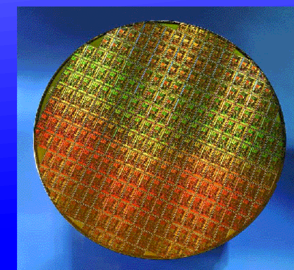
Session 21

CANTILEVER FORCE SENSORS

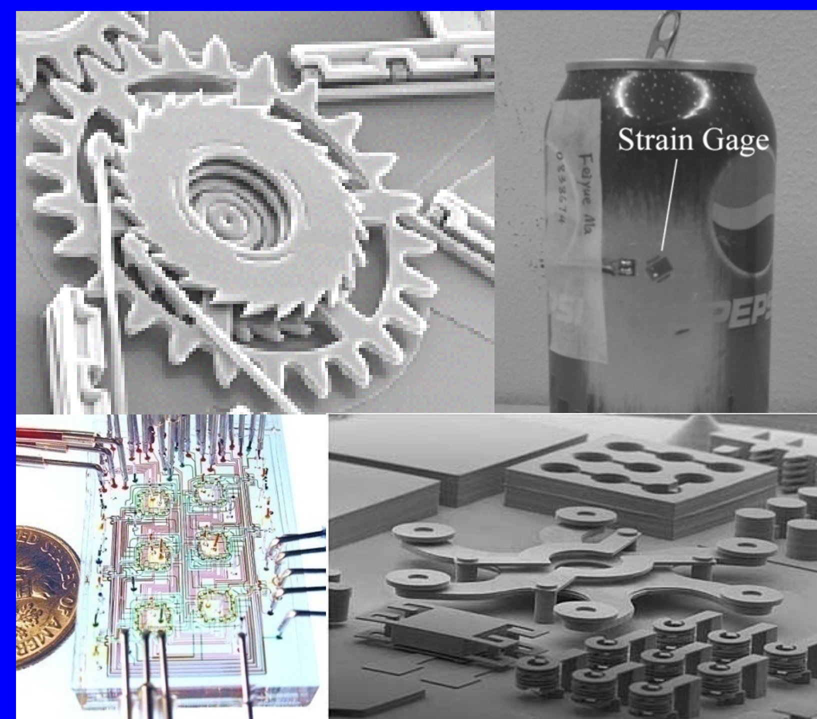
MicroElectroMechanical Systems

- Sensors and Actuators
  - Strain gauges, Pressure Sensors, Accelerometers Micromirrors, BioMEMS, etc.
  - Combined electrical, mechanical, optical, material, fluid, chemical, and/or biological systems



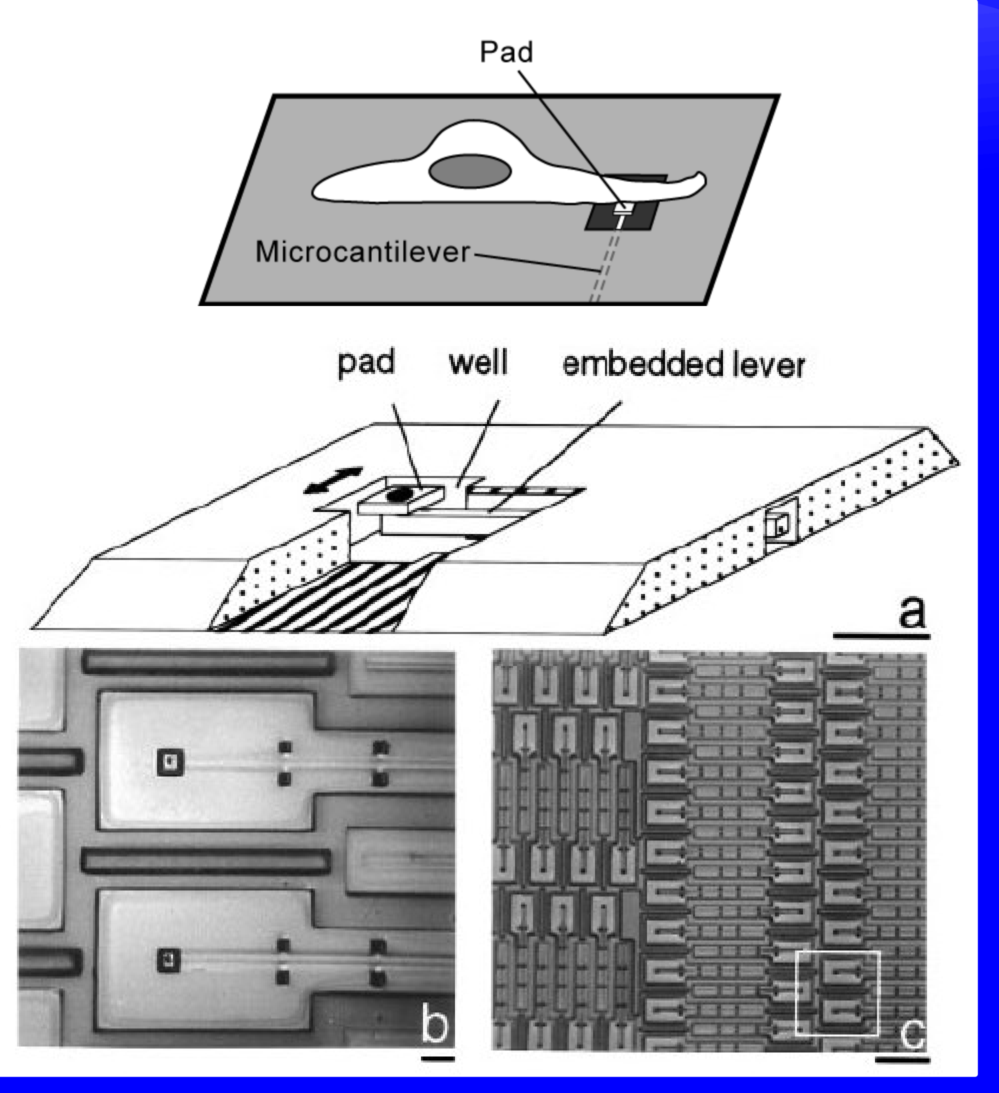
IC

MEMS



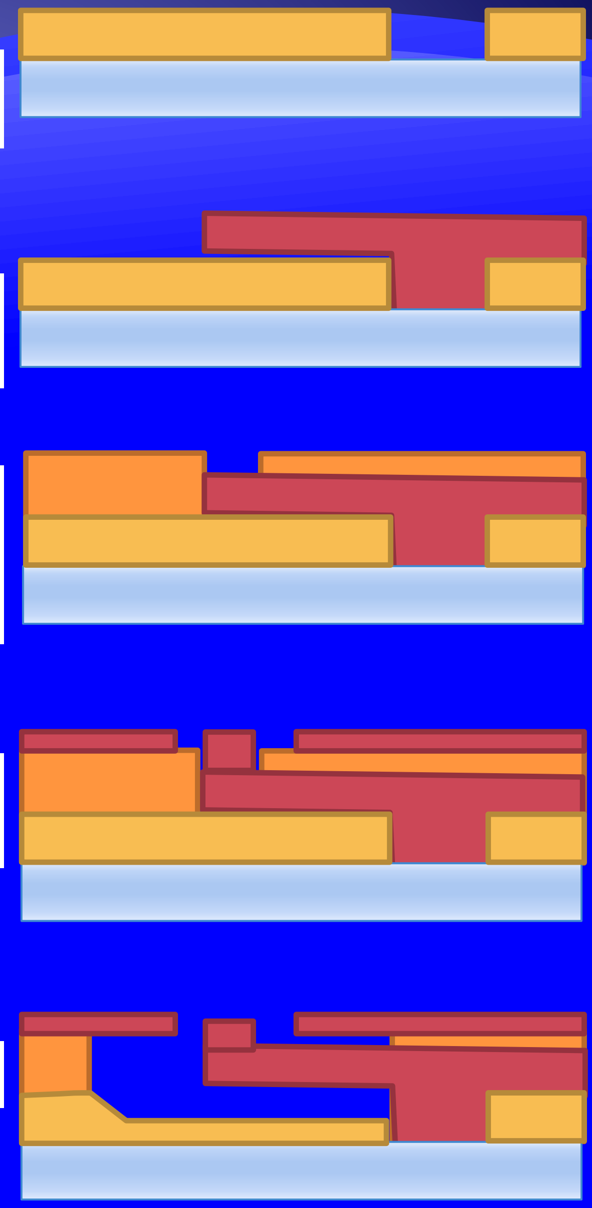
Horizontal Cantilever

- Micromachined device to measure individual focal adhesions
- Dynamic measurements of traction forces during cell migration



