf.org
+1 (216) 445 9523

Director Computational Biomodeling (CoBi) Core
Department of Biomedical Engineering
Lerner Research Institute
Cleveland Clinic

Research Interests:

- Simulation-based medicine, emphasizing biomechanics and physics-based computational modeling.
- Leveraging computational modeling as a routine, reliable, and efficient tool for healthcare delivery and biomedical science.
    1. Developing databases of anatomically and physiologically realistic virtual specimens and subjects
    2. Using computational modeling in the clinical workflow to support patient-specific decision making and to realize individualized care.
    3. Culture change in the modeling community and establishment of “good practices” to enhance credibility, reproducibility, and reusability in modeling and simulation

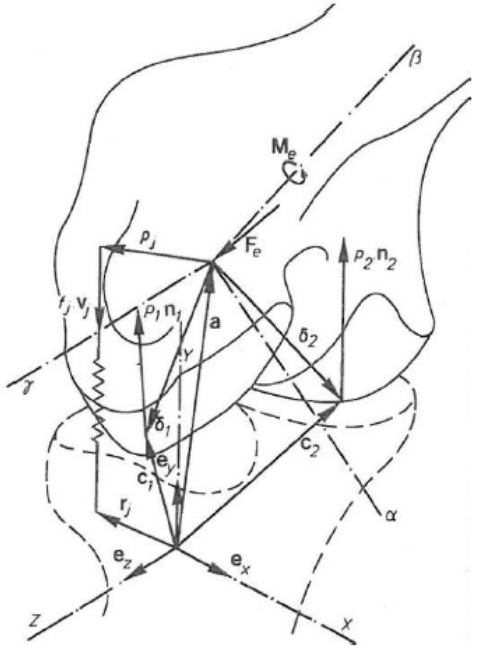
CoBi Core

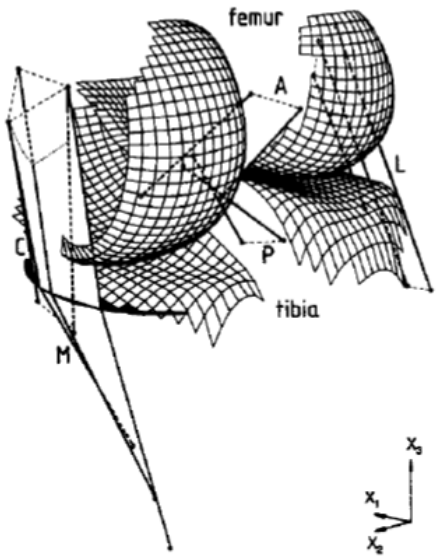
Cleveland Clinic

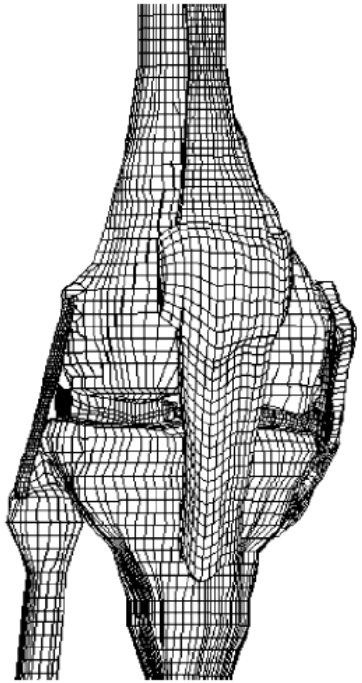
Modeling of the knee has greatly improved

