Essential equations

$$\frac{p_2}{p_1} = K_{eq} = \frac{k_+}{k_-} = \exp\left[-\frac{(G_2 - G_1) - F(x_2 - x_1)}{k_B T}\right]$$

$$k_+ = C \exp\left[-\frac{(G_a - G_1) - F(x_a - x_1)}{k_B T}\right]$$

$$k_- = C \exp\left[-\frac{(G_a - G_2) - F(x_a - x_2)}{k_B T}\right]$$

“Progress in science depends on new techniques, new discoveries and new ideas, probably in that order.” (Sydney Brenner)

Nobel Prize in Physiology (with MIT’s Robert Horvitz) in 2002

Photograph removed due to copyright restrictions.

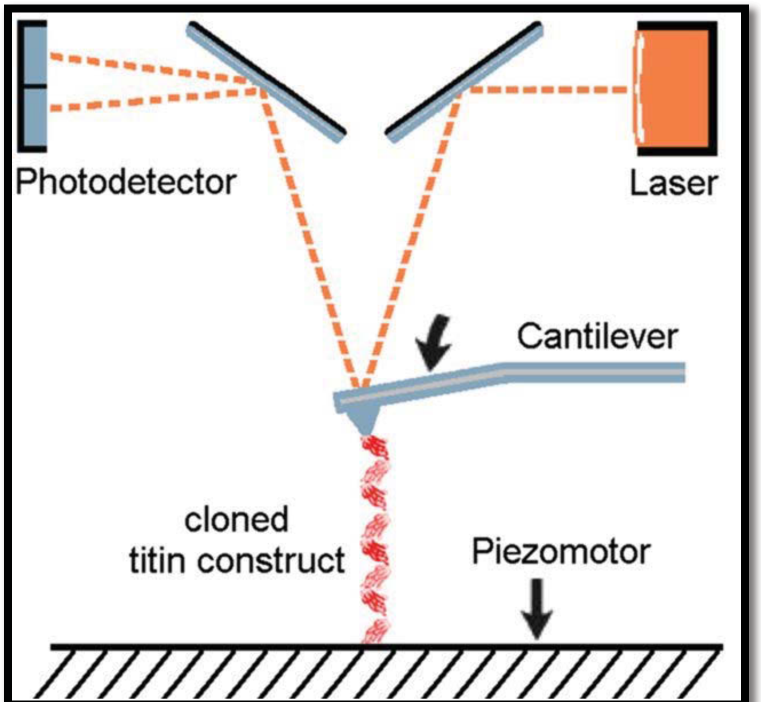
Forces at the molecular level

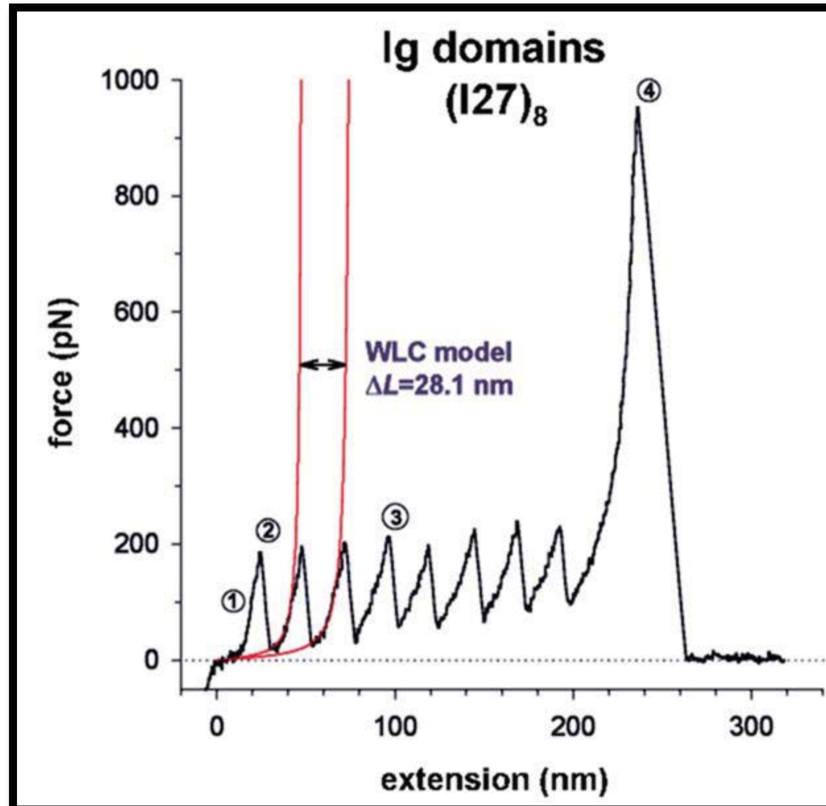
Type of Force	Example	Rupture Force*	Length	Energy
Breaking of a covalent bond	C-C	~1600 pN	0.1-0.5 nm	~ 1.6×10^{-19} J ~ 90-350 kT
Breaking of a noncovalent bond.	Biotin/streptavidin	~5-160 pN	~ 1 nm	~ 1.6×10^{-19} J ~40 kT
Breaking of a weak bond.	Hydrogen bond	~4-20 pN	~ 0.3nm	~ 4-8 $\times 10^{-21}$ J ~ 1 kT
Developed by molecular motor	Kinesin walking on microtubule	~5 pN	8 nm (step size)	~ 40×10^{-21} Nm ~10 kT

1 nm = 10^{-9} m
1pN = 1×10^{-12} N
[Energy] = F L = [N m] or [J]
$k = 1.38 \times 10^{-23}$ J/K
$kT = 4.14 \times 10^{-21}$ J = 4.14 pN * 1 nm