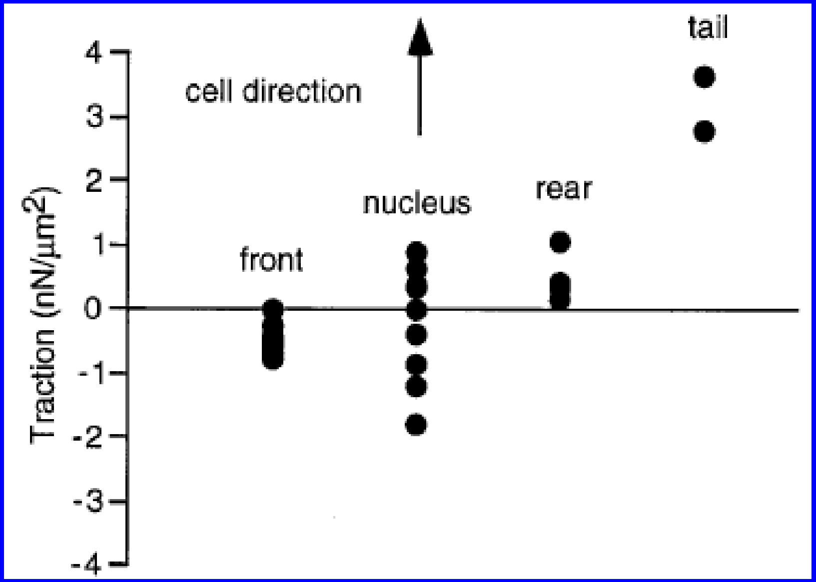
Fabrication

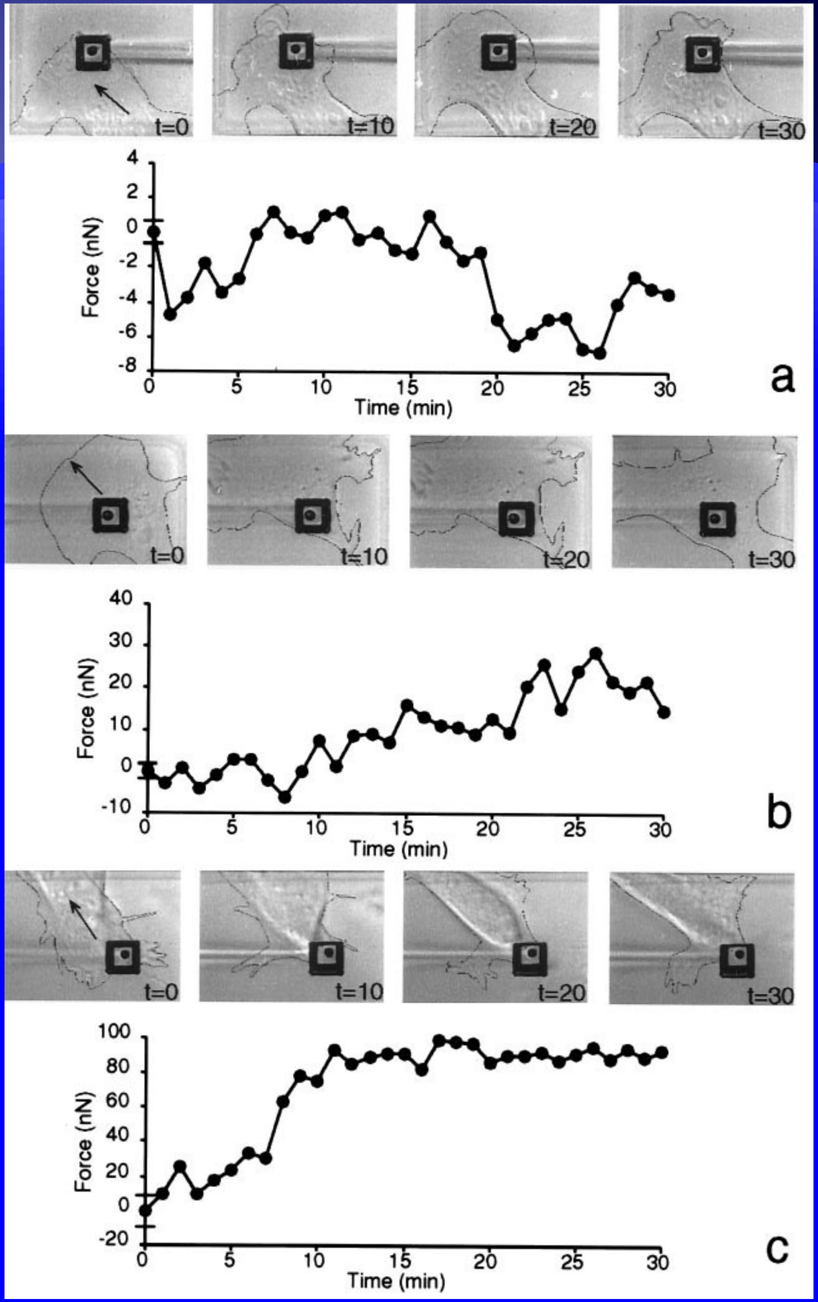
- Phosphorous-doped Glass
  - Deposit
  - Lithography
  - Etching
- Poly-Silicon #1
  - Deposit
  - Lithography
  - Etching
- Spin-on-Glass
  - Deposit
  - Lithography
  - Etching
- Poly-Silicon #2
  - Plasma deposit
  - Lithography
  - Etching
- Etch-Release



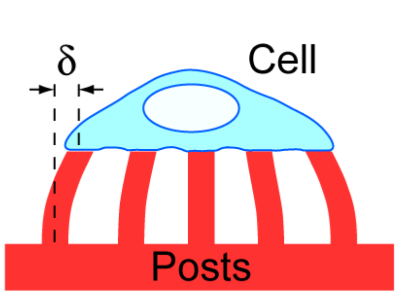
Measurement

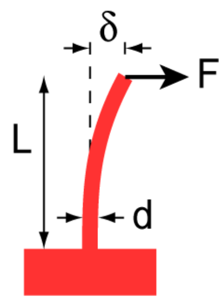
- Cells pull in the front and retract in the rear
- Retraction force at rear releases adhesions





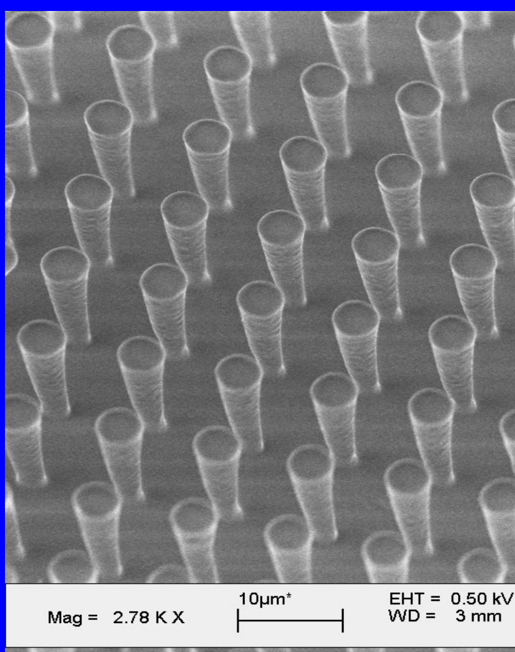
Microposts to Measure Cell Forces



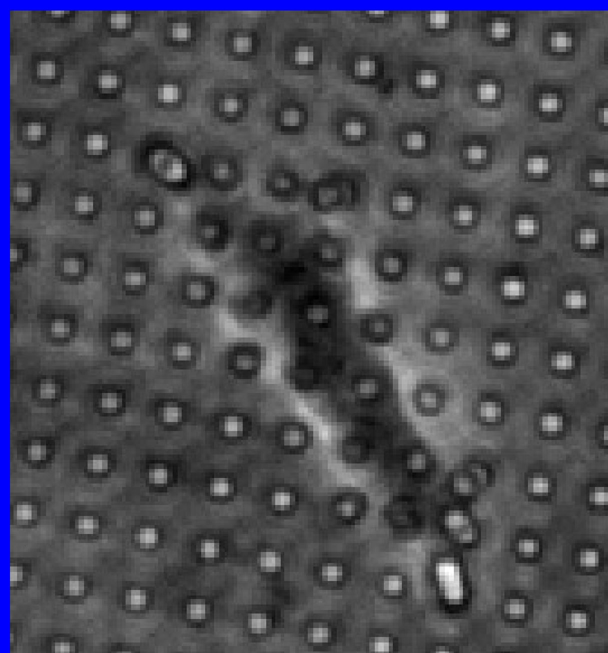


$$F = \left(\frac{3\pi E d^4}{64 L^3} \right) \delta$$

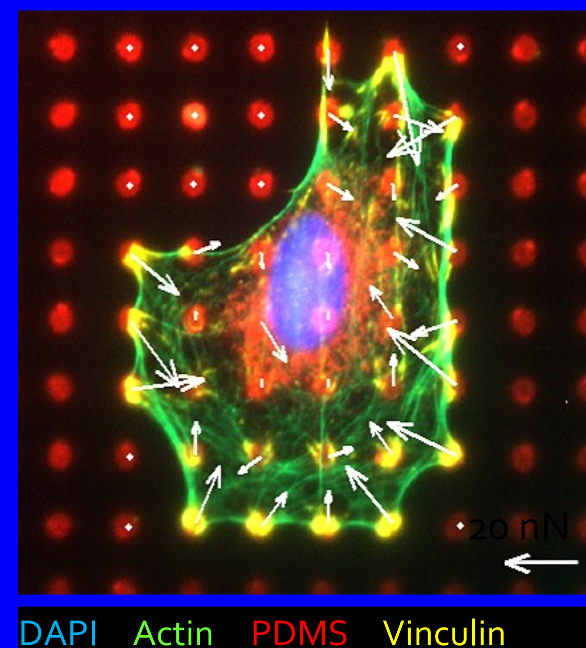
F	Traction Force
δ	Displacement
E	PDMS Modulus of Elasticity
d	Post Diameter (3 μm)
L	Post Length (5-11 μm)