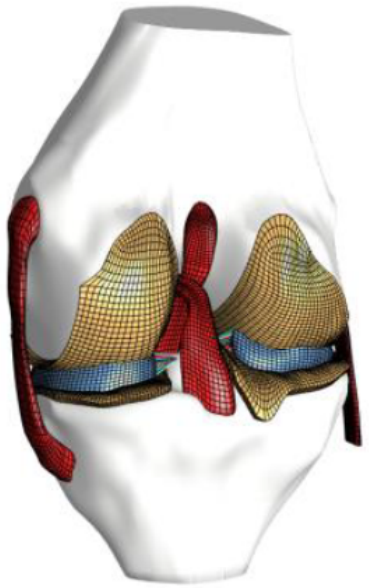
Knee Modeling

80's → 90's → 00's → 10's









Wismans, J Biomech 1980

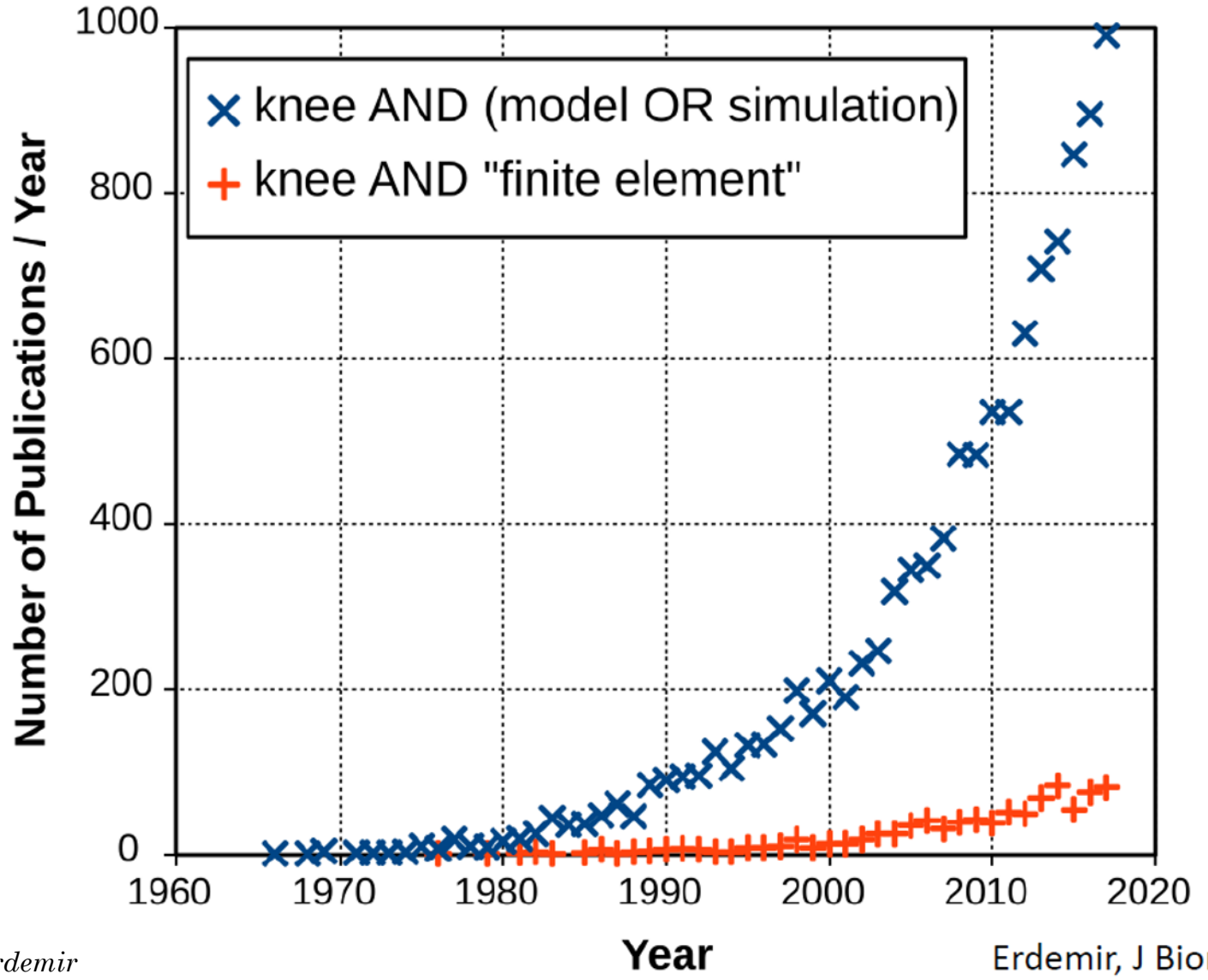
Blankevoort, J Biomech 1996

Doblare, J Biomech 2006

Erdemir, J Knee Surg 2016

Carl Imhauser

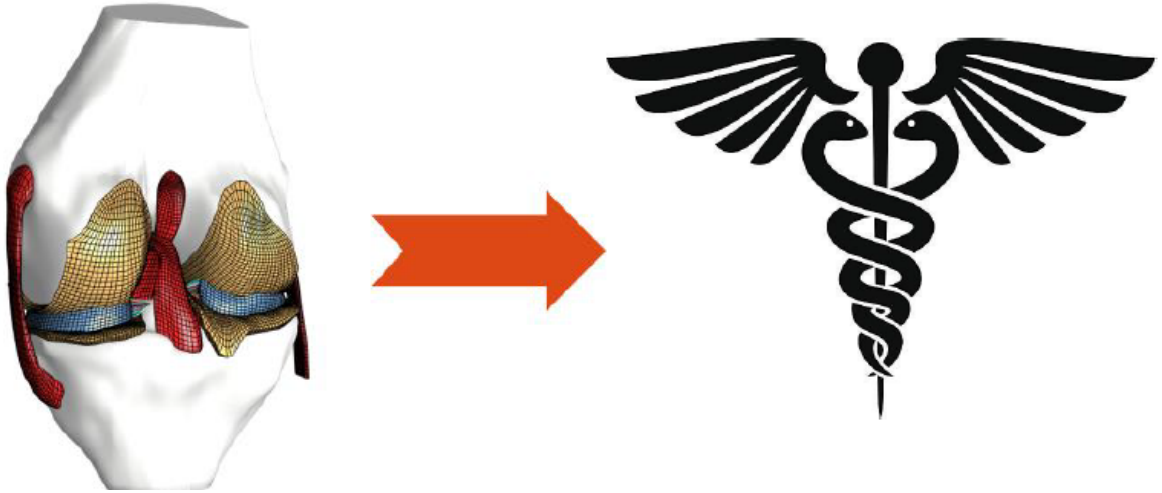
Rapid increase in publications on knee models



Erdemir, J Biomech Eng, In Review

Importance of model reproducibility

- Low rate of clinical translation of preclinical findings
- High profile failures cause public to lose faith in research
