Multiscale Modeling in Cell Biomechanics

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Molecular Cell Biomechanics | Berkeley Biomechanics

NASEM FORD FELLOWS

Mechanical Engineering
UNIVERSITY OF CALIFORNIA, BERKELEY

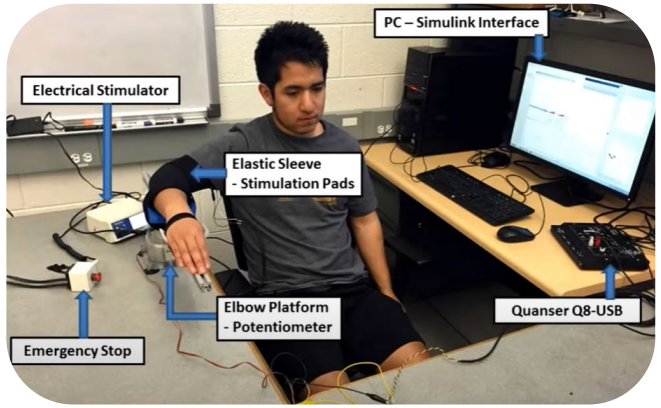
PHILIPS

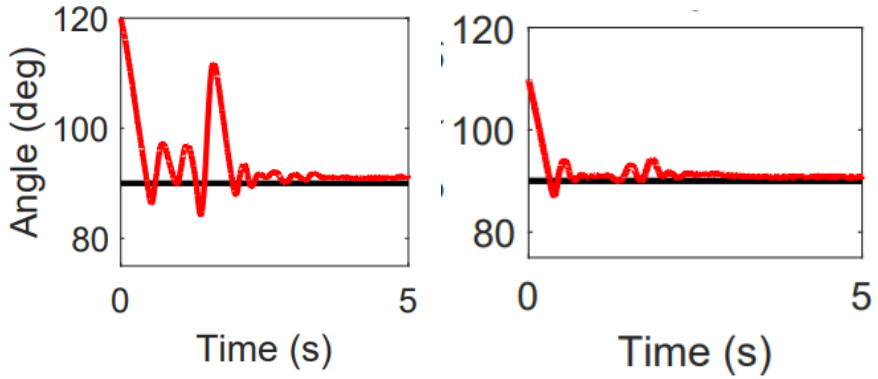
SCHOOL OF MINES 1874 COLORADO

amontes@berkeley.edu

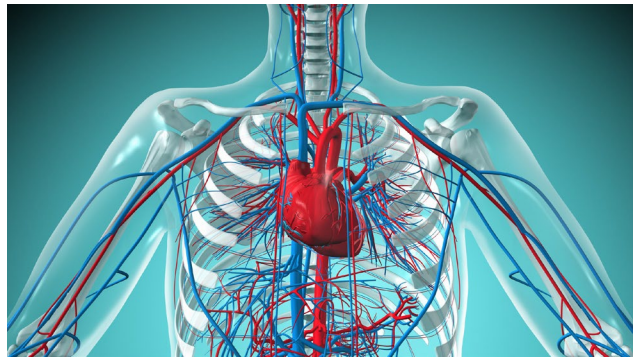
The Body is a multiscale system

Neuromuscular[1]





Cardiovascular



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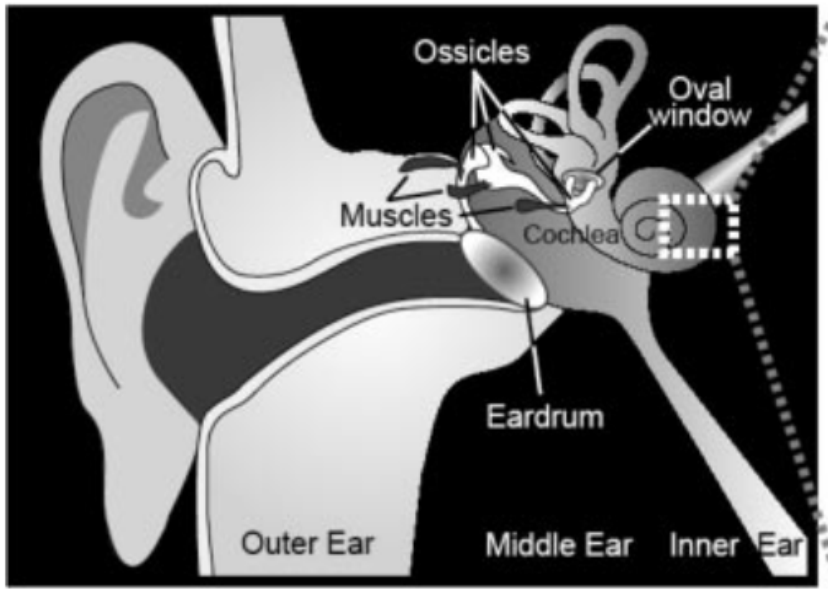
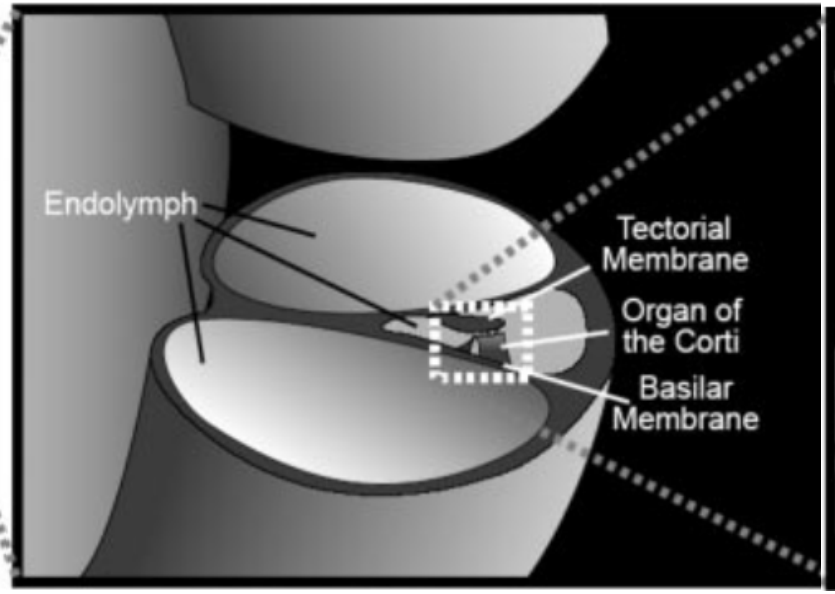
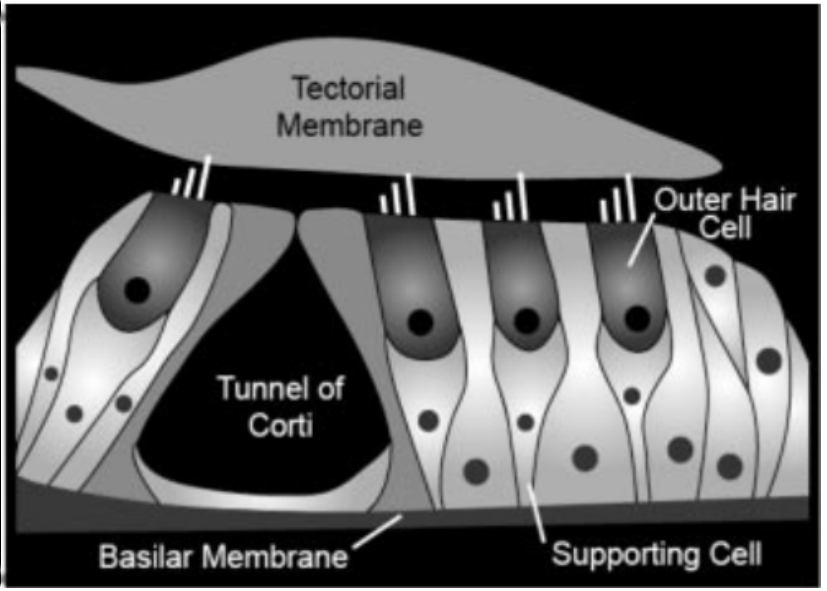
1. Harris et al. *Proceedings ASME DSCC*. 2016.

So… cell biomechanics?

