Kinetic Monte Carlo Simulation of Traction Force Dynamics

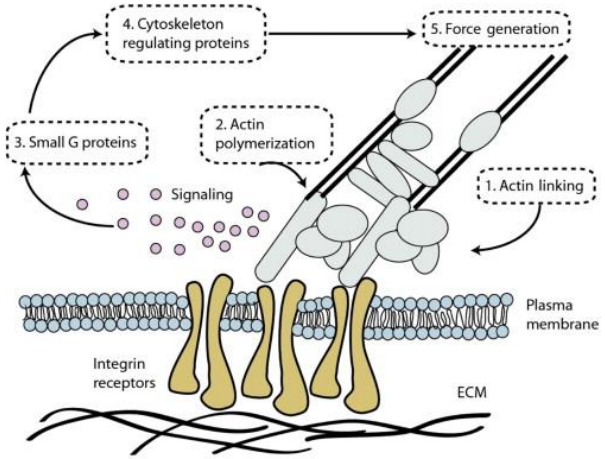
Barituziga Banuna CHEME 7770 FINAL PROJECT May 13, 2020

What is Force Transduction

- Method by which cells respond to physical stimuli around them

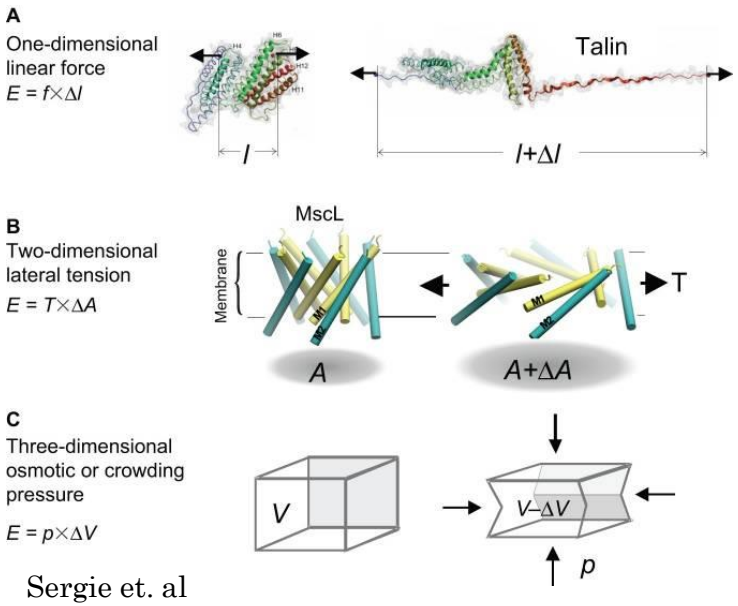
Three Identified Kinds:

Protein Mediated



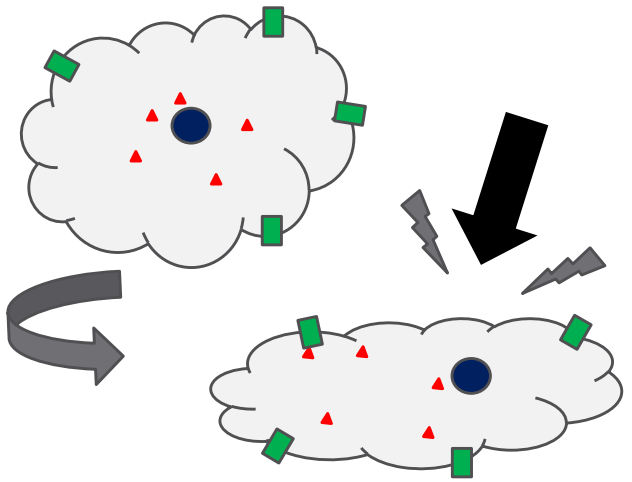
Hasse et. al

Lipid-Initiated Protein



Sergie et. al

Spatial Alteration



Motor Clutch Mechanism

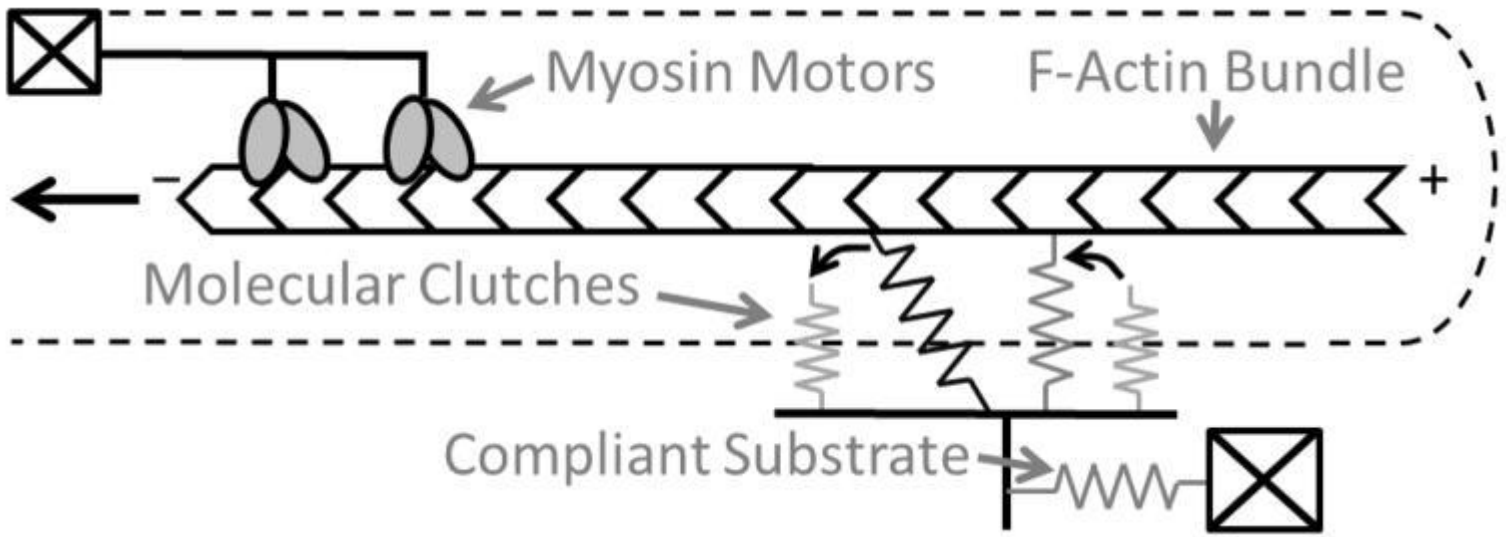
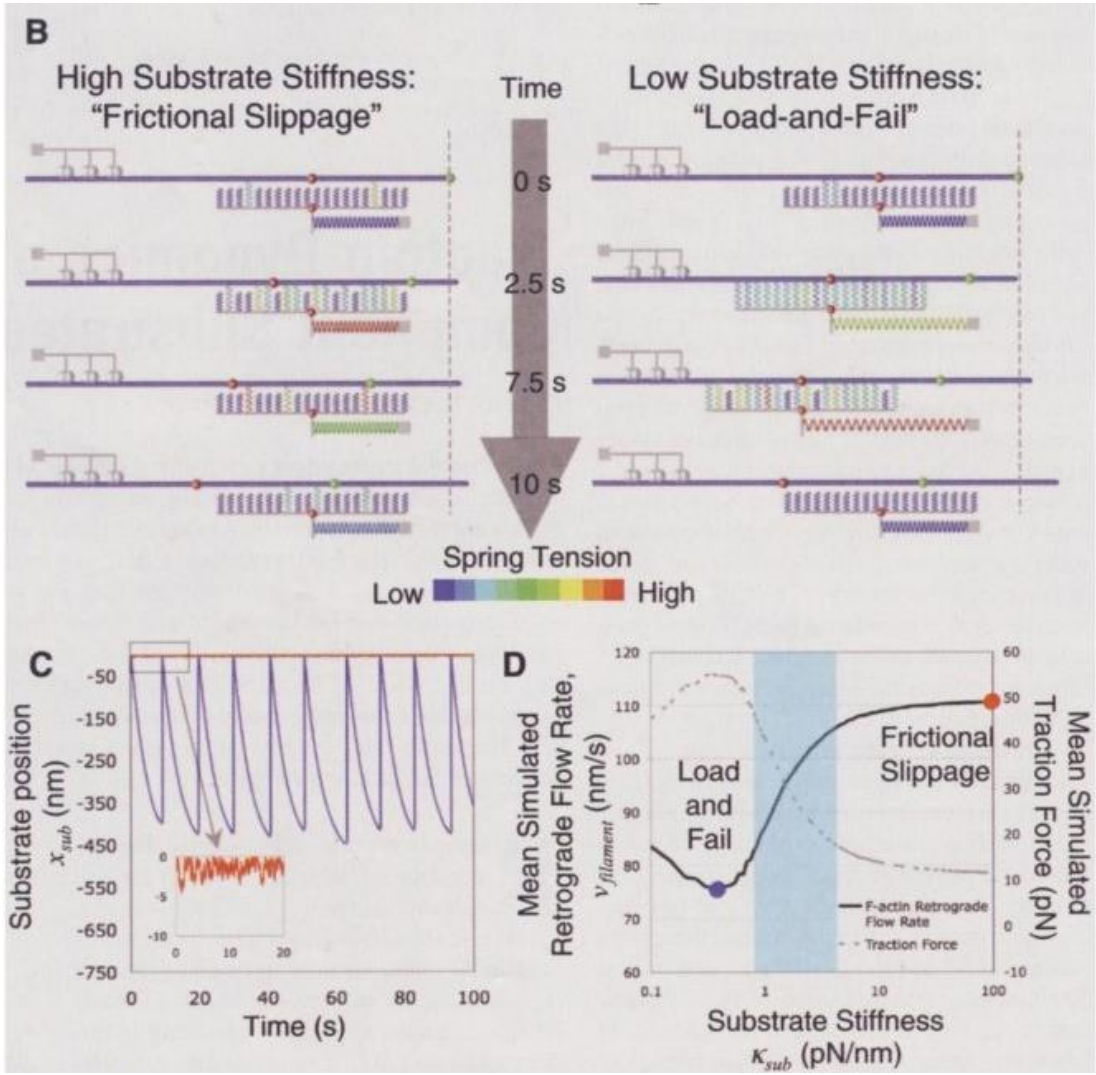