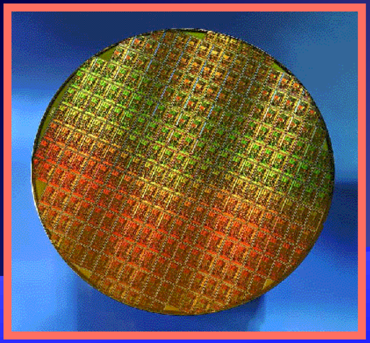
PDMS microposts

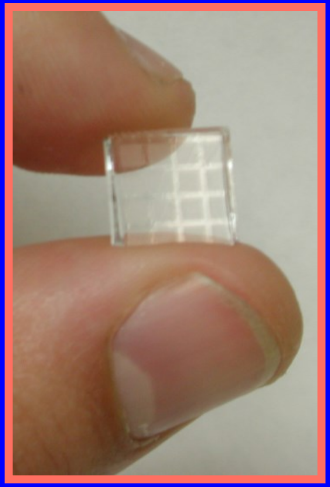


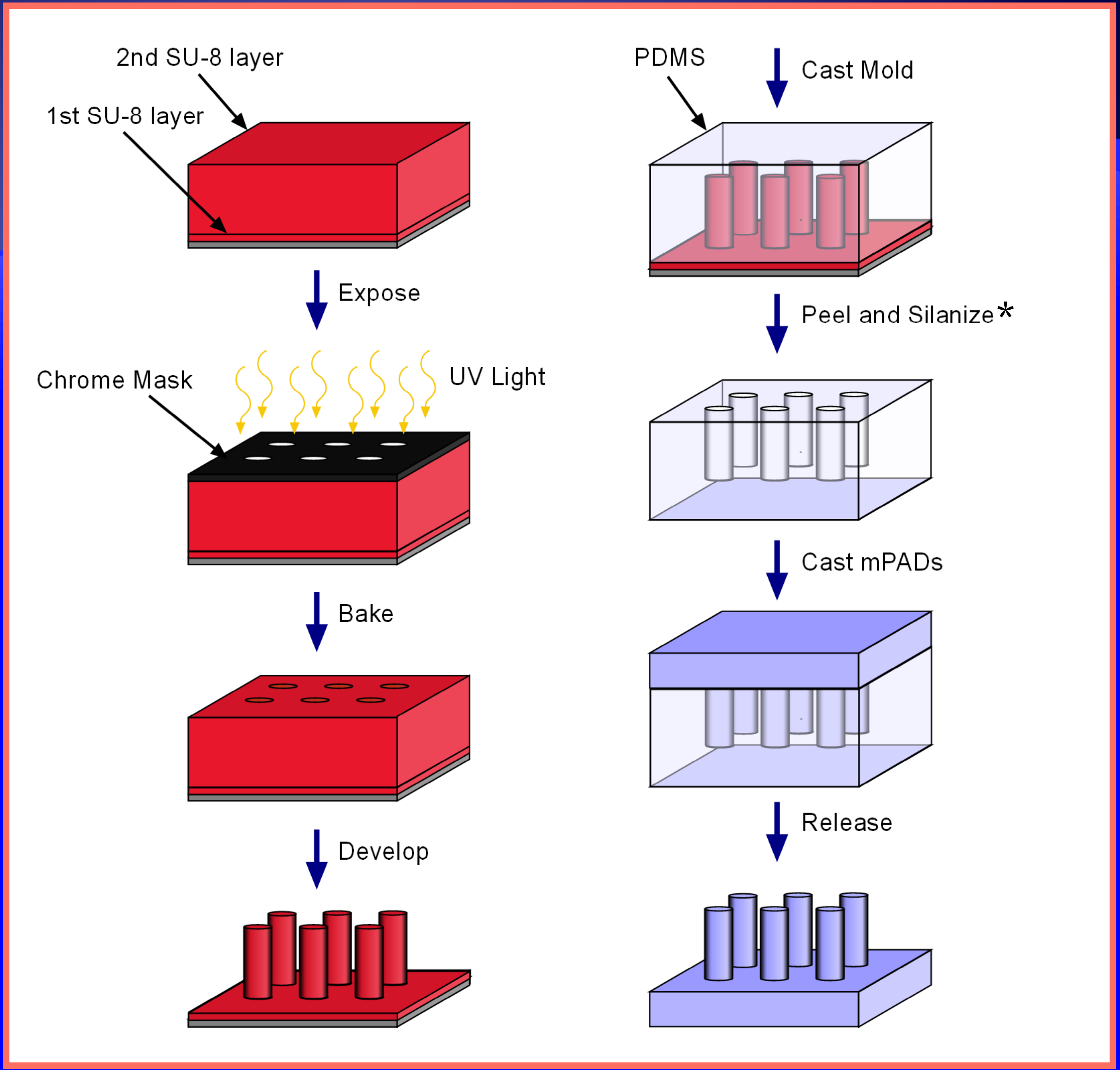
Deflection Measurements



Immunofluorescence

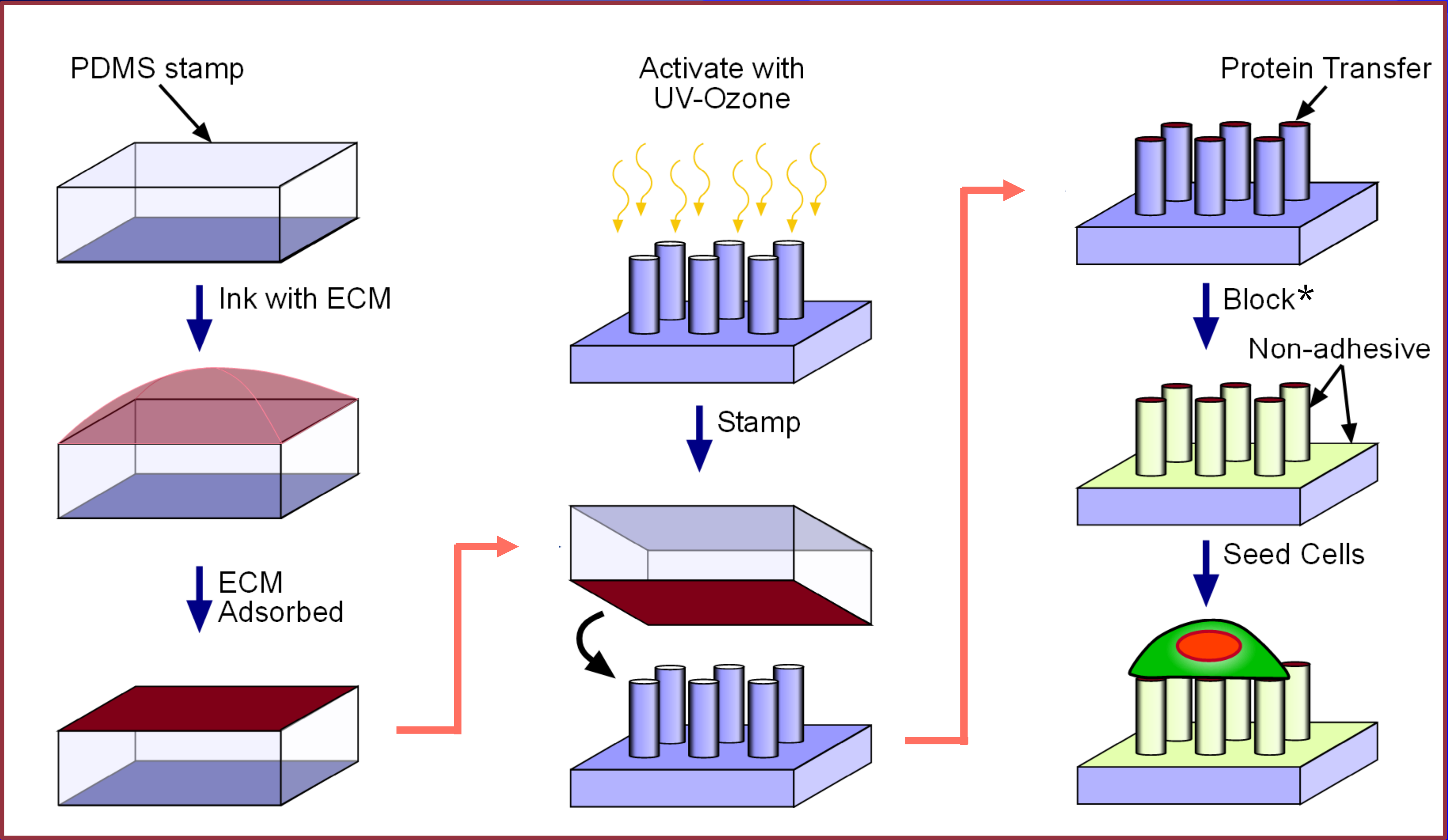






* (tridecafluoro-1,1,2,2-tetrahyrooctyl)-1-trichlorosilane

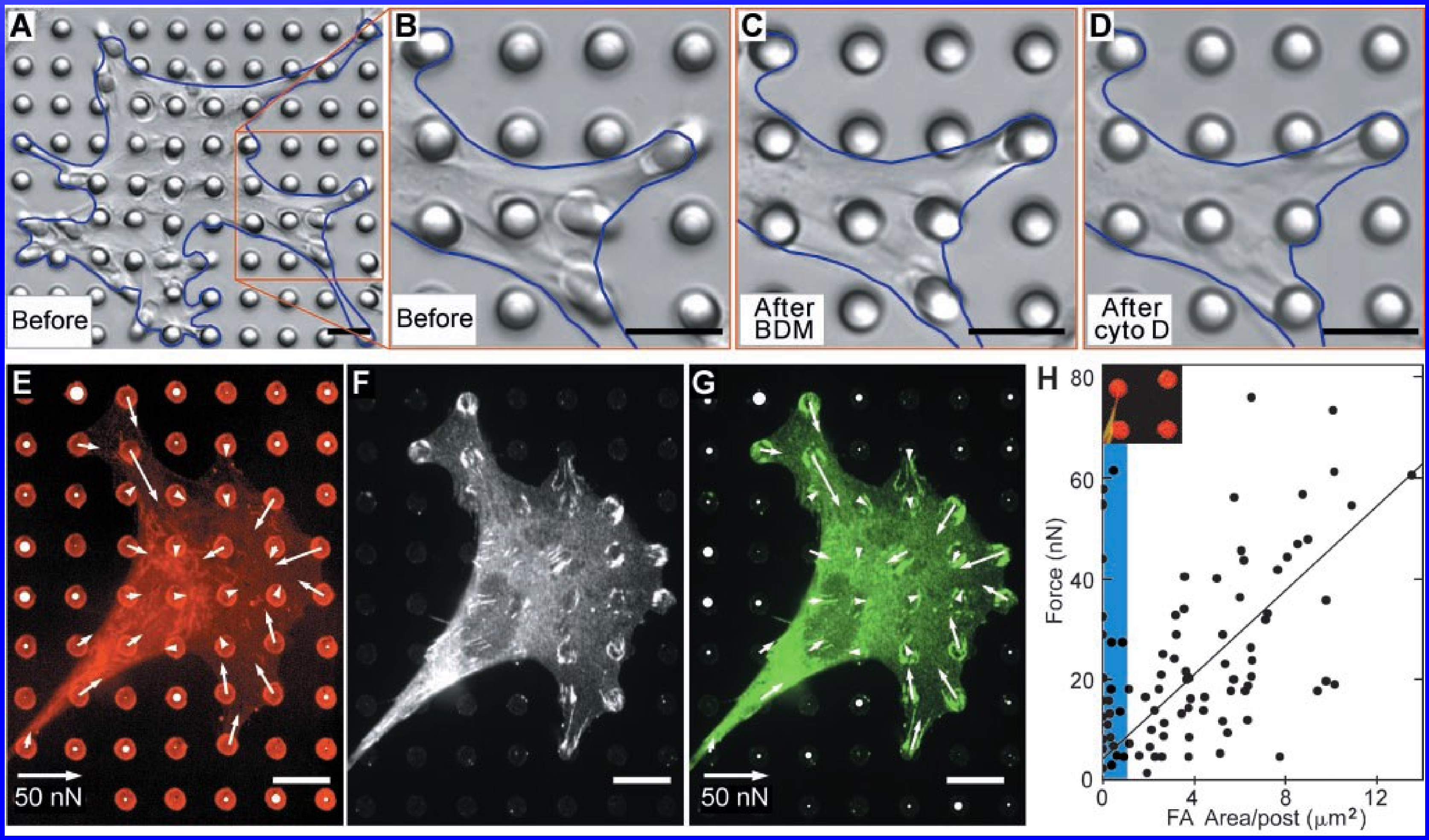
Biofunctionalizing the Posts



* 0.2% (w/v) Pluronics® F127 difunctional block copolymer surfactant

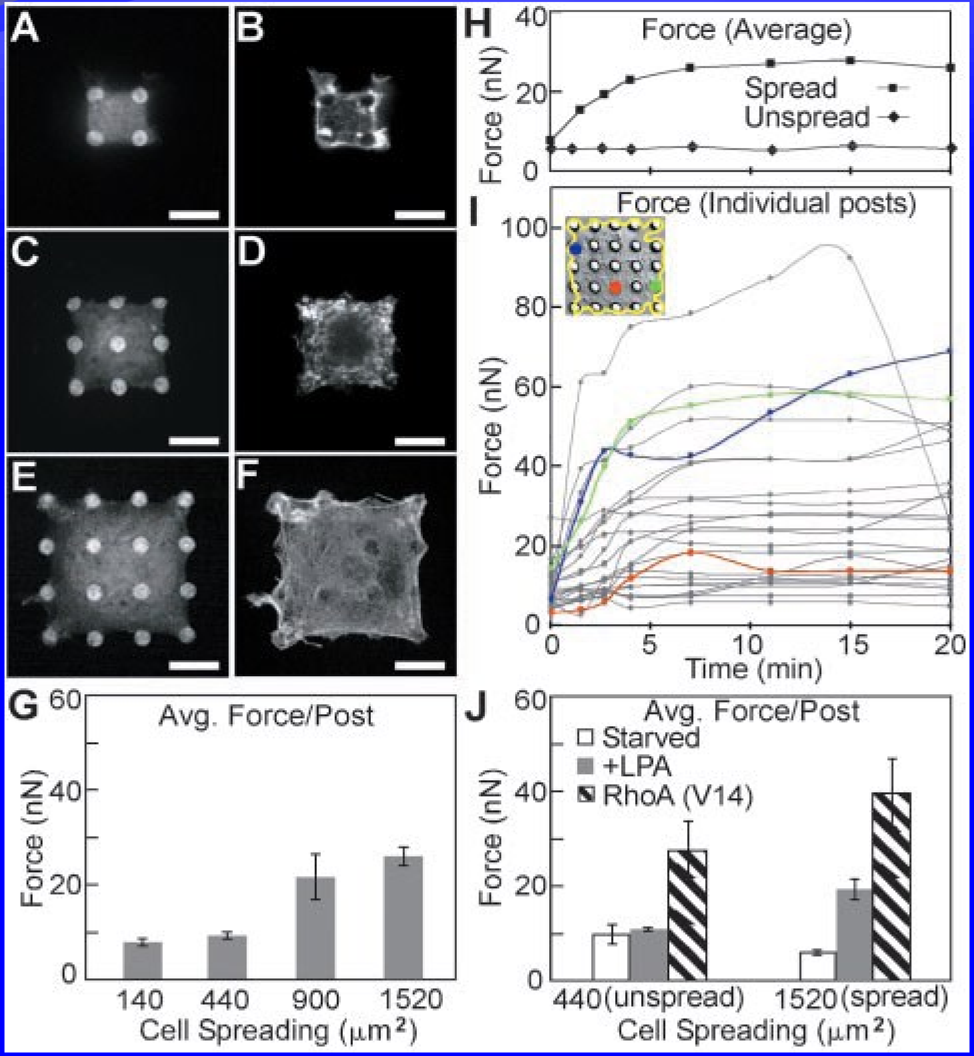
