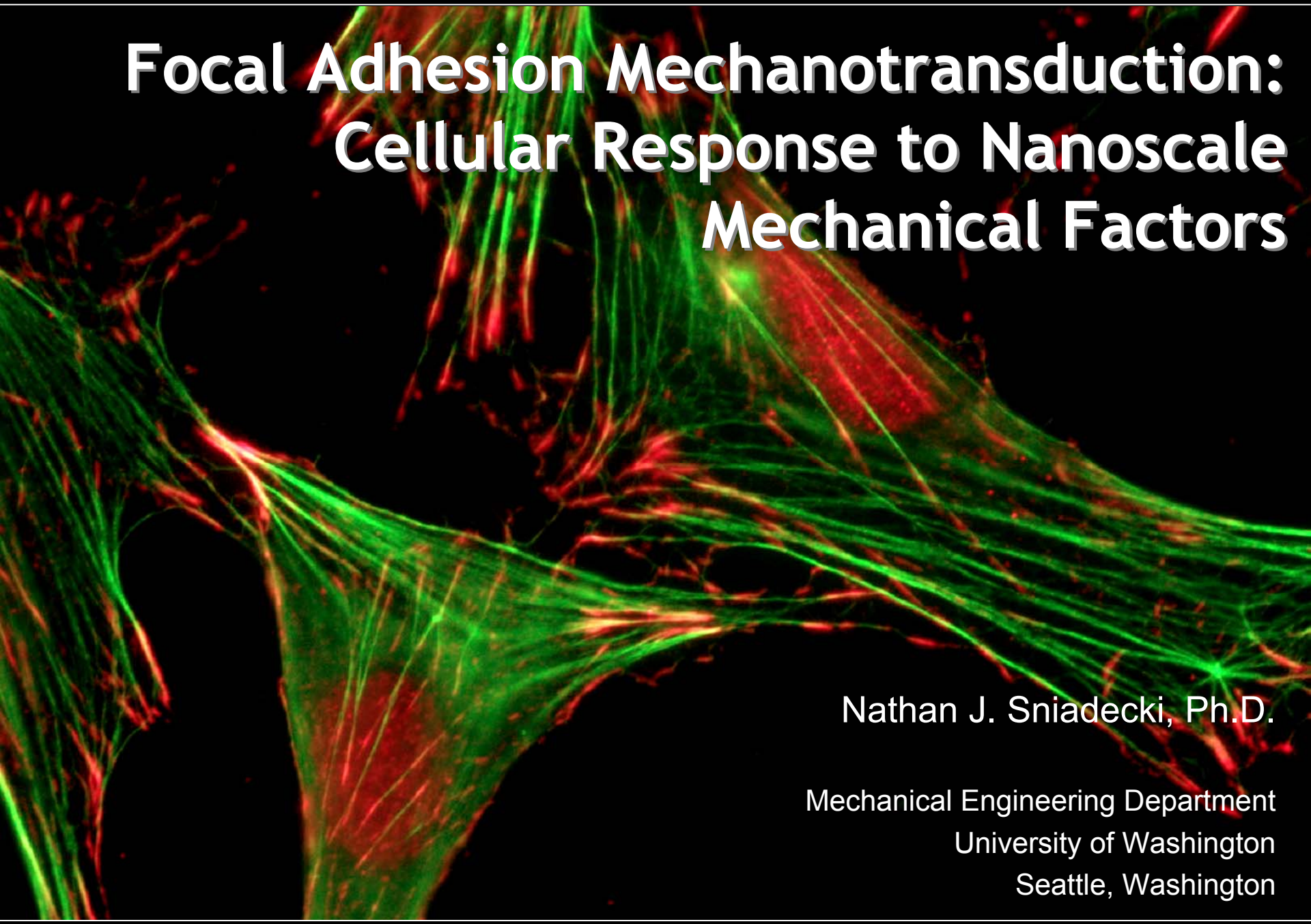
Focal Adhesion Mechanotransduction: Cellular Response to Nanoscale Mechanical Factors



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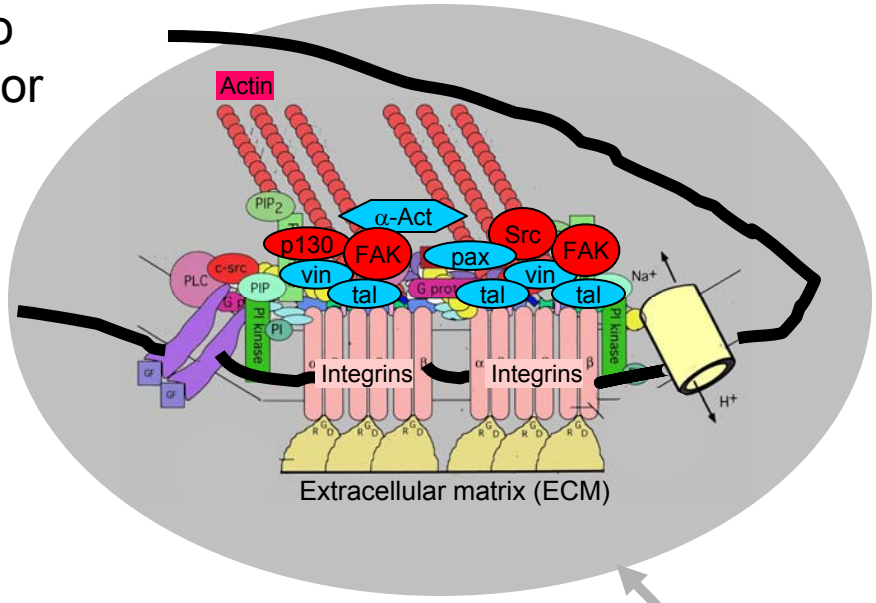
Mechanotransduction at Focal Adhesions