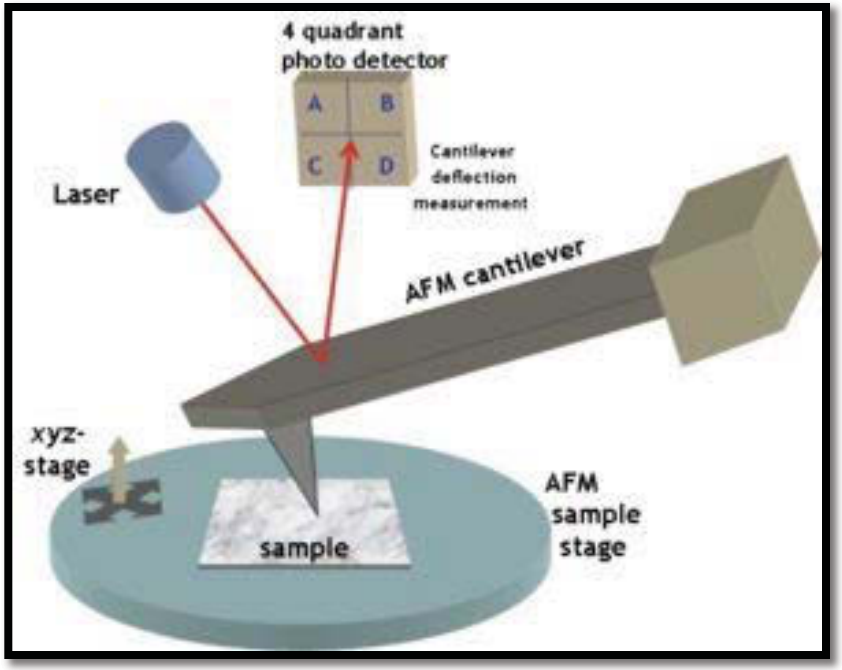
* Rupture forces generally depend on the rate of force application! Faster force application requires higher rupture forces!

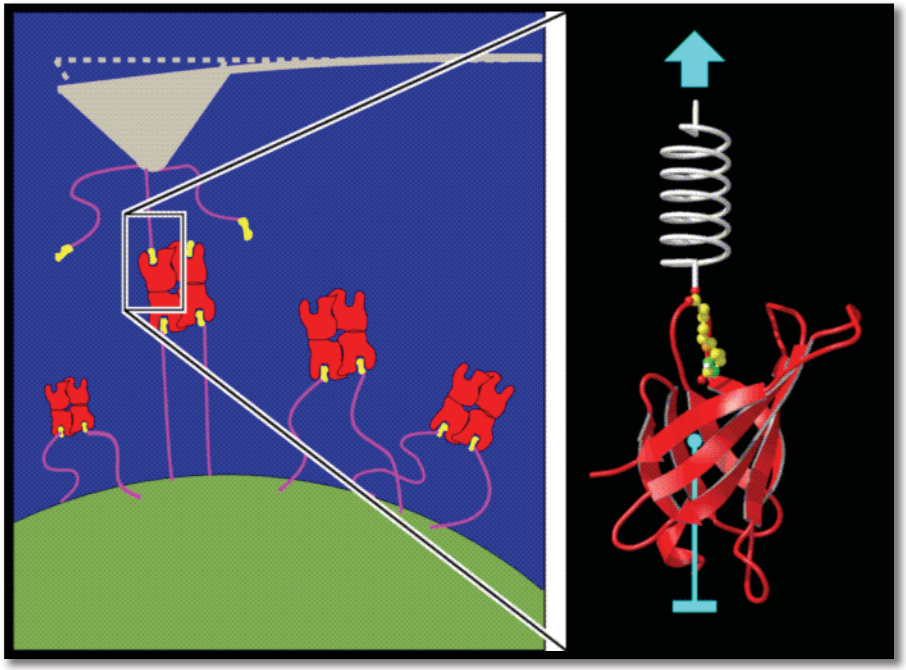
Example:
Unfolding of titin under force





Atomic force microscope

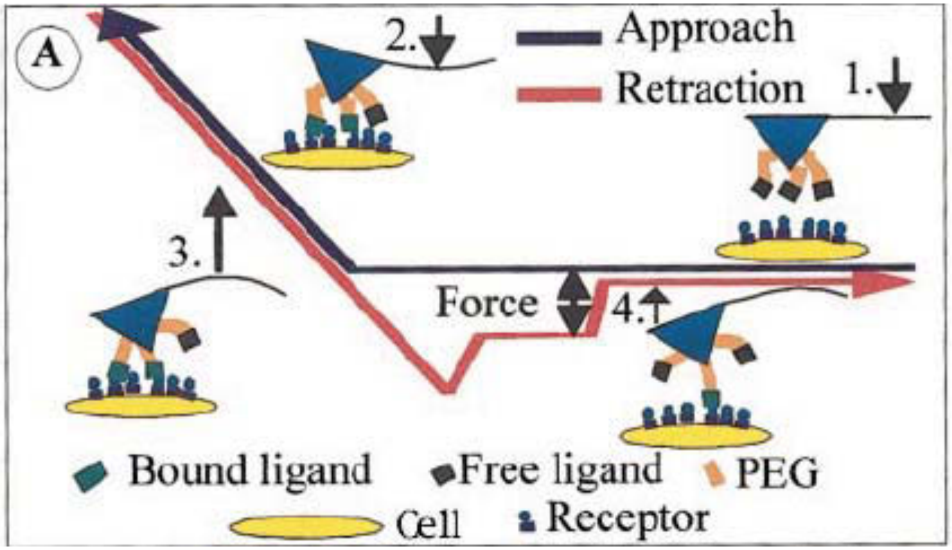




Force: pN –> nN (or higher)
depending on cantilever stiffness

Resolution: better than nm

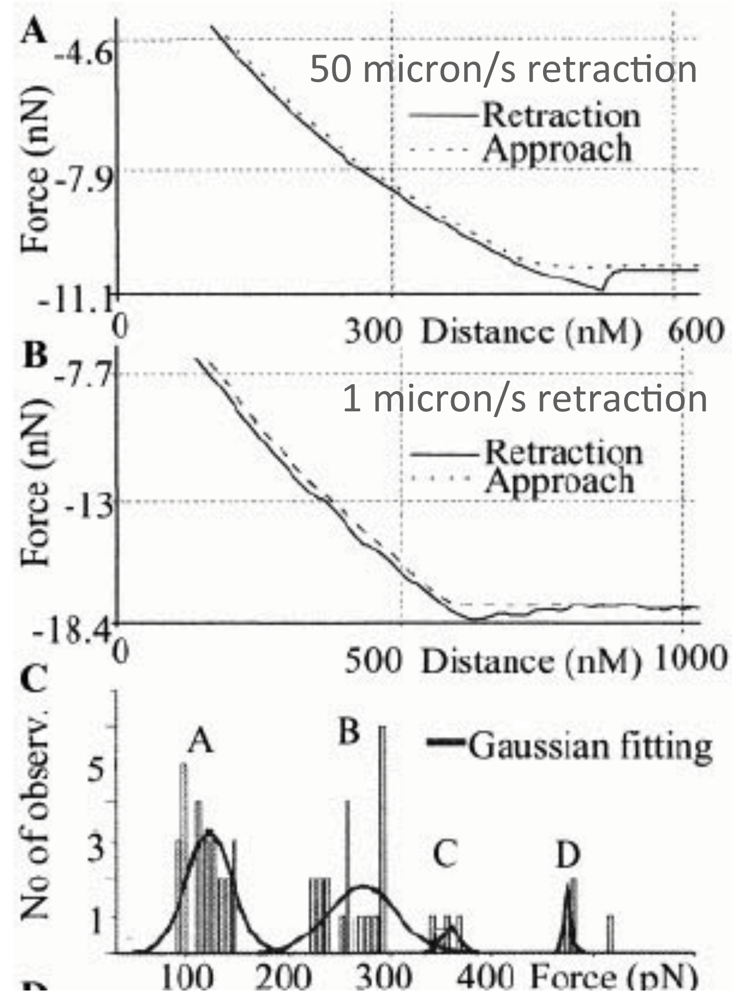
Strength of integrin bonds to ECM ligands



AFM used to measure the strength of integrin bonds to various RGD ligands.