The Body is a multiscale system: Hearing Example

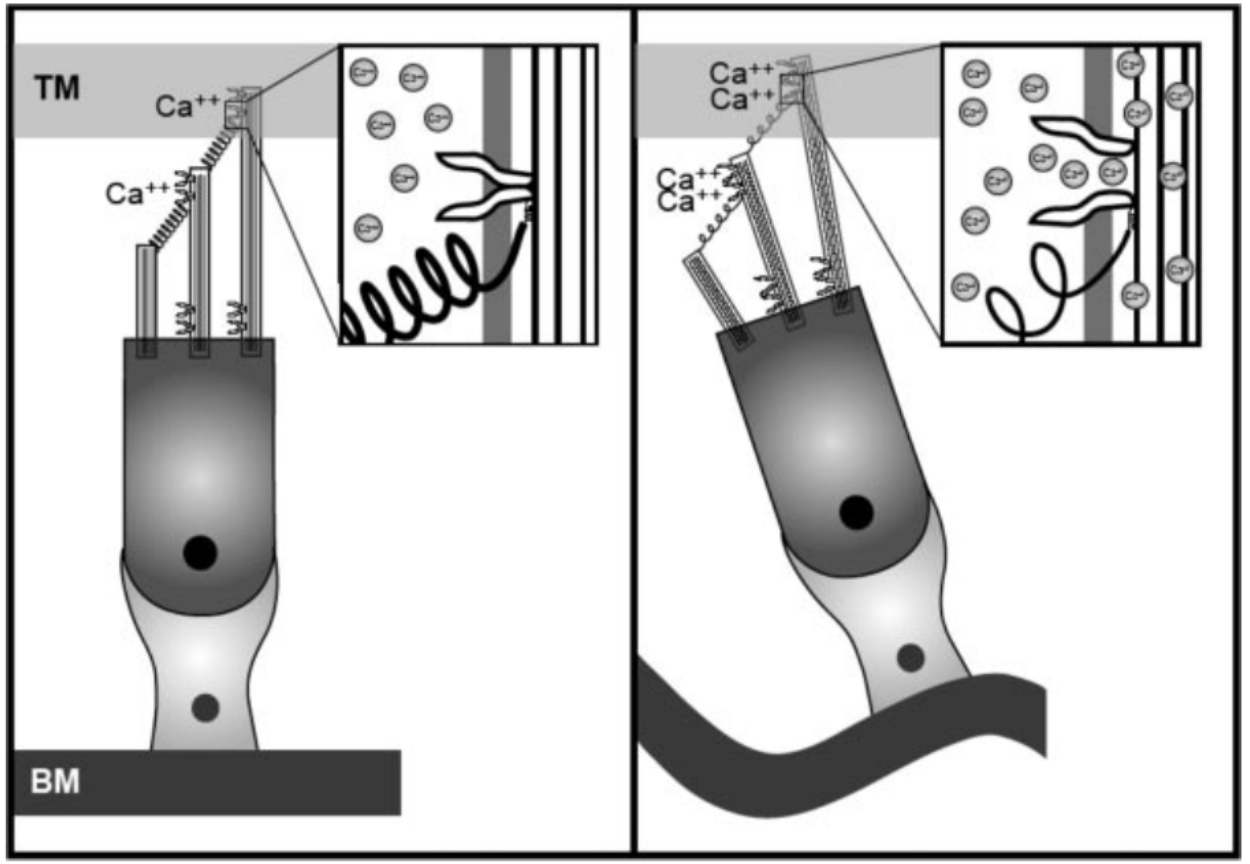






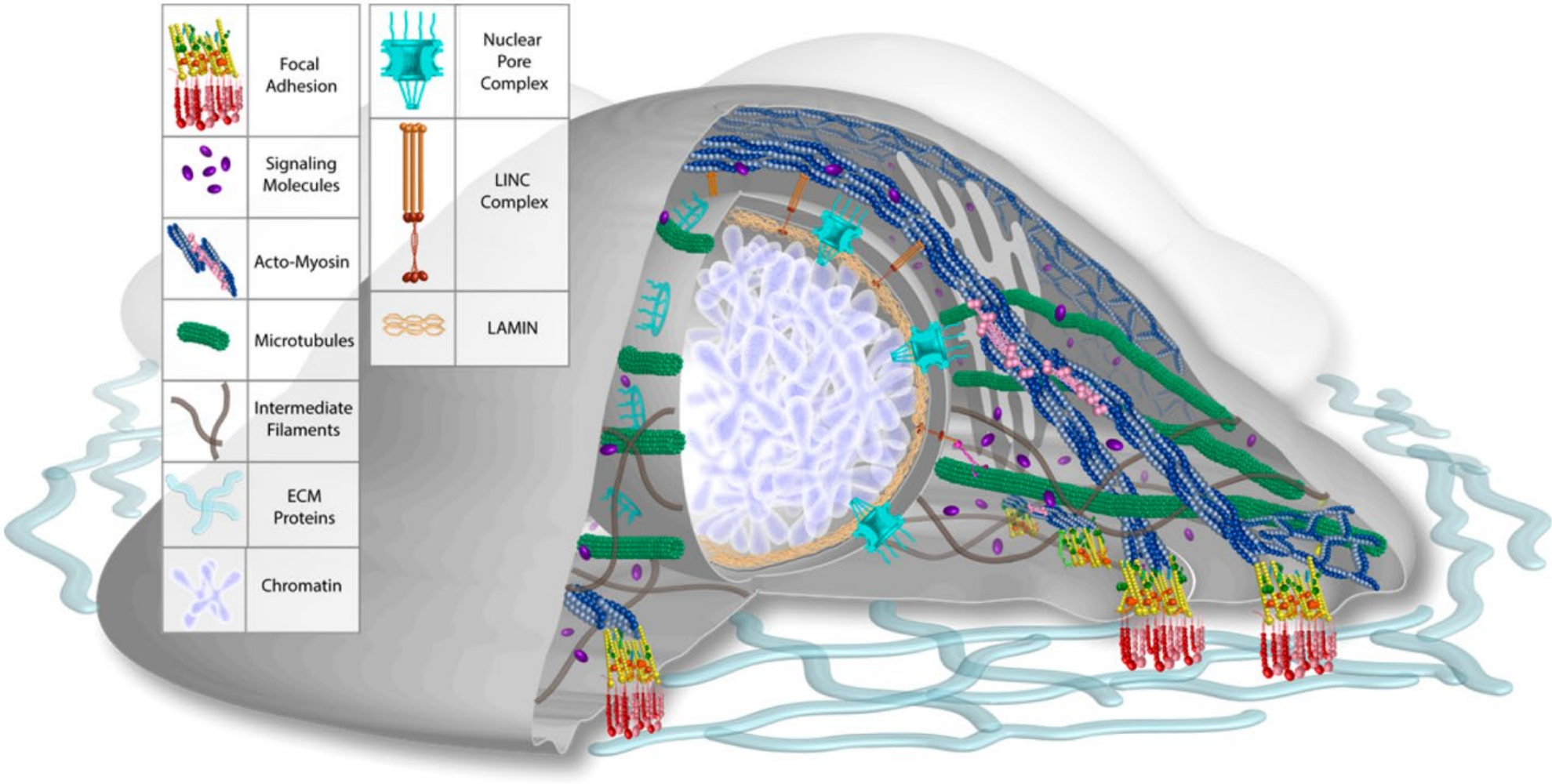
Ingber. *FASEB.* 2006.

The Body is a multiscale system: Hearing Example



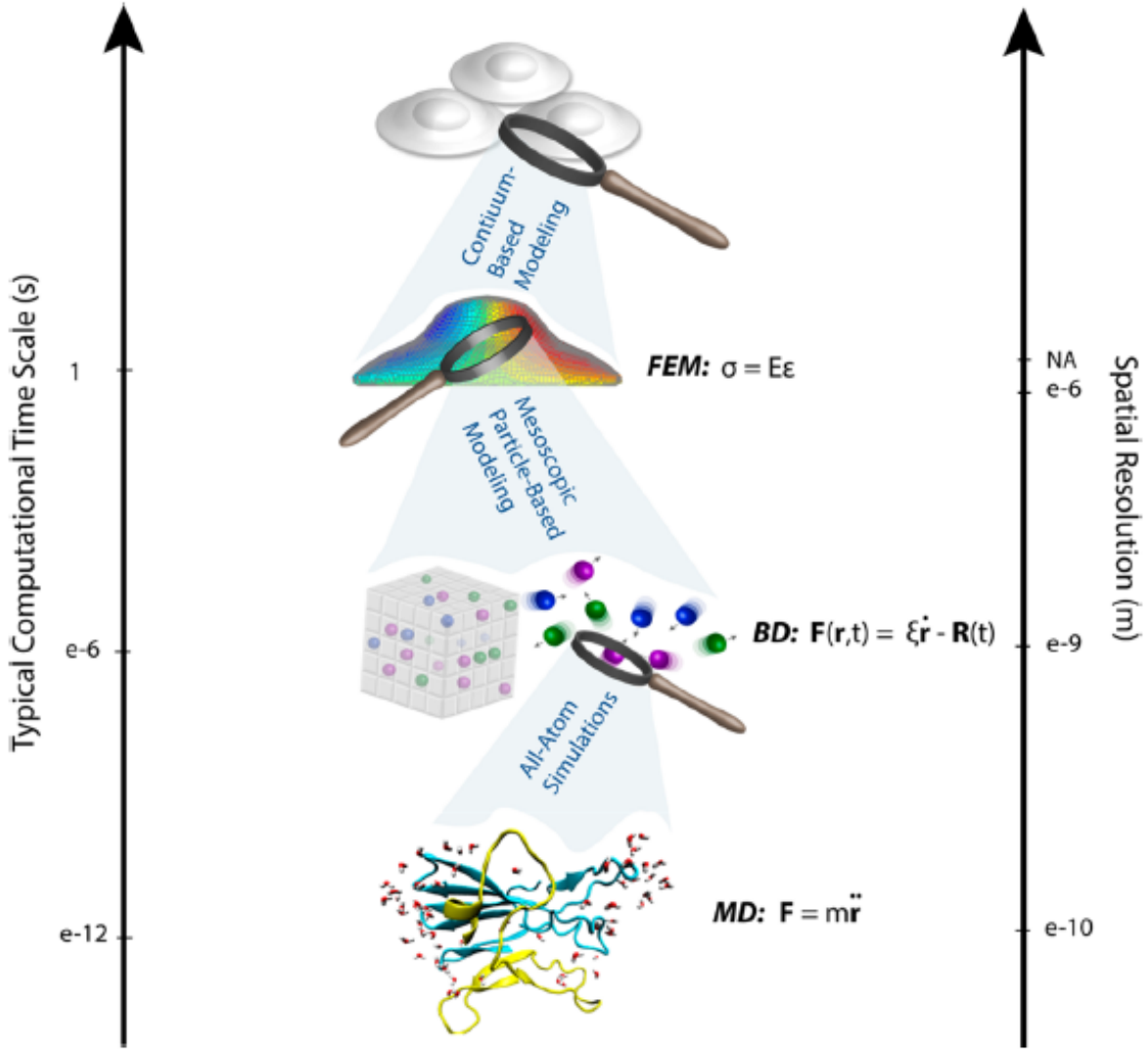
Ingber. *FASEB.* 2006.

Cell as a multiscale biomechanical system



Shams et al. *ACS Biomater. Sci. Eng.* 2017.

Modeling multiscale cell mechanics with appropriate methods



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Shams et al. *ACS Biomater. Sci. Eng.* 2017.

Cell Modeling: A (brief) History

The cell as a water balloon

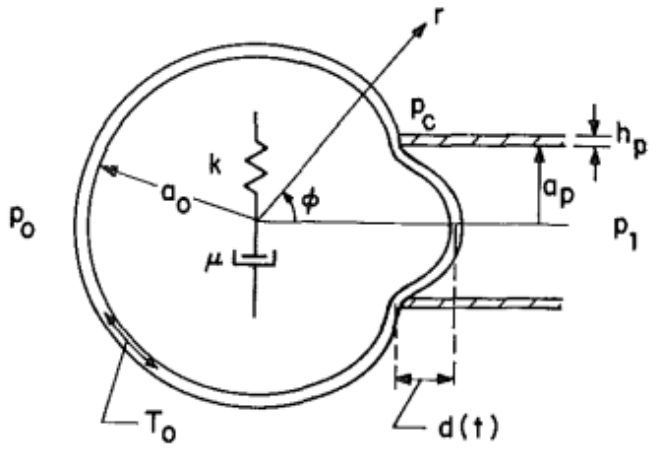


Fig. 2(*a*) Sketch of a cell in a micropipette aspiration test

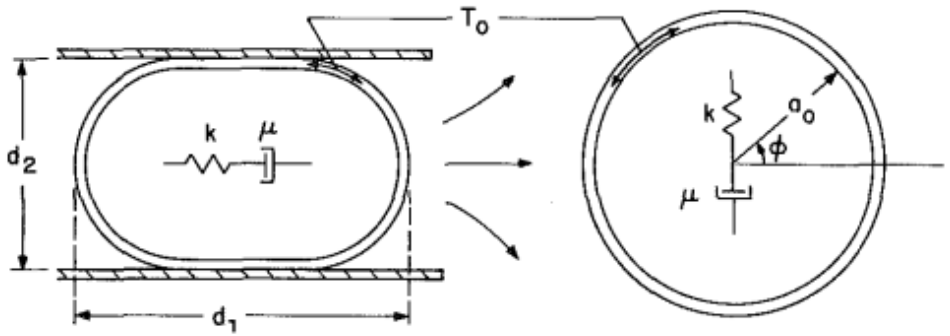


Fig. 2(*b*) Sketch of a leukocyte in recovery test, before and after the spherical shape is recovered

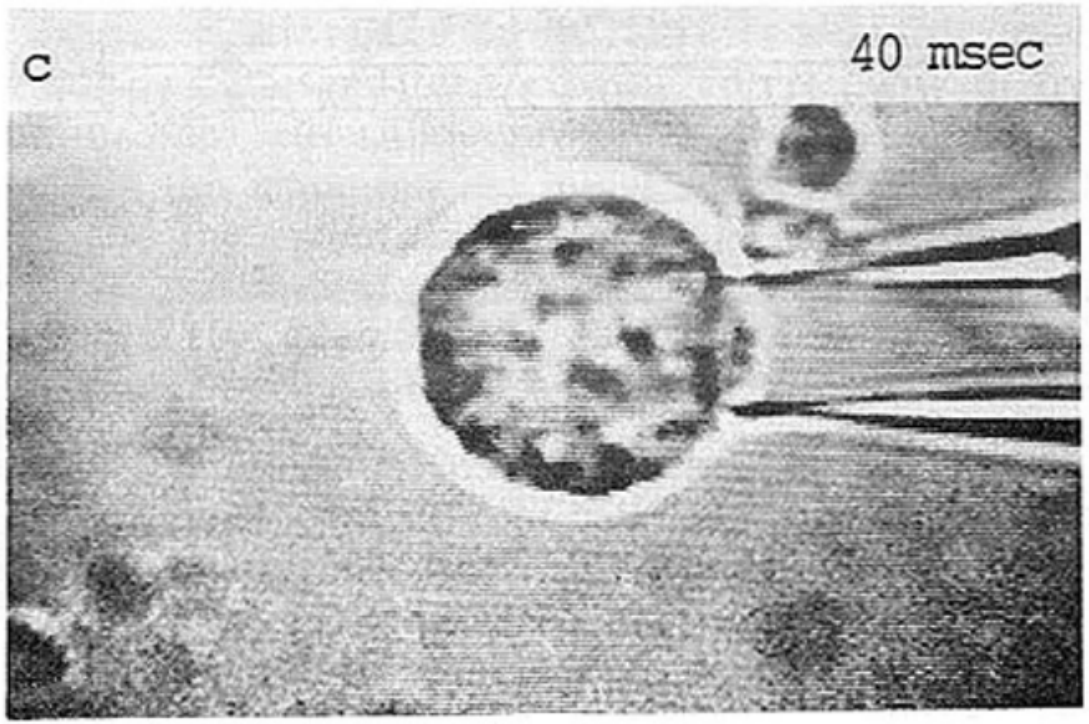
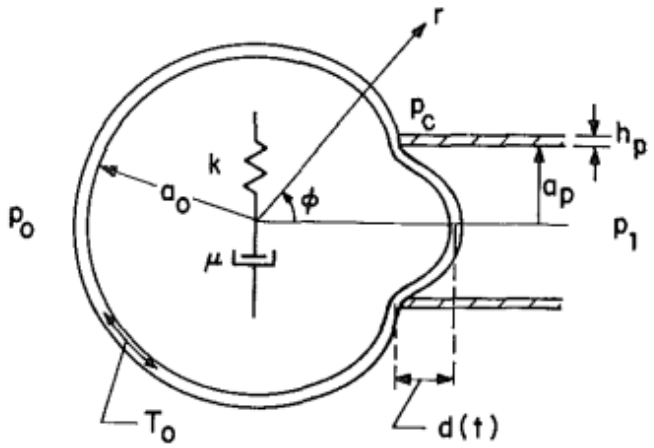


Fig. 3(*c*)

Dong et al. *J of Biomechanical Engineering.* 1988.