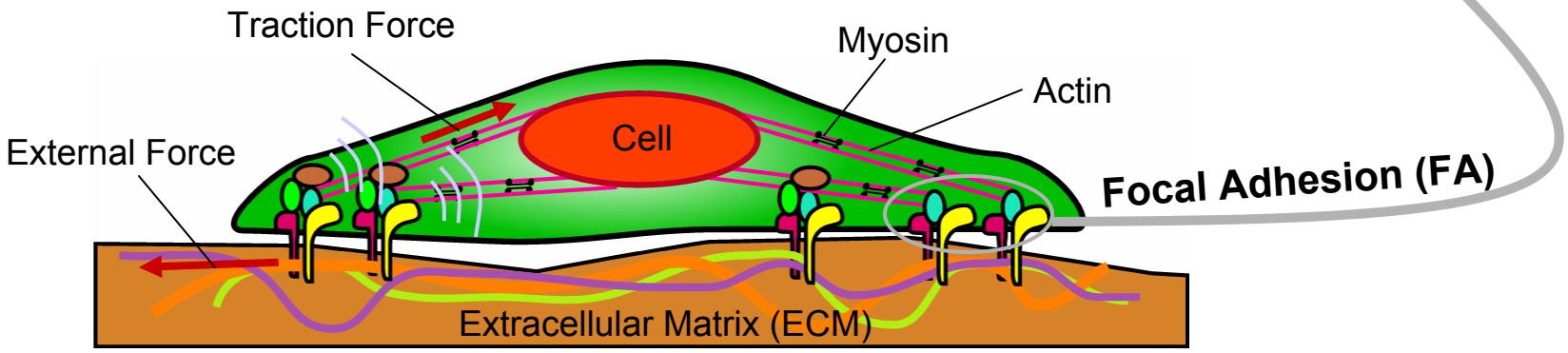
Focal adhesions are force sensitive integrin-receptor complexes (100 nm – 1 μm).

Structural proteins link integrins to actin to develop traction force for cellular migration or contraction

Signaling proteins activated with integrin-matrix binding and force

Traction forces or external forces are transduced into biological signals that can regulate cell function

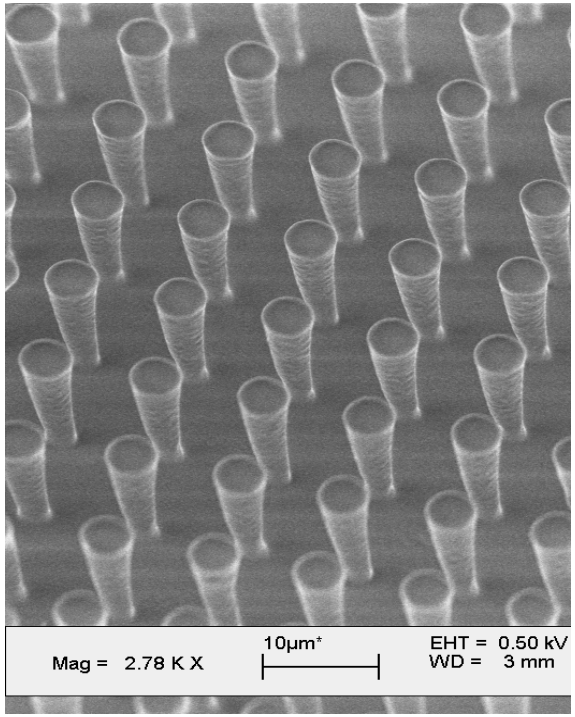


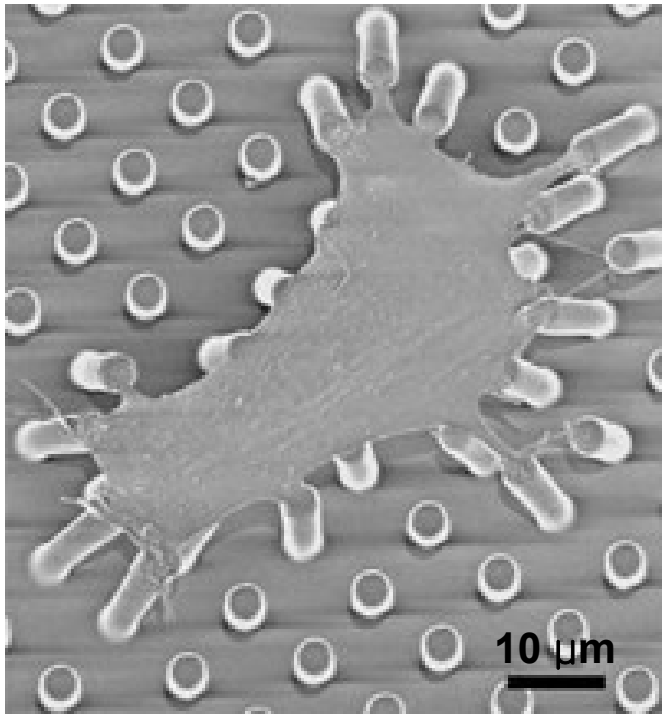


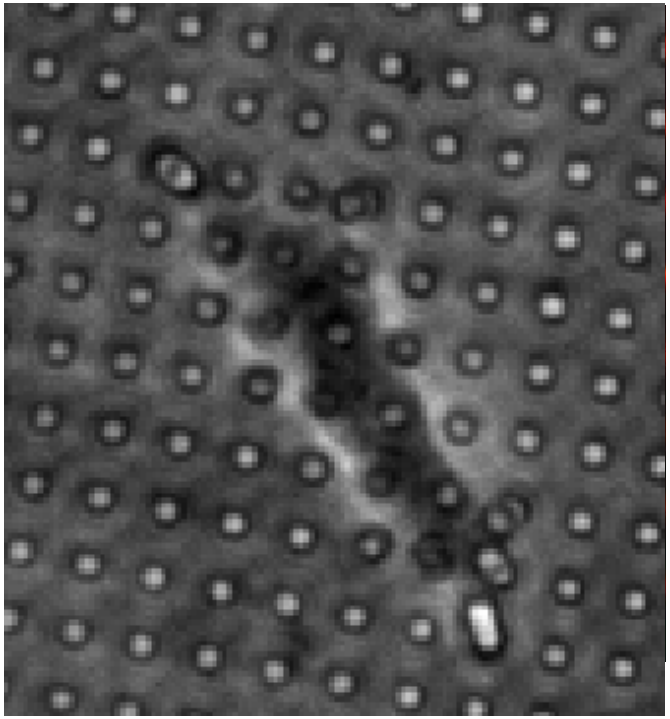
Traction Force Sensor Array

Arrays of flexible microposts to measure traction forces

Made with soft lithography of polydimethlysiloxane (PDMS)