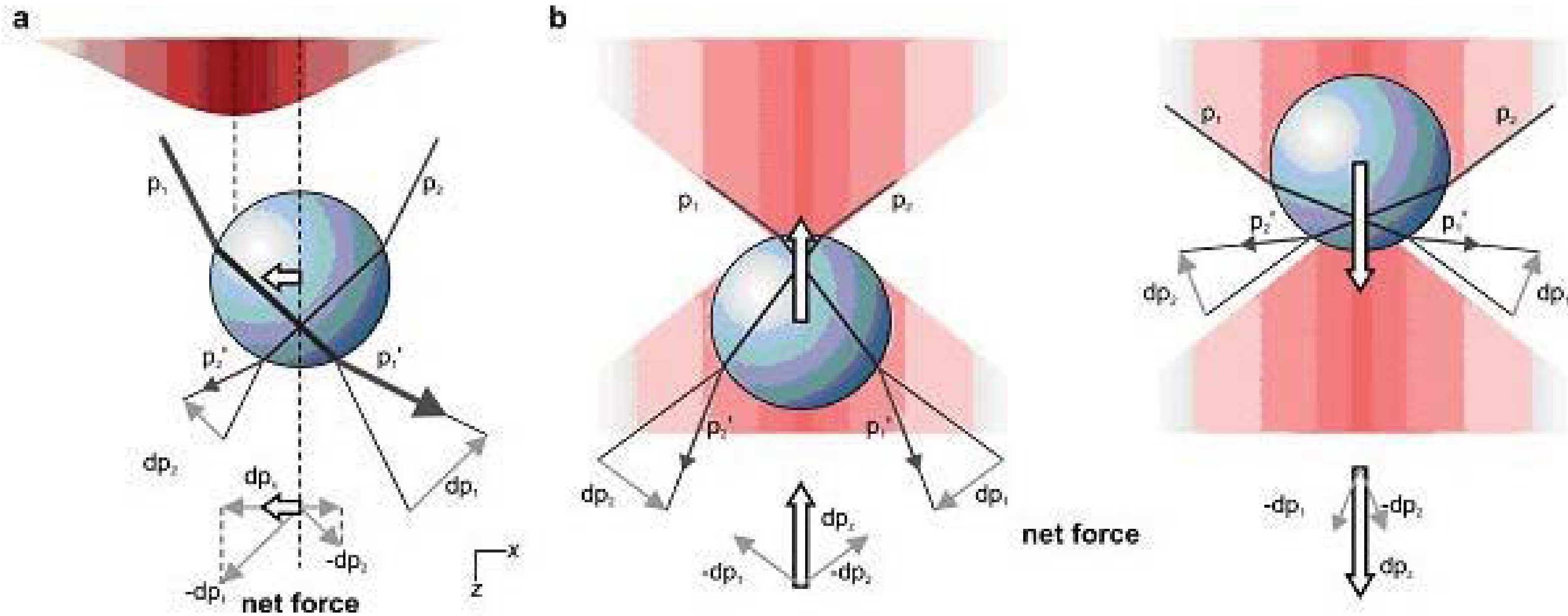
Single bond forces were 32-97 pN.

Lower forces (~ 10 pN or less?) are likely adequate to produce conformational changes.



Lehenkari & Horton, BBRC, 1999

Optical trapping



Qualitative picture of the origin of the trapping force. [a] Lateral gradient force of a Gaussian laser beam profile. Since rays p1 and p2 have different intensity, the momentum changes of these rays (Δp1 and Δp2, respectively) differ in magnitude, causing a net reaction force on the refracting medium in the direction of highest intensity. The x–projection of this force Δpx tends to counteract a displacement from the laser beam axis, pulling the particle to the center of beam. [b] Axial gradient force towards the focus of the trapping light. The white arrows indicate the net restoring force in the respective directions.

Optical traps

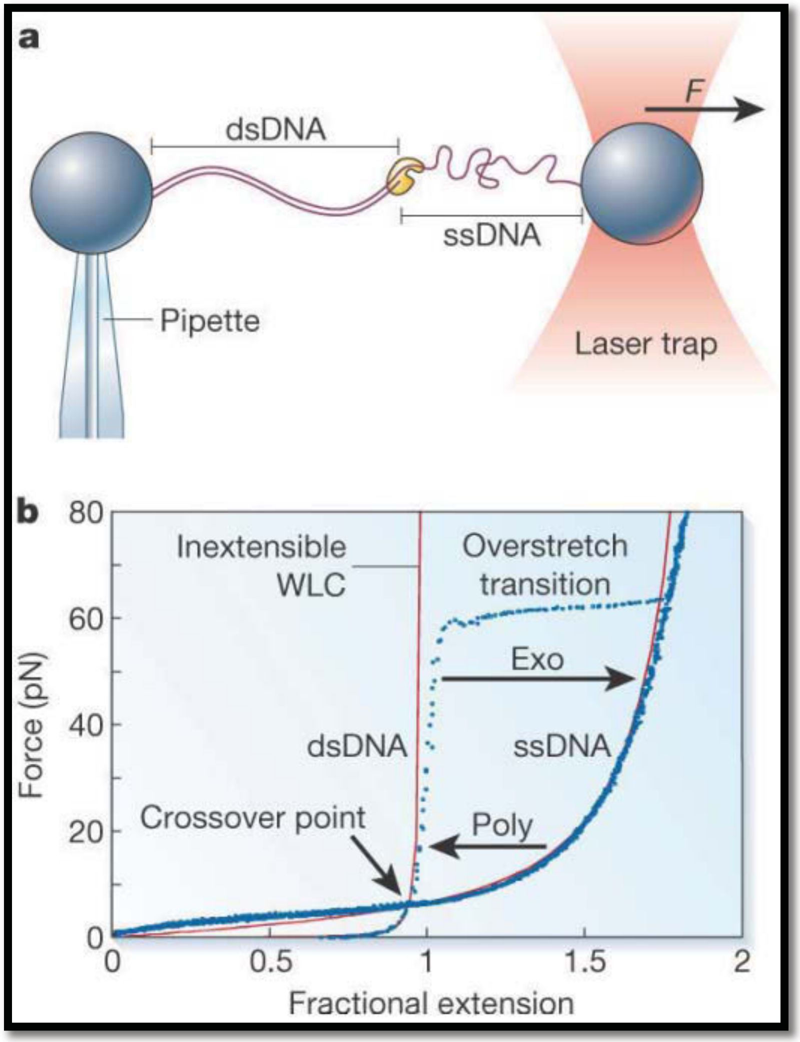
Force application:

~10-200 pN

limited by laser power

Resolution (bead):

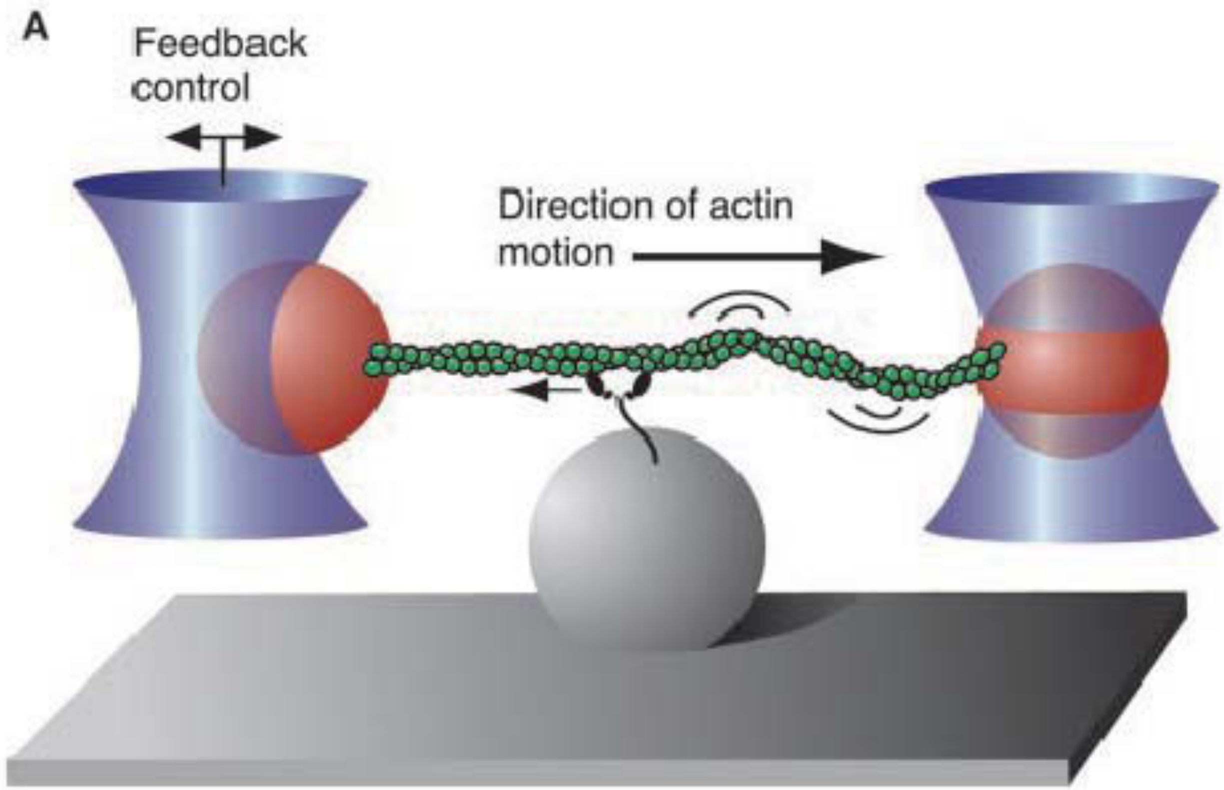
Better than 1 nm!