The cell as a water balloon



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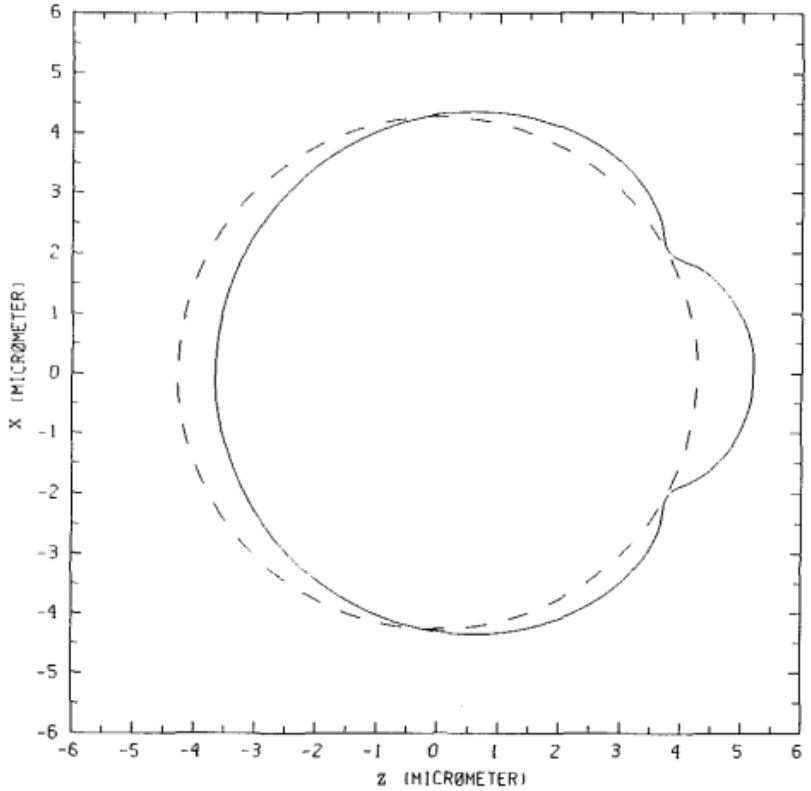

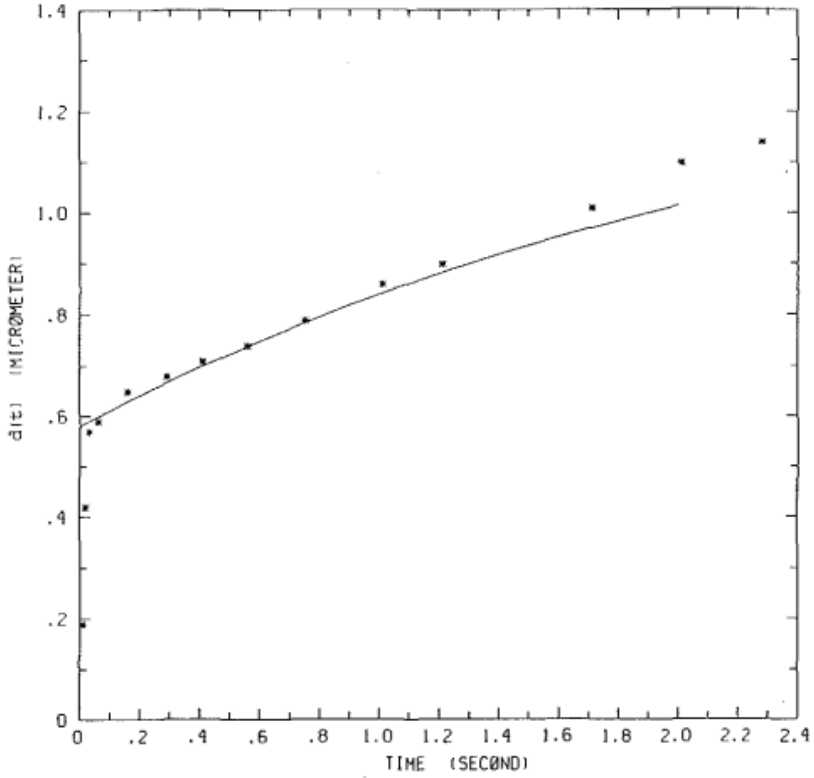

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Dong et al. *J of Biomechanical Engineering.* 1988.

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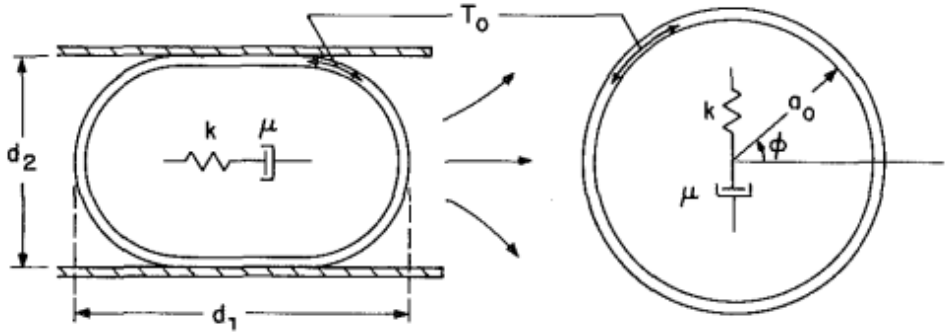

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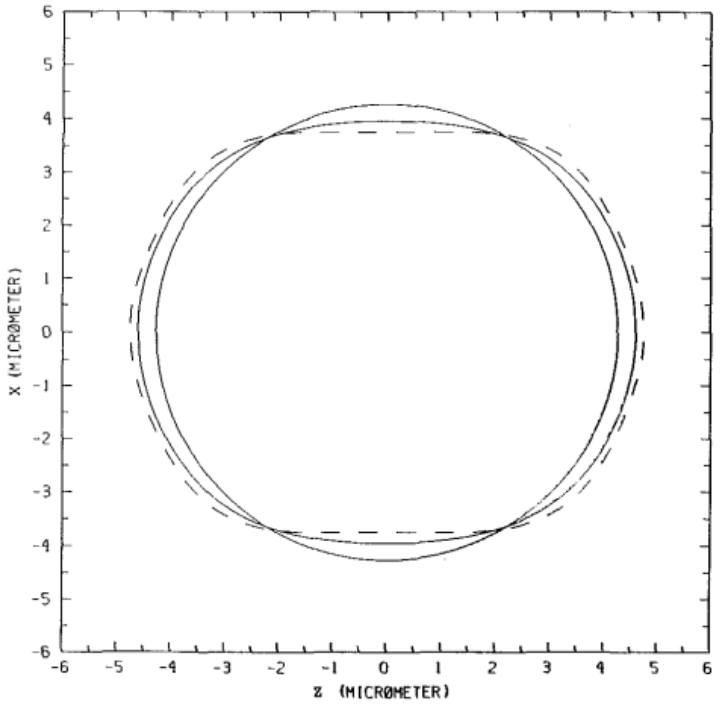

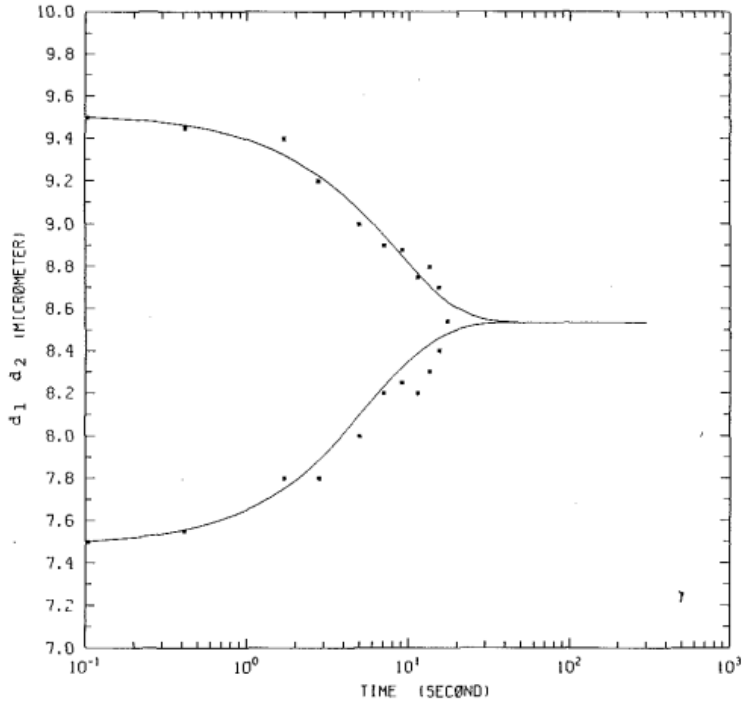

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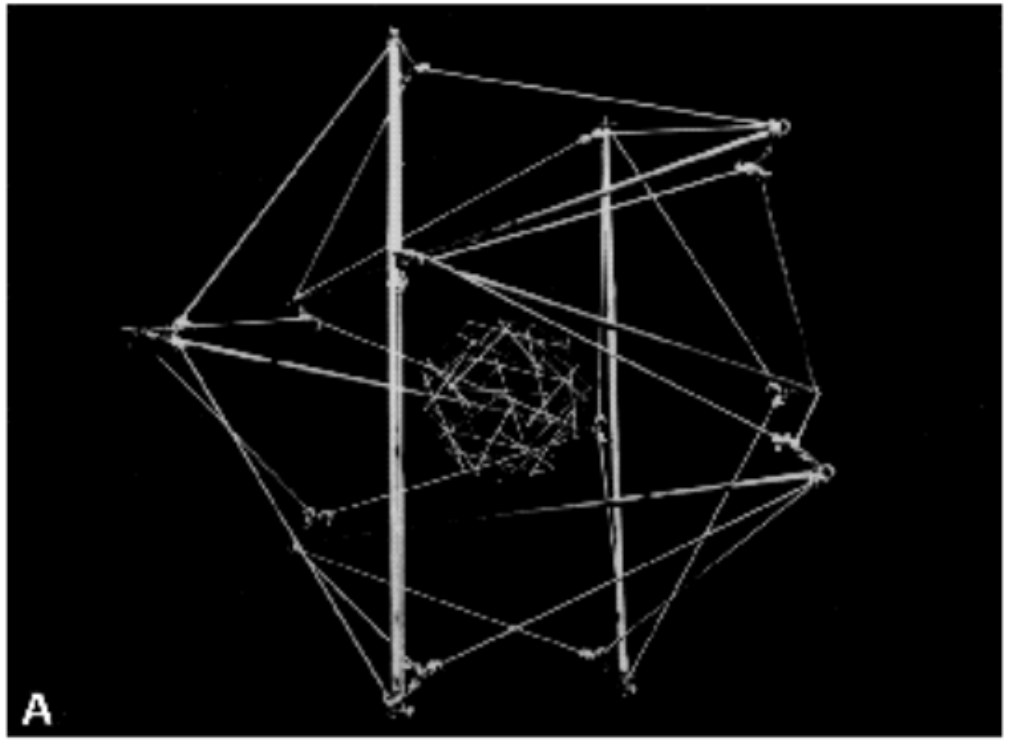
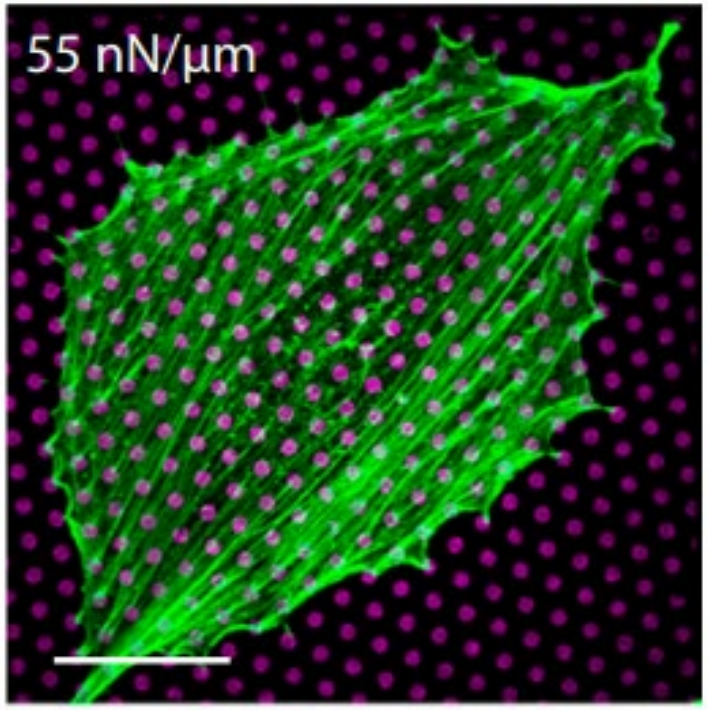
Dong et al. *J of Biomechanical Engineering.* 1988.