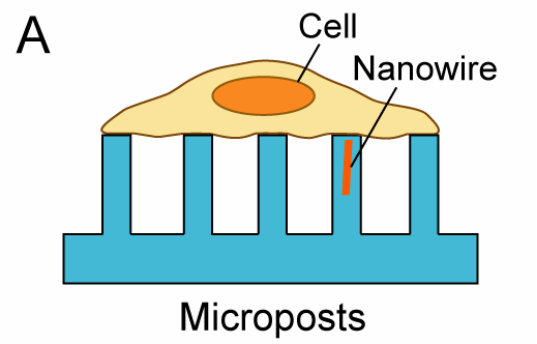


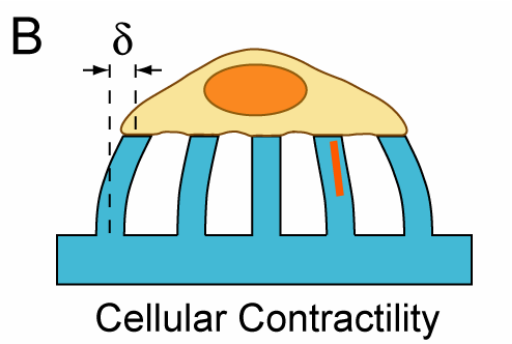


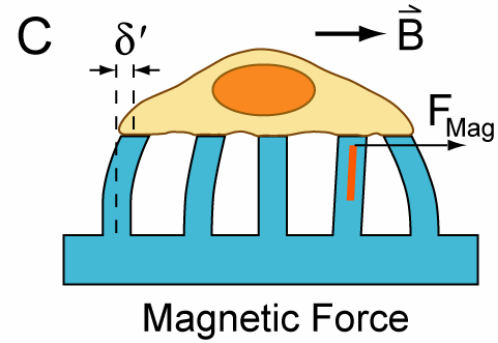


3-µm diameter, 10-µm height microposts

Magnetic Microposts







Sensor and Actuator System

- Measure traction forces with microposts

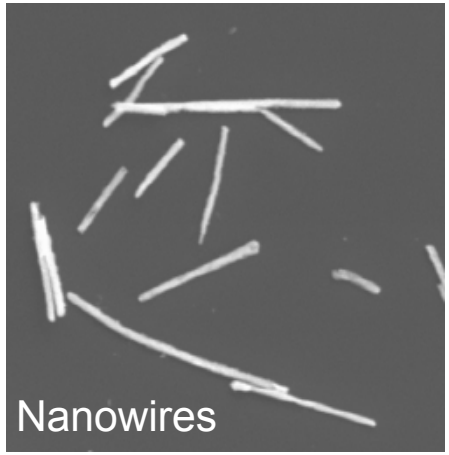
$$F_{tr} = K\delta = \left(\frac{3\pi \mathrm{E}^{\mathrm{d}}}{64\mathrm{L}^3}\right)\delta$$

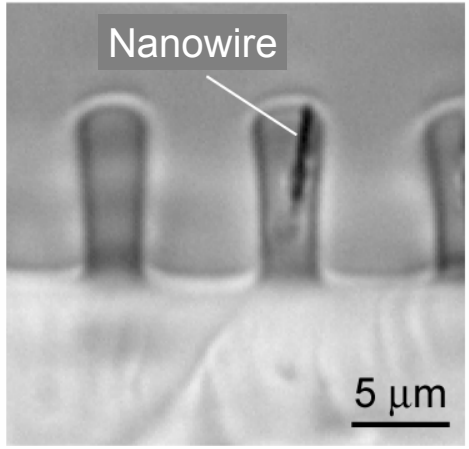
- Apply forces with magnetic nanowires

$$\tau = \mu_{\perp} \cdot \mathrm{B} \qquad F_{Mag} = \frac{3\tau(L + L_w)}{2(L^2 + L_w L + L_w{}^2)}$$