Focal Adhesions and Force

- Positive correlation of FA and local force



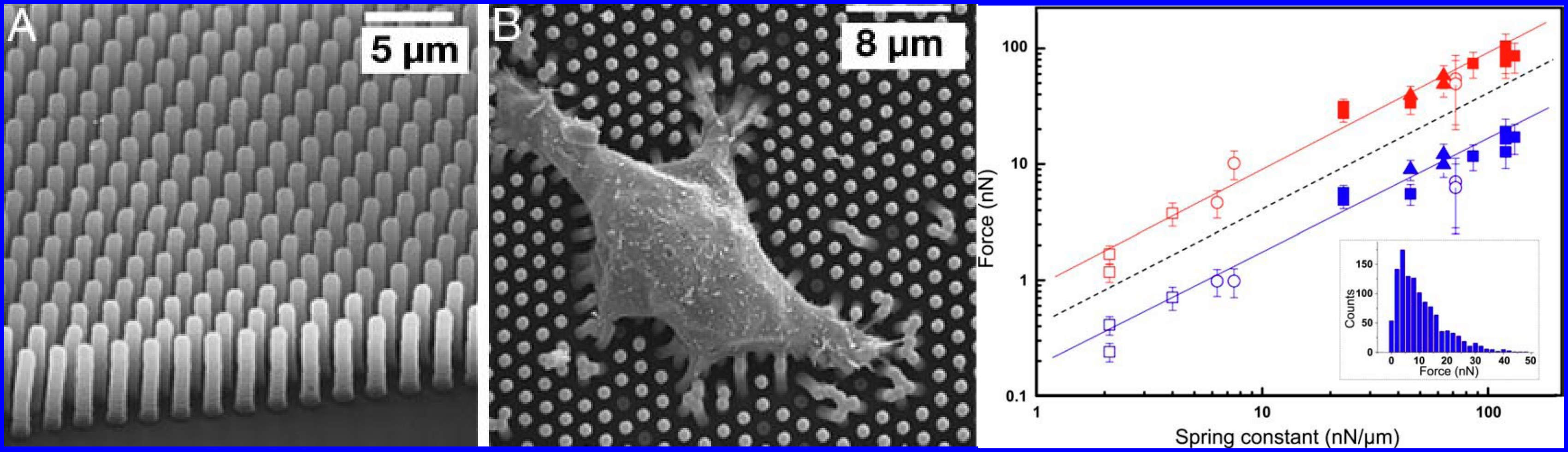
Spread Area and Force

- Contact area, i.e. cell spreading, promotes larger traction forces
- Constitutively active RhoA mutant causes large forces at low contact area



Hexagonal Packed Posts

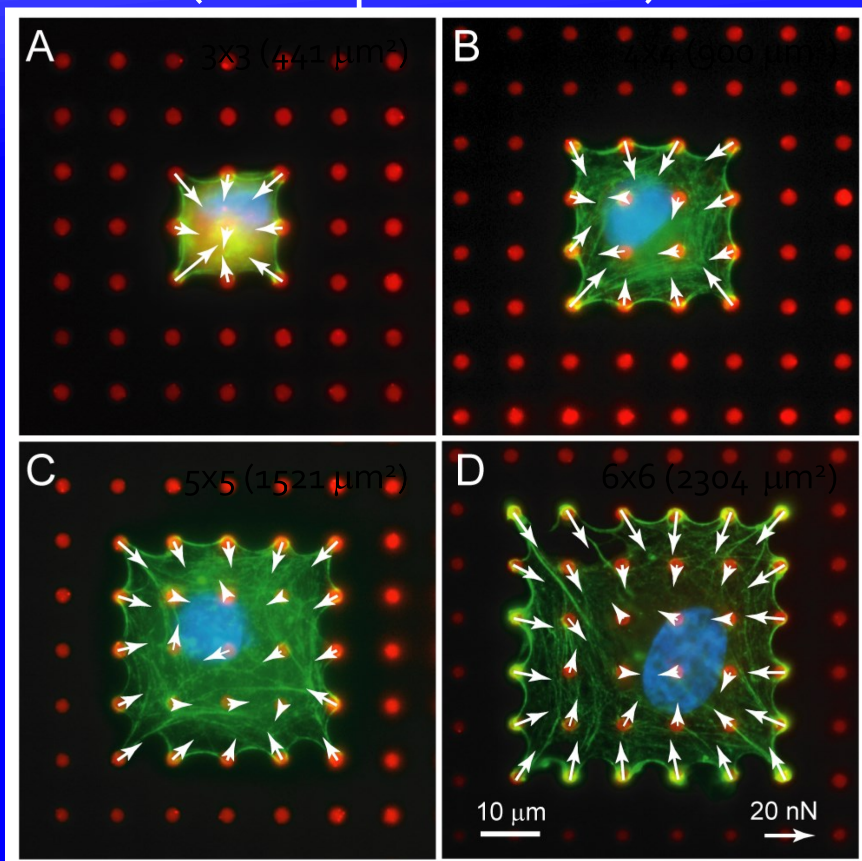
- Closer spacing between smaller posts
- Positive correlation between stiffness and force