- As a Knee M&S Community, we want to be proactive about this as we translate modeling tools to clinical use



Carl Imhauser

Question about knee model reproducibility

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

Focus on joint and tissue level mechanics

National Institute of Biomedical Imaging and Bioengineering

R01EB024573

Ahmet Erdemir

Ahmet assembled a group of engineers

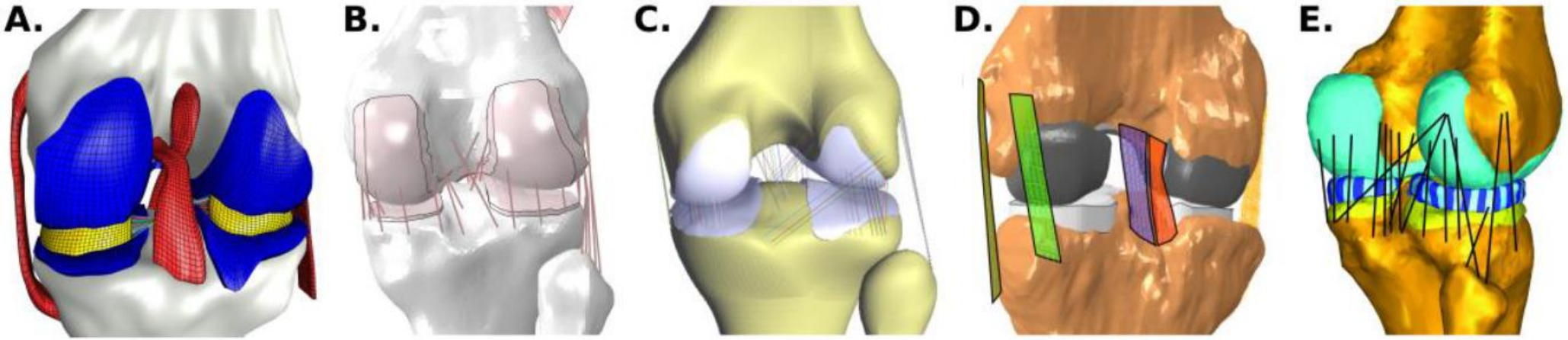
Kevin Shelburne, PhD
University of Denver