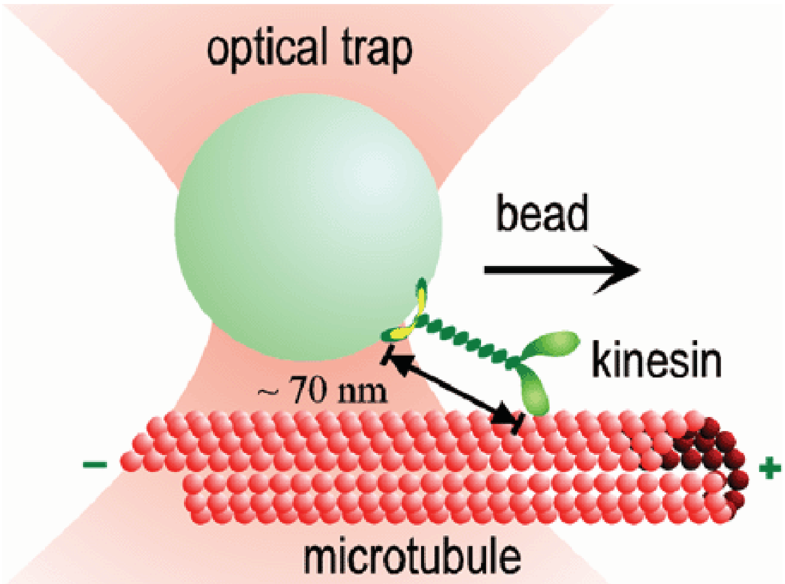


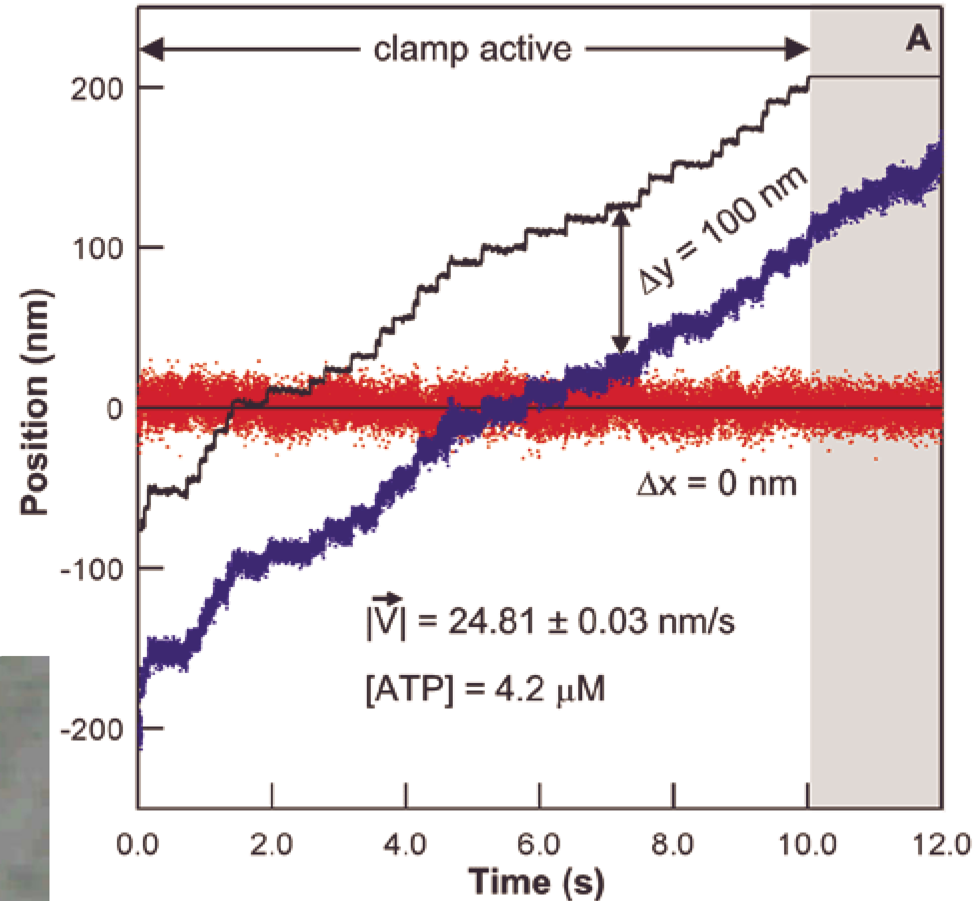
Source: Bustamante, Carlos, et al. "Ten Years of Tension: Single-molecule DNA Mechanics." *Nature* 421, no. 6921 (2003): 423-7.

Bustamante *et al. Nature*

Myosin experiments, dumbell geometry

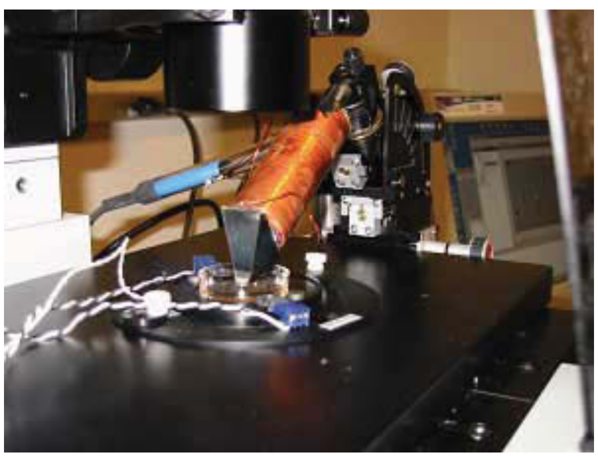






https://web.stanford.edu/group/blocklab/kinesin/kinesin.html

Magnetic trapping



Courtesy of Peter So. Used with permission.