Cobalt Nanowires

- 300 nm diameter, 5-7 μm long
- High magnetic moment (μ) along long axis

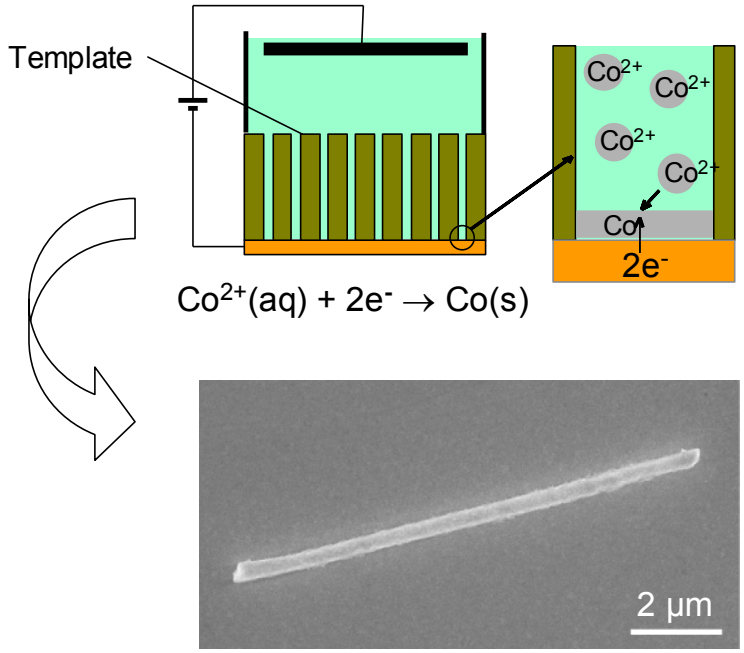




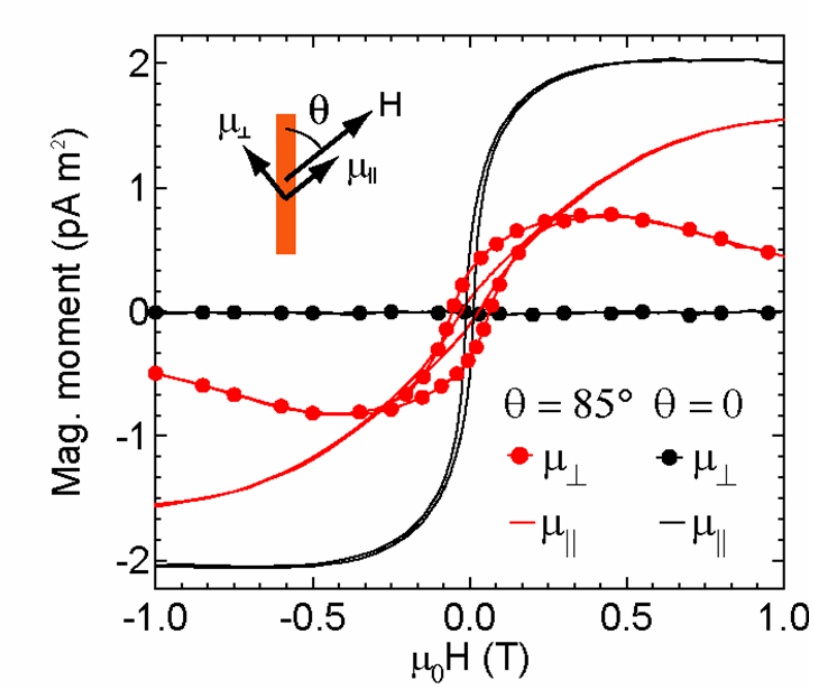
N.J. Sniadecki, et al., *PNAS*, 2007, 104:114553-8
N.J. Sniadecki, et al., *Rev Sci Instr*, 2008, 79, 044302

Magnetic Nanowires

Cobalt Electrodeposition



Vibrating Sample Magnetometer



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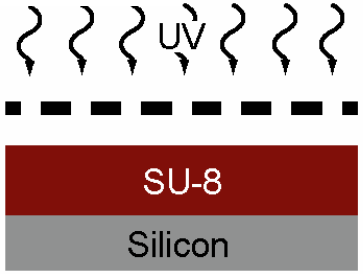
N.J. Sniadecki, et al., *Rev Sci Instr*, 2008, 79, 044302

Fabrication

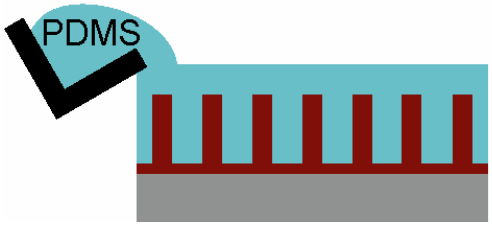
Nanowires magnetically embedded into PDMS mold