The cell as a tensegrity structure



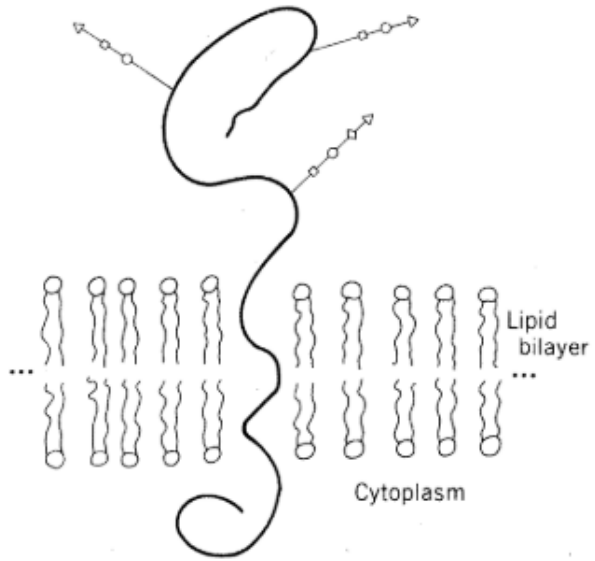


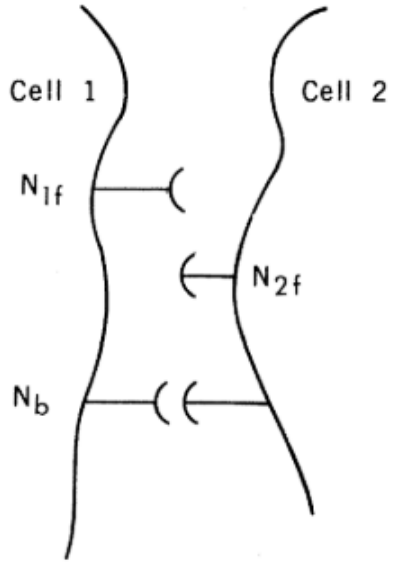
Ingber. *J of Cell Science.* 1993.
Doss et al. *PNAS.* 2020.

Models for the Specific Adhesion of Cells to Cells

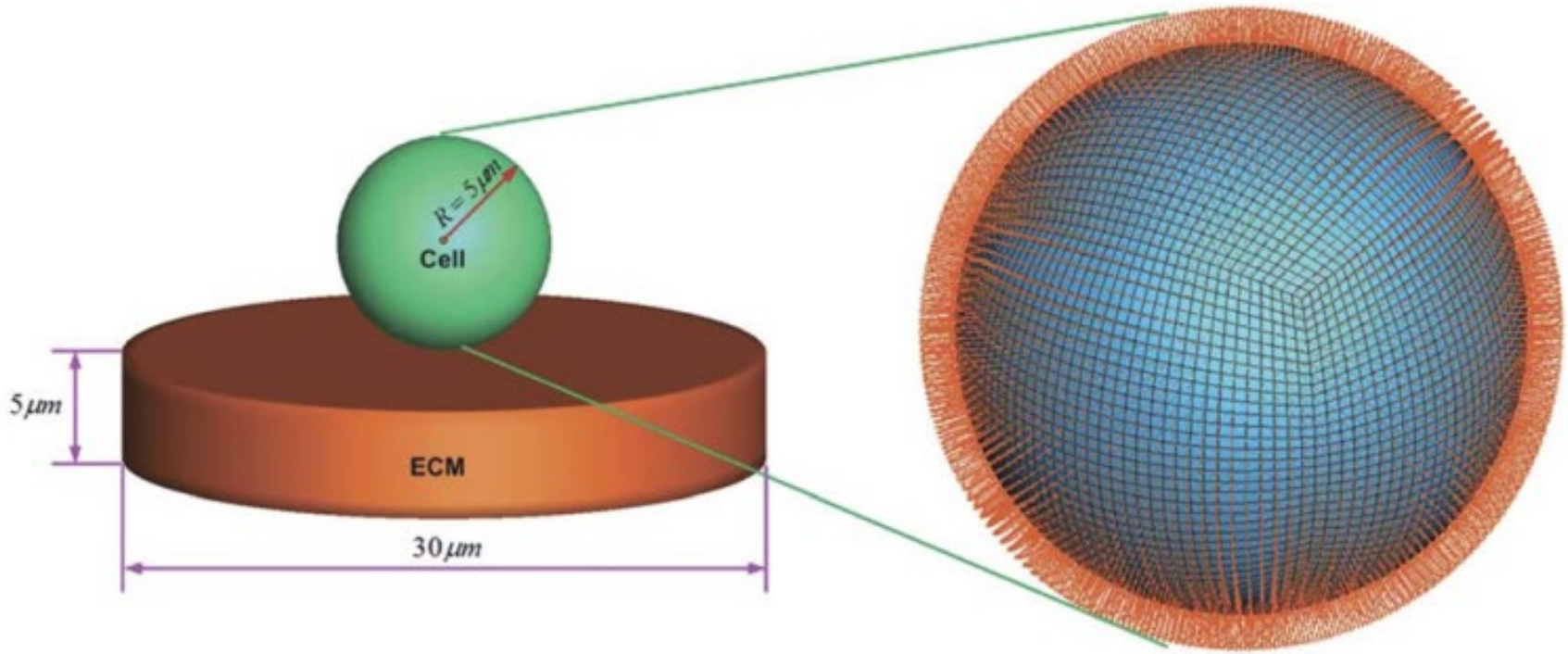
A theoretical framework for adhesion mediated by reversible bonds between cell surface molecules

George I. Bell



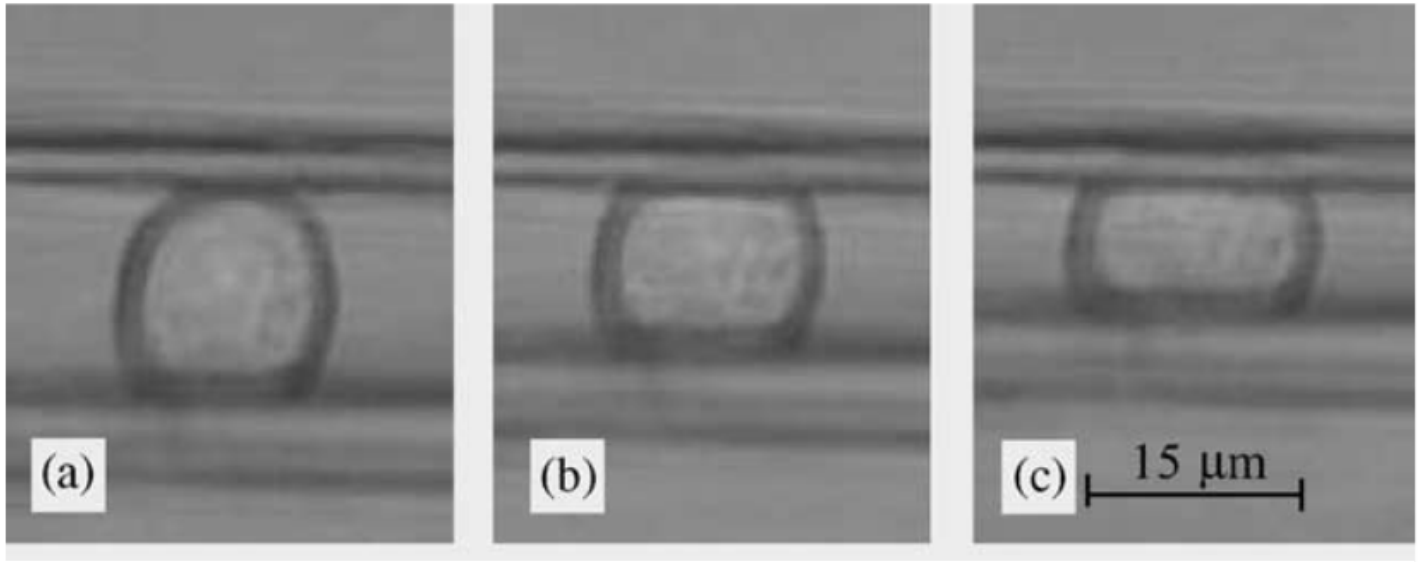


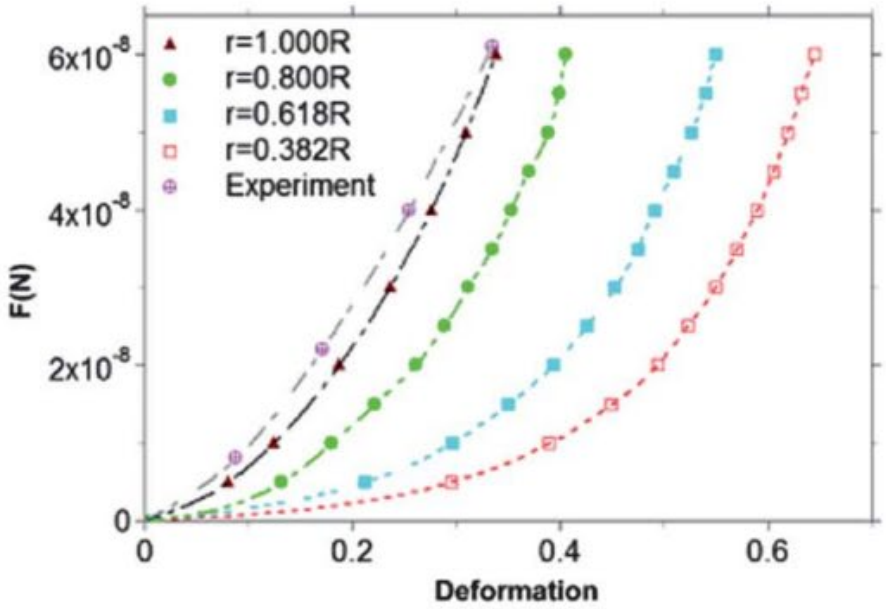
3D soft matter cell model for cell spreading



Zeng and Li. *Soft Matter*. 2011.

3D soft matter cell model validation





Zeng and Li. *Soft Matter.* 2011.
Caille et al. *J of Biomechanics.* 2002.

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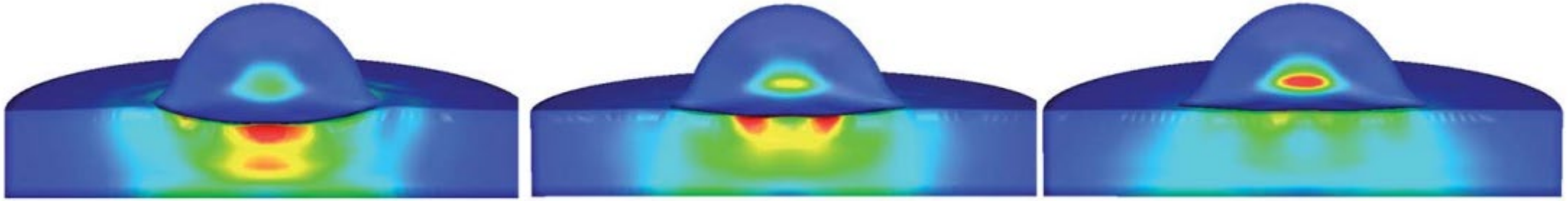

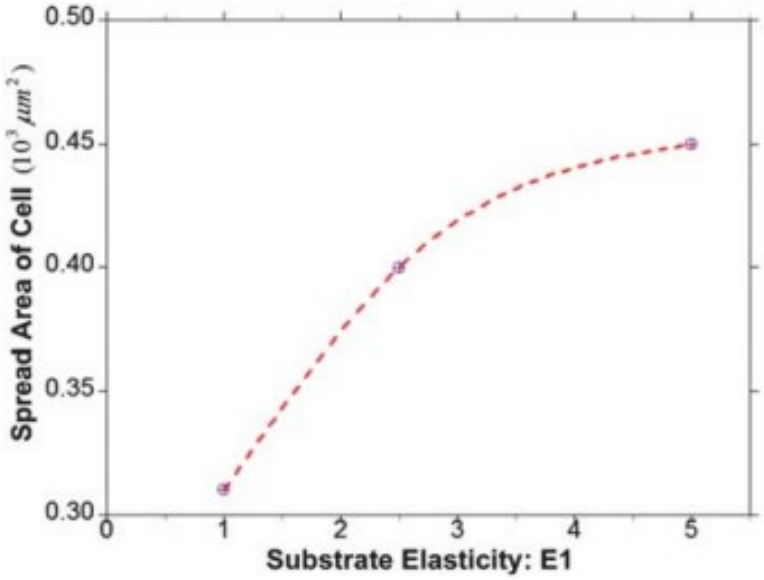

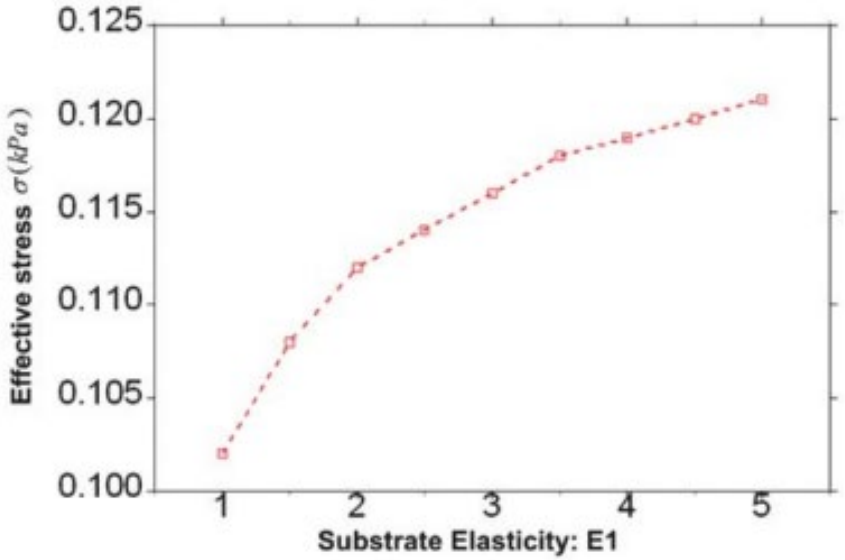

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Zeng and Li. *Soft Matter*. 2011.