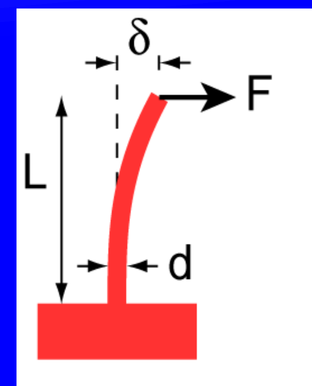
du Roure, *et al*. (2005) *PNAS*, 102:2390
Saez, *et al*. (2005) *Biophys J*, doi: 10.1529/biophysj.105.071217

Stiffness vs. Spreading

Micro-Contact Printing (Cell Spread Area)



Micropost Dimensions (Substrate Stiffness)

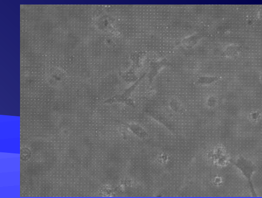


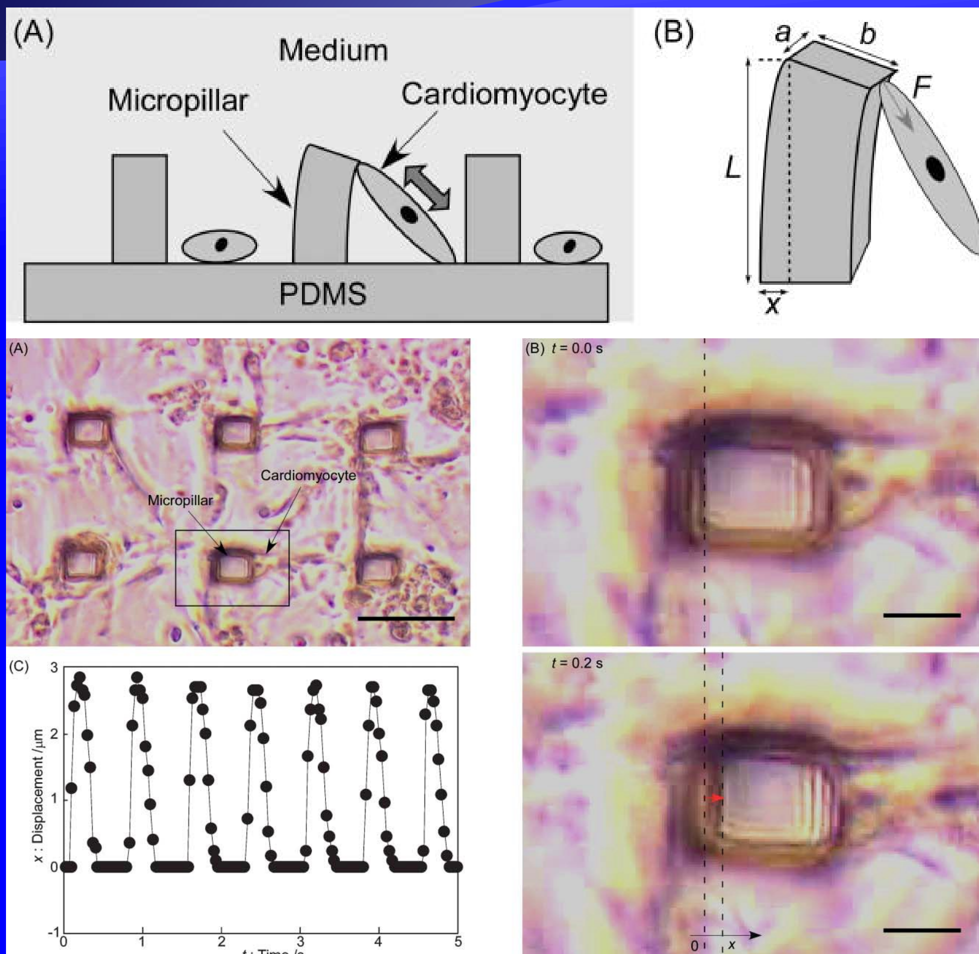
$$F = \frac{3\pi E d^4}{64 L^3}\delta$$

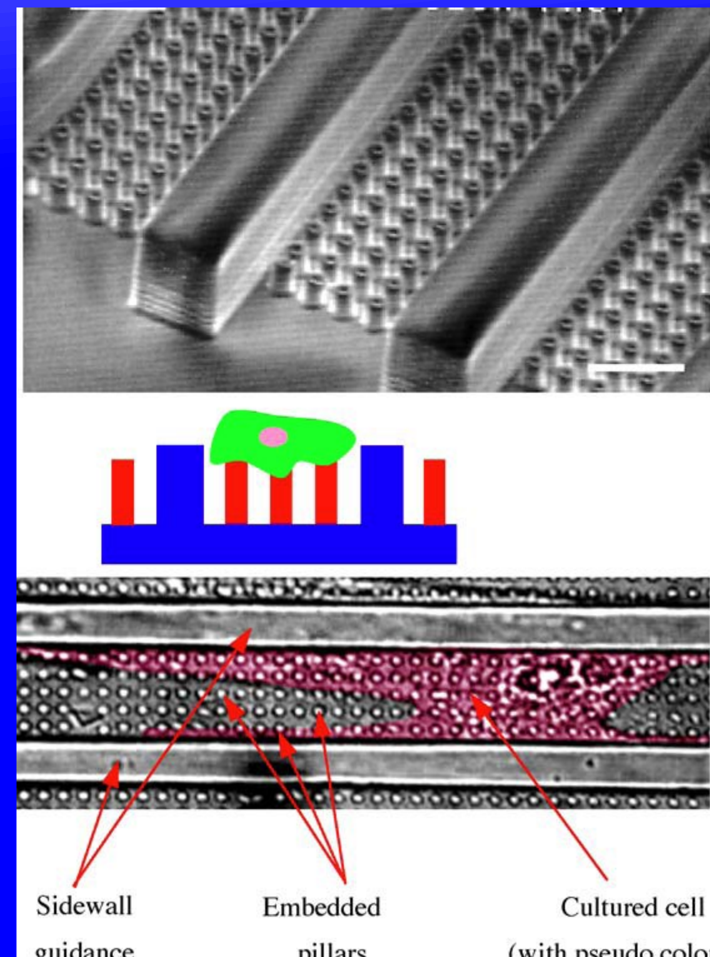
Array	L (µm)	d (µm)	k (nN/µm)
1	8.96 ± 0.36	2.14 ± 0.03	10.7 ± 2.3
2	7.44 ± 0.28	2.04 ± 0.06	15.5 ± 3.6
3	7.19 ± 0.22	2.22 ± 0.10	24.1 ± 6.3
4	7.45 ± 0.20	2.42 ± 0.05	30.5 ± 6.2
5	6.70 ± 0.13	2.50 ± 0.07	47.8 ± 10

Han, S.J., Ting, L.H., Bielawski, K.S., Rodriguez, M.L., Sniadecki, N.J. (2012). Biophys J. 103(4): 640-8.

Muscle Posts





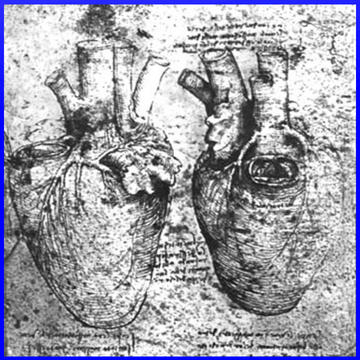


Tanaka, et al, (2006) *Lab on a Chip*, 6:230

Zhao Y, Zhang X, (2006) *Sensors and Actuators*, 127:216

Twitch Forces Increase with Stiffness

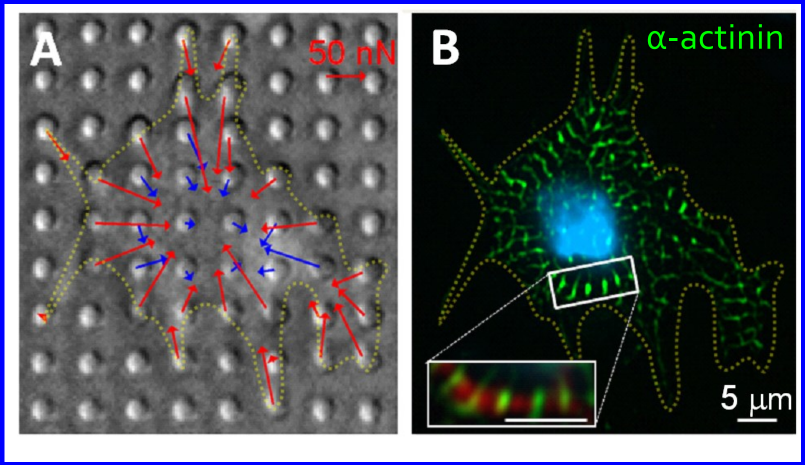
During development, myocardial stiffness coincides with increased contractile performance.