1. Lithography

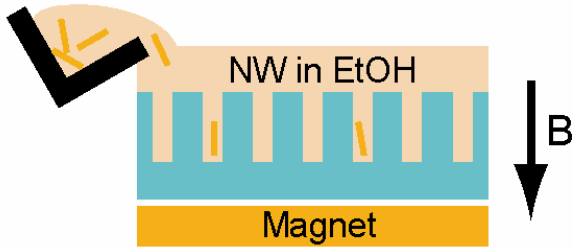


2. Develop

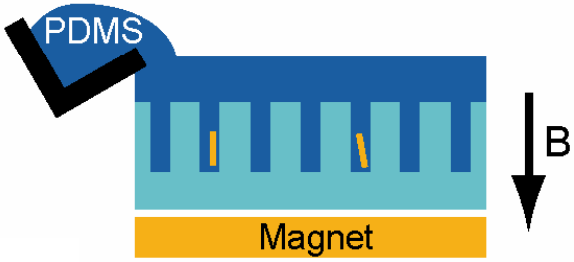
3. Cast in PDMS



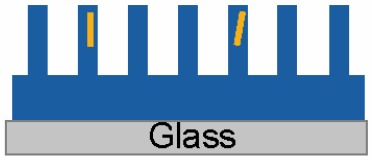
4. Deposit Nanowires



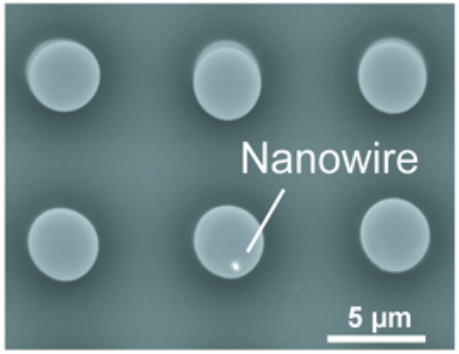
5. Encase in PDMS



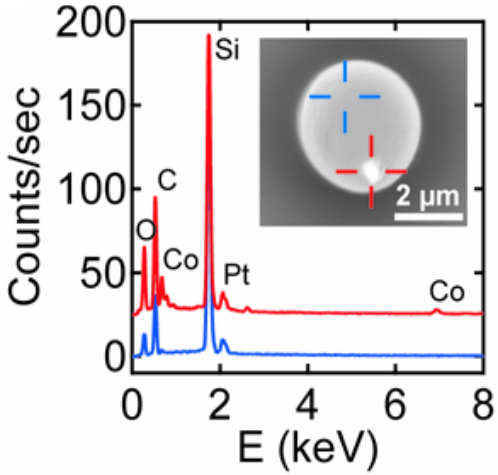
6. Release



SEM Image



EDS Measurement



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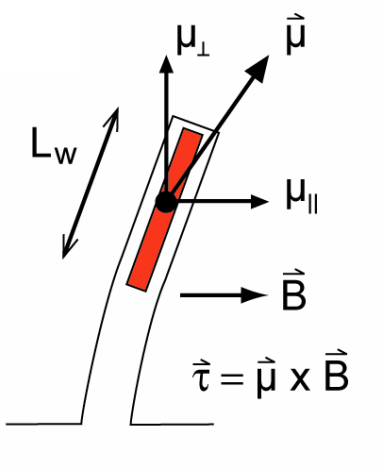
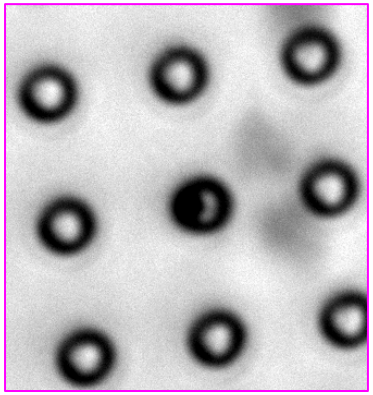
N.J. Sniadecki, et al., *Rev Sci Instr*, 2008, 79, 044302