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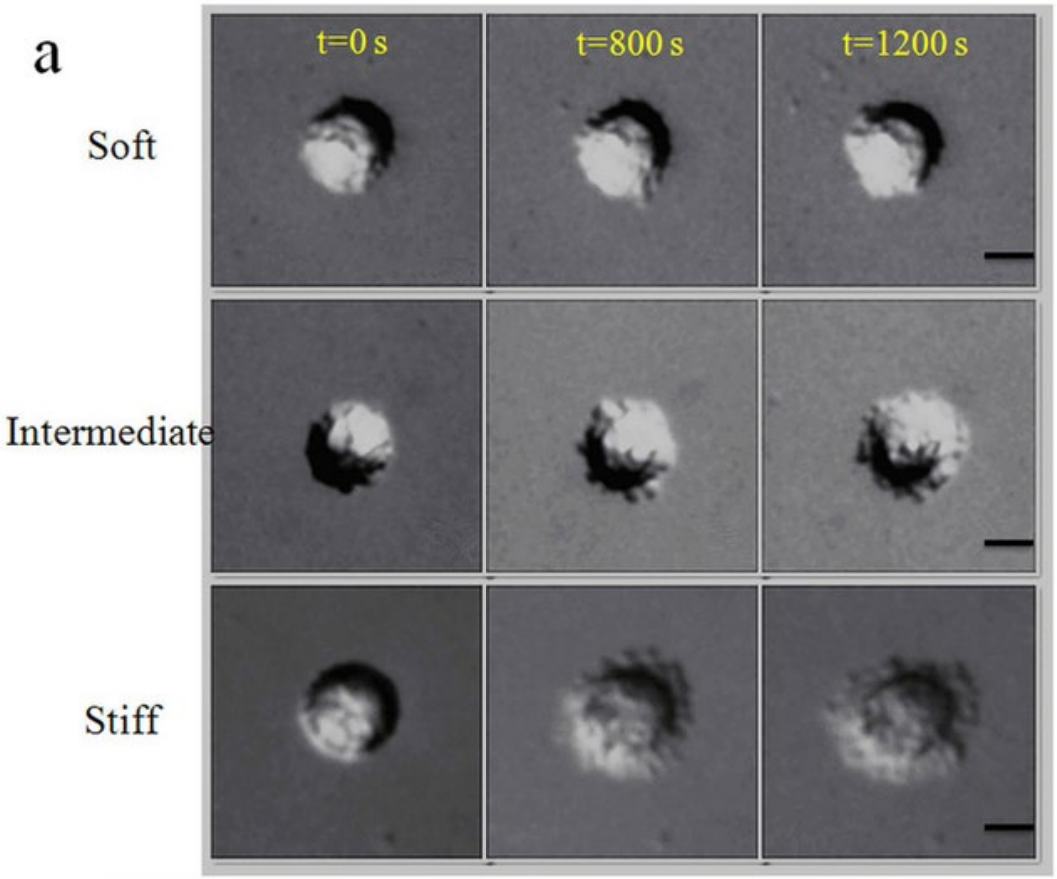
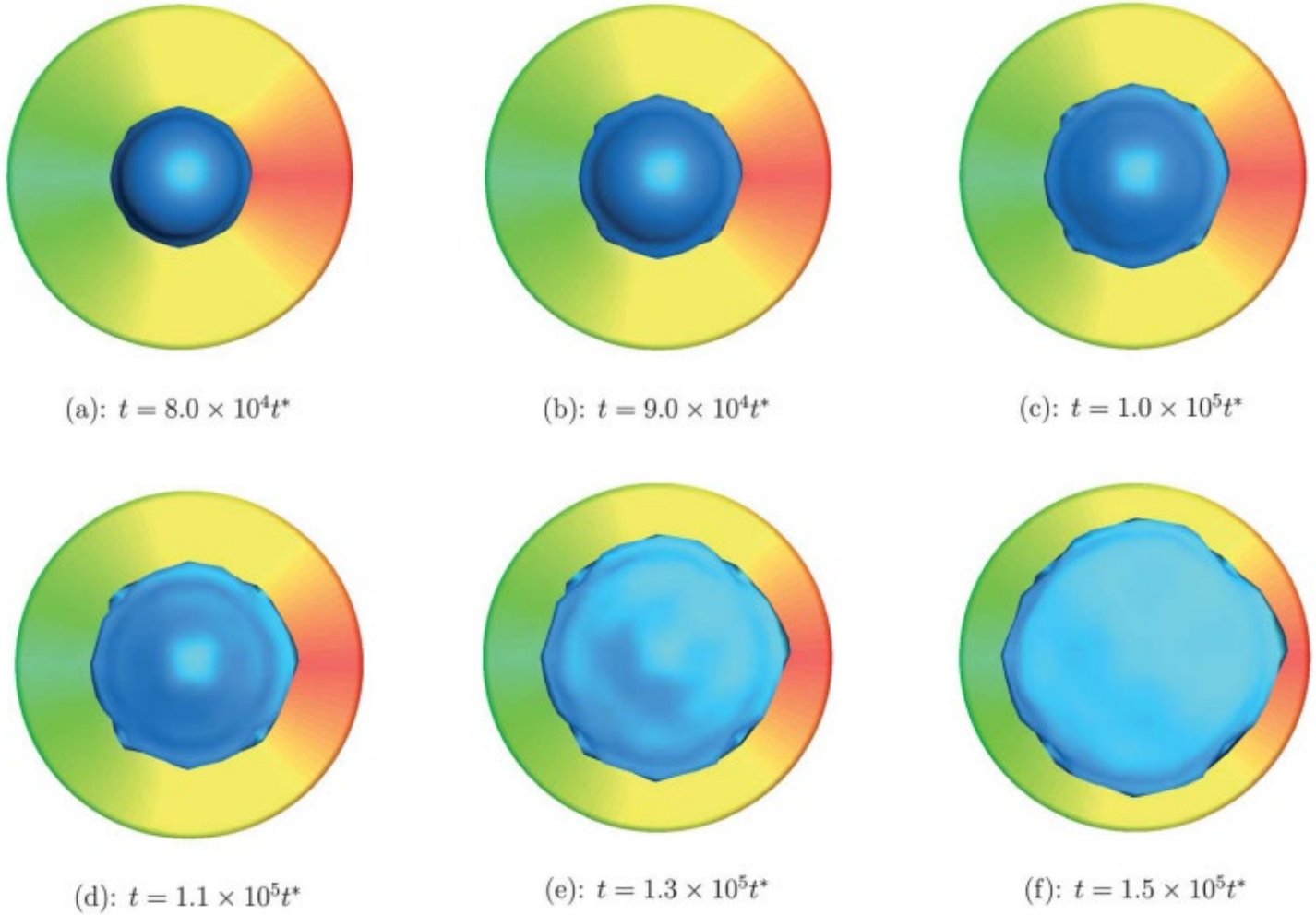




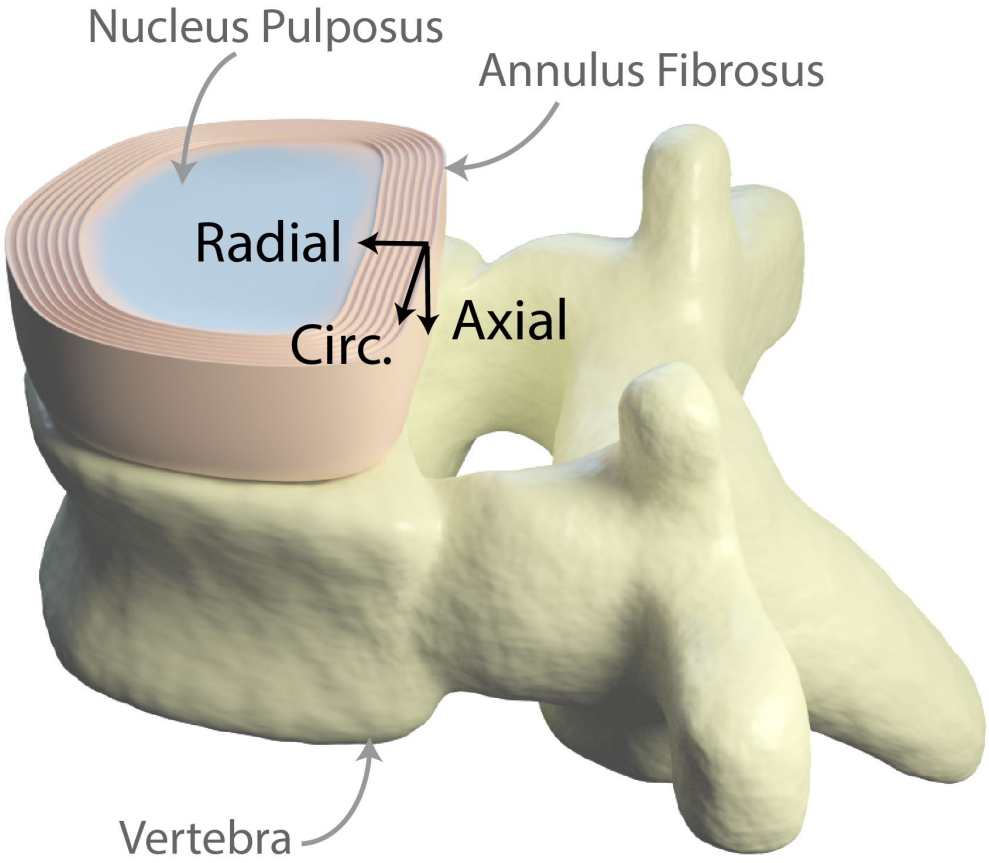
Zeng and Li. *Soft Matter.* 2011.
Li et al. *Scientific Reports.* 2014.

Case Study: A Micromechanical System for the Spine

The Intervertebral Disc of the Spine as a multiscale system

Disc Degeneration:

- 8M spine pathologies / year[1]
- $100B healthcare costs / year[2]



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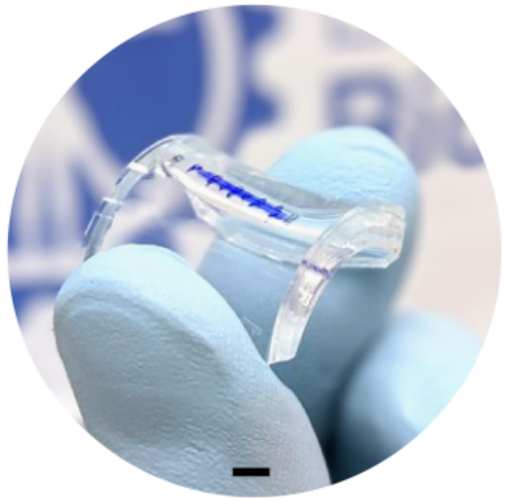
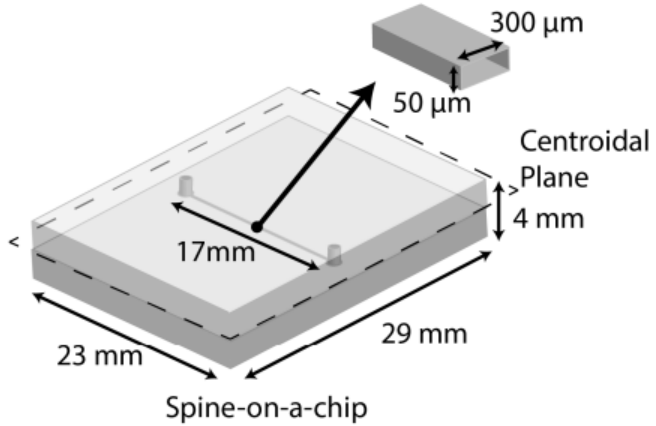
1. Centers for Disease Control and Prevention (CDC), *MMWR Morb Mortal Wkly*, 2009.
2. Katz, J et al., *The J. of Bone and Joint Surgery*, 2006.