So lab magnetic force

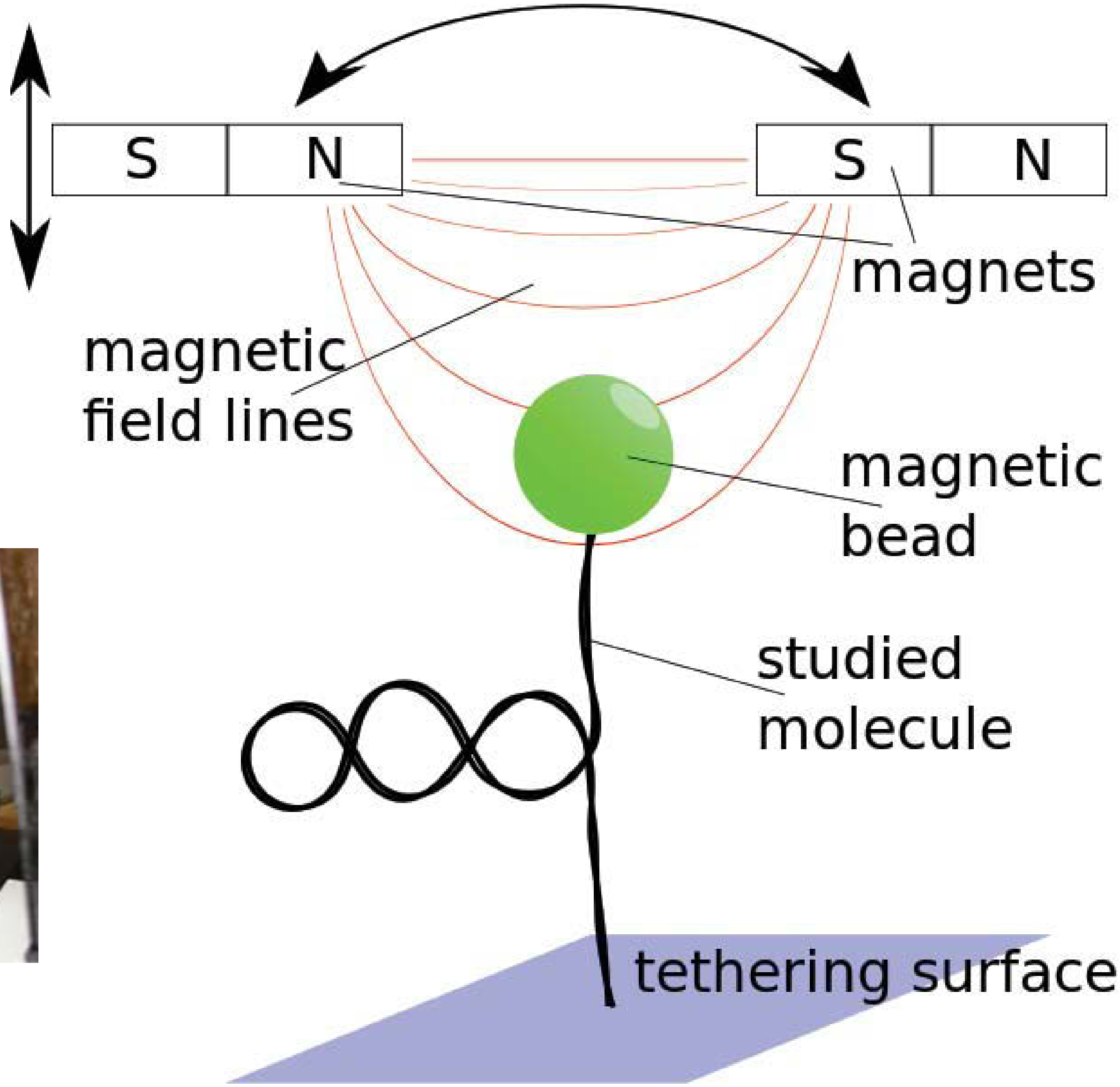
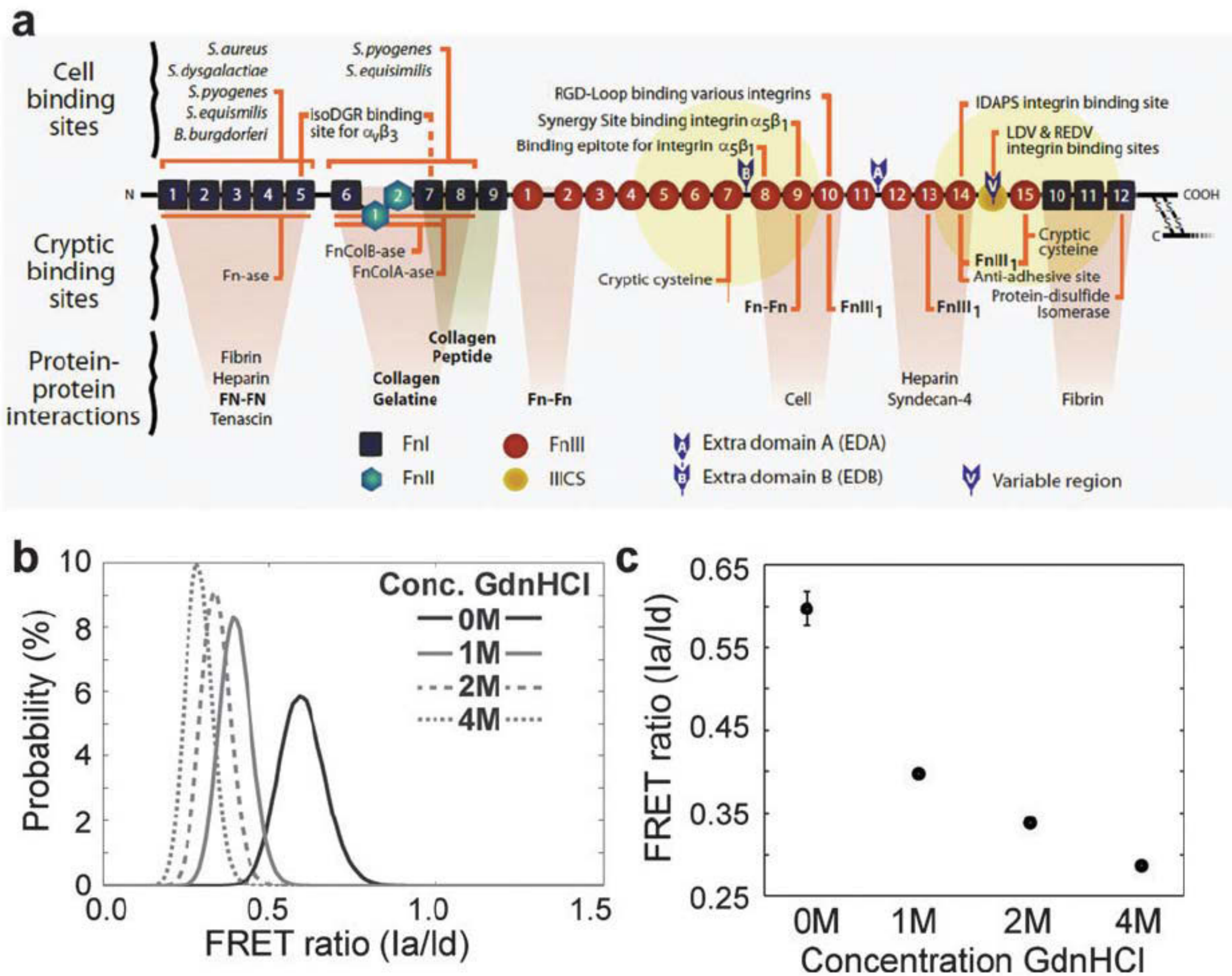


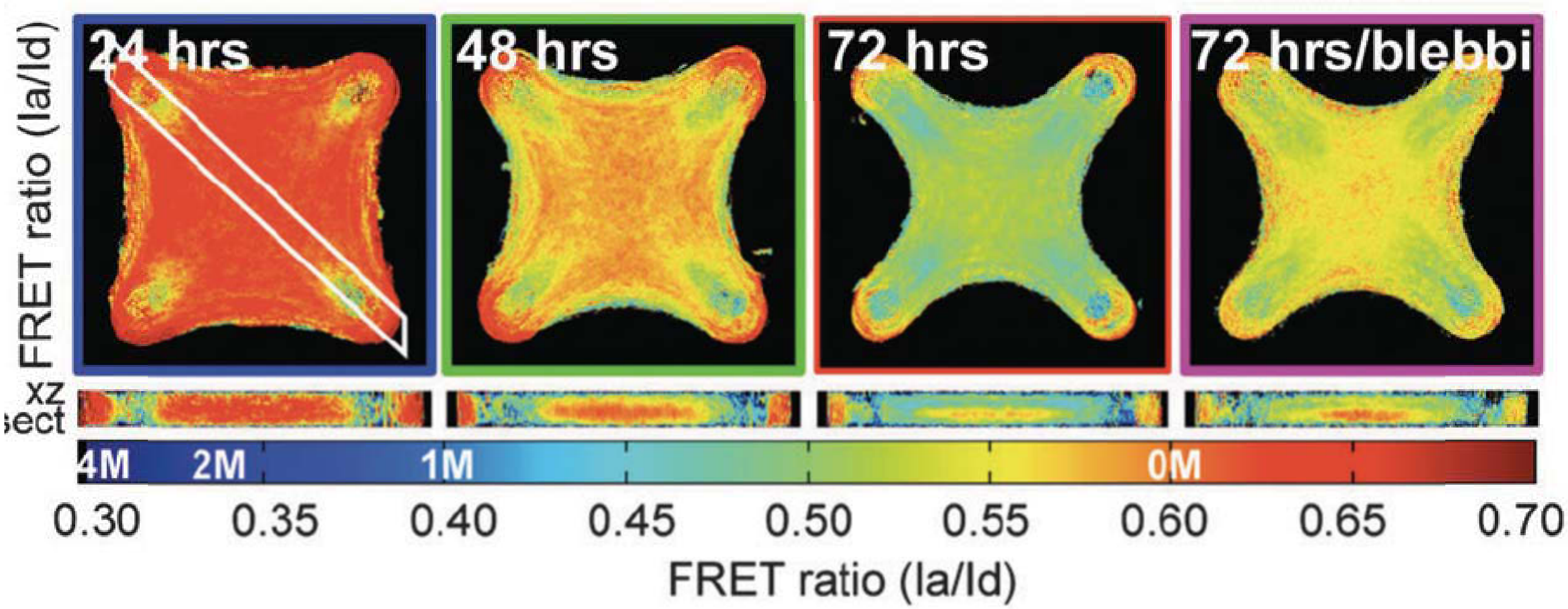
Image is by Daniel Förster and is in the public domain.