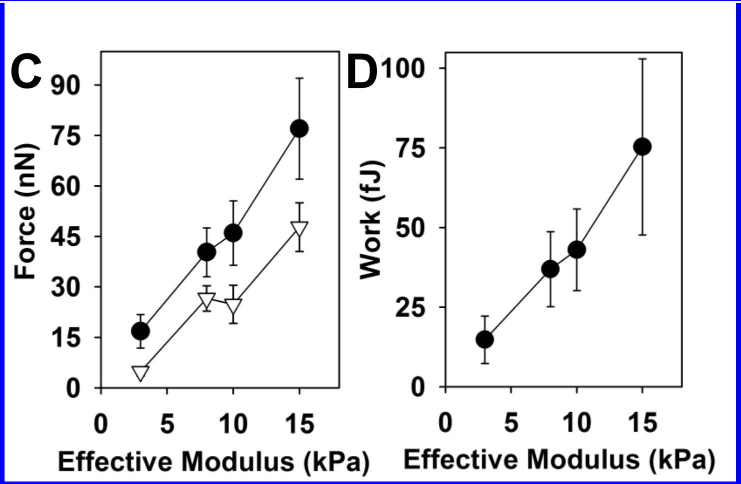


Stiffness	E (kPa)	G (kPa), ν ≈ 0.5
Prenatal	12 ± 4	≈ 4
Neonatal	39 ± 7	≈ 13

Values adapted from Jacot et al. *J. Biomech.* 2010

Neonatal Rat Ventricular Cardiomyocytes

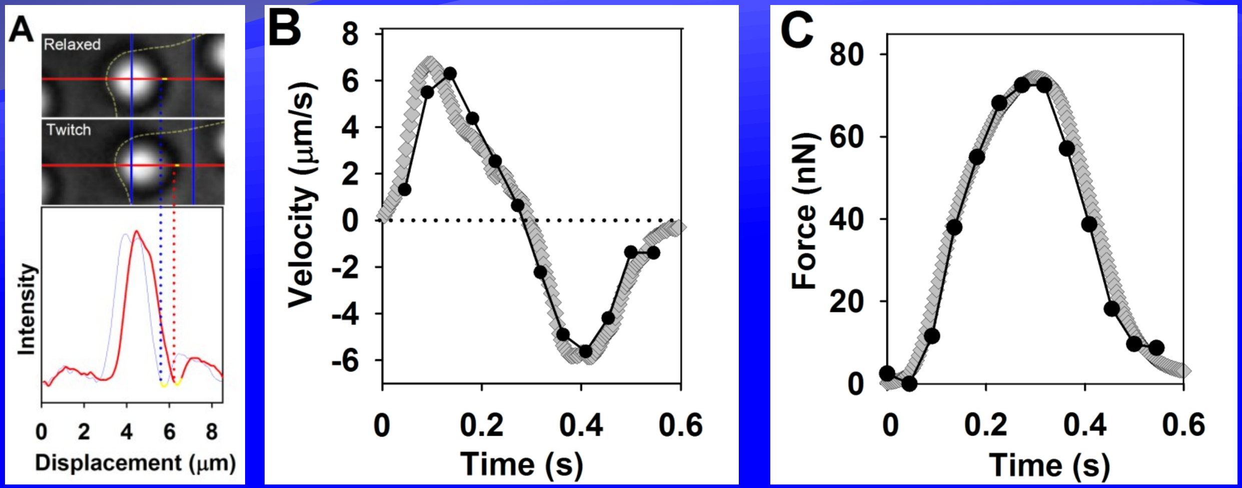


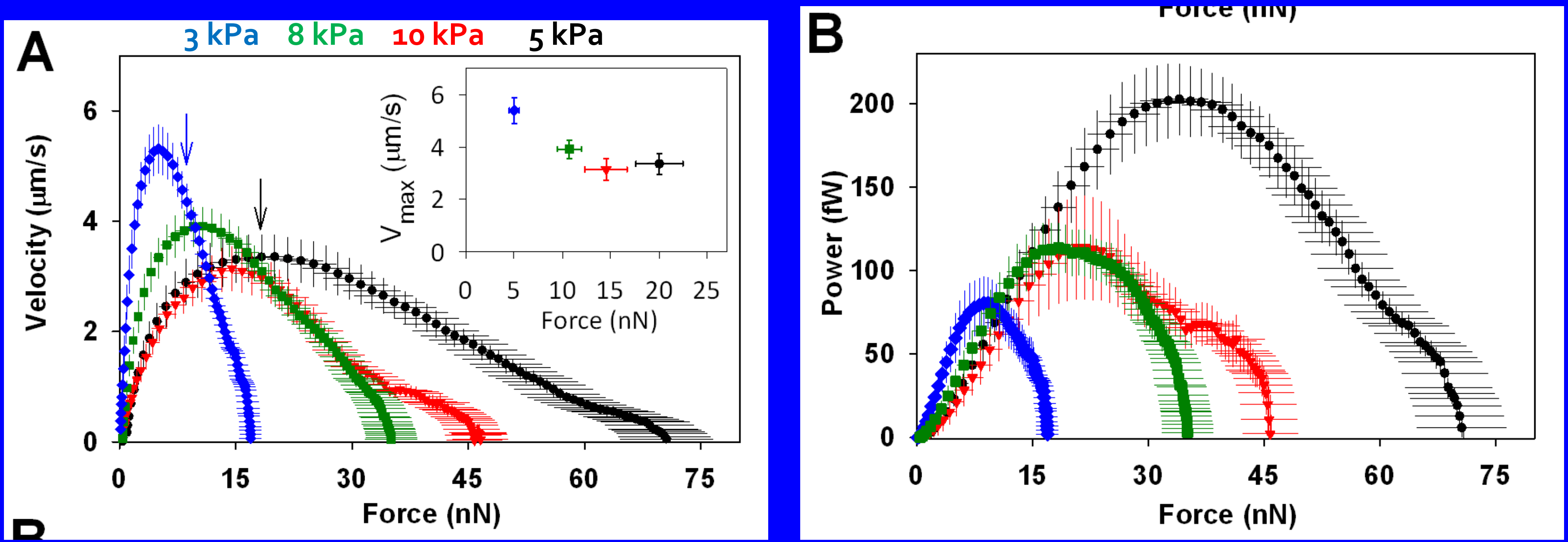


Rodriguez, A.G., Han, S.J., Regnier, M. Sniadecki, N.J. (2011) *Biophys J* 101(11):2455-64

Twitch Power increases with Stiffness

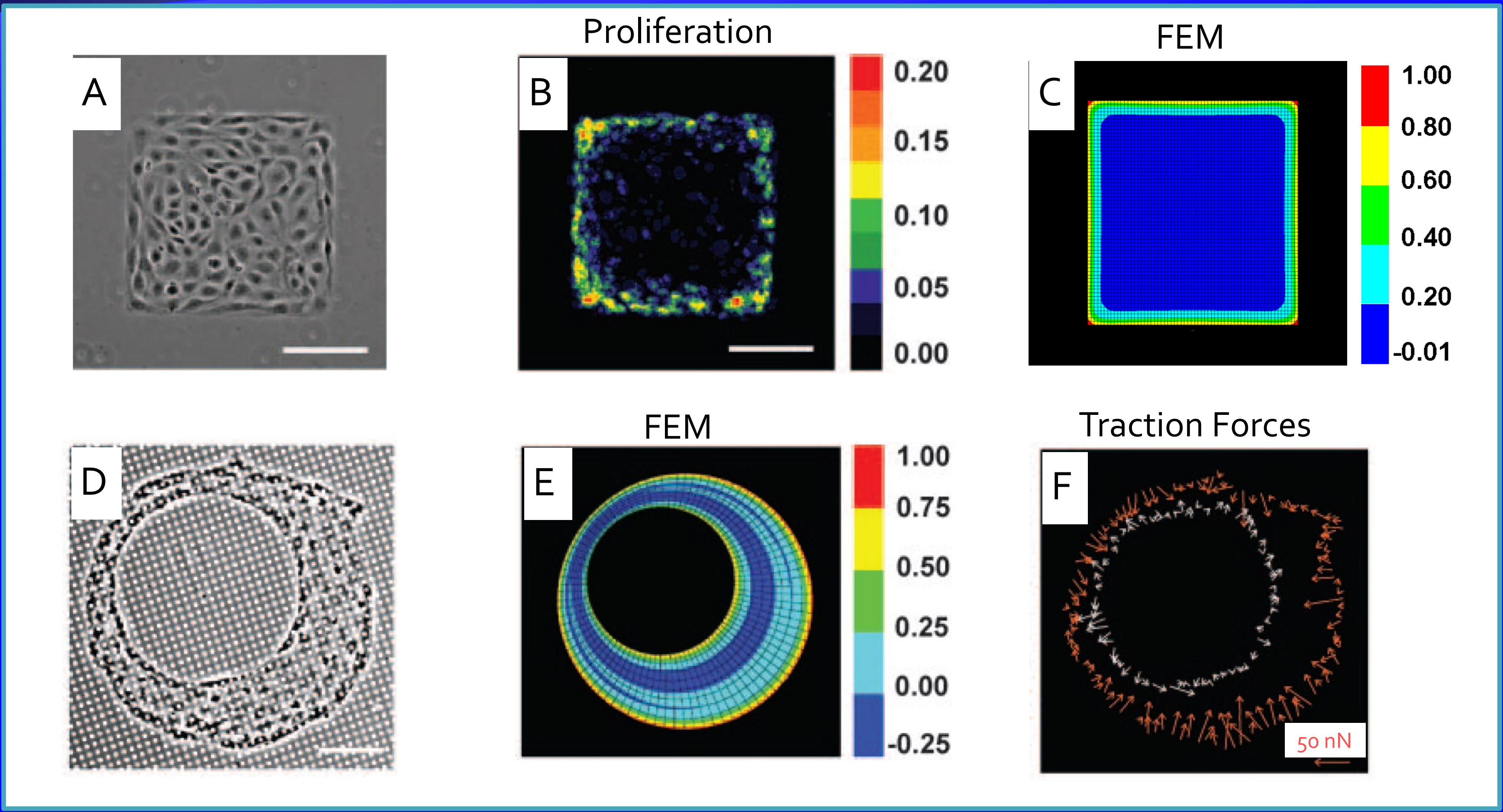
- Fast line scanning for velocity, power.