Micromechanical chip design

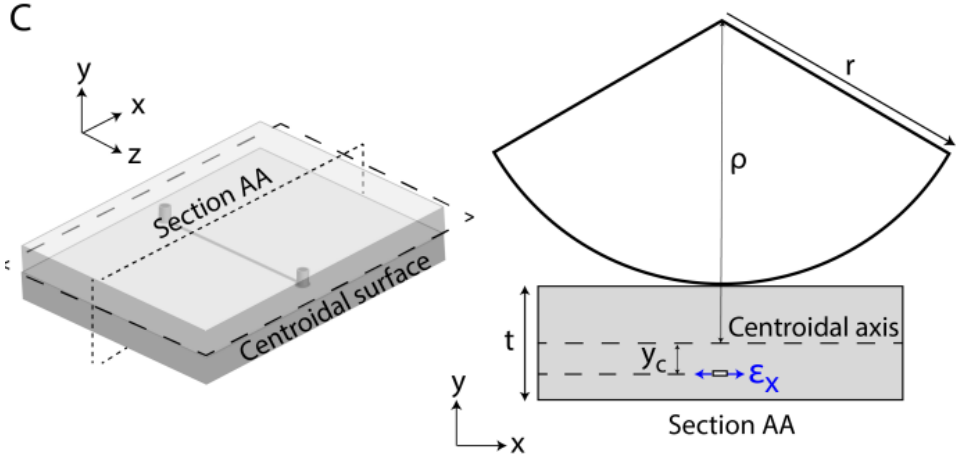
A



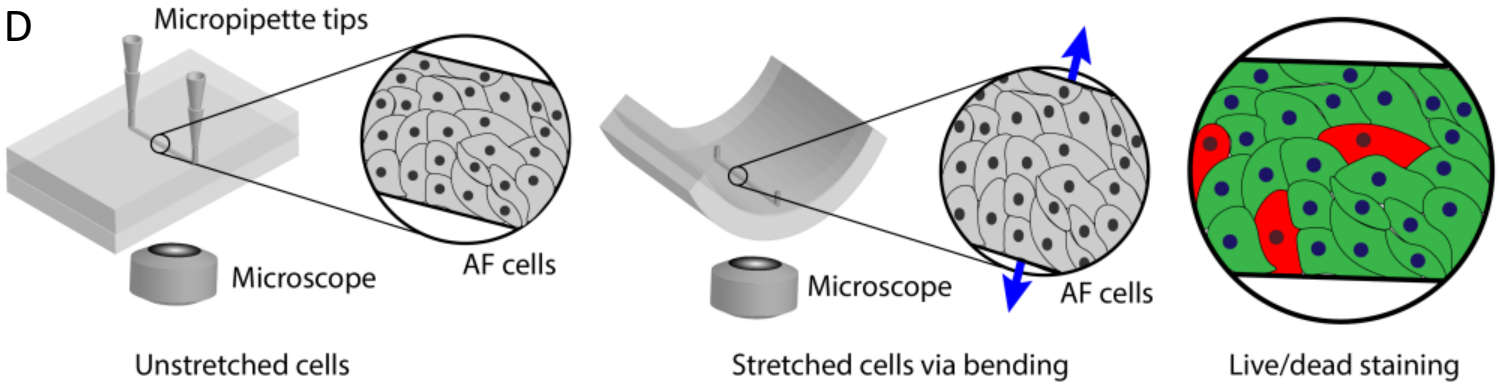
B



C



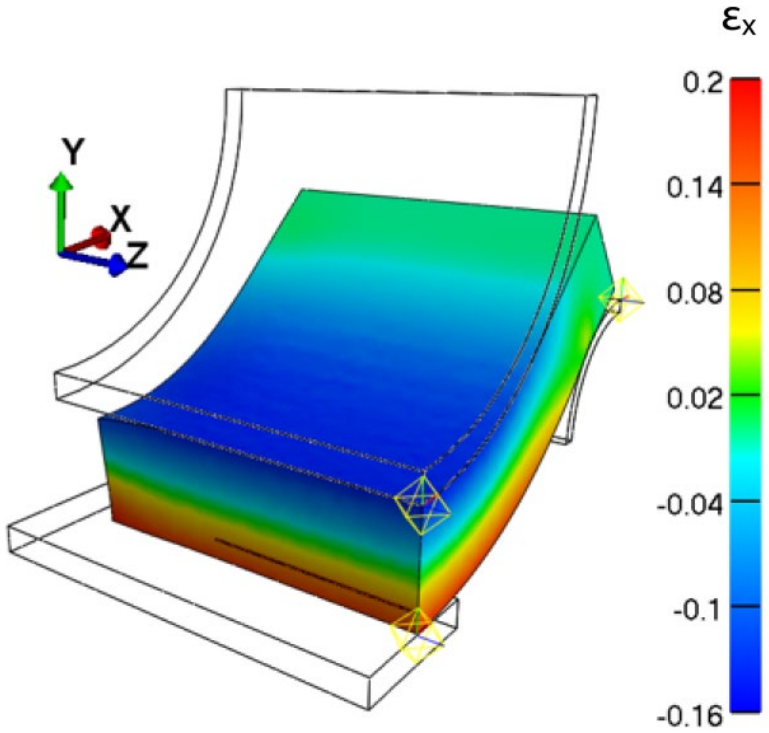
D

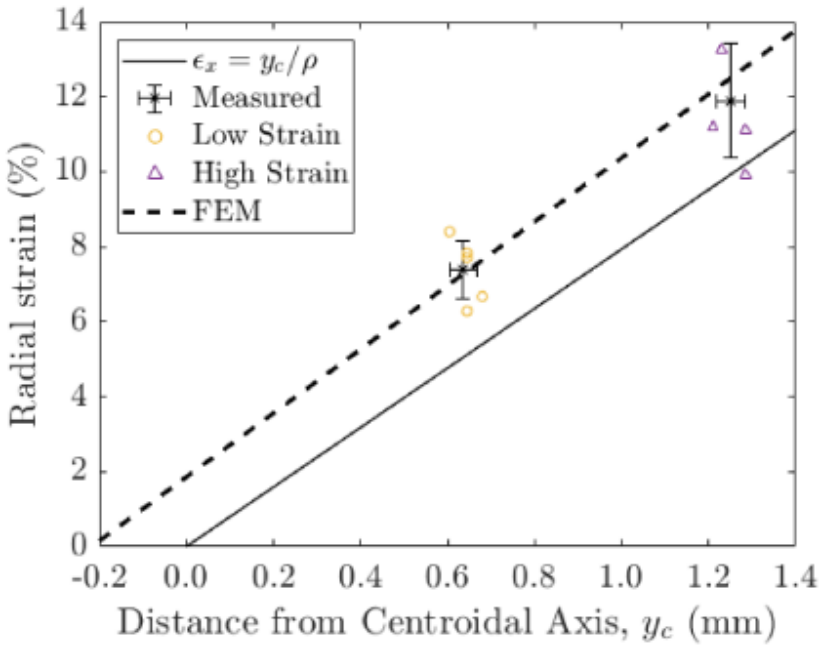


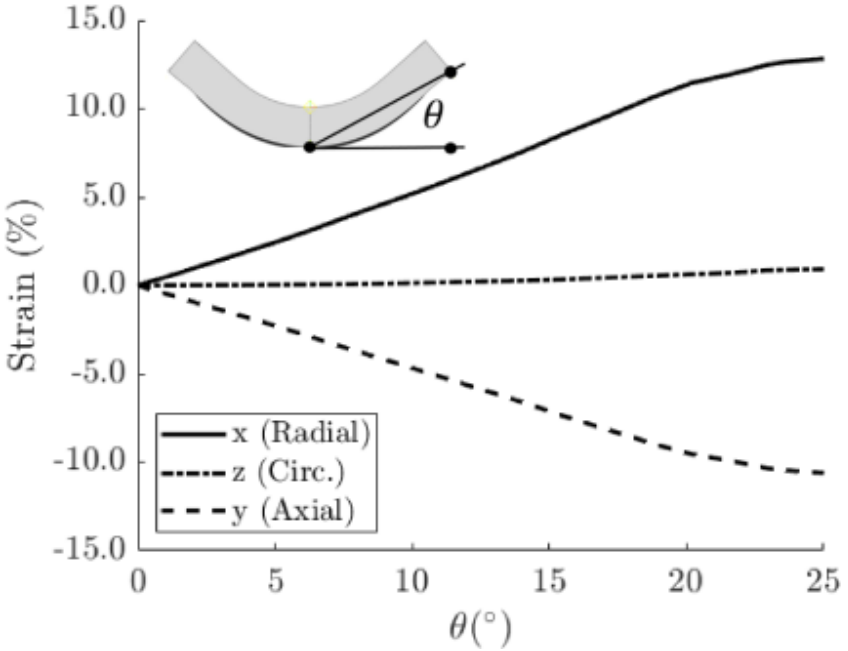
$$\varepsilon_x = \frac{y_c}{\rho} = \frac{y_c}{r + \frac{t}{2}}$$

McKinley et al. *In press.* 2022.

Micromechanical chip model







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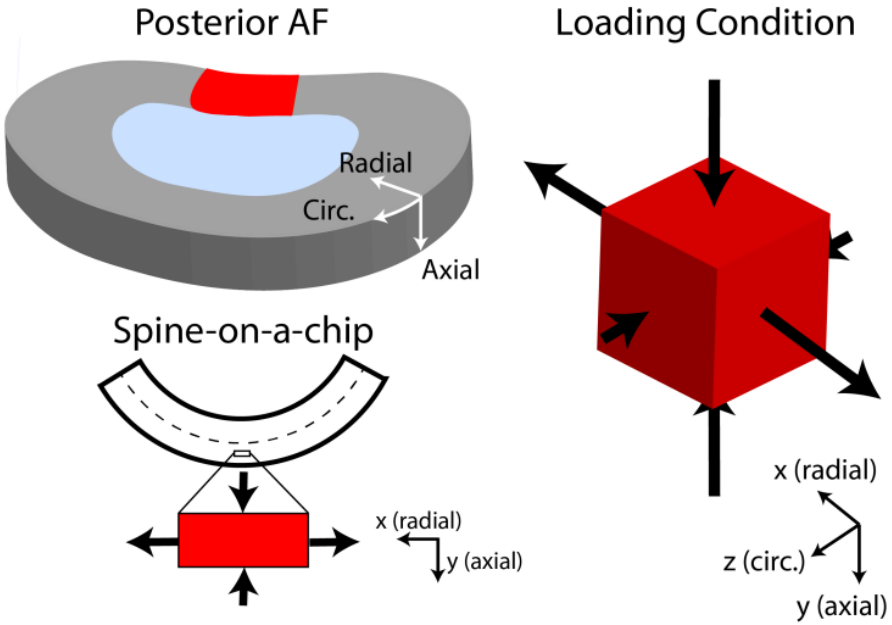
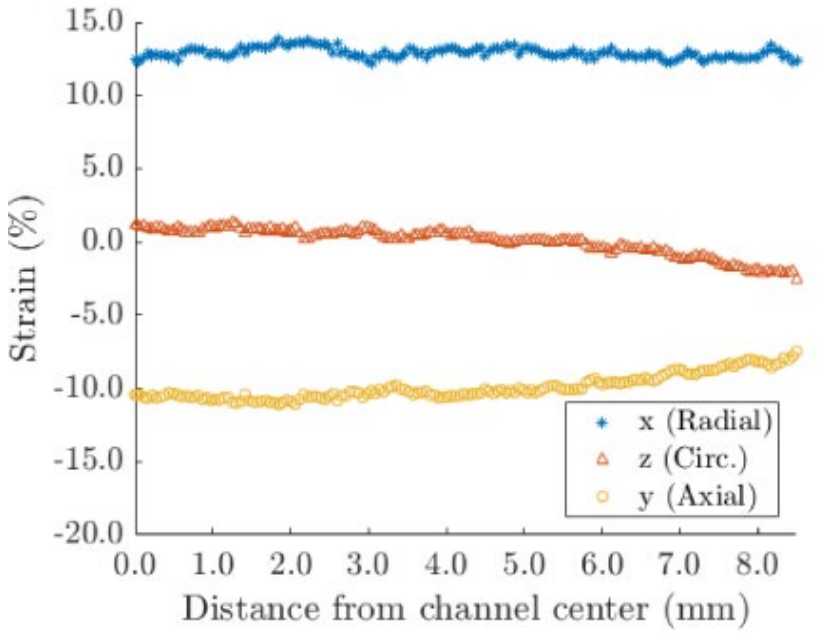
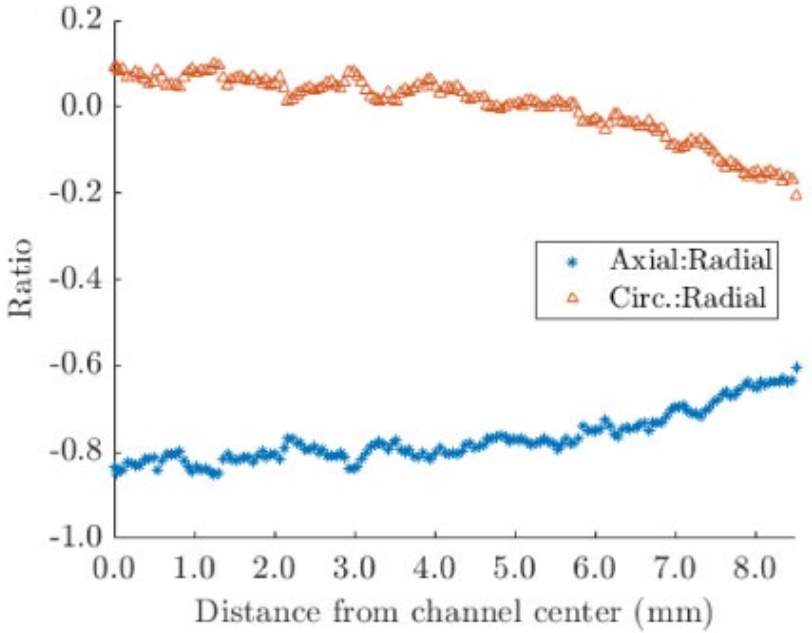
McKinley et al. *In press.* 2022.