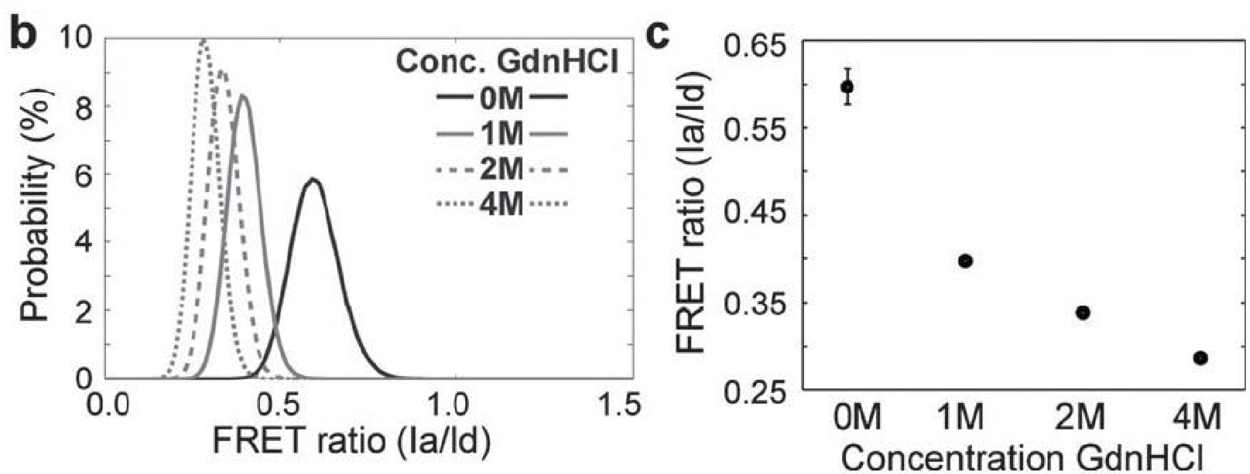
Force-induced fibronectin assembly and matrix remodeling in a 3D microtissue model of tissue morphogenesis†

Wesley R. Legant,[a] Christopher S. Chen*[a] and Viola Vogel*[b]



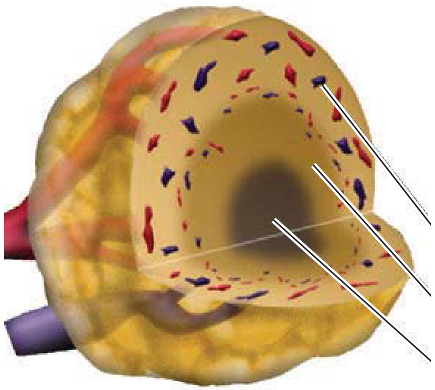
Source: Legant, Wesley R., et al. "Force-induced Fibronectin Assembly and Matrix Remodeling in a 3D Microtissue Model of Tissue Morphogenesis." *Integrative Biology* 4, no. 10 (2012): 1164-74.

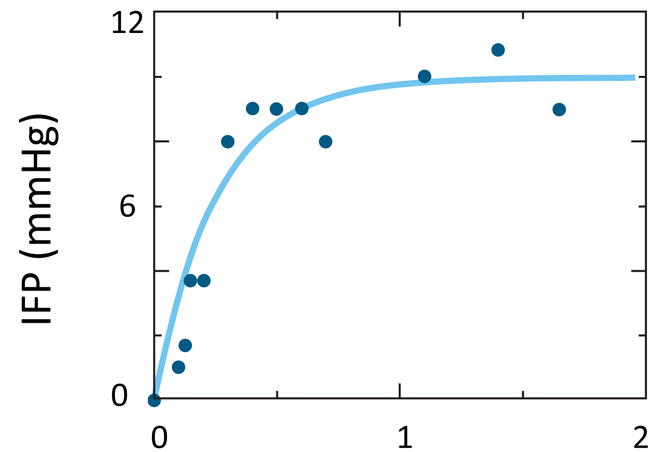




Source: Legant, Wesley R., et al. "Force-induced Fibronectin Assembly and Matrix Remodeling in a 3D Microtissue Model of Tissue Morphogenesis." *Integrative Biology* 4, no. 10 (2012): 1164-74.

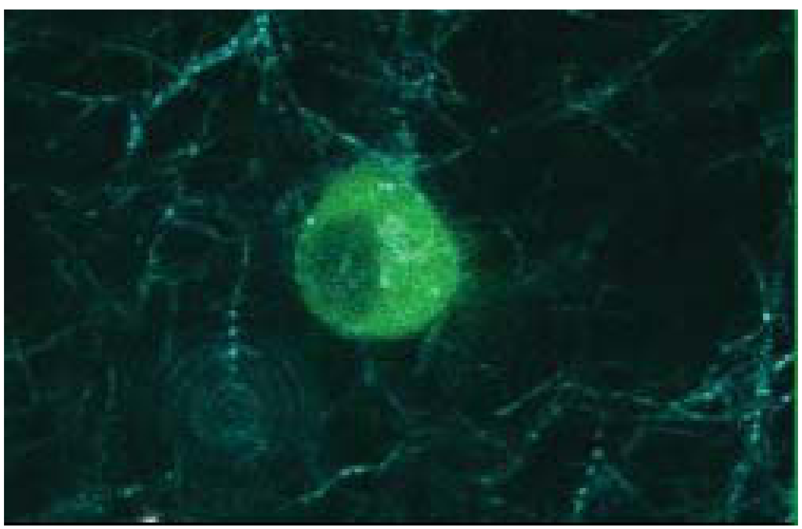
Interstitial flow alters tumor transport environment