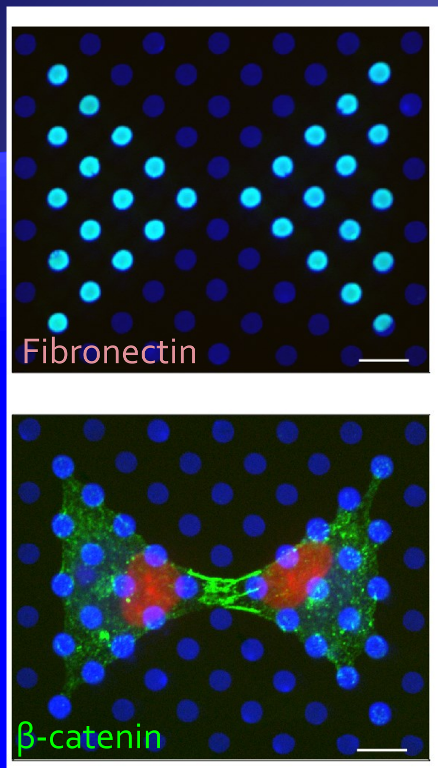
Multicellular Measurements

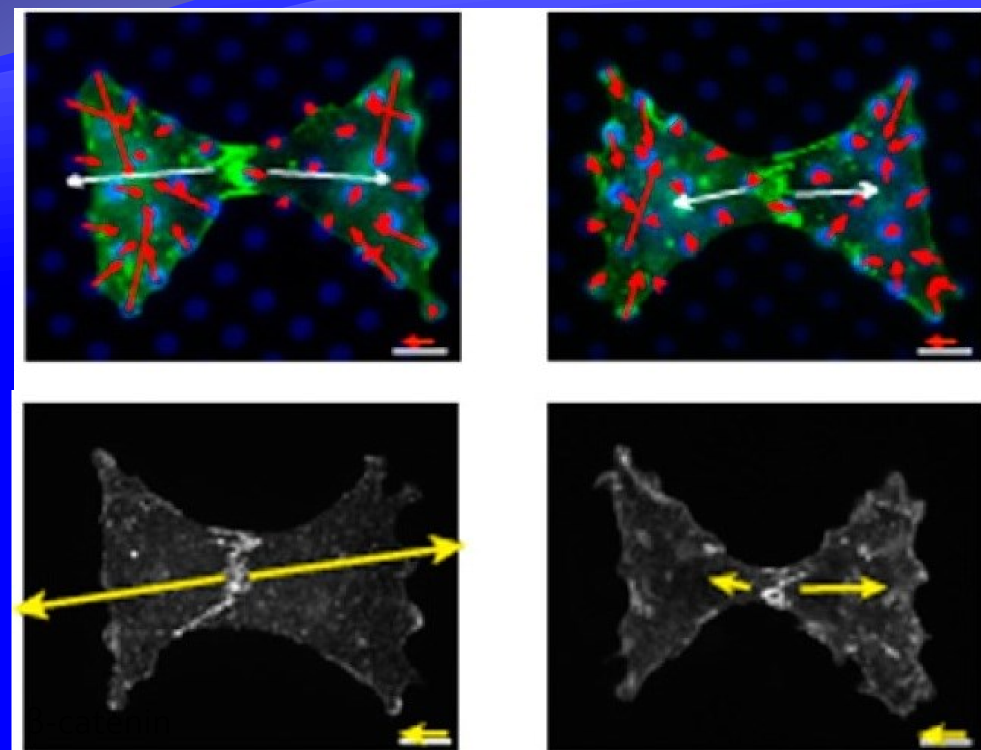
- Force correlates with cell growth



Nelson, *et al*. (2005) *PNAS*, 102(33):11594

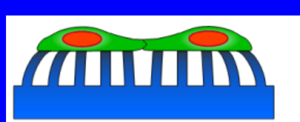
Bowties to Measure "Tugging" Force

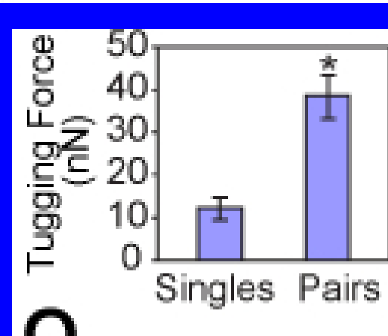


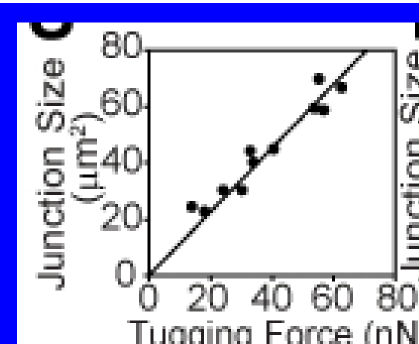


Single

Pairs



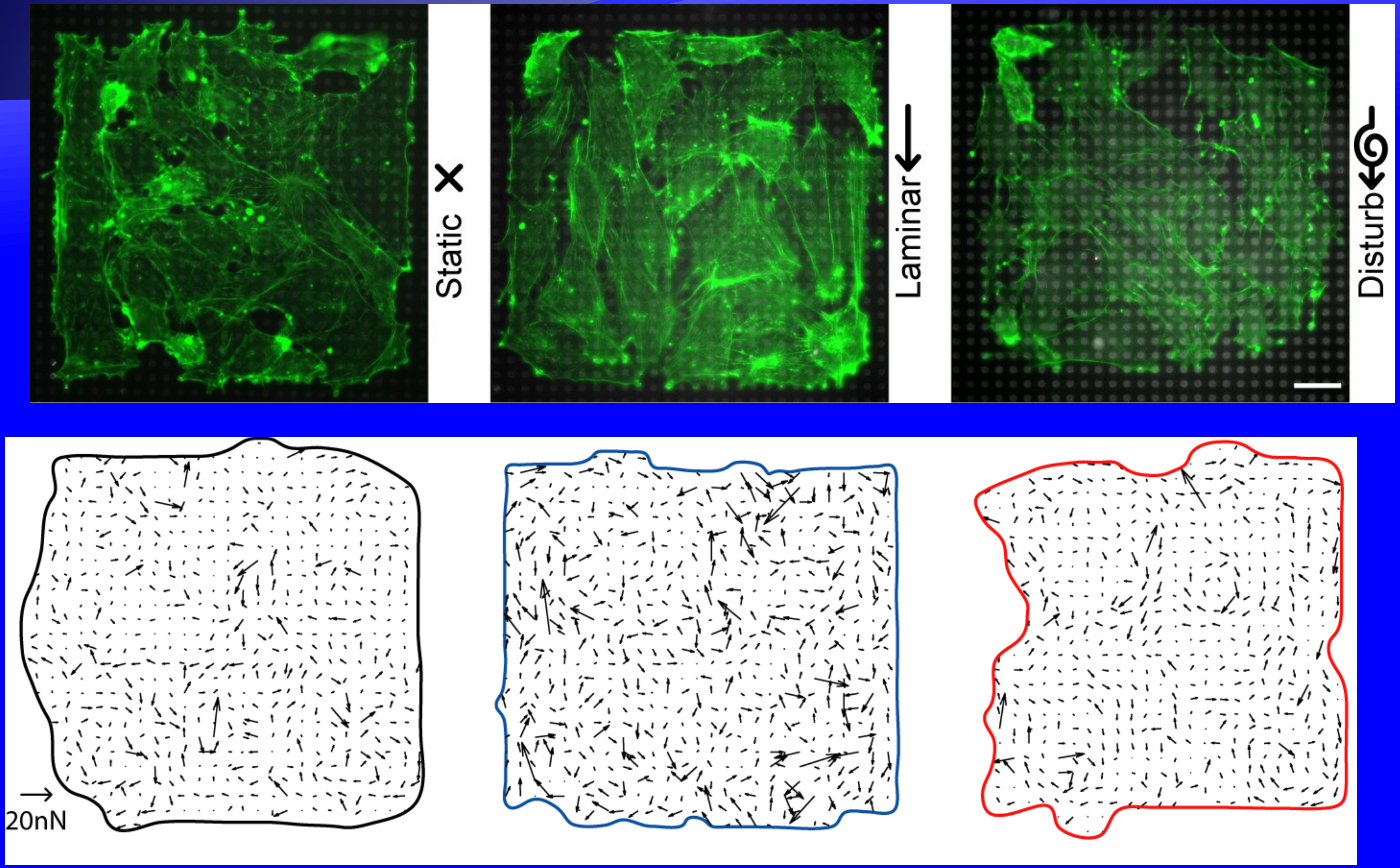




For graphs: *, $p < 0.05$ (Student-t test)

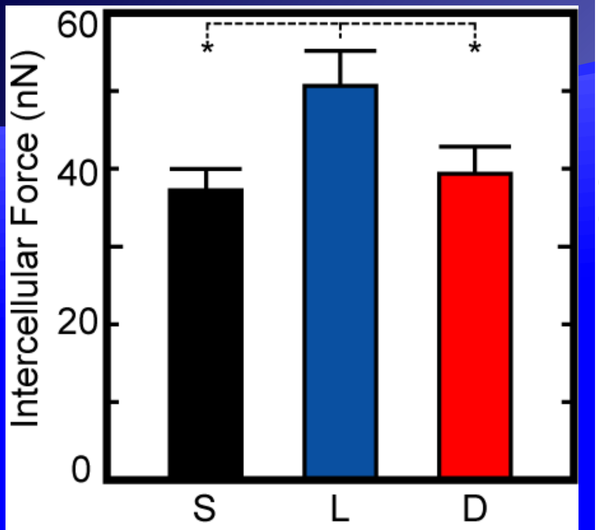
Liu, Z., et al. (2010) *Proc Nat Acad Sci*. 107: 19944-9