Establishing physiological relevancy





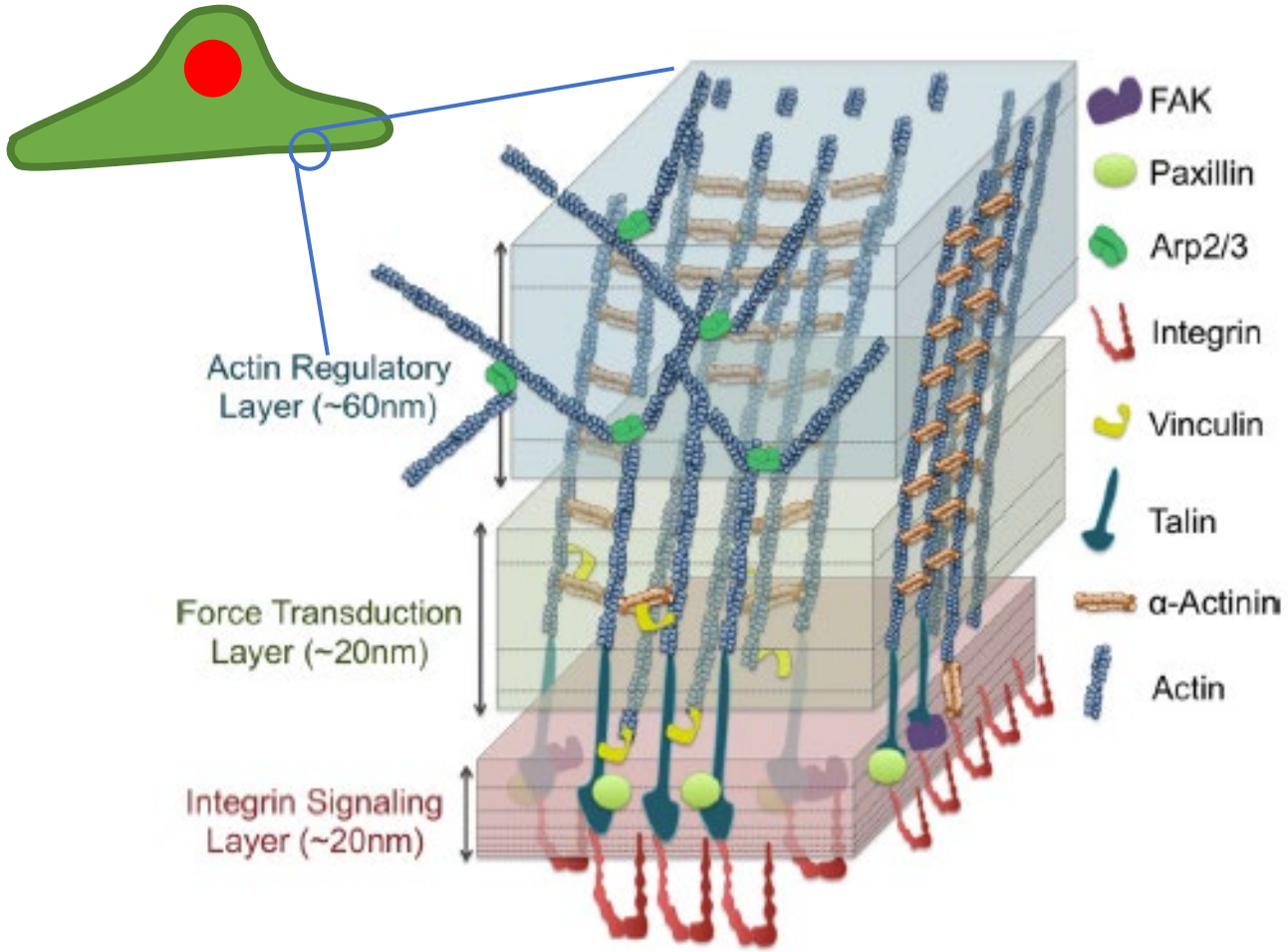


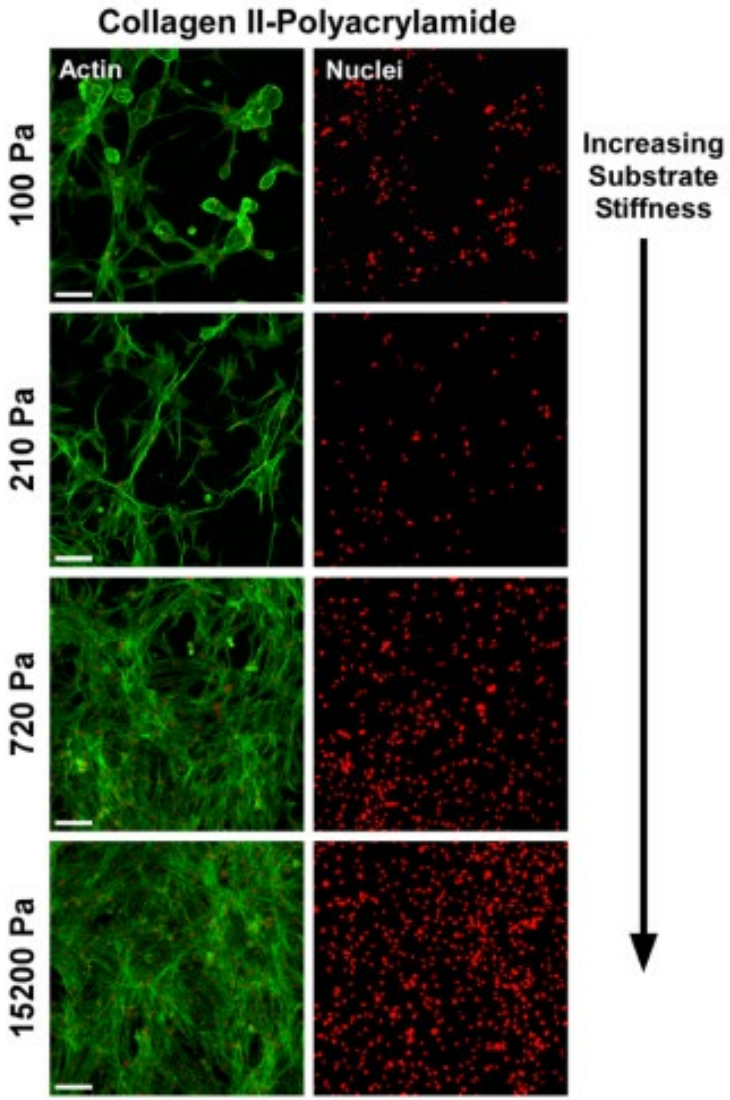
	Circumferential:Radial	Axial:Radial
Posterior AF	0.05 ± 0.35 [31]	-0.95 ± 1.17 [31]
Spine-on-a-chip	-0.0025 ± 0.07	-0.77 ± 0.06
Uniaxial Cell Stretcher*	n/a	-0.55 to -0.4 [38]

*Strex Cell (Strex Inc.)

McKinley et al. *In press.* 2022.

What about the loads imparted to the cells and molecules?





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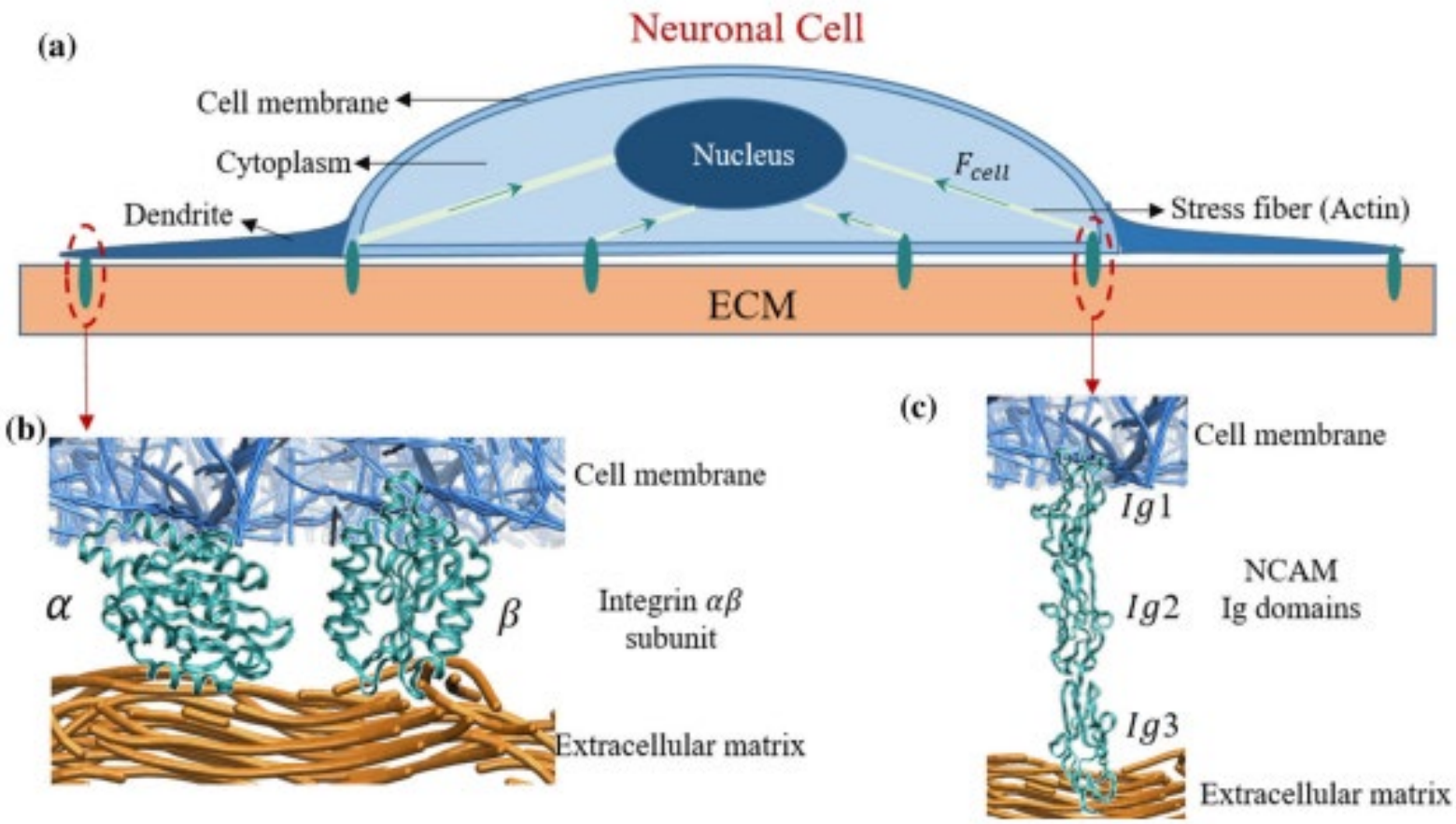
Shams et al. *J. of Biomech. Eng.* 2018.
Gilchrist et al. *PLoS One.* 2011.