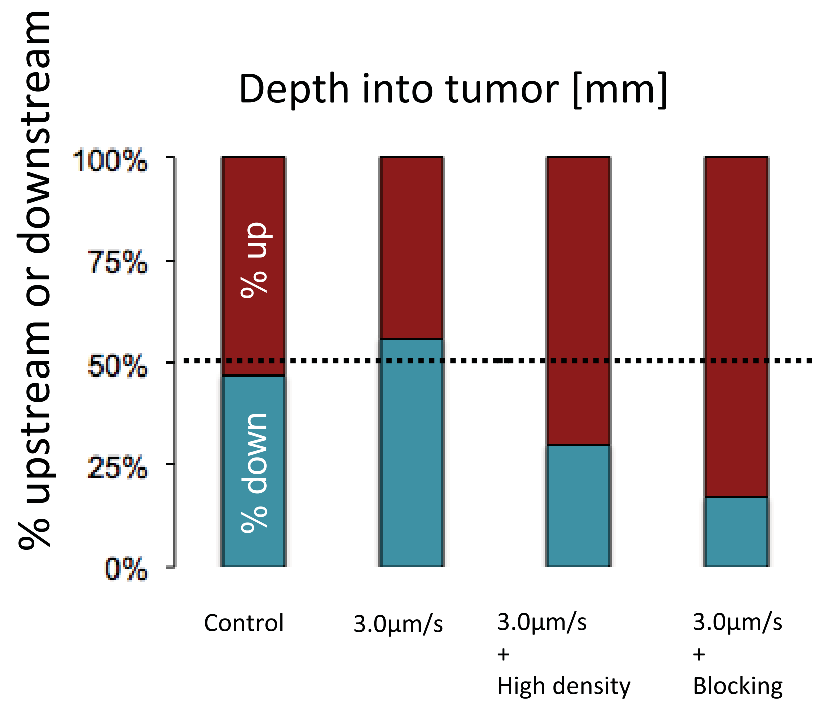




Source: Chauhan, Vikash P., et al. "Delivery of Molecular and Nanoscale Medicine to Tumors: Transport Barriers and Strategies." *Annual Review of Chemical and Biomolecular Engineering* 2 (2011): 281-98.

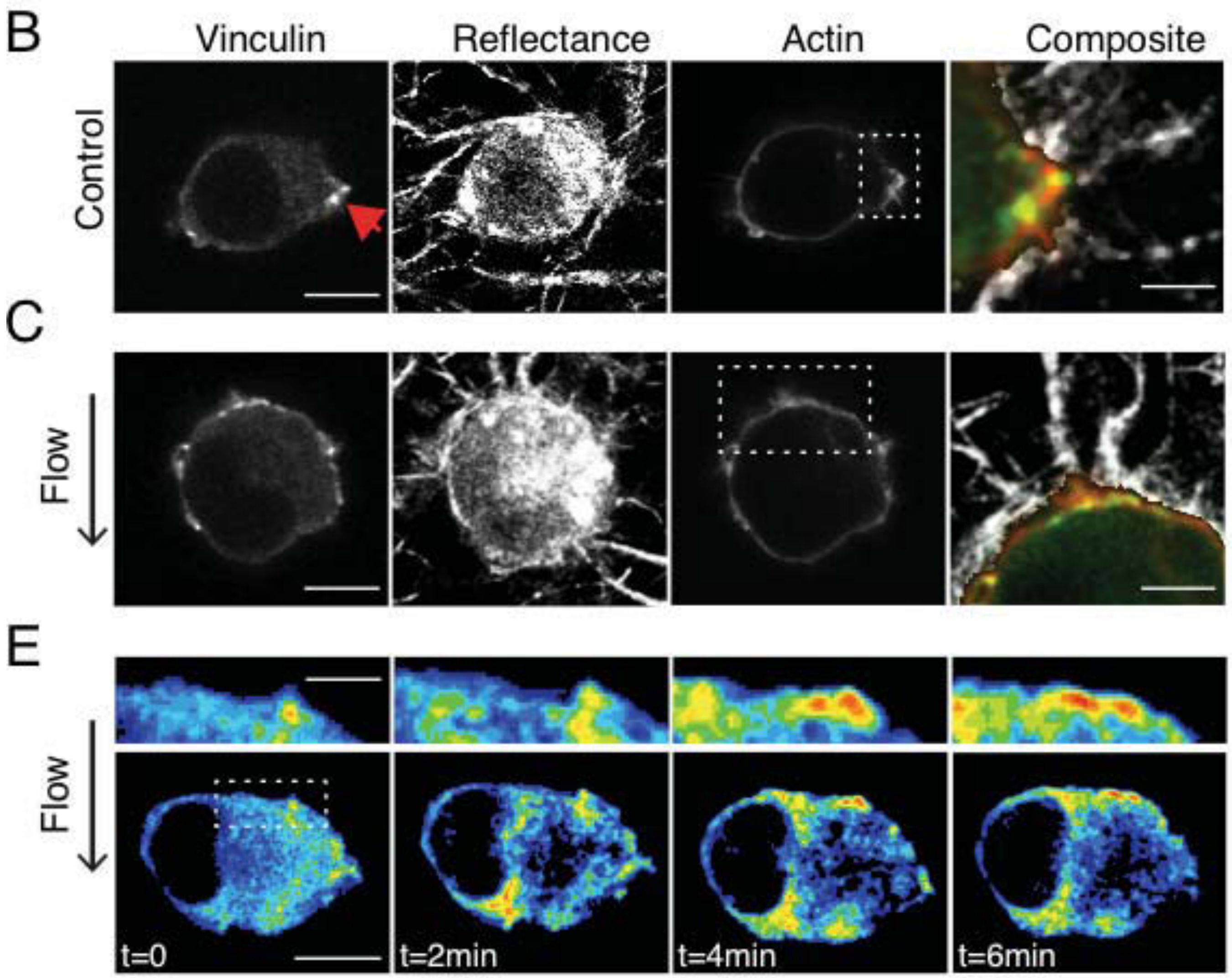
[Chauhan et al. Ann. Rev. Chem. Bio. Eng. 2011]





Polacheck et al., PNAS, 2012

Focal adhesion proteins localize to sites of tension at matrix adhesions



Vinculin recruitment over 6 min after start of flow

Source: Polacheck, William J., et al. "Mechanotransduction of Fluid Stresses Governs 3D Cell Migration." *Proceedings of the National Academy of Sciences* 111, no. 7 (2014): 2447-52.

Polacheck et al., PNAS, 2014

20.310J / 3.053J / 6.024J / 2.797J Molecular, Cellular, and Tissue Biomechanics
Spring 2015