Figure 1: Taken from Bangasser, Benjamin L, and David J Odde. "Master equation-based analysis of a motor-clutch model for cell traction force." *Cellular and molecular bioengineering* vol. 6,4 (2013): 449-459. doi:10.1007/s12195-013-0296-5

Monte Carlo Simulation

Key Take-Aways:

- High Stiffness Substrates Exhibit "Frictional Slippage" behavior
- Compliant Substrates Exhibit "Load-and Fail" behavior



Odde et. al

Key Equations

- Bell Model

$$K_{off,i} = K_{off} \exp\left(\frac{F_{c,i}}{F_b}\right)$$

- Hook's Law

$$F_s = kx$$

Simulation Specifics

- Test 10 regimes of substrate stiffness
- 100000 events
- Contested Binding and Unbinding times

USED PARAMETERS

nm=50 Number of myosin motors

Fm=-2 Motor stall force in pN

vu=-120 Unloaded motor velocity in nm/s

nc=50 Number of molecular clutches

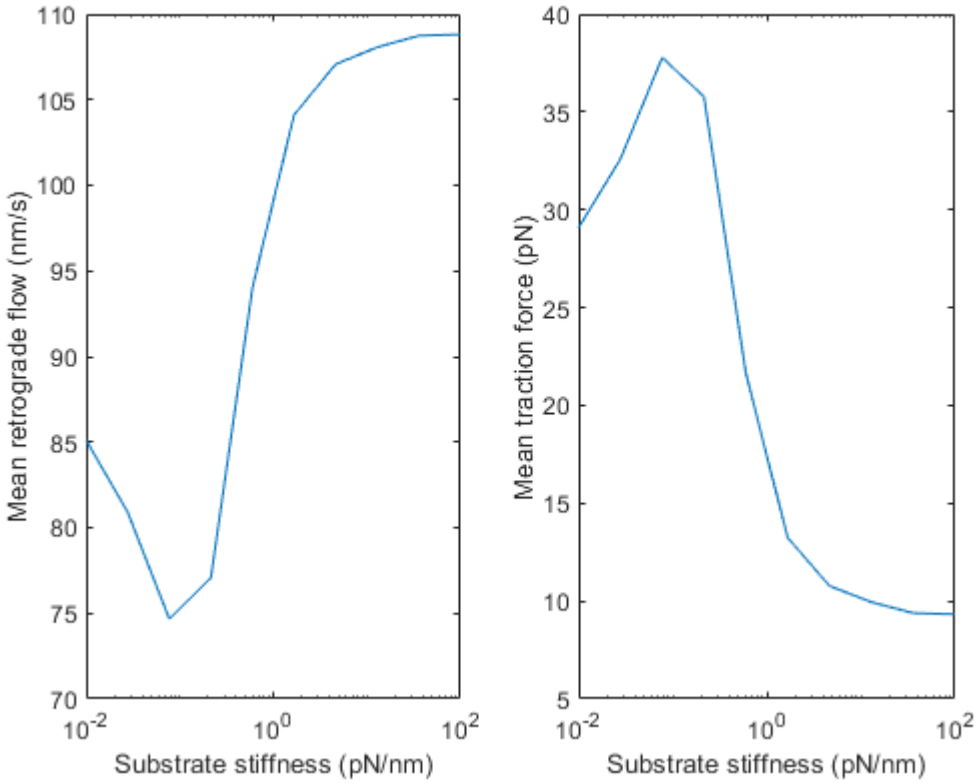
kon=0.3 On rate constant in 1/s

koff=0.1 Off rate constant in 1/s

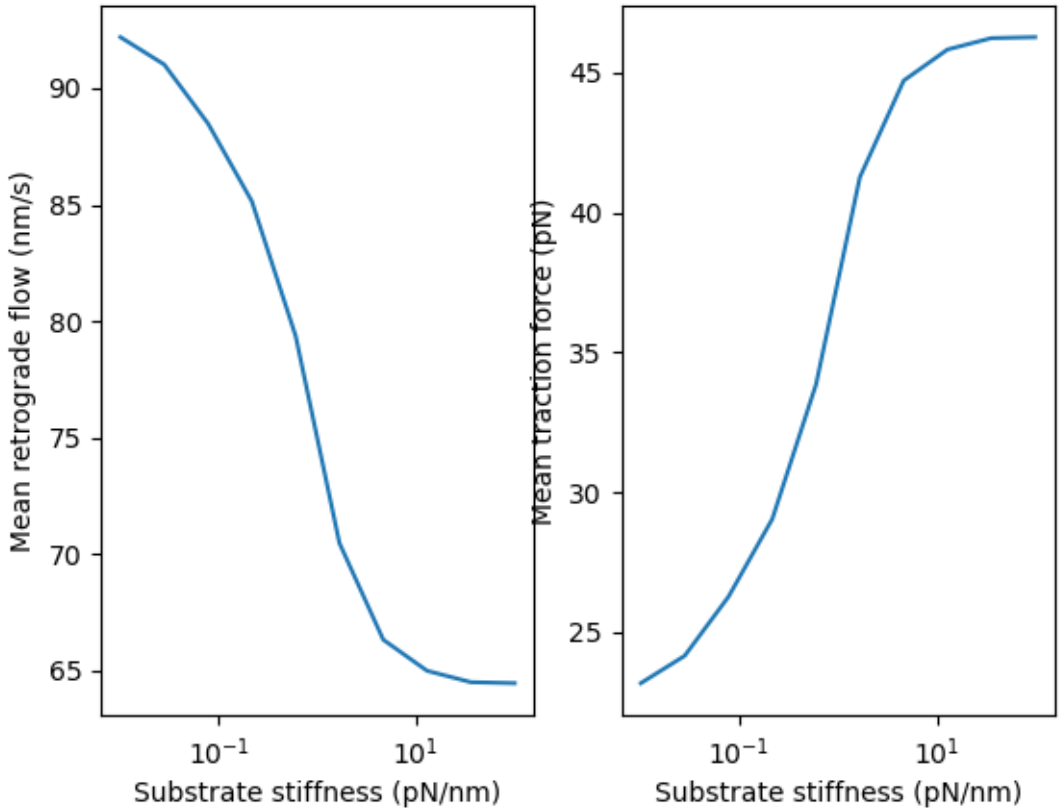
Fb=-2 Bond rupture force in pN

Kc=0.8 Clutch spring constant in pN/nm

Replication of Simulation



Odde & Bangasser SIM



My Attempt

Code for original simulation can be found at http://oddelab.umn.edu/software.html

Expansion of Model

- Viscoelastic Consideration – Non-linear stress response
- Time Assay

References

1. Bangasser, Benjamin L et al. “Determinants of maximal force transmission in a motor-clutch model of cell traction in a compliant microenvironment.” *Biophysical journal* vol. 105,3 (2013): 581-92. doi:10.1016/j.bpj.2013.06.027