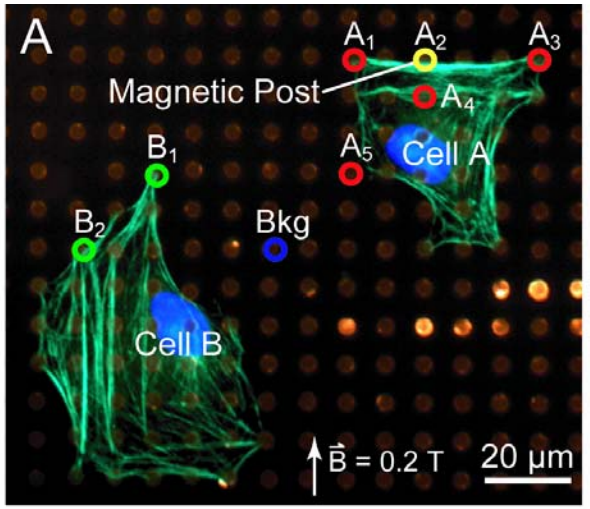
Magnetic Stimulation

Magnetic actuation for external force

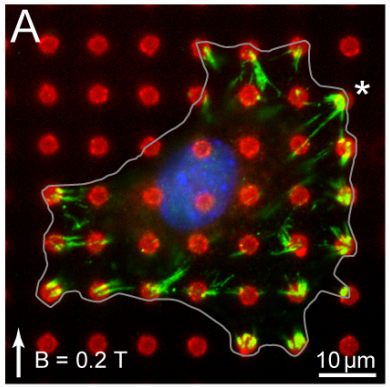


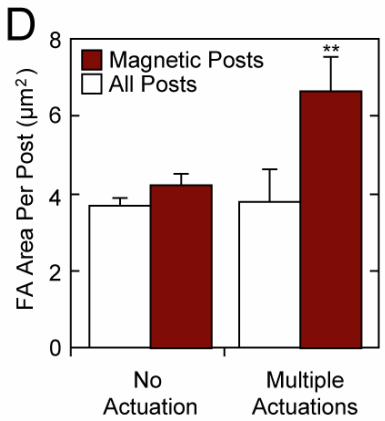


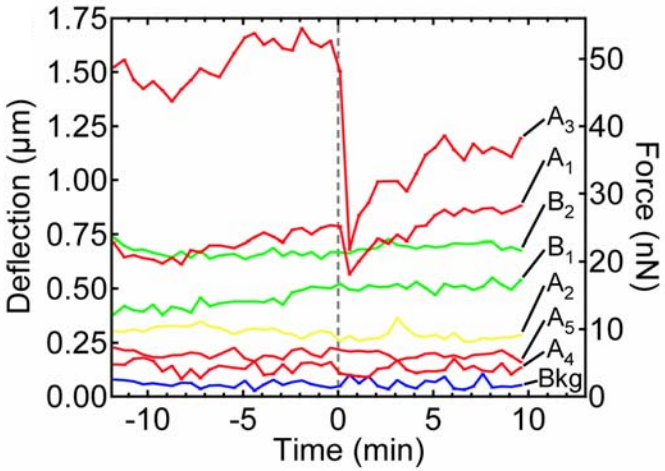
Stimulation relaxes traction forces



Focal adhesion protein recruitment



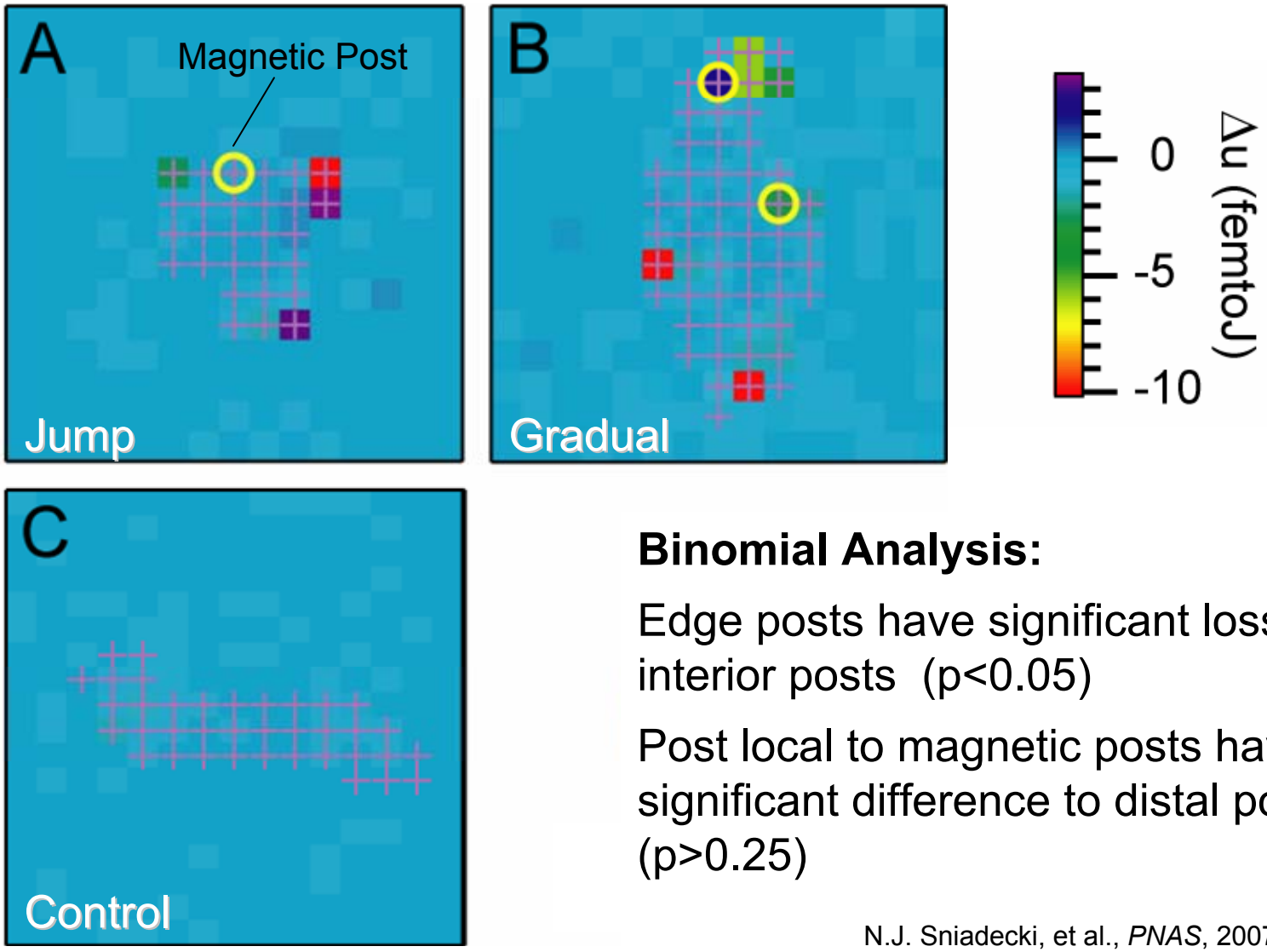




N.J. Sniadecki, et al., *PNAS*, 2007, 104:114553-8

Spatial Response

Relaxation occurs at remote sites along cell periphery but not at interior posts



Binomial Analysis:

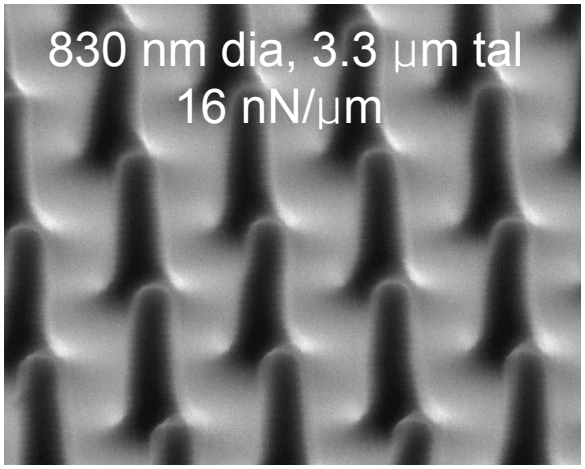
Edge posts have significant loss versus interior posts ($p<0.05$)

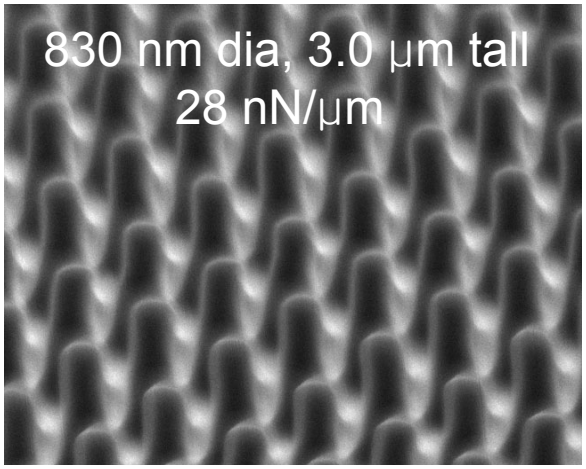
Post local to magnetic posts have no significant difference to distal posts ($p>0.25$)

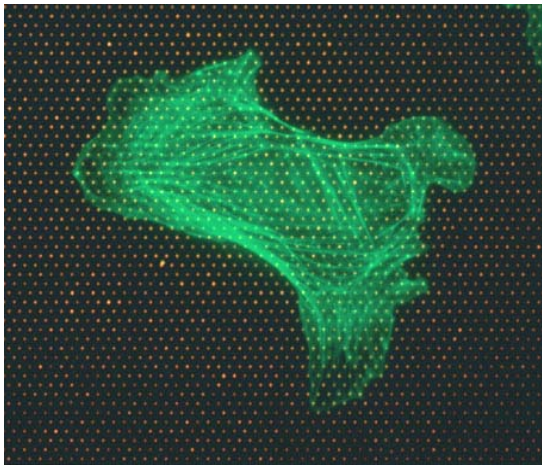
N.J. Sniadecki, et al., *PNAS*, 2007, 104:114553-8

