MEMS Devices for Force Sensing in Biology

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PASI on MEMS
6/21/04

STANFORD UNIVERSITY

Theme

- **MEMS devices may be good for many things.**
- **A large fraction of MEMS sensors detect signals by detecting physical force. Often these forces are very small**
- **There are some interesting scientific applications for miniature, sensitive force sensors, especially in Biology.**

Some Definitions

- <u>MEMS</u> : Micro Electro Mechanical Systems

- <u>Micromachining</u> : The use of IC Fab tools to make micromechanical structures

Why are MEMS Interesting?

Technological Applications

inertial, automotive, optical, biochemical

Interesting Fundamentals

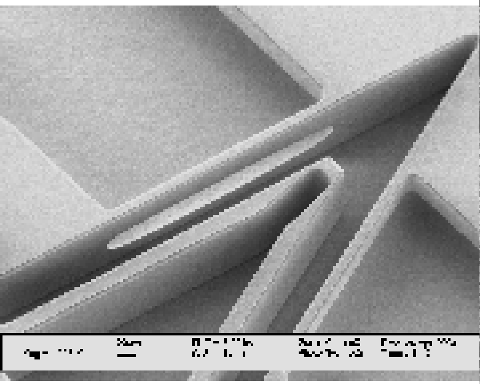
small forces, novel interactions, science
Measurement opportunities

Science Opportunities

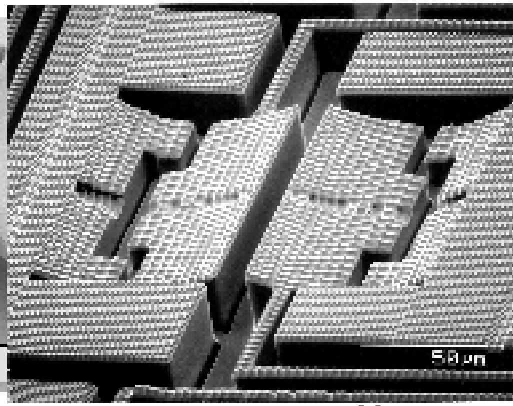
new materials, design and performance
implications, little quality work done

Variety!

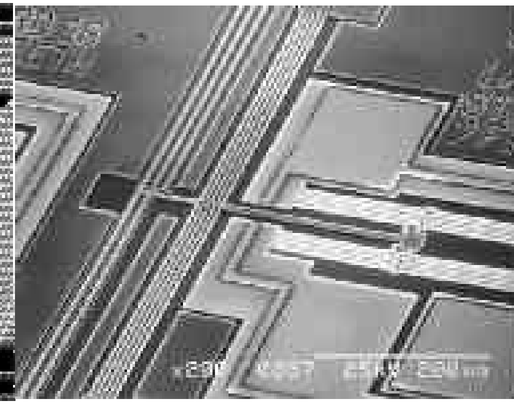
MEMS Devices in Bewildering Variety have been demonstrated on the surfaces of wafers.



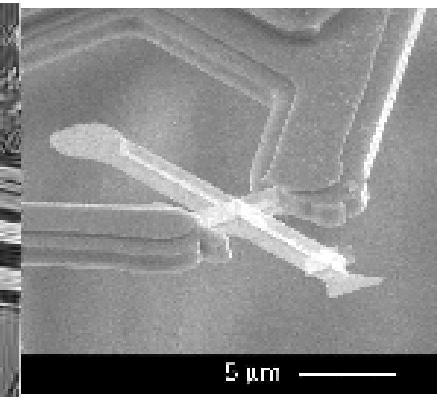
Frank, Pisano, UC Berkeley



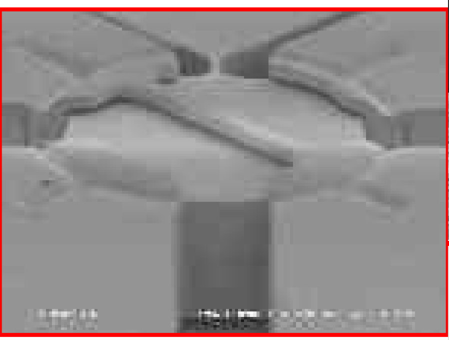
Rao, Aimi, MacDonald
UCSB



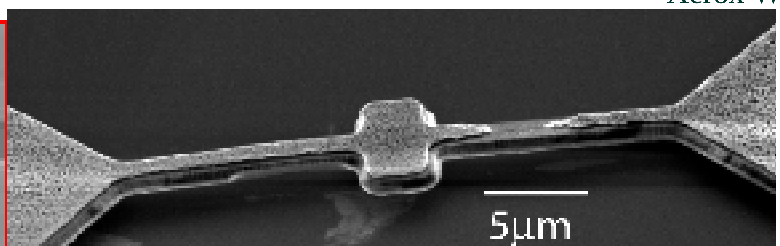
Gulvin, et.al
Xerox Wilson



Chui, et.al, IBM Almaden



Pourkamali, Ayazi,
Ga. Tech



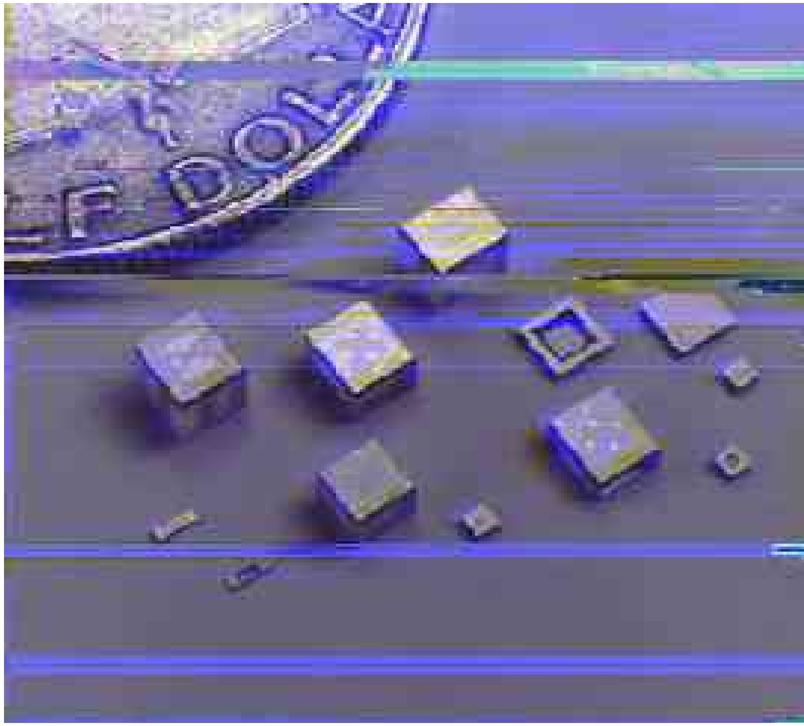
Carter, Kang, White, Duwel, Draper Labs

Li, et.al, MIT

All from Proceedings,
Hilton Head '04

MEMS Force Measurement Example

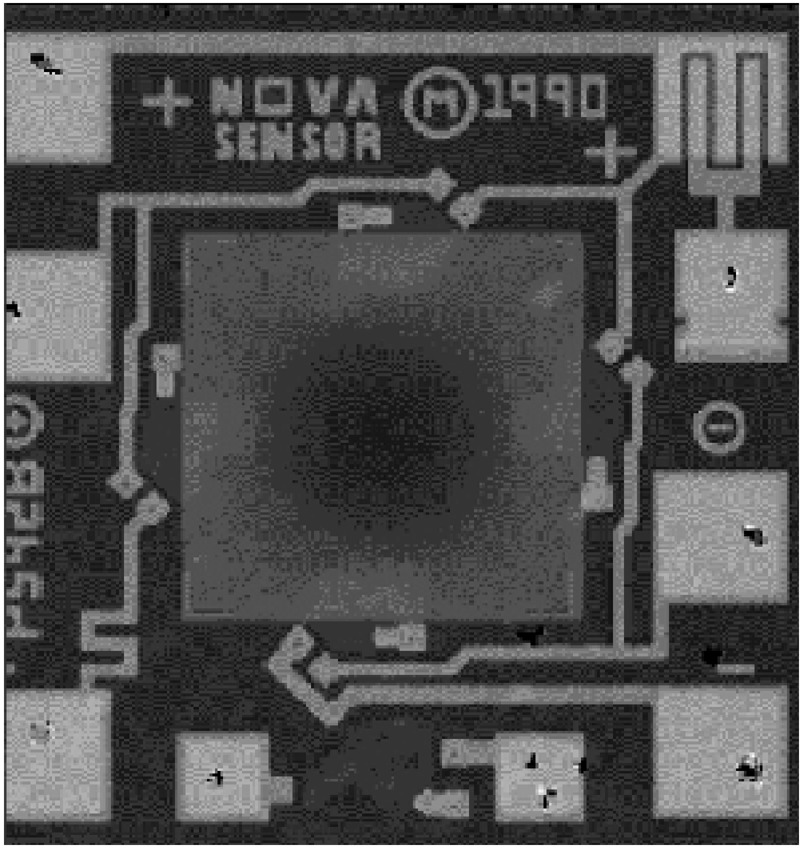
Commercial Piezoresistive Pressure Sensor



Lucas Novasensor

Doped Silicon Strain Gauges for Diaphragm Strain Detection.

Force in a Silicon Pressure Sensor



Lucas Novasensor

Model NP301

- **Range : 5 PSI -> 100 kPa**
- **Accuracy : 0.5% FullScale**
- **Diaphragm Area : 0.5 mm x 0.5 mm**
- **Full Scale Force is 25 mN, Specified Errors correspond to 100 µN.**
- **The RMS noise is less than 10 nN/√Hz.**

How Small is a nanoNewton?

Examples (in 1g)

- **A drop of water weighs 10 µN**
- **The Si diaphragm of the Novasensor Pressure sensor weight about 50 nN**
- **An eyelash weighs 100 nN**
- **Polysilicon micromachined structures can weigh about 1 nN**

Scaling Issues for Force Sensors

Forces get smaller

- For Pressure Sensors, F ~ Area = L^2
- For Inertial Sensors, F ~ Volume = L^3

Transducers Lose Sensitivity

- Capacitors scale as Area = L^2
- Optical, Piezoelectric, Piezoresistive also lose sensitivity as size is reduced

These trends oppose miniaturization

Scaling Issues for Force Sensors

Noise generally does not improve with miniaturization

- **Electrical Noise will probably be the same.**
- **Energy Fluctuations ($k_B T$) will result in larger errors.**
  - **Thermomechanical noise scales as $1/\sqrt{m}$**
- **Some 1/f noise becomes more significant**
  - **Increased surface/volume**