Peter Laz, PhD
University of Denver

Thor Besier, PhD
University of Auckland

Jason Halloran, PhD
Cleveland State University

Carl Imhauser, PhD
Hospital for Special Surgery



R01EB024573

Ahmet Erdemir

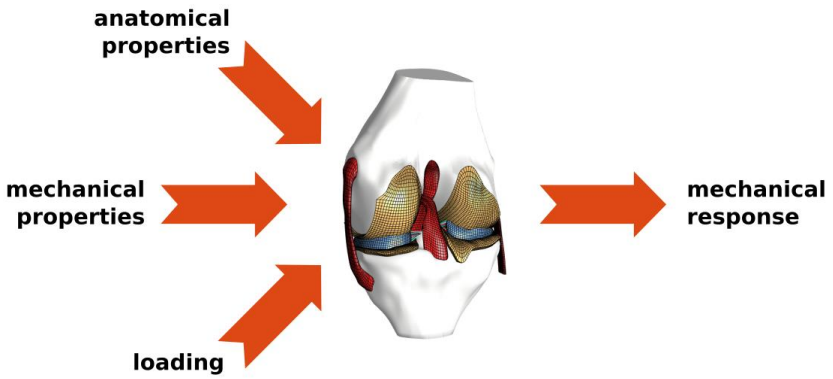
REPRODUCIBILITY & "ART" OF KNEE MODELING

The model
Virtual biomechanical knees
Physics-based (Newton's laws)
continuum mechanics
rigid body dynamics

What is new inside?
Computational techniques are not new.
Modeler's interpretation, i.e., their "art", vary.
What's new is the overall strategy
to document modeler's choices, and
to understand their impact on reproducibility.

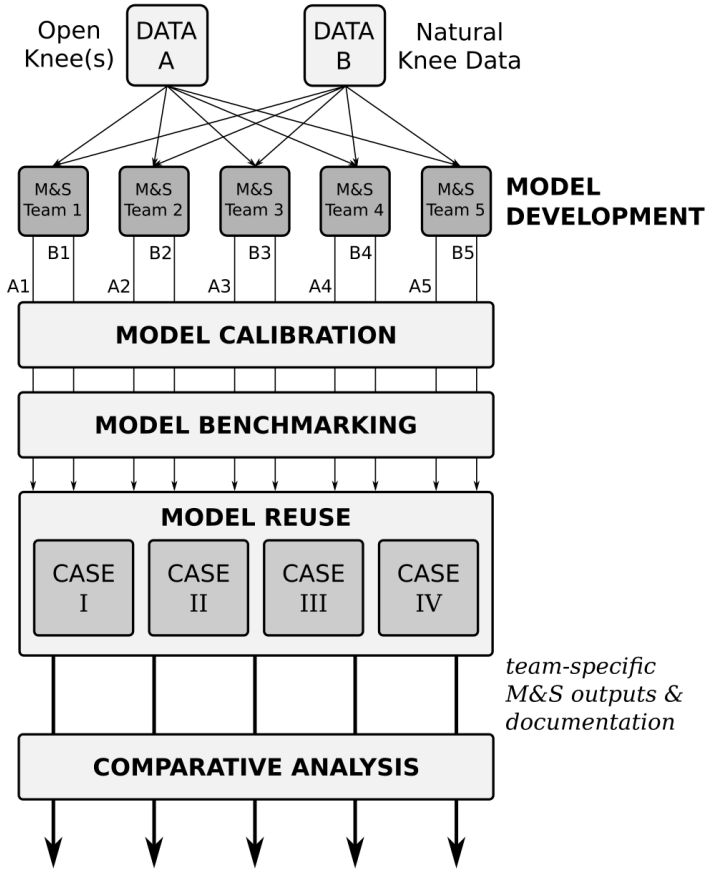
How will this change current practice?
Emergence of good practices
Demonstration of competing implementations
Documentation and exchange of simulation workflows
Increased credibility in modeling & simulation (M&S)