Multiscale model to predict cell deformation with varying ECM Stiffness



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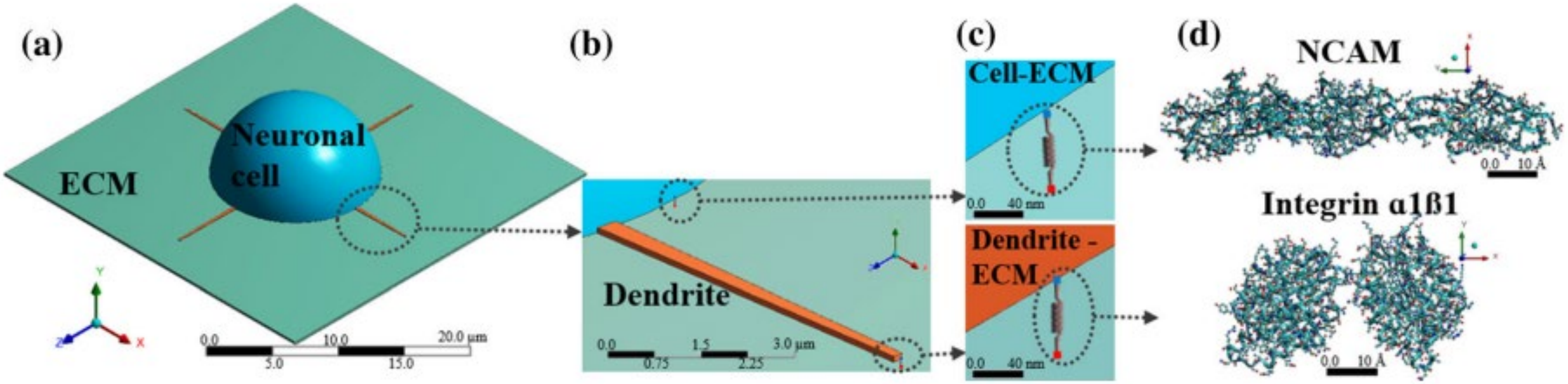
Yasodharababu et al. *Cell and Mol. Bioeng.* 2020.

Multiscale model to predict cell deformation with varying ECM Stiffness



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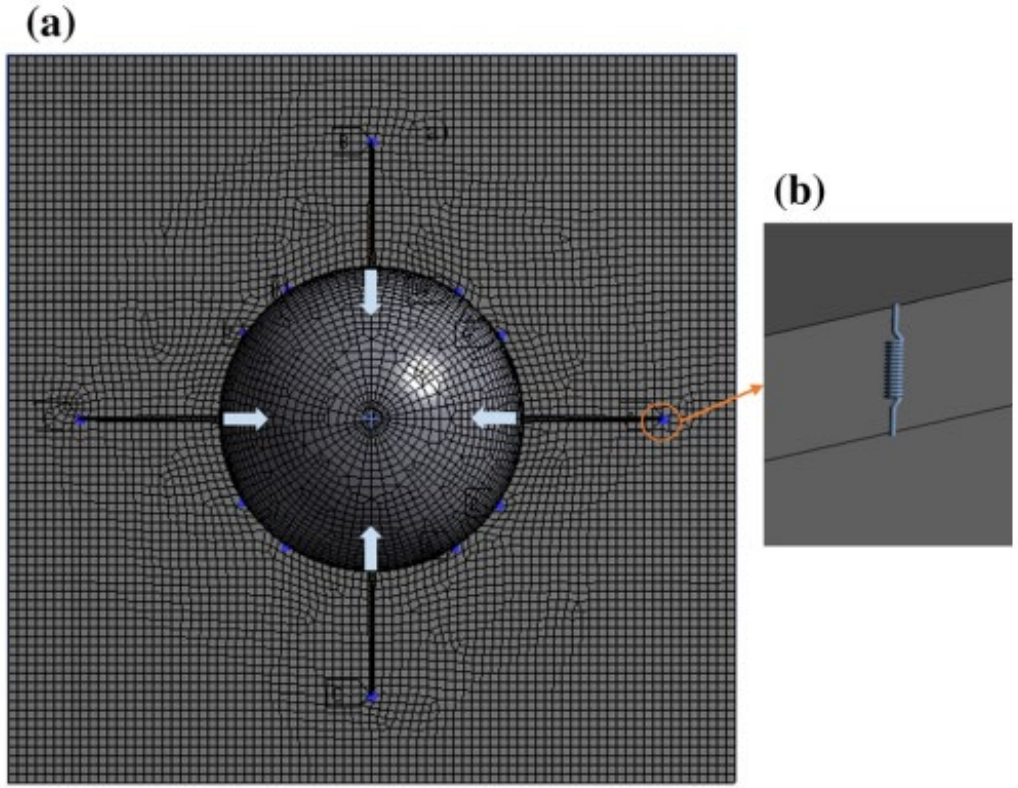

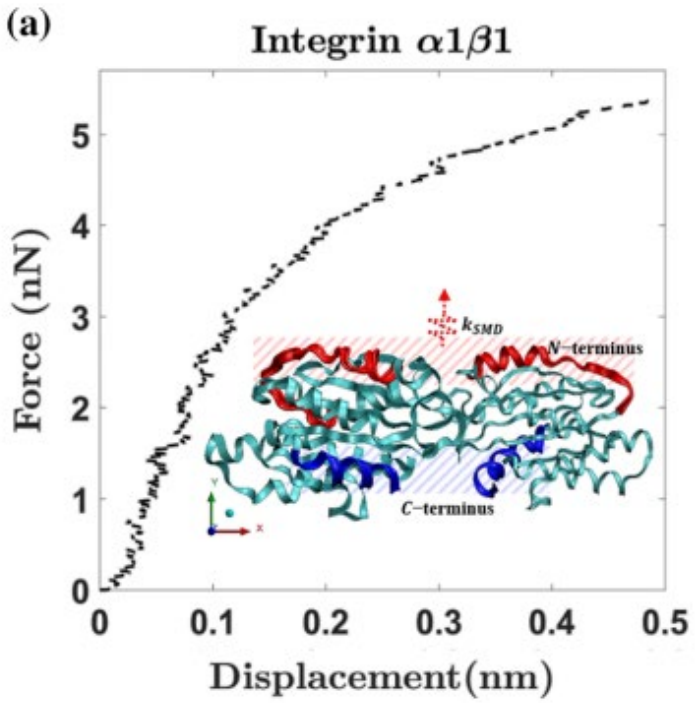

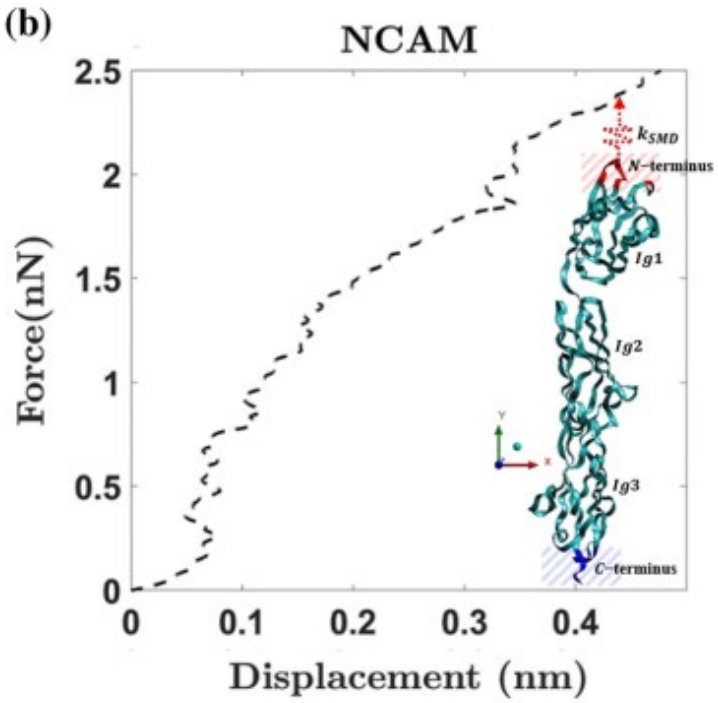

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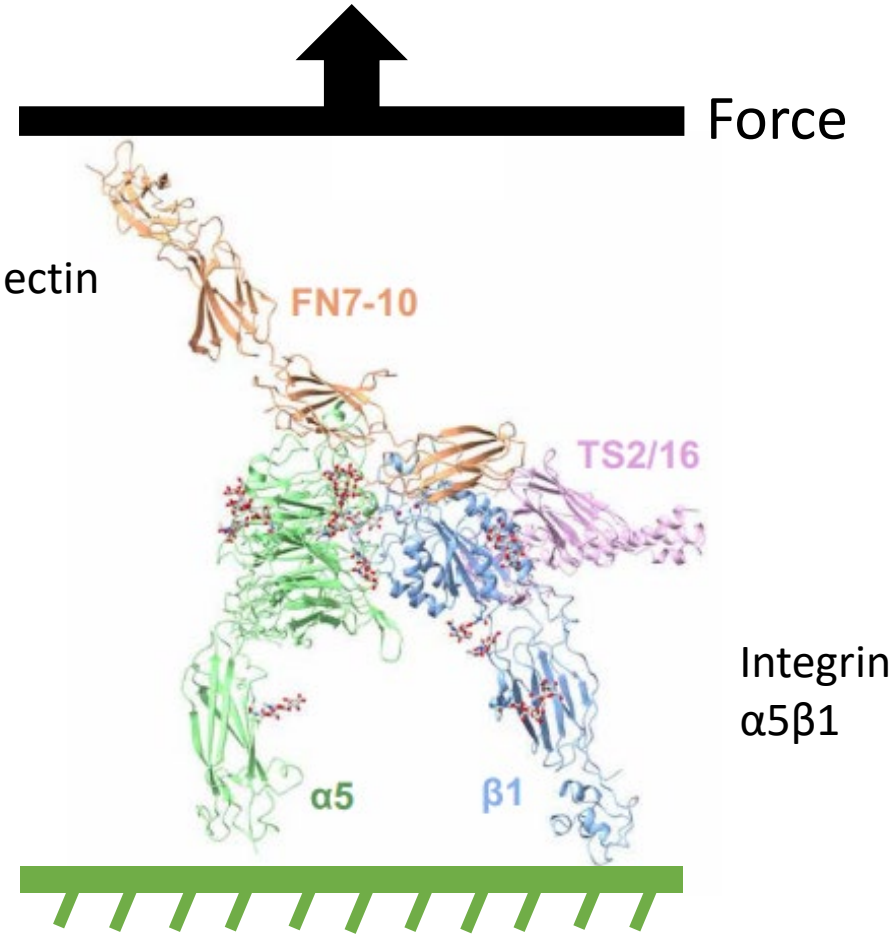
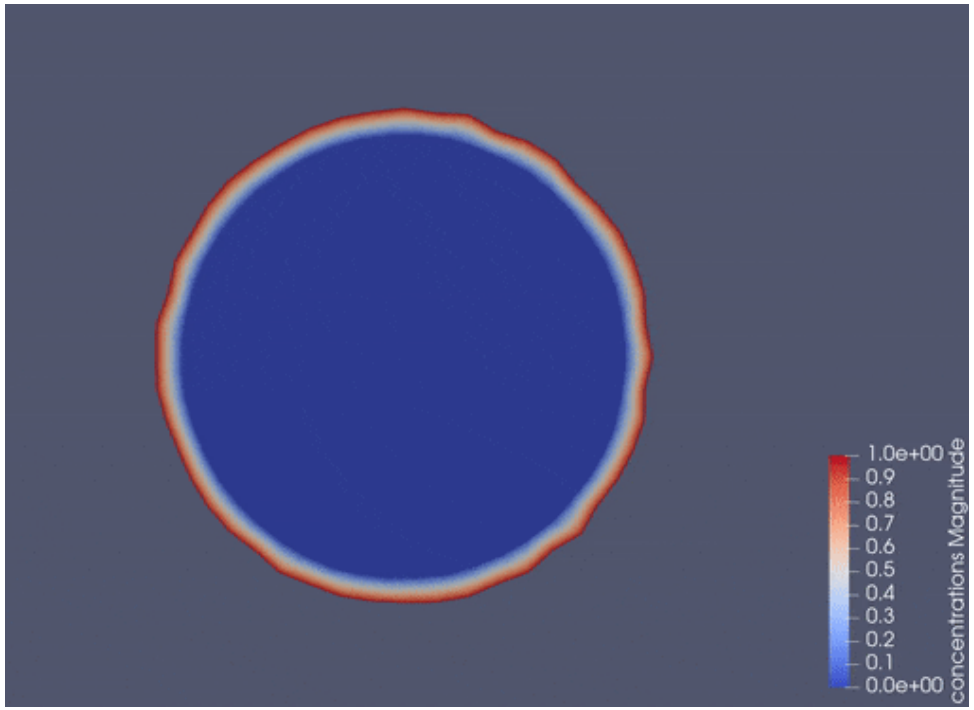
Yasodharababu et al. *Cell and Mol. Bioeng.* 2020.

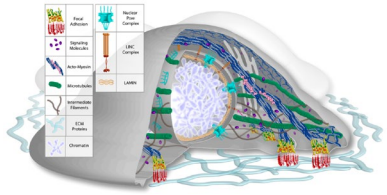
What about the loads imparted to the cells and molecules?





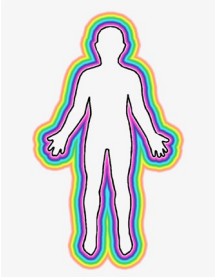
Schumacher et al. *Science Advances.* 2021.

Advantages of multiscale modeling in cell biomechanics



Representative of the system

Detail-oriented



Holistic-ish

Multiscale modeling limitations

Expensive

Excessive

Cumbersome to validate

The cell is a multiscale biomechanical system that can be modeled using multiscale mechanics

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