ADXL202 Example

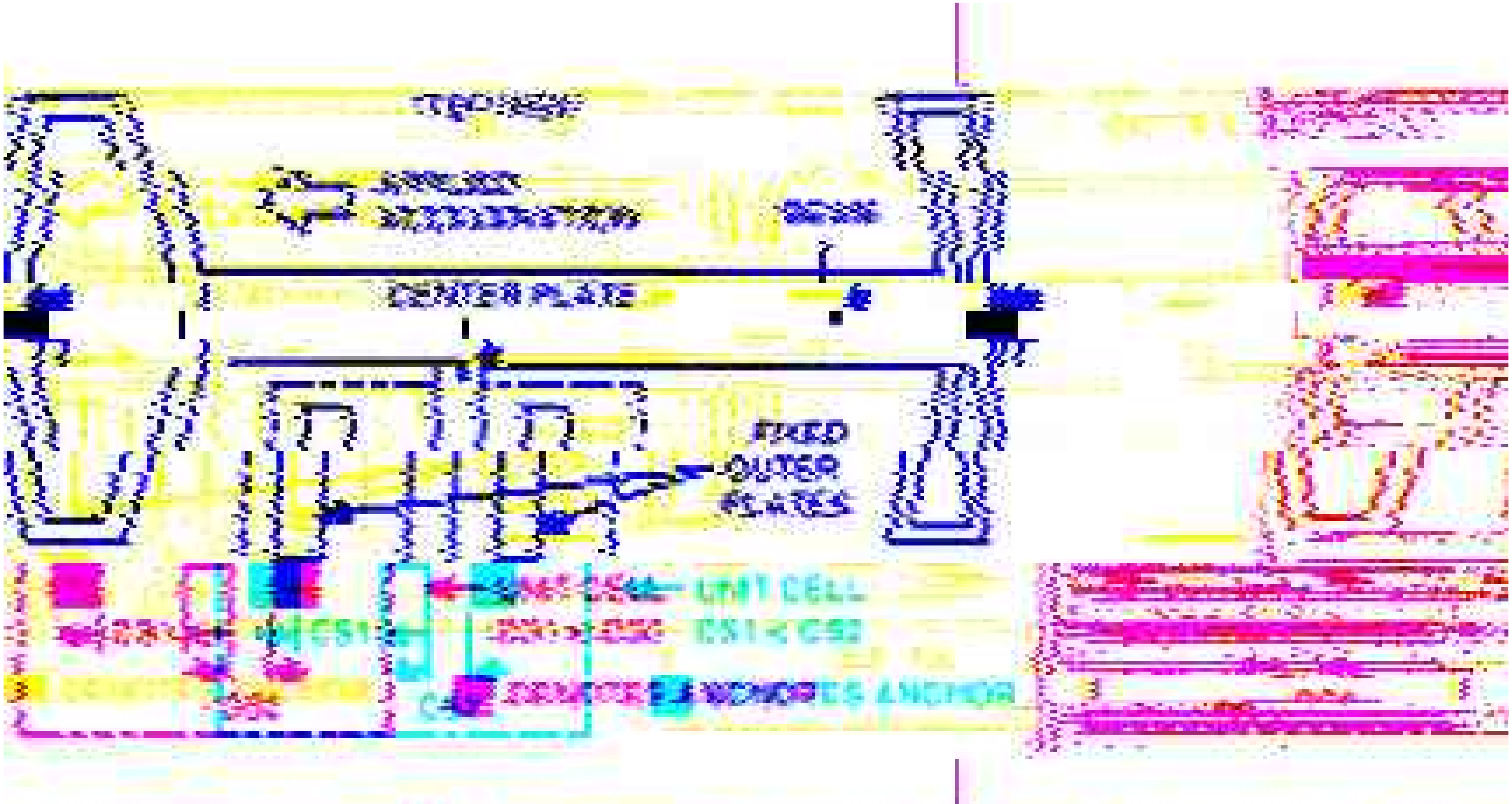


Figure 17. The ADXL05 Sensor Momentarily Responding to an Externally Applied Acceleration

ADXL202 Example

- **This Accelerometer has the following Fundamental Parameters :**

Structural Thickness = ~ 2 μm

Mass = ~ 1 x 10^{-10} kg

Suspension Stiffness = ~ 1 N/m

Resonant Frequency = ~ 10 kHz

Detectable Acceleration = 0.5 mg/

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Suspension Stiffness = ~ 1 N/m

Resonant Frequency = ~ 10 kHz

Detectable Acceleration = 0.5 mg/

Detectable Displacement = 0.005Å/

Detectable Force = 0.5 pN//

Thermodynamics in Accelerometers

Thermal fluctuations in micromechanical systems exert a noise force, which cannot be distinguished from inertial forces.

- The minimum detectable acceleration from thermal noise is

$$A_n =$$

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Thermal fluctuations in micromechanical systems exert a noise force, which cannot be distinguished from inertial forces.

- The minimum detectable acceleration from thermal noise is

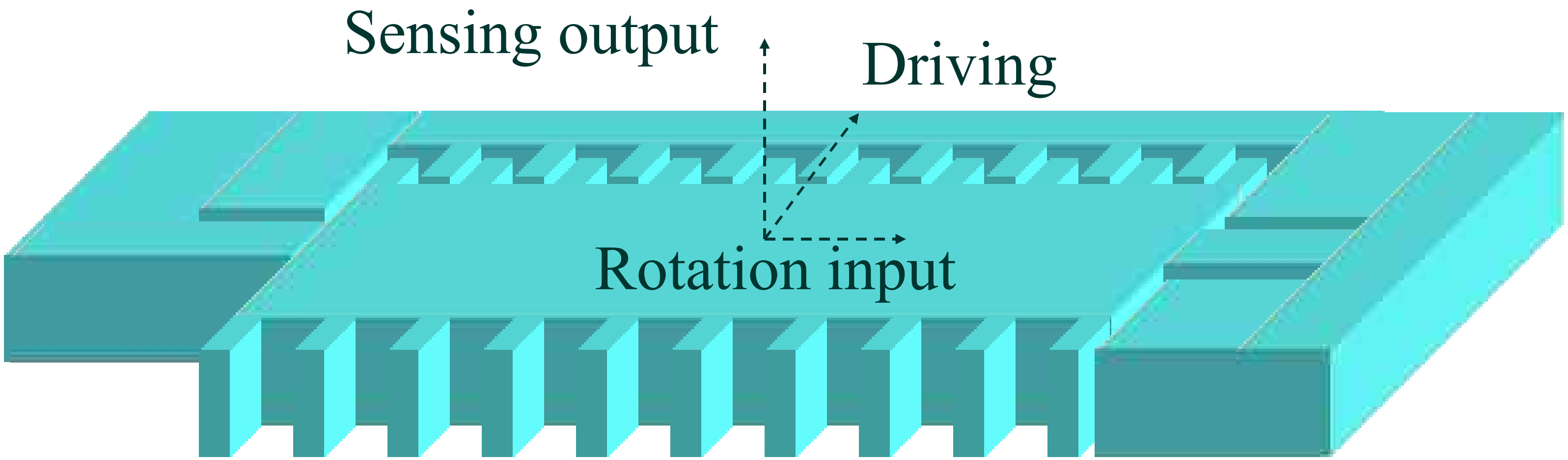
$A_n =$

$\omega_o = 10$ kHz, $m = 0.1\ \mu gm$, $Q = 0.7$

$A_n = 0.3\ mg/$

Force Sensing in Gyroscopes

MEMS gyros operate by detection of Coriolis Forces applied to moving masses $F = m\omega \times v$



Force Sensing in Gyroscopes

- **MEMS gyros operate by detection of Coriolis Forces applied to moving masses $F = m\omega \times v$**
- **Need large amplitude, high-frequency oscillation for large signals.**
- **Example : Robert Bosch Automotive Skid Control Gyro**

Structural Thickness ~ 12 μm	Mass ~ 3 x 10^{-9} kg
Suspension Stiffness ~ 0.5 N/m	Resonant Frequency ~ 2 kHz
Amplitude of Oscillation ~50 μm	Velocity ~ 0.6 m/s
Detected Rotation ~ 0.1 deg/sec	

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Suspension Stiffness ~ 0.5 N/m	Resonant Frequency ~ 2 kHz
Amplitude of Oscillation ~50 µm	Velocity ~ 0.6 m/s
Detected Rotation ~ 0.1 deg/sec	Detected Force ~ 4 pN

Thermodynamics in Gyroscopes

Thermal fluctuations in micromechanical systems exert a noise force, which cannot be distinguished from Coriolis forces.

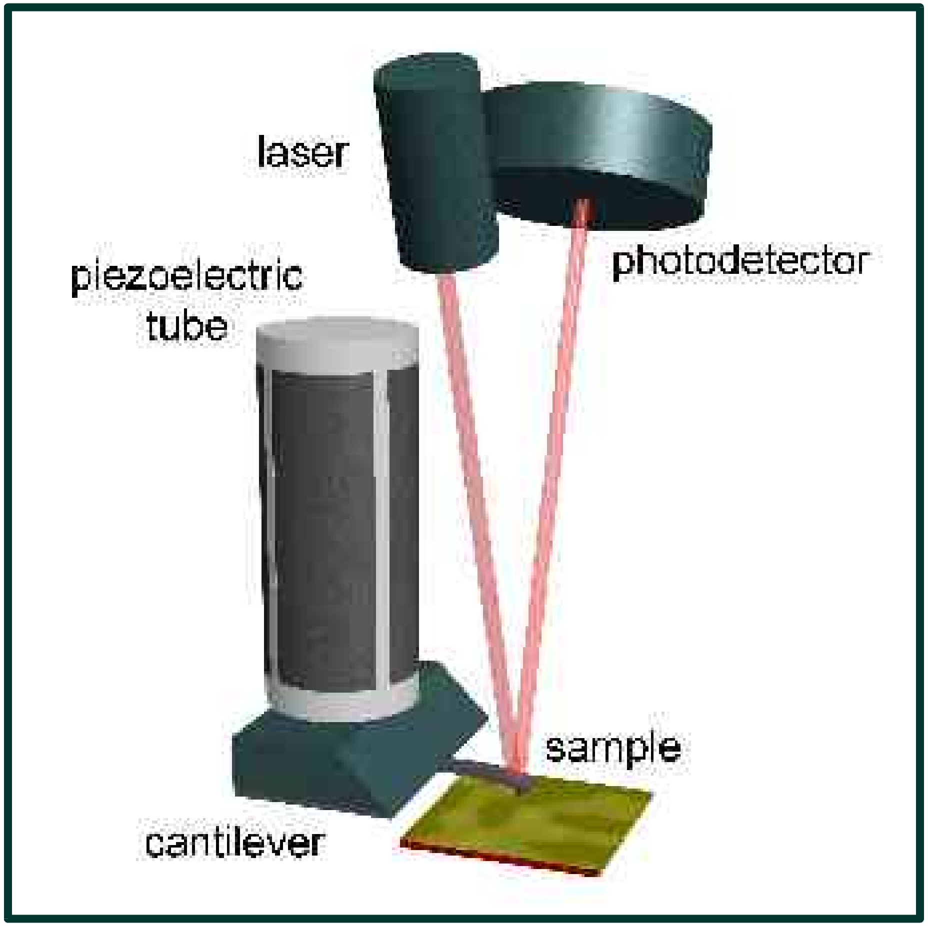
F.Ayazi and K.Najafi, JMEMS 10,169 (2001).

From this, we clearly see that maximizing amplitude and frequency are important, and that maximizing Q is also important.

The Bosch Skid-Control Gyro is also operating very close to thermodynamic limits

Force Sensing Cantilevers

- **In AFM, cantilevers are used to detect surface topography by measuring nN forces.**

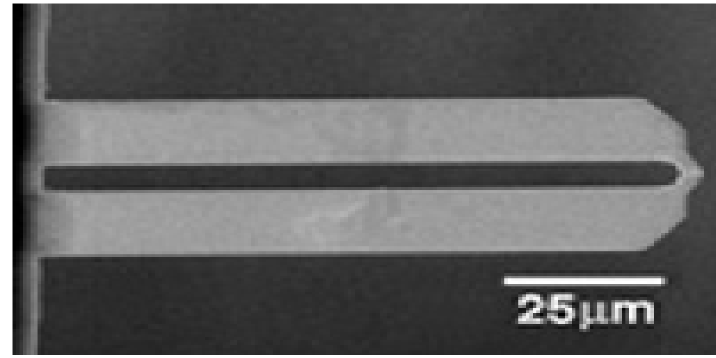


Piezoresistive Cantilevers

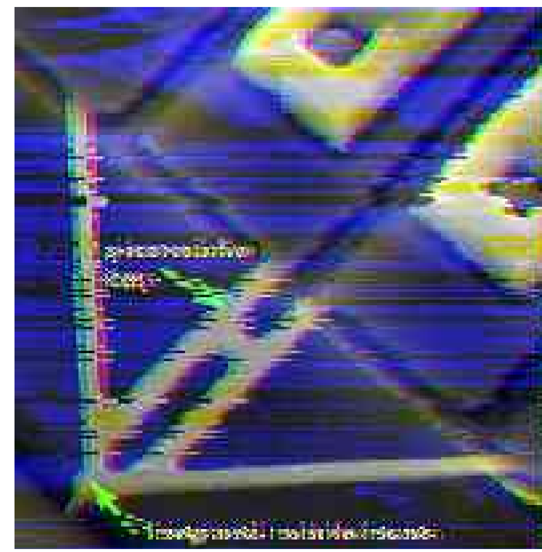
- In AFM, piezoresistive cantilevers are used for measurement of 100 pN forces near surfaces
- Important when Optical methods are inconvenient
- Sensitivity scales as $1/t^3$, so reductions in thickness are very important to pursue

Thinner Piezoresistive Cantilevers

Thin piezolever examples



- 1 µm thick -> 20 pN/√Hz
  - » (Chui, APL'96)



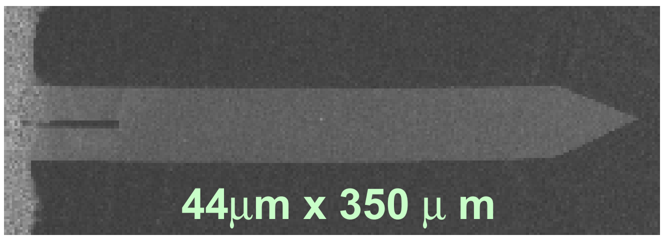
- 0.35 µm thick -> 1 pN/√Hz
  - » (Reid, Transducers'97)

Issue : Avoiding Diffusion of Doped Si Strain Gauge throughout Cantilever Thickness during High-Temperature Steps in Processing. Very hard as devices are thinner than 1 µm.