End users
Knee biomechanists who rely on computational models
Broader biomedical M&S community to adopt demonstrated practices
Decision-makers in M&S regulation and policy making



Same data
Same reuse cases

Different models?
predictions?
conclusions?



Are M&S predictions influenced by variations in M&S decisions?

Cleveland Clinic
University of Denver
Cleveland State University 1964
Hospital for Special Surgery
Auckland Bioengineering Institute, The University of Auckland New Zealand

Ahmet Erdemir (CC)
Kevin Shelburne & Peter Laz (DU)
Jason Halloran (CSU)
Carl Imhauser (HSS)
Thor Besier (ABI)

NIBIB - R01EB024573
https://simtk.org/projects/kneehub

Ahmet Erdemir

The project uses the SimTK platform

National Institute of Biomedical Imaging and Bioengineering

R01EB024573

https://simtk.org/docman/?group_id=1061

What is SimTK?

SimTK is a **free project-hosting platform** for the **biomedical computation community** that:

- Enables you to easily share your software, data, and models
- Tracks the impact of the resources you share
- Provides the infrastructure so you can support and grow a community around your projects
- Connects you and your project to thousands of researchers working at the intersection of biology, medicine, and computations

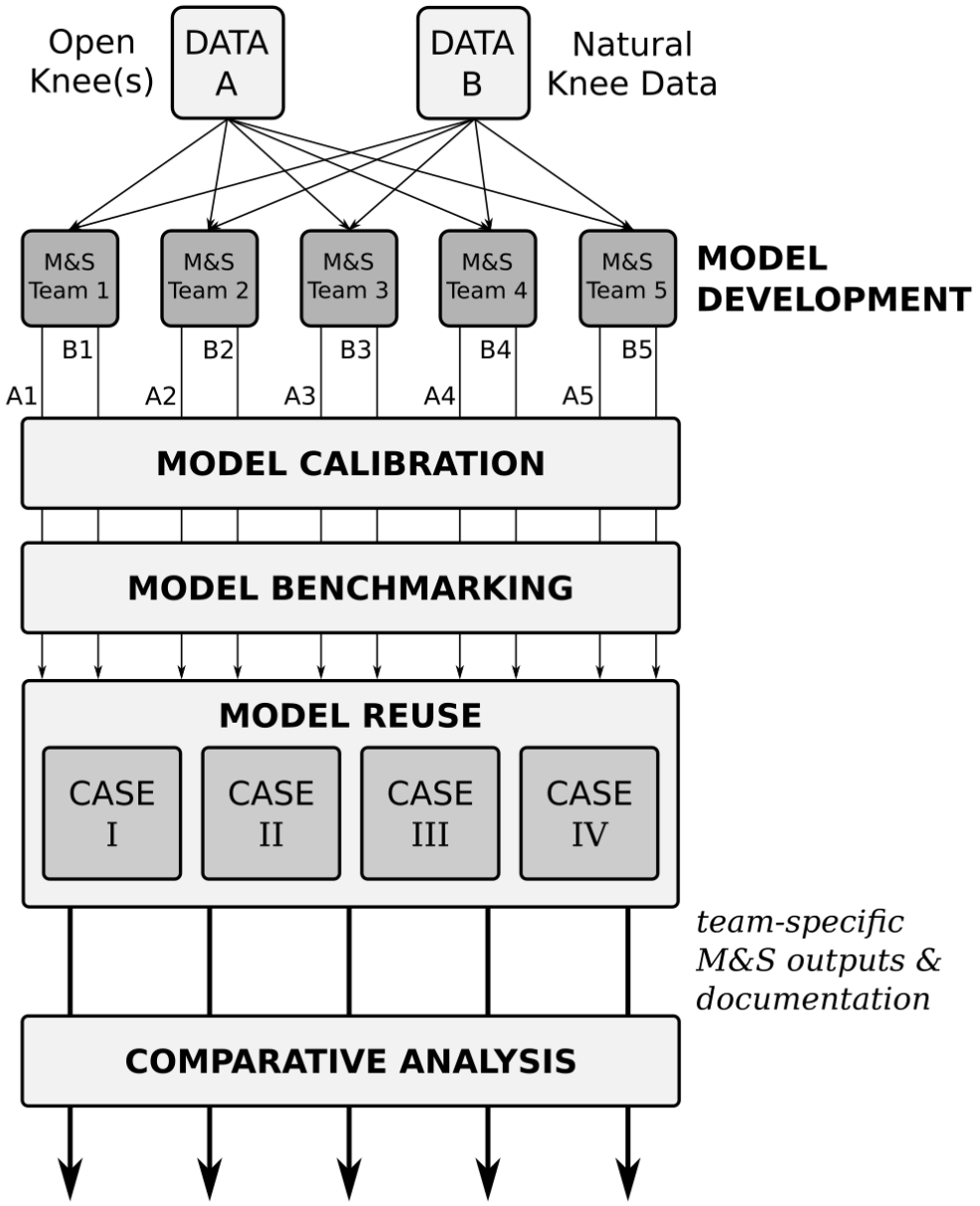
SimTK

Enabling groundbreaking biomedical research via open access to high-quality simulation tools, accurate models, and the people behind them.

1178 projects
808210 downloads
82466 members

Research Plan

- Reuse existing input data on knee anatomy and mechanics
- Develop 5 specimen-specific knee models.
- Calibrate all knee models, including measures of fit error and loading conditions.
- Benchmark all models using data from combined data sets.