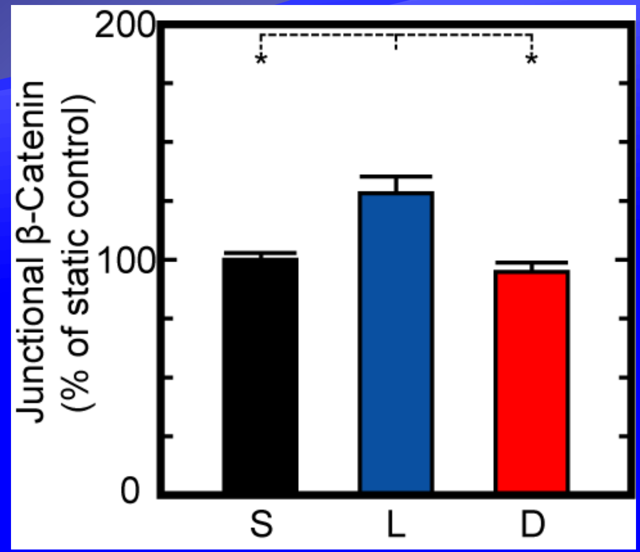
Shear Flow Mechanotransduction

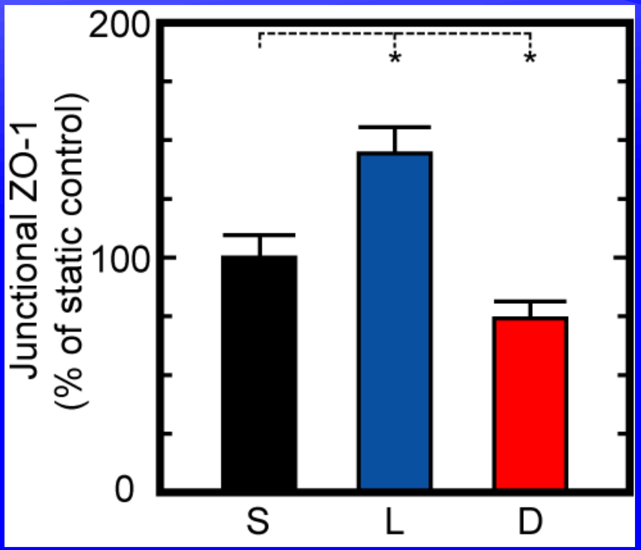


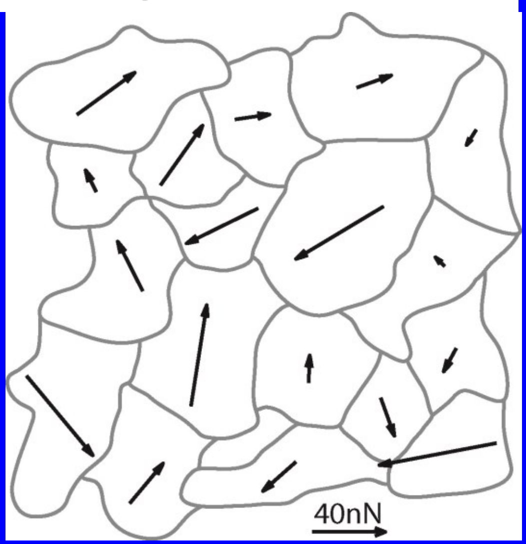
Ting, L.H., Jahn, J.R., Jung, J.L., Shuman, B.R., Feghhi, S., Han, S.J., Rodriguez, M.L., Sniadecki, N.J. (2012). AJP Heart. 302: H2220.

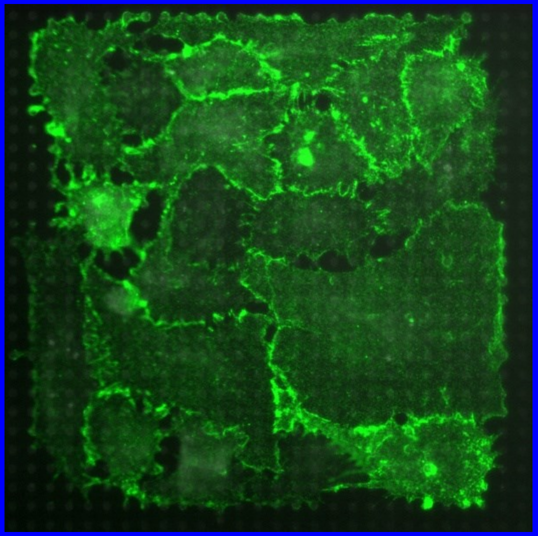
Cell-Cell Junctions Under Flow

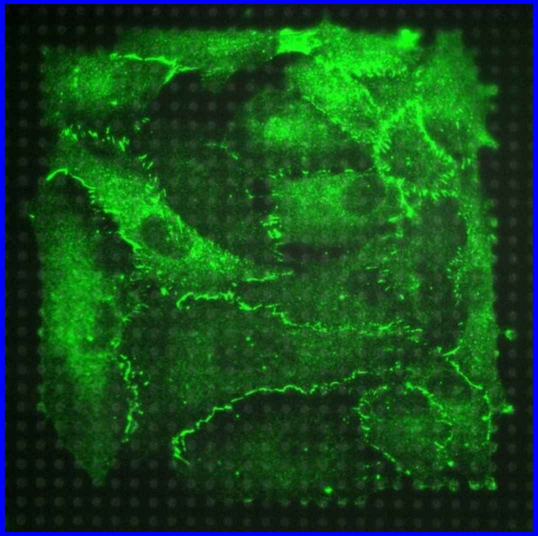








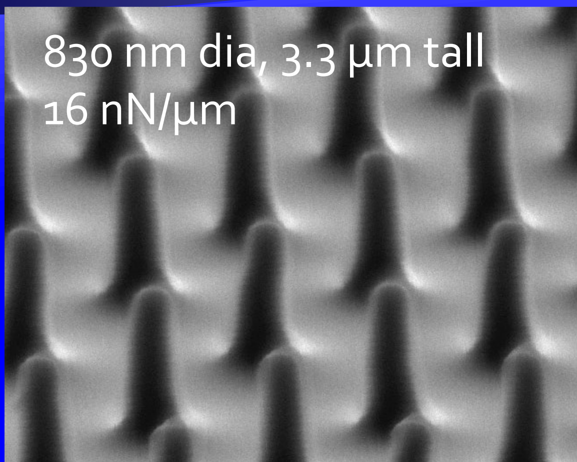


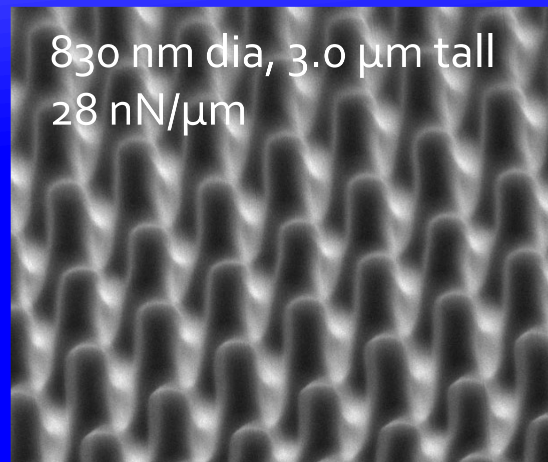


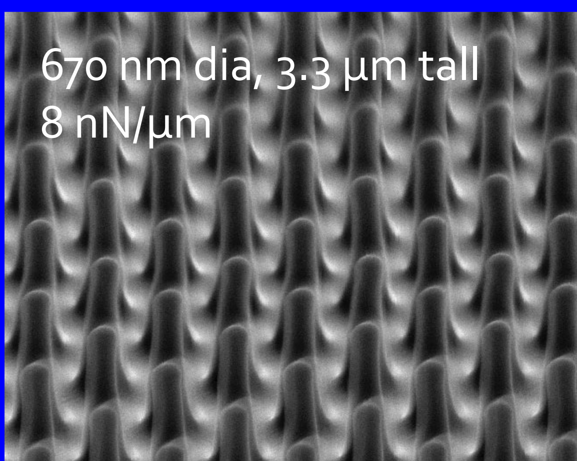
Ting, L.H., Jahn, J.R., Jung, J.L., Shuman, B.R., Feghhi, S., Han, S.J., Rodriguez, M.L., Sniadecki, N.J. (2012). AJP Heart. 302: H2220.

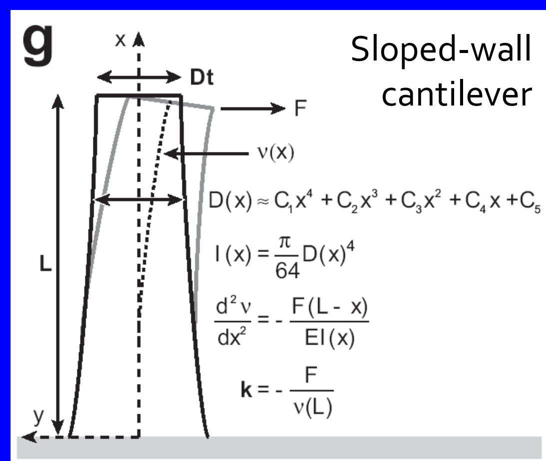
Nanoposts

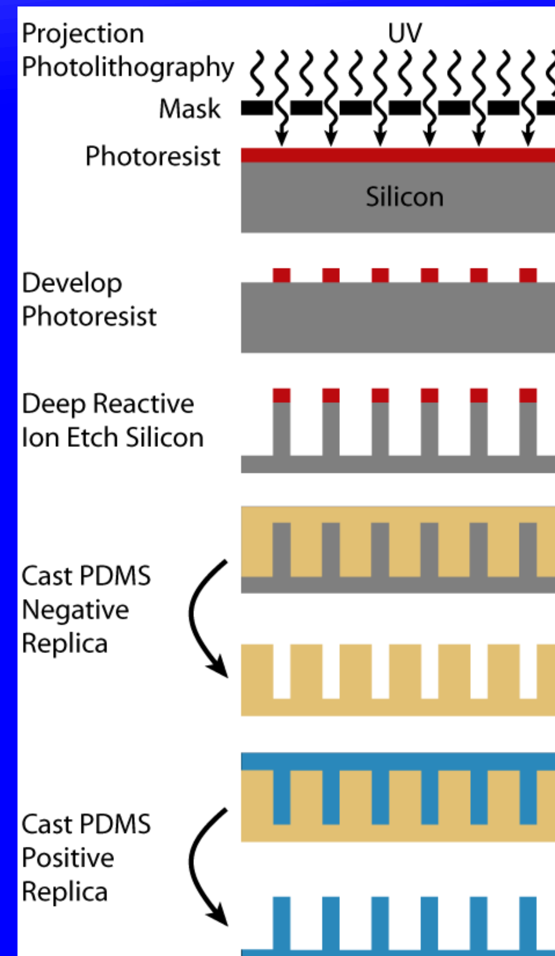
- High resolution force measurements











Yang, *et al.* (2007) *Adv Materials*, 19:3119