2. Bangasser, Benjamin L, and David J Odde. “Master equation-based analysis of a motor-clutch model for cell traction force.” *Cellular and molecular bioengineering* vol. 6,4 (2013): 449-459. doi:10.1007/s12195-013-0296-5

3. Chan and Odde (2008), Traction dynamics of filopodia on compliant substrates, Science, DOI: 10.1126/science.1163595

4. Elosegui-Artola et al. (2016), Mechanical regulation of a molecular clutch defines force transmission and transduction in response to matrix rigidity, Nature Cell Biology, doi:10.1038/ncb3336

5. Gong, Z.; Szczesny, S. E.; Caliari, S. R.; Charrier, E. E.; Chaudhuri, O.; Cao, X.; Lin, Y.; Mauck, R. L.; Janmey, P. A.; Burdick, J. A.; Shenoy, V. B. Matching material and cellular timescales maximizes cell spreading on viscoelastic substrates. https://www.pnas.org/content/115/12/E2686 (accessed May 14, 2020).

6. Haase, K.; Al-Rekabi, Z.; Pelling, A. E. Mechanical Cues Direct Focal Adhesion Dynamics. https://www.sciencedirect.com/science/article/pii/B9780123946249000051 (accessed May 14, 2020)

7. P. Bieling et. al Force Feedback Controls Motor Activity and Mechanical Properties of Self-Assembling Branched Actin Networks. Cell VOLUME 164, ISSUE 1-2, P115-127, JANUARY 14, 2016. DOI:https://doi.org/10.1016/j.cell.2015.11.057

8. Paul A. Janmey David A. Weitz. Dealing with mechanics: mechanisms of force transduction in cells. Cell VOLUME 29, ISSUE 7, P364-370, JULY 01, 2004. DOI:https://doi.org/10.1016/j.tibs.2004.05.003

9. Sukharev, Sergei, and Frederick Sachs. “Molecular force transduction by ion channels: diversity and unifying principles.” *Journal of cell science* vol. 125,Pt 13 (2012): 3075-83. doi:10.1242/jcs.092353