- Test model reuse in 4 simulation cases (passive flexion, sit-to-stand, etc)
- Third party comparison to assess model reuse credibility.



Are M&S predictions influenced by variations in M&S decisions?

Ahmet Erdemir

Project Status

All teams have provided comprehensive documentation of their workflow and all the products of modeling and simulation lifecycle.

- Publicly available data were earmarked and each team were asked to write their **model development specifications** (e.g., their own standard operating procedure).
- Teams processed the public data through various analysis stages to create **derivative data** (e.g. segmentations, geometries from anatomical images).
- Teams submitted all these derivative data along with a working model with the results of a predefined simulation case.
- They also submitted a document recording all their protocol deviations and justifications.

Project Status

The goal is to determine whether the “art” of a modeler affects ability to obtain consistent and actionable knowledge from the model. If so, at what stage of modeling or simulation lifecycle?

How? This project will enable a third party to test the reproducibility potential of workflows by:

- taking a team's specification and protocol deviation documents
- following their steps to generate all derivative data, models, and simulation results
- then comparing the results with the third party results.

Implications of project findings

$=$	If predictions are the same across teams?	Awesome!
$\neq$	If predictions **differ** across groups?	Tremendous opportunity to learn what drives variability in knee model predictions

Thanks to:

Ahmet Erdemir (Cleveland Clinic) and Carl Imhauser (Hospital for Special Surgery), from the KneeHub project.

Grace Peng (NIBIB)

Andrew McCulloch (UCSD)