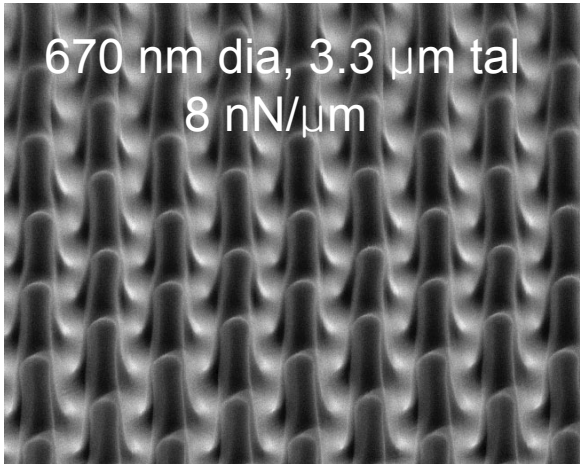
Nanoposts

High Spatial Resolution of Traction Forces

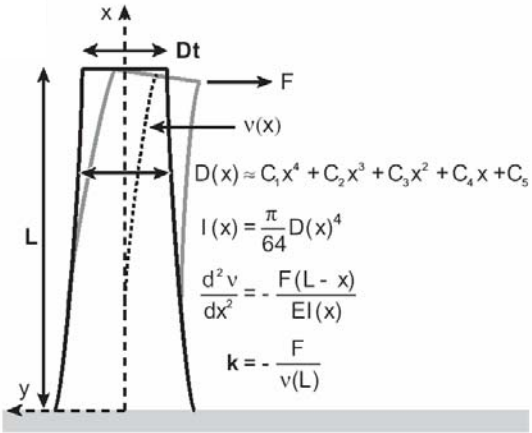


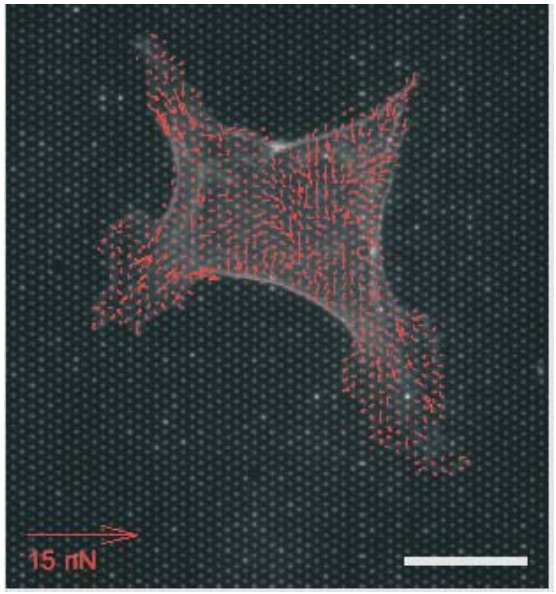






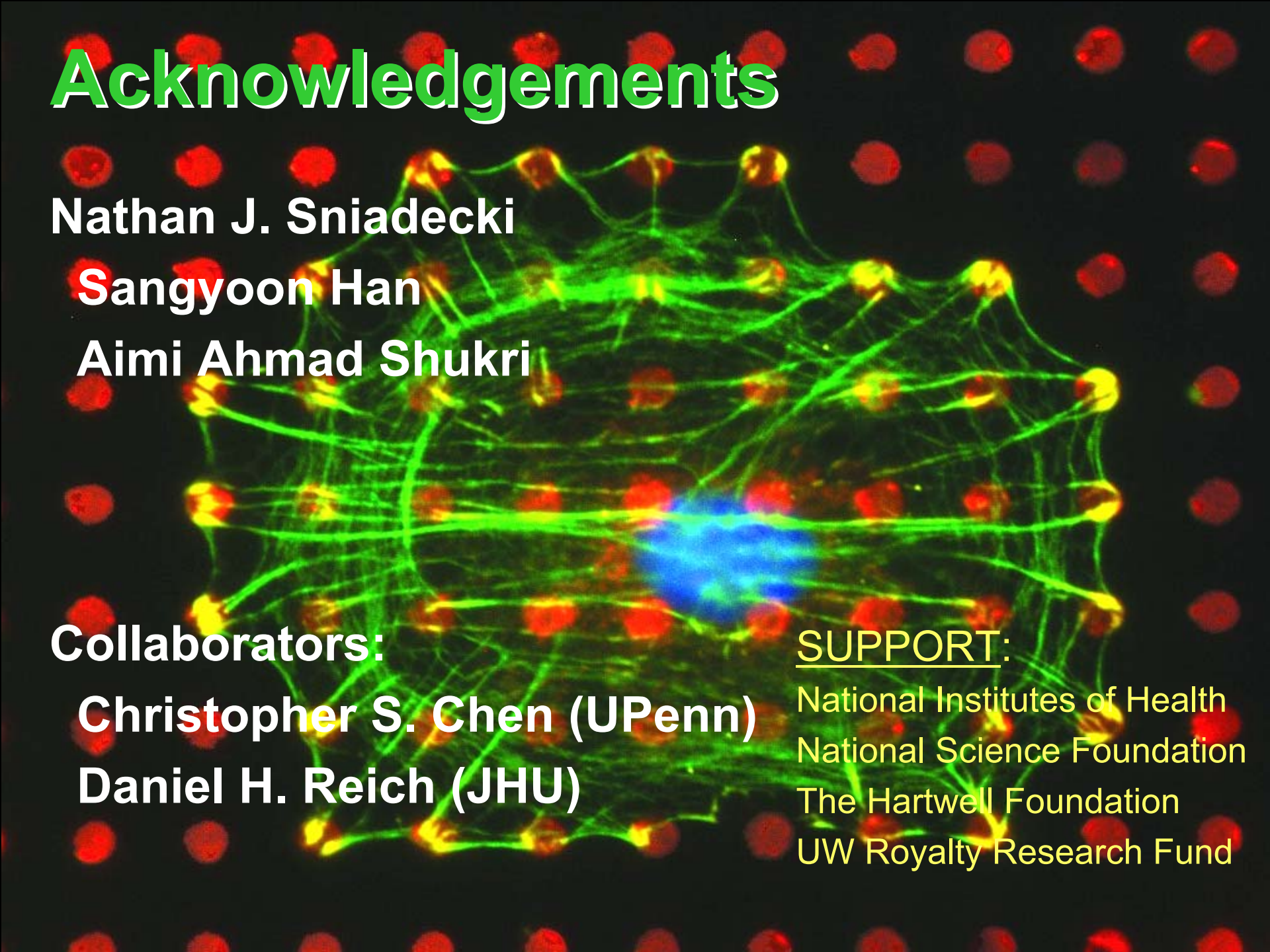
Sloped-wall cantilever





M.T. Yang, N.J. Sniadecki, C.S. Chen, *Adv Mat*, 2007, 104:114553-8

Acknowledgements



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Aimi Ahmad Shukri

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Daniel H. Reich (JHU)

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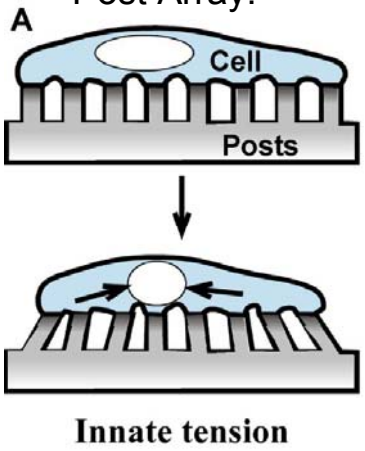
National Science Foundation

The Hartwell Foundation

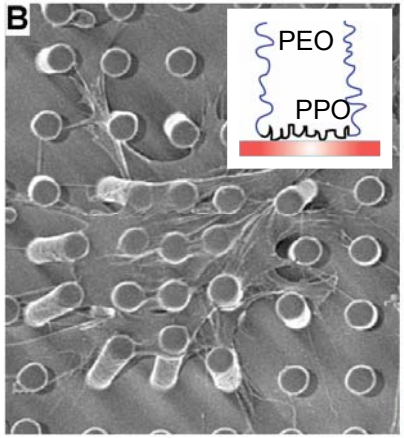
UW Royalty Research Fund