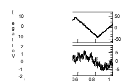
Ultrathin Epi-Doped Cantilevers

Strain gauge formed by epitaxial growth of 30 nm doped layer

97 nm thick



Cantilever response to Applied Load
(1 Hz to 1.2 kHz bandwidth)



V

F(pN)

500 fN resolution
(10 Hz to 1 kHz)

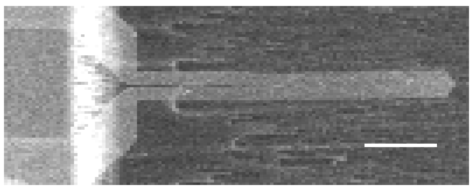
8 fN/√Hz at 1 kHz

J. A. Harley et al, 'High Sensitivity Piezoresistive Cantilevers under 1000Å Thick', Appl. Phys. Lett., Vol 75, No. 2, pp. 289-291, 1999

Ultrathin n-type Piezoresistive Cantilevers

- N-type piezos have higher sensitivity and lower noise.
- Epi-Si, plasma etching process allows fabrication

70 nm thick

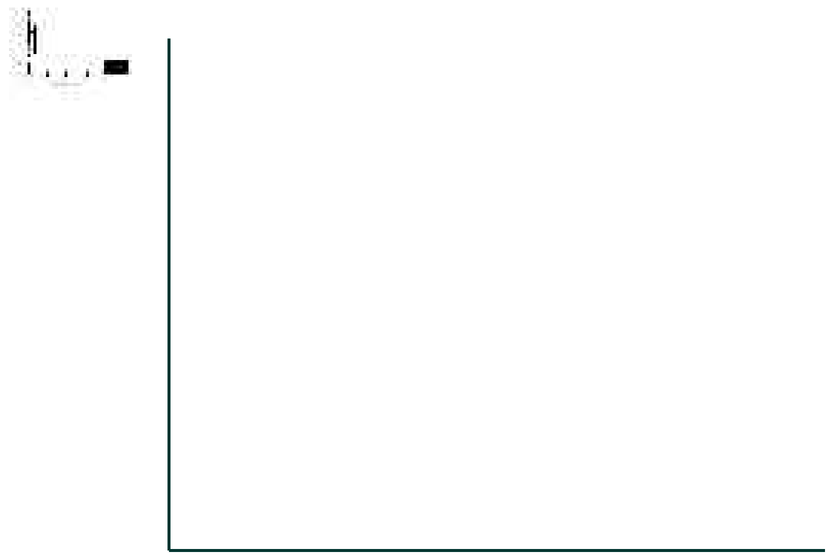


8 μm x 144 μm

120 fN resolution
(10 Hz to 1 kHz)

1.6 fN/√Hz at 1 kHz

Cantilever noise measurement

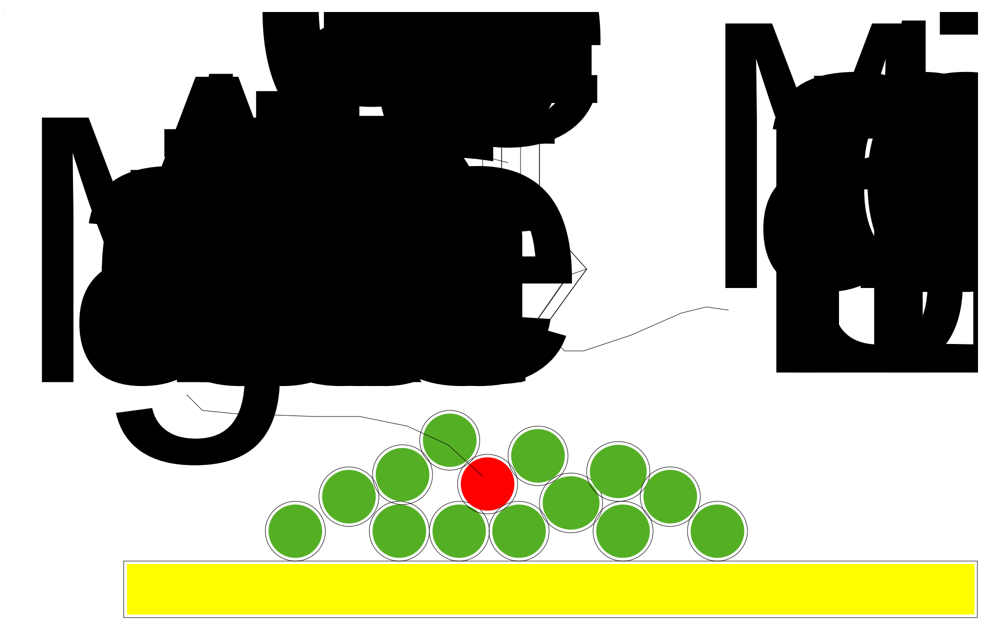


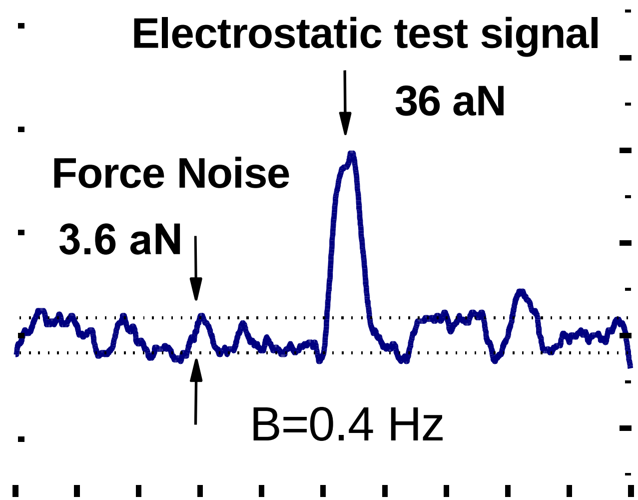
Yiching Liang

Y. Liang, S-W Ueng, T.W. Kenny, "Performance Characteristics of Ultra-Thin n-Type Piezoresistive Cantilevers", Proceedings Transducers '01, Munich Germany, p. 998 (2001).

Example Problem : MRFM

- Force detection of magnetic resonance should enable atomic resolution, 3-D, chemically selective imaging.
- Magnetic forces from individual atoms are <u>very</u> small.





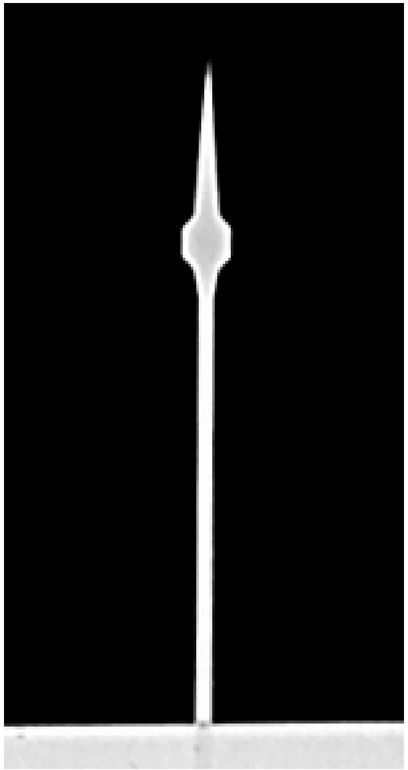
T.D. Stowe, et.al. “attoNewton Force Detection using Ultrathin Silicon Cantilevers”, Appl. Phys. Lett. 71, 288-290 (1997).

Tim Stowe, Kevin Yasumura, Anu Tewary

With Rugar, Mamin, Stipe, Yannoni, Botkin : IBM Almaden

Ultrathin Cantilever

- **thickness (*t*)** 600 Å
- **temperature** 5 K
- **pressure** 10^{-6} Torr
- **$f_0 = \omega_o/2\pi$:** 1.7 kHz
- ***Q*** 6,700
- ***k*:** $6\mathrm{x}10^{-6}$ N/m
- **Fmin** **0.820 aN/√Hz**



50 μm

T.D. Stowe, et.al. "attoNewton Force Detection using Ultrathin Silicon Cantilevers", Appl. Phys. Lett. 71, 288-290 (1997).

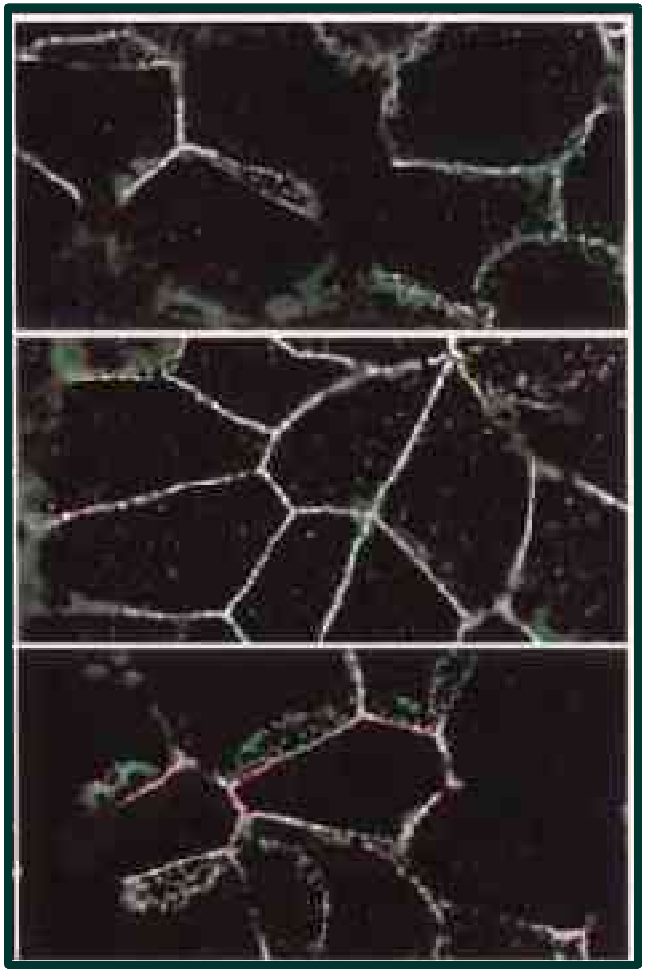
Biology Force Measurement Opportunities

- **Antibody-Antigen Binding** (100 pN)
  - » Lee and Colton, 1994
- **Cellular Adhesion** (5-100 pN)
  - » Adams, Chen, Smith and Nelson (1998)
- **Actin-Myosin Mechanical Behavior** (10 pN-10nN)
  - » Finer, Simmons and Spudich (1994)
- **Protein Folding** (0.1-100 pN)
  - » Powers, Daburesse, Noller (1993)
- **Insect Biomechanics** (nN-mN)
  - » Full, Federle (1993)
- **Small Animal Locomotion/Adhesion** (nN-mN)
  - » Autumn, Full

Many current topics in Biology are related to measurements of forces

Cadherin Molecule Background

- Cadherins - A model system
  - » Used to hold sheets of cells, such as skin, together.
  - » Important for development of an organism from fertilized egg to multicellular individual.
  - » Defects in cadherins lead to cancer.
- Diverse family of molecules
  - » N-cadherin, E-cadherin, K-cadherin, etc.
  - » Many types of interactions to study.
  - » Adhesion contrast for different pairings expected
- Have been cloned, which allows for mutational studies.
- Single-molecule interactions are expected to be 10-200 pN.



(Nelson, et. al., 1998).

Cadherins - Background

- A transmembrane protein
  - » Two functionally significant domains - Extracellular and cytoplasmic
  - » Extracellular domain has five repeats
  - » Distal four domains contain Ca++ binding sites

Structure of the Cadherin/Catenin complex

Extracellular Domain provides adhesion

- Only the N-terminal domain is involved in cell-cell adhesion
- Dimerizes with adjacent cadherin on the same cell

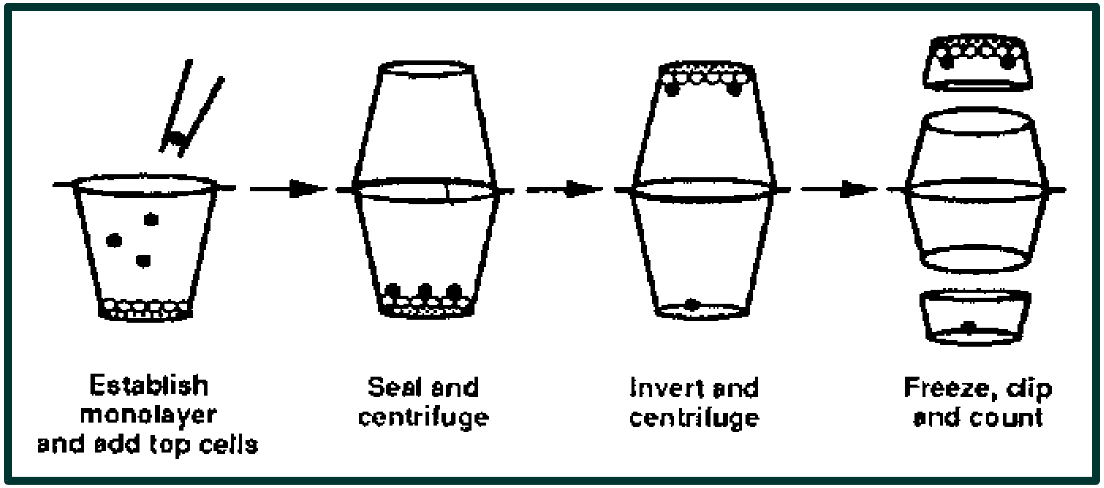
- **Dimer then binds to another cadherin dimer in a homophilic reaction**
  - » **A weak interaction (<< 1 nN)**
  - » **Clustering or other cooperative phenomena are thought to be involved**
    - – **May take a zipper form.**
    - – **Stronger bonds are thought to form through clustering (Yap, et. al. 1997)**
    - – **Interactions with the cytoskeleton strengthen bonds (Adams and Nelson, 1998)**

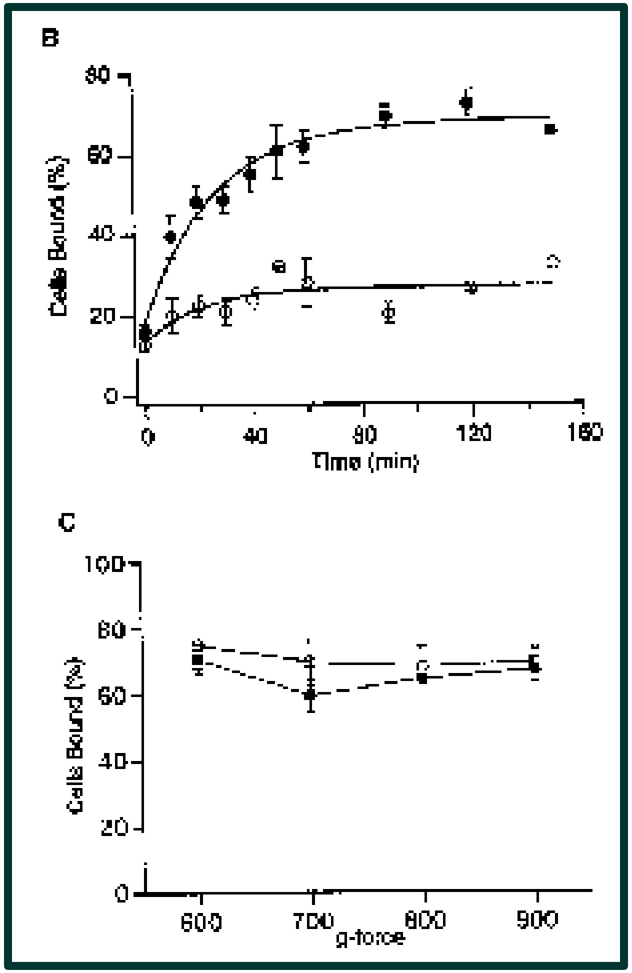
Dimeric structure of cadherin, shown in

a diagram of the zipper model.

Whole-Cell Force measurements

- Laminar flow to assay adhesion based on resistance of cells to detachment from capillaries coated with purified E-cadherin (Yap, et. al., 1997).
  - » Cell adhesion rates
- Adhesion rates of cells subject to centrifugation





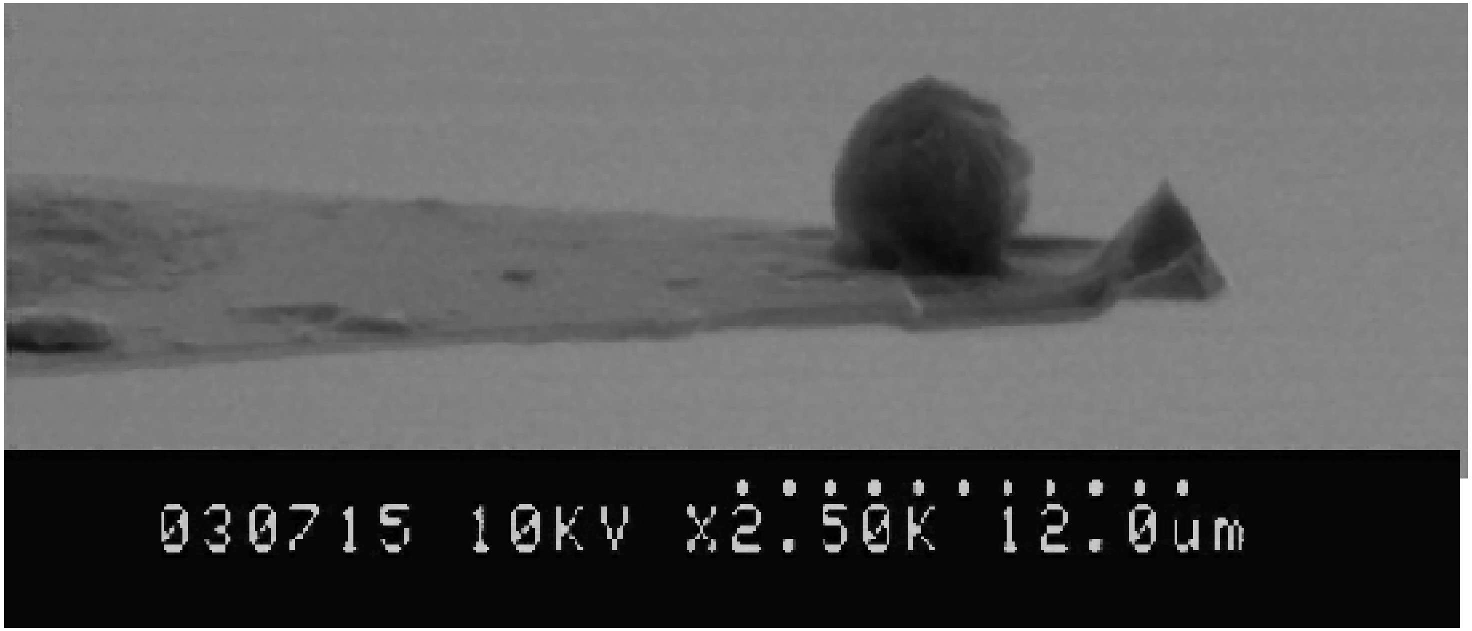
(Yap, et. al., 1997).

MEMS Adhesion Measurement

Mechanical Properties of Molecules

Interaction Forces near 100 pN expected. Many complications (underwater operation,surface chemistry issues)

Bead Attachment



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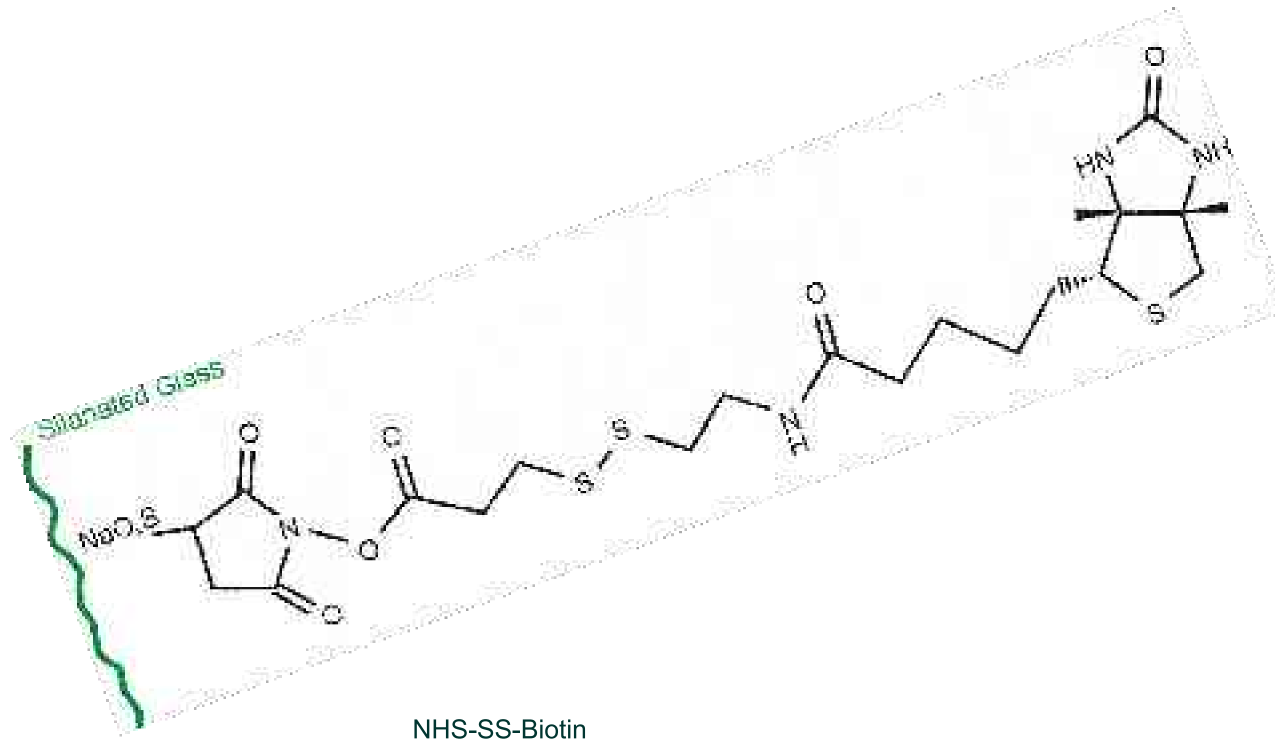
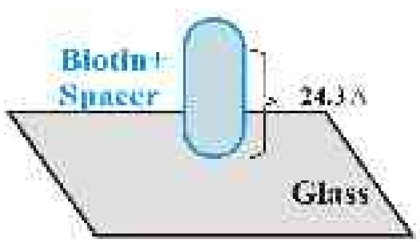
- Pre-prepared 2 µm Polystyrene Bead with neutravadin/biotin coating
- Manual attachment to cantilever prior to AFM experiment.

Cadherins are “tethered” to a slide via a chain of other molecules



NHS-SS-Biotin

Cover-slip	Length (Å)
NHS-SS-Biotin	24.3



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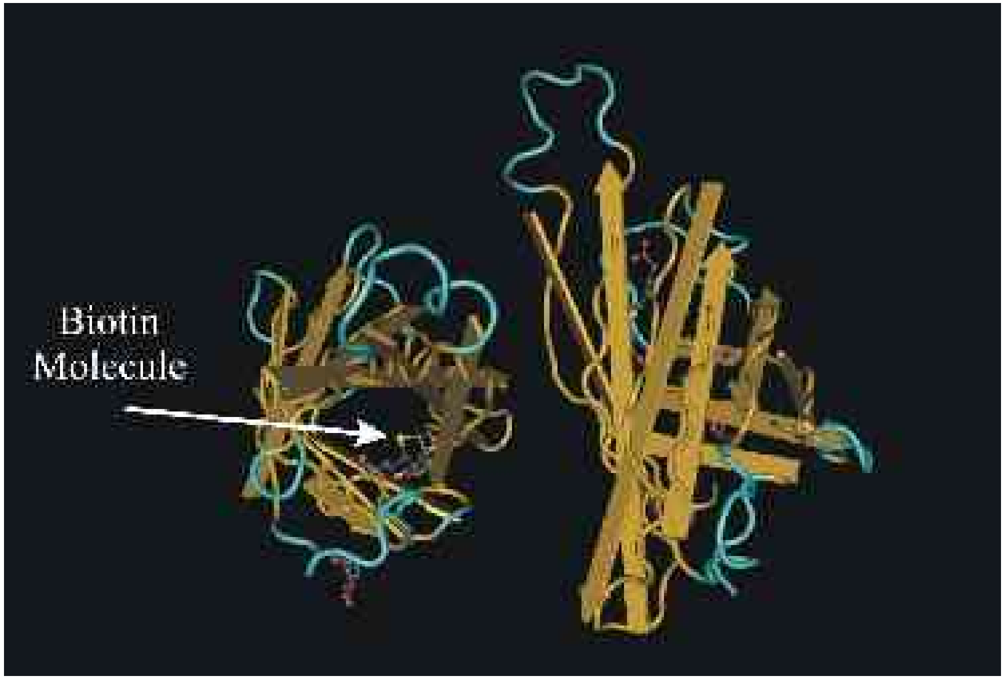
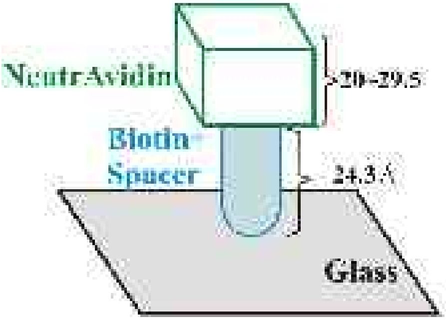


Biotin-Avidin complex. Biotin binding pocket indicted. PDB ID: 2AVI

Cover-slip	Length (Å)
NHS-SS-Biotin	24.3
NeutrAvidin	20 to 29.5



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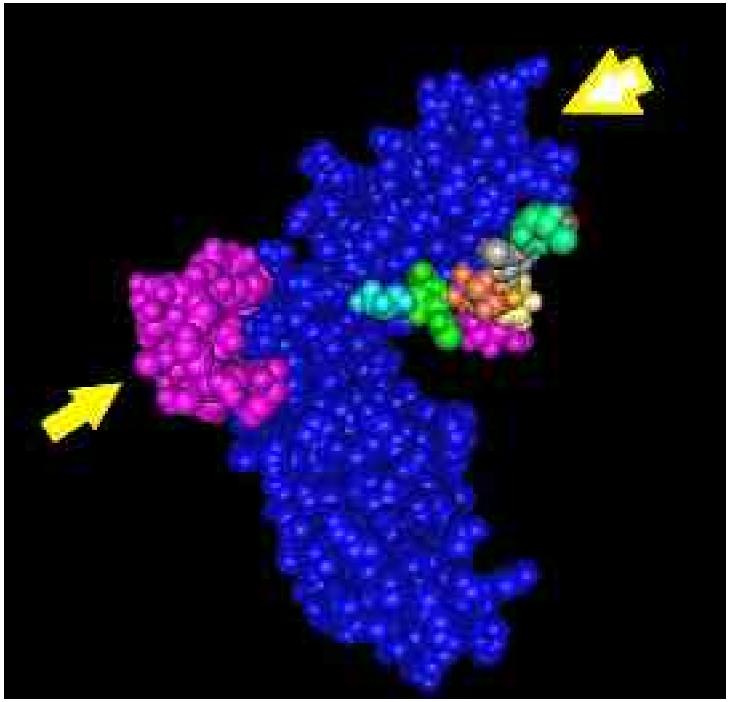
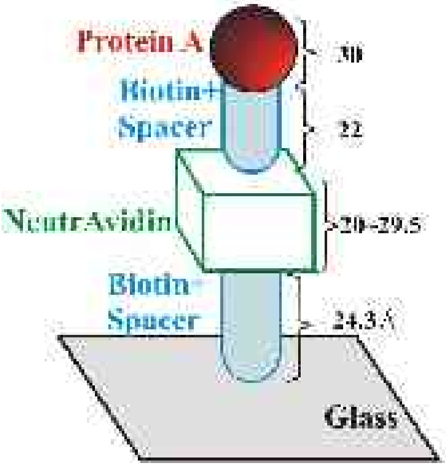


The Protein A-Fc complex, Binding sites indicted. PDB ID: 1FC2

Cover-slip	Length (Å)
NHS-SS-Biotin	24.3
NeutrAvidin	20 to 29.5
Biotinylated Protein A	22+30



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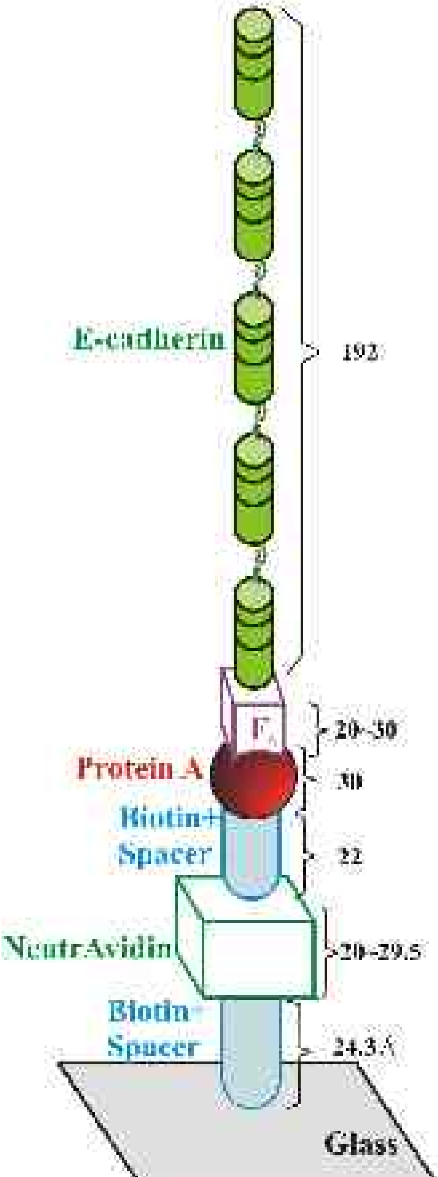
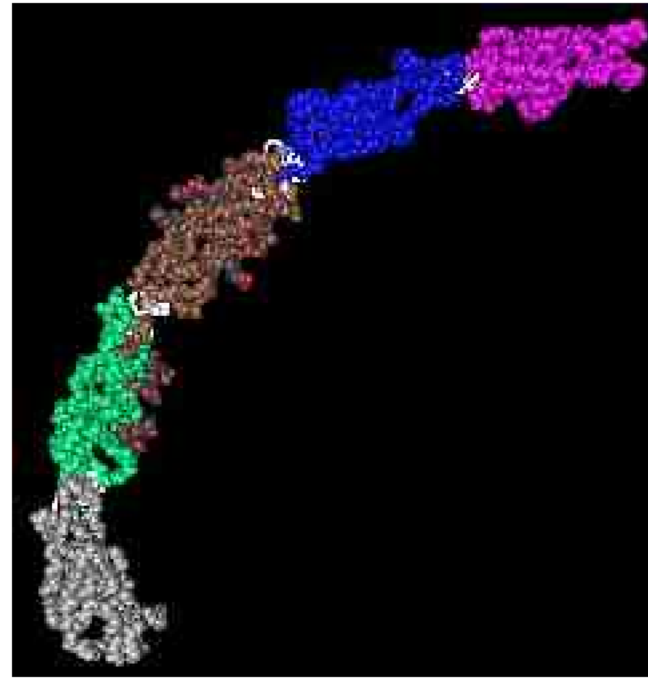
Cadherins are "tethered" to a slide via a chain of other molecules





C-Cadherin Ectodomain from Boggon T.J., (PDB ID: 1L3W)

Cover-slip	**Length (Å)**
NHS-SS-Biotin	24.3
NeutrAvidin	20 to 29.5
Biotinylated Protein A	22+30
F_c-E-Cadherin	30 to 40 +192.5 to 250
Sub-total	**318.8 to 395.8**

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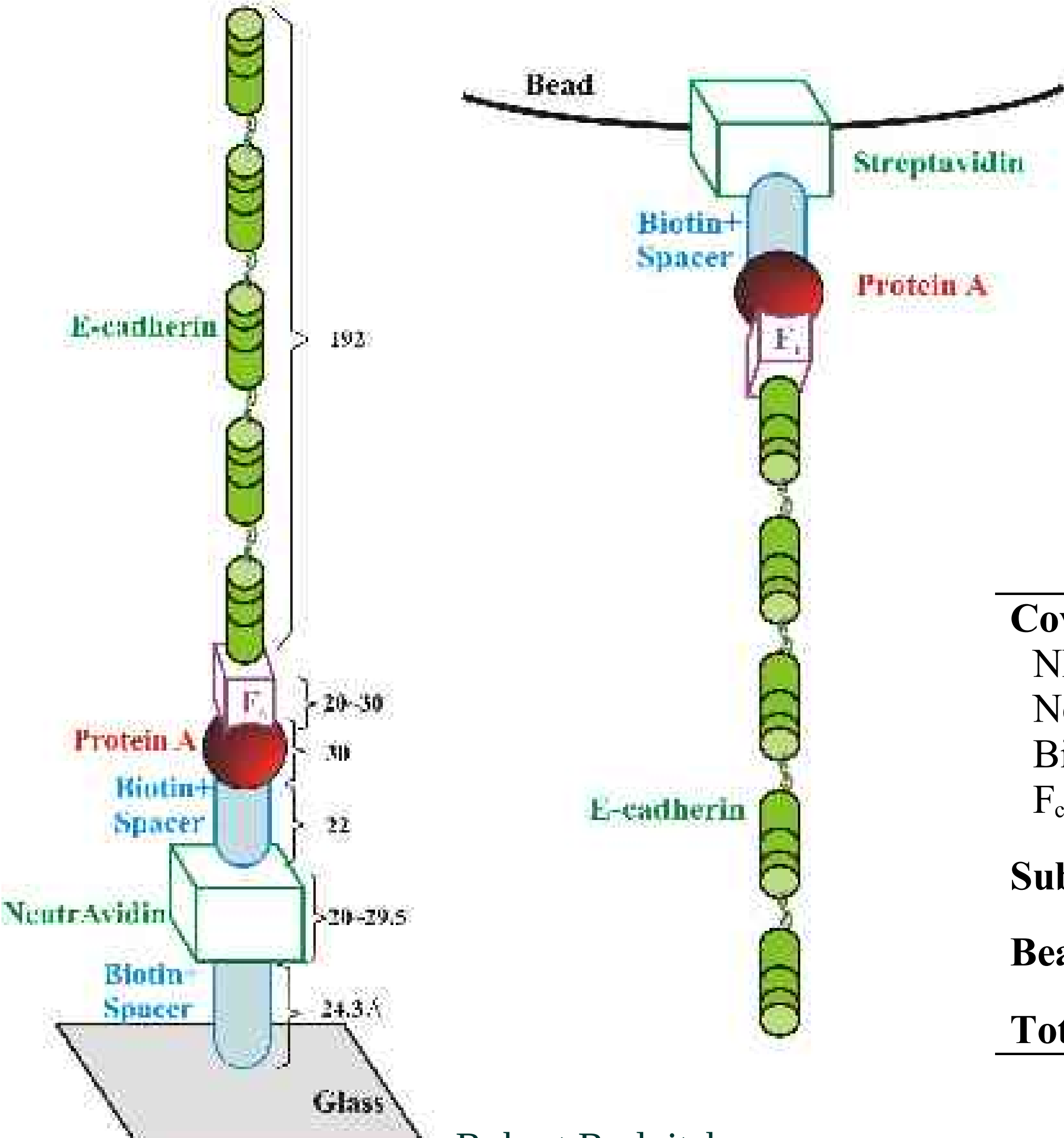
Cadherins are "tethered" to a slide via a chain of other molecules



Cover-slip	Length (Å)
NHS-SS-Biotin	24.3
NeutrAvidin	20 to 29.5
Biotinylated Protein A	22+30
F_c-E-Cadherin	30 to 40 +192.5 to 250
Sub-total	**318.8 to 395.8**
Bead	**294.5 to 371.5**
Total	**613.3 to 767.3**

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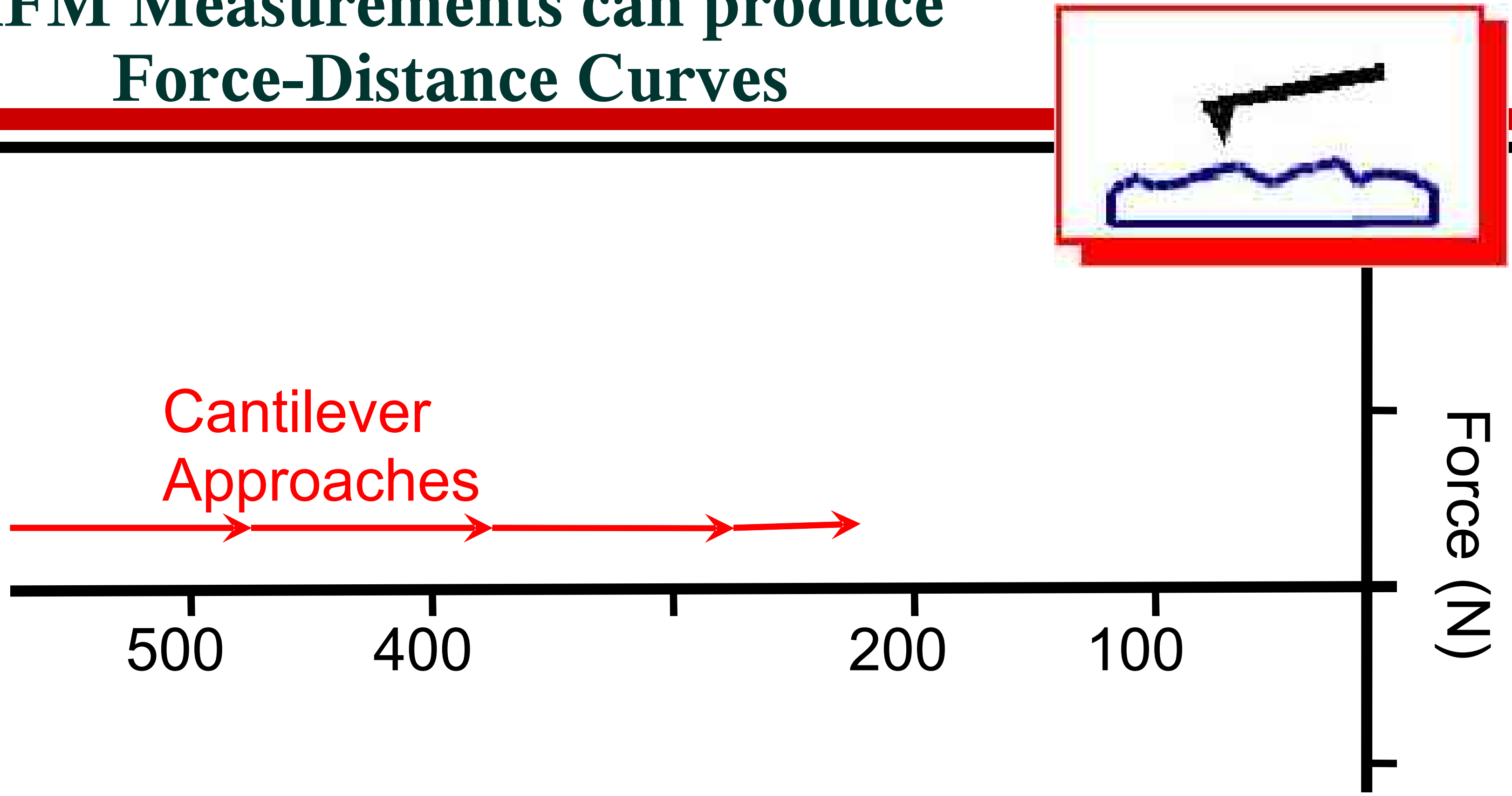
Unanswered questions remain

What is the actual binding force?

- **Does the binding force scale linearly with density?**
- **What are the forces for *heterophilic* interactions?**
- **How does the cadherin molecules' structure affect binding?**

AFM Measurements can produce Force-Distance Curves



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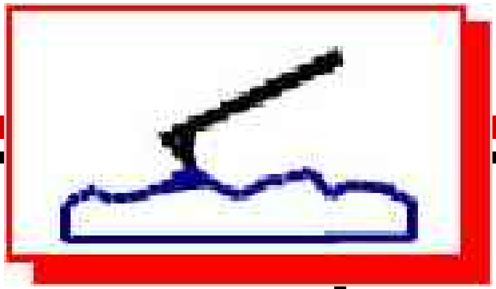

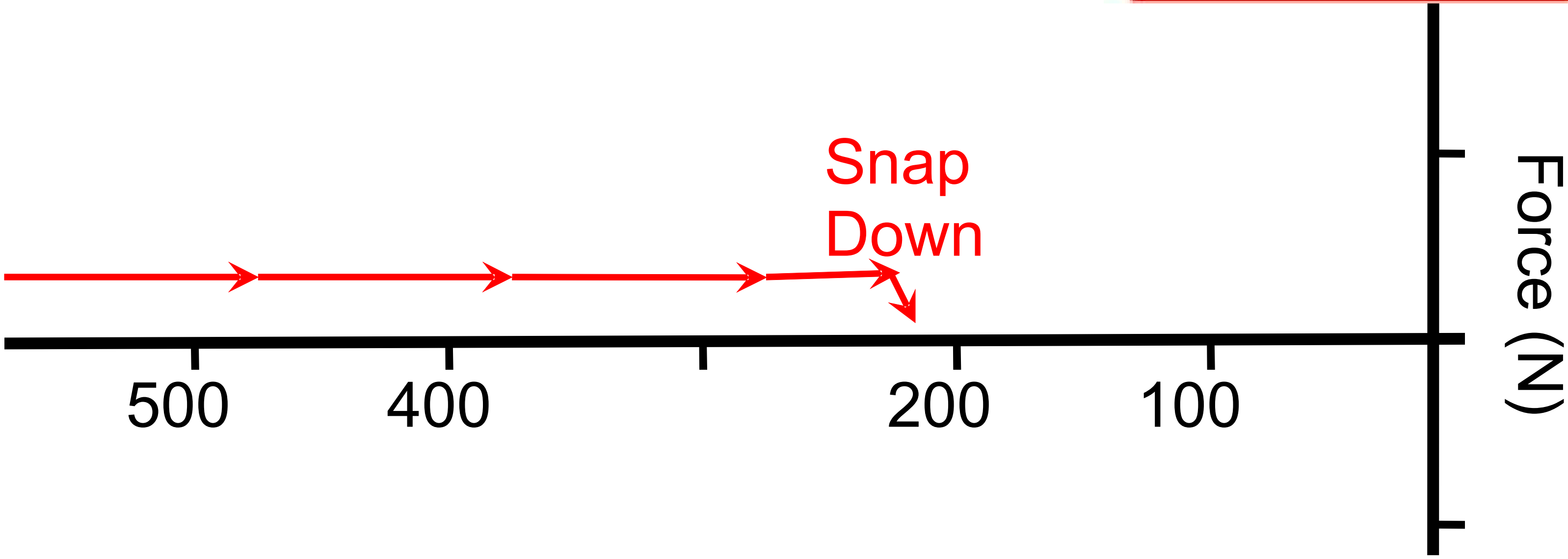

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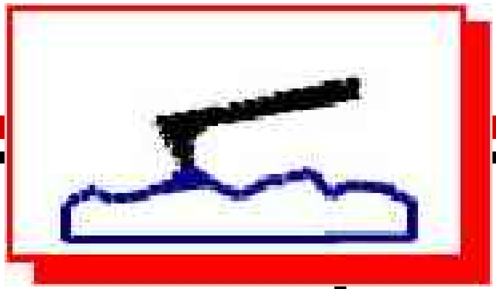

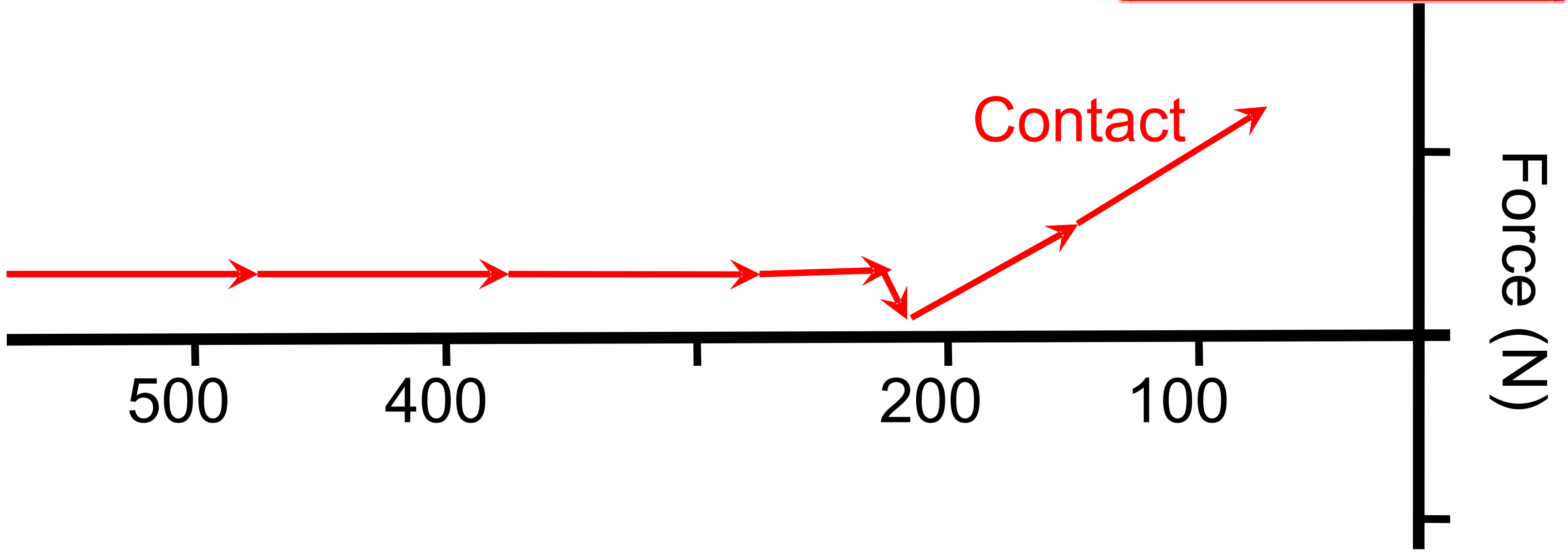

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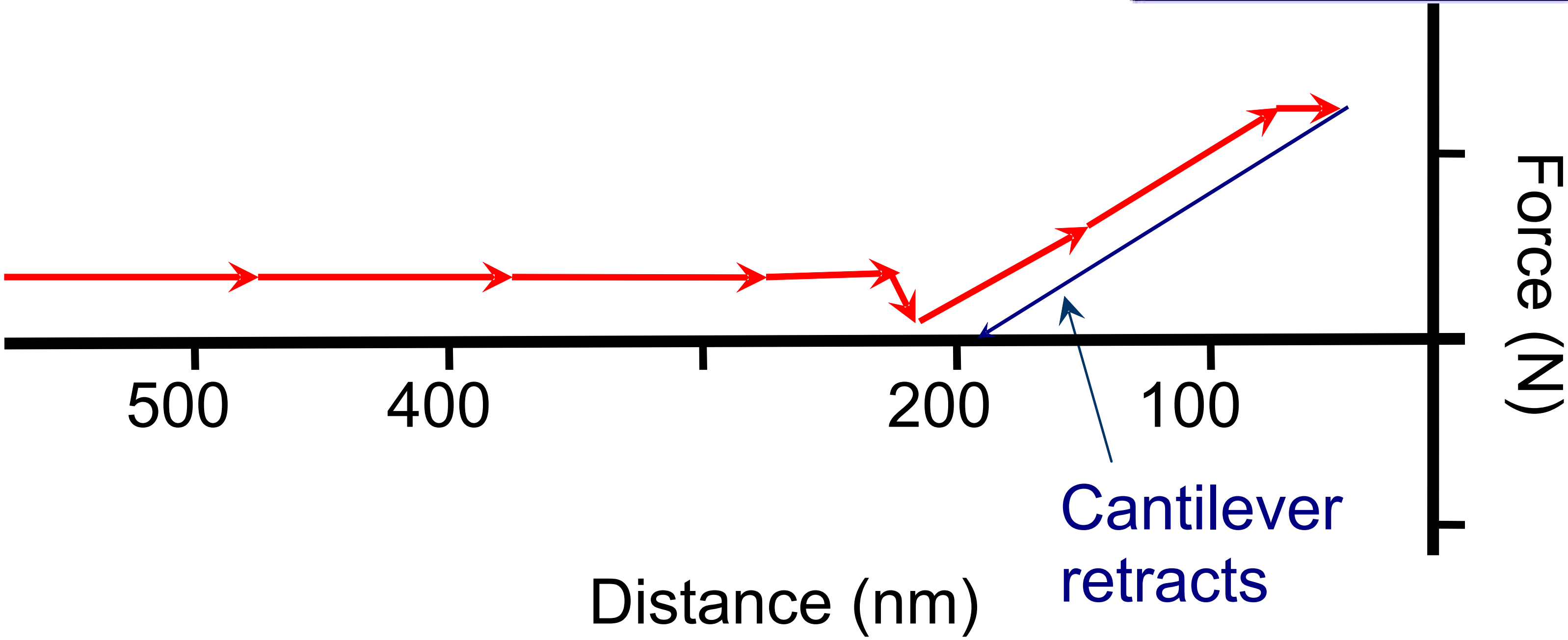

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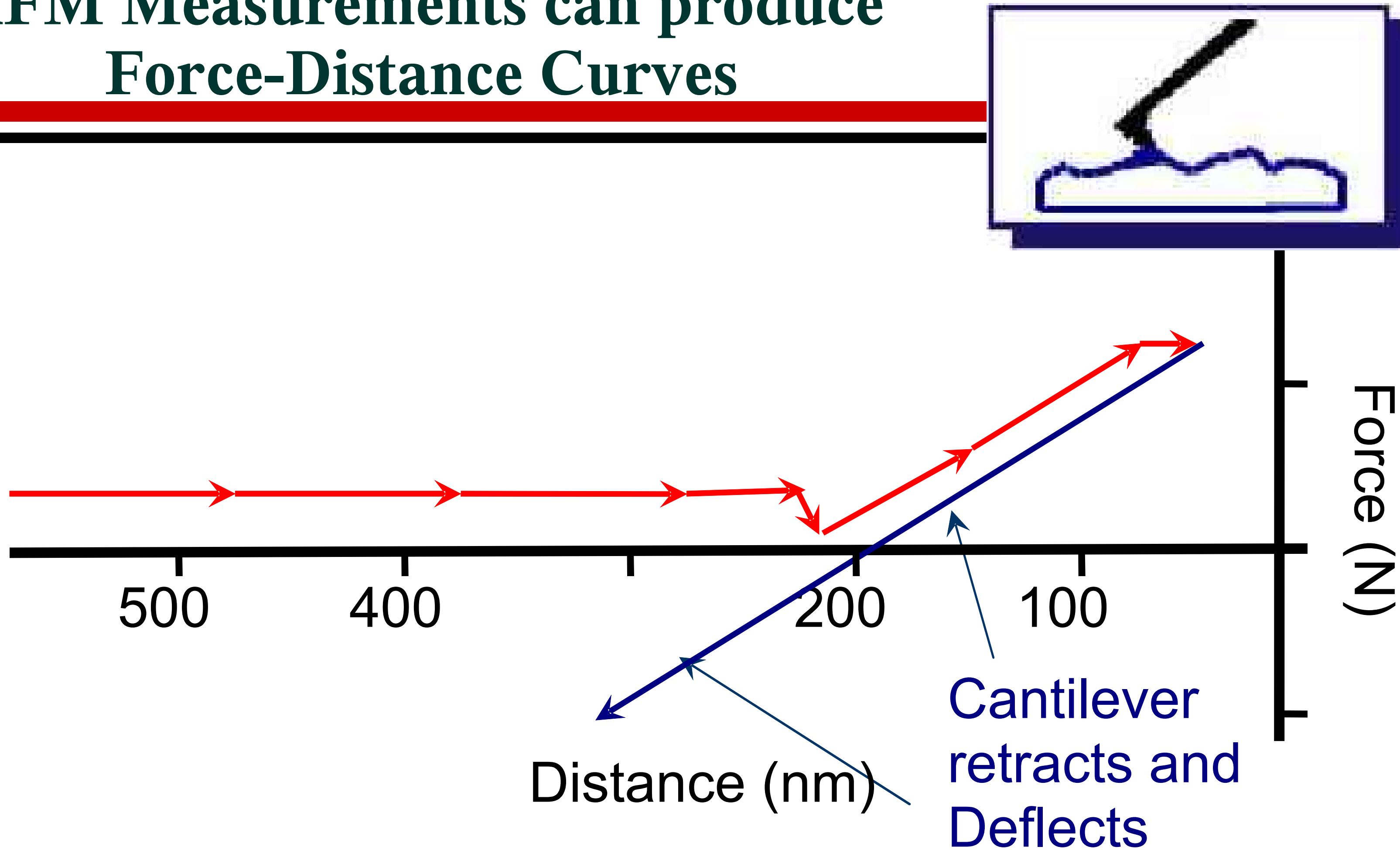

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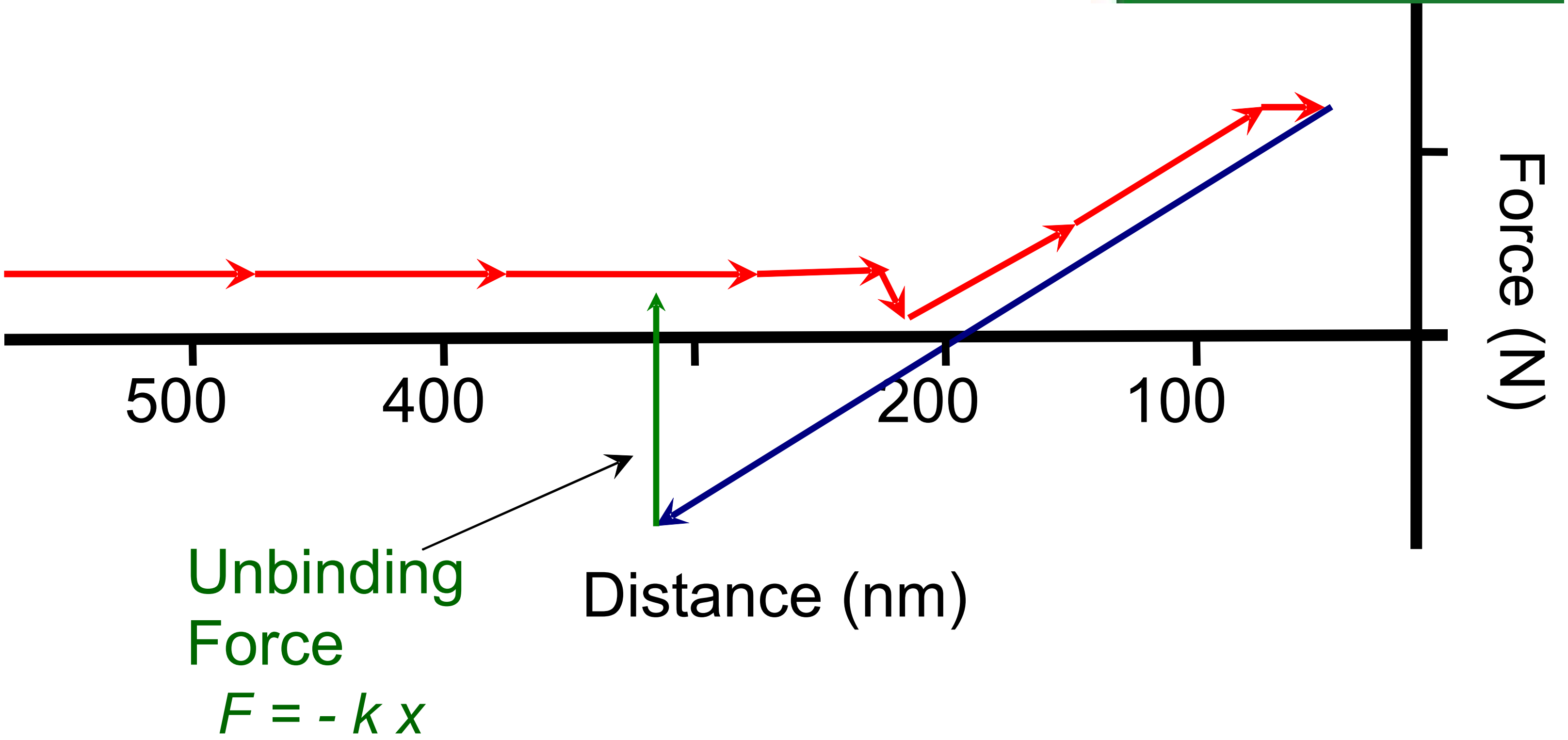
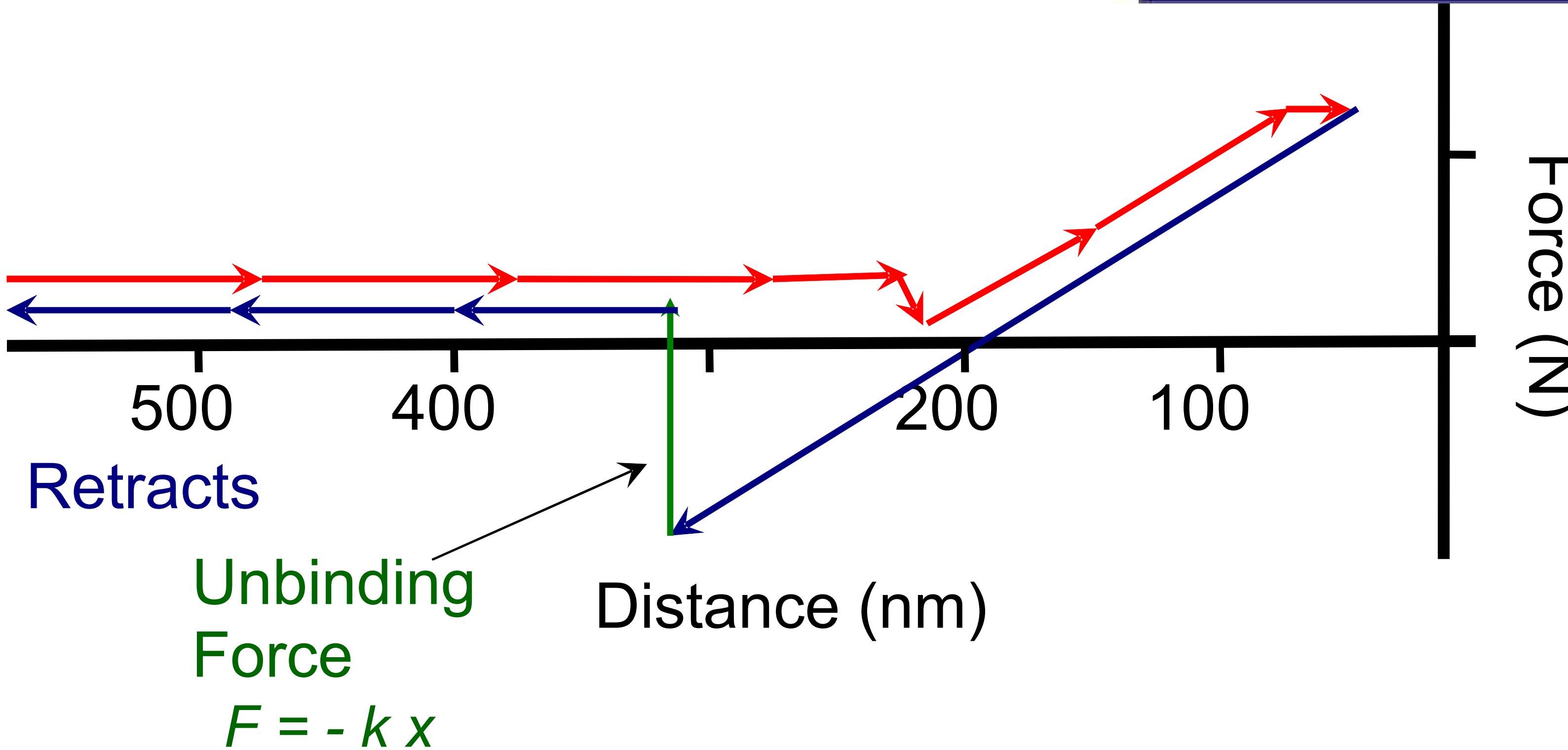


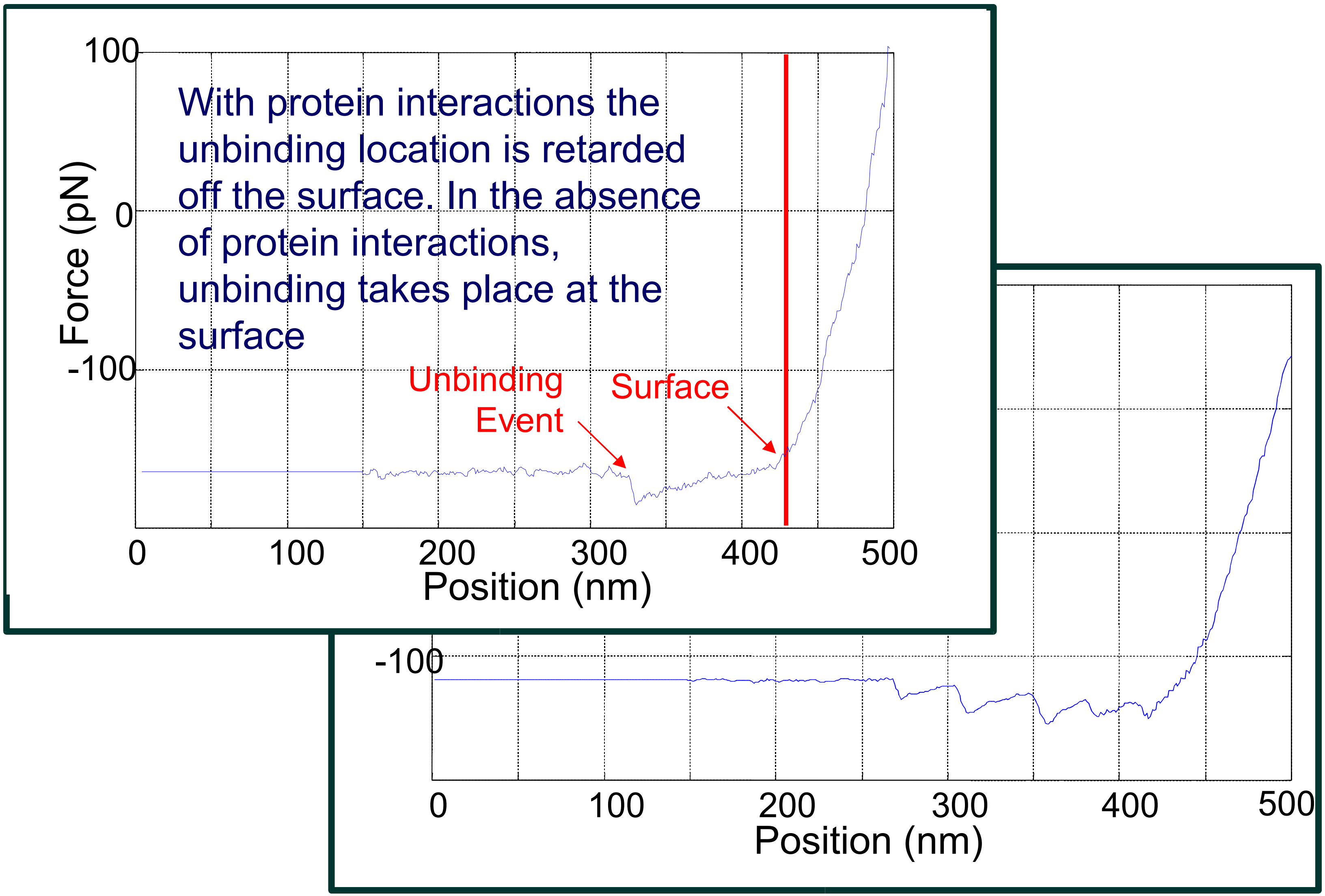
Adhesion forces can be detected by measuring the cantilever's deflection.

AFM Measurements can produce Force-Distance Curves



Adhesion forces can be detected by measuring the cantilever's deflection.

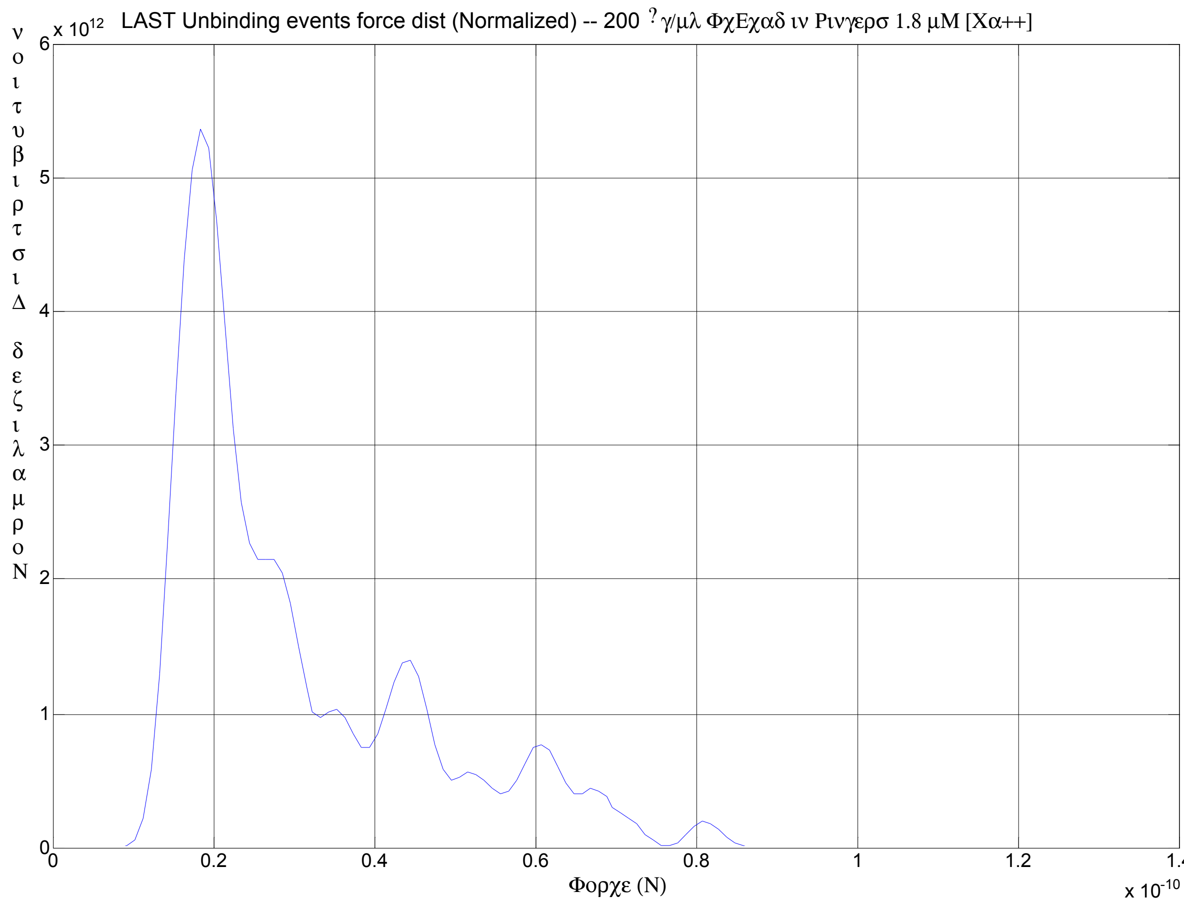
Single and multiple adhesions are observed



Force probability distributions show evidence of multiple binding events

- **Force increment of ~ 20 pN**
- **Peaks at:**
  - » 18-21 pN
  - » 41-43 pN
  - » 59-61
  - » 81-83 pN

perhaps indicating single, double, triples and quadruple unbinding events.



Ongoing Work

- **Does the binding force scale linearly with density?**
- **What are the forces for *heterophilic* interactions?**
- **How does the cadherin molecules' structure affect binding?**
- **Is there a measureable time interval for the binding interaction?**

More Biology Force Measurement Examples

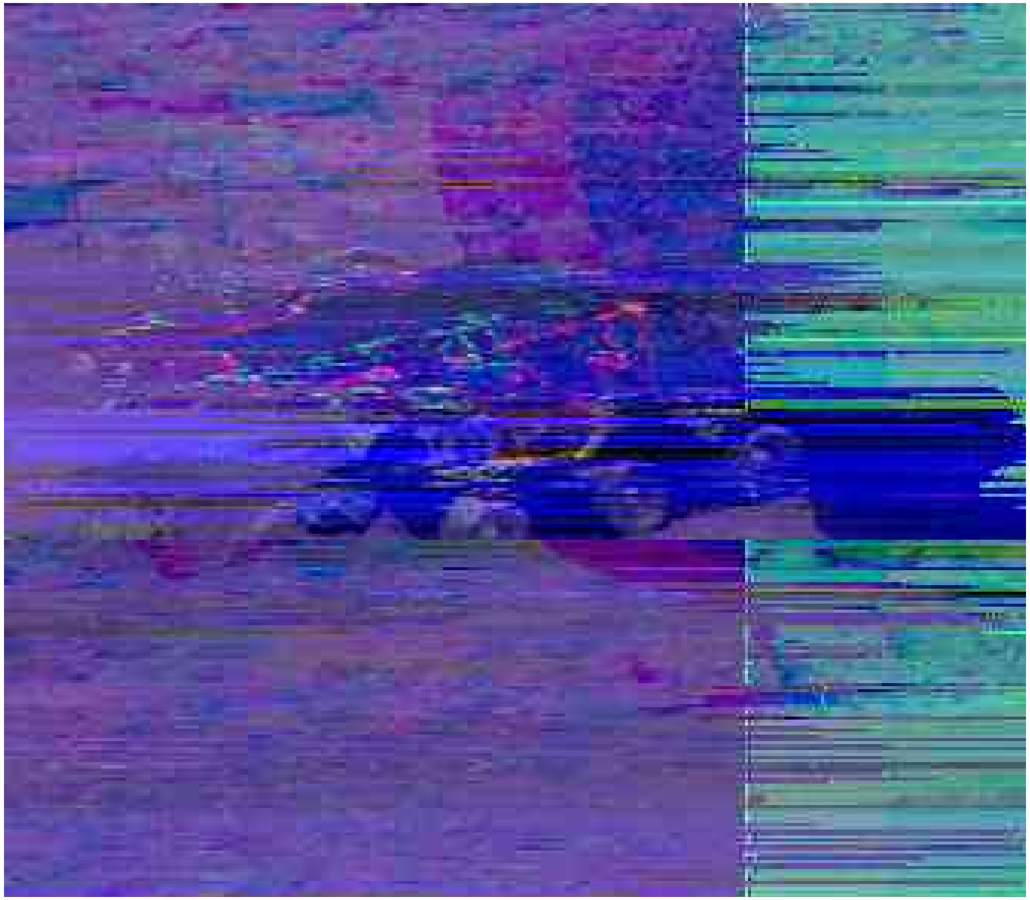
- **Small Animal/Insect Locomotion**
  - » **There are many examples of small animals which are remarkably agile yet simple and relatively unintelligent.**

Blaberus discoidalis, Death-Head Cockroaches, Female and Male

Michael Bartsch, Mark Cutkosky, Walter Federle, Bob Full

More Biology Force Measurement Examples

- **Man-Made Robot Locomotion**
  - » **There are many examples of man-made robots which are very sophisticated and expensive, yet rather clumsy and fragile.**



Mars Pathfinder Rover, JPL, 1999

Man-Made Robot Locomotion

Day 59

- The rover partway down "Half Dome"

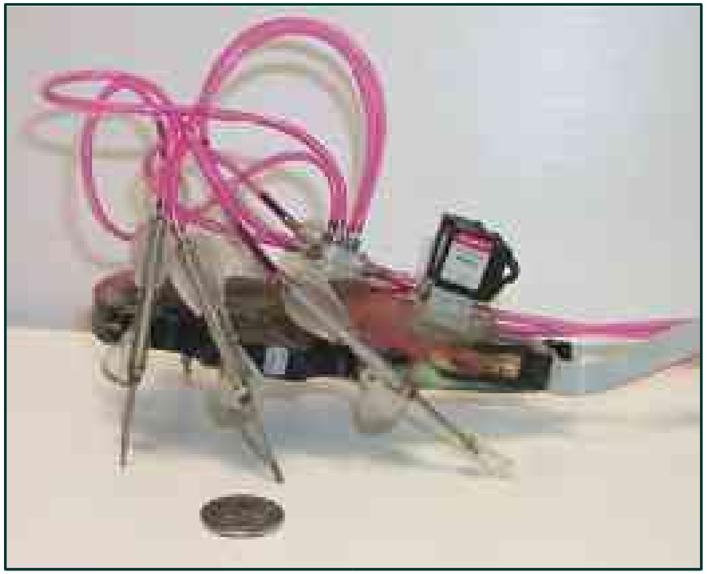
Day 64