Micropost Force Sensors

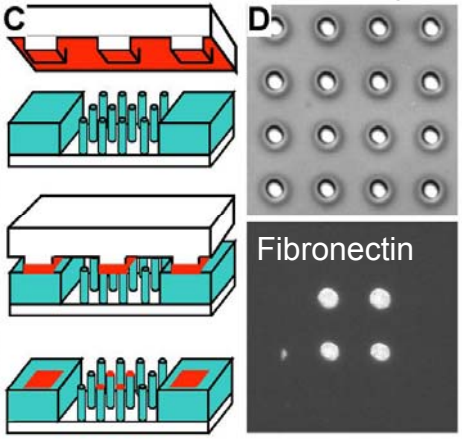
Post Array:



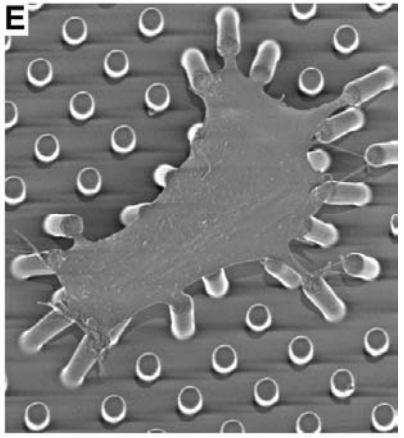
No adhesion blocking:



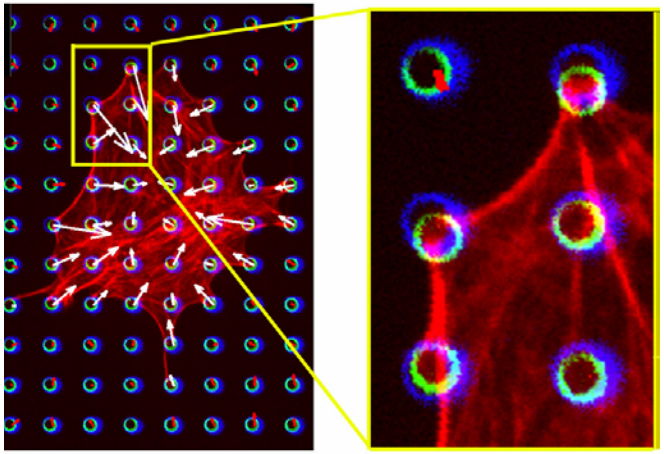
Microcontact printing:



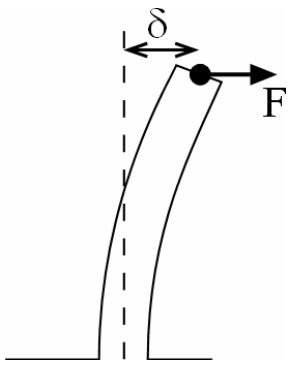
Adhesion only on tips:



Measurements:



Posts deflects as simple cantilever springs:



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

- F … Cellular Force
- K … Spring Stiffness (32 nN/μm)
- δ … Displacement
- E … Elasticity Modulus of PDMS
- d … Post diameter (3 μm dia)
- L … Post Length (10 μm)

J. L. Tan, et al., *Proc. Nat. Acad. Sci.*, 2003, 100:1484-1489
C. A. Lemmon, et al., *Mech. & Chem. Biosystems.*, 2005, 2(1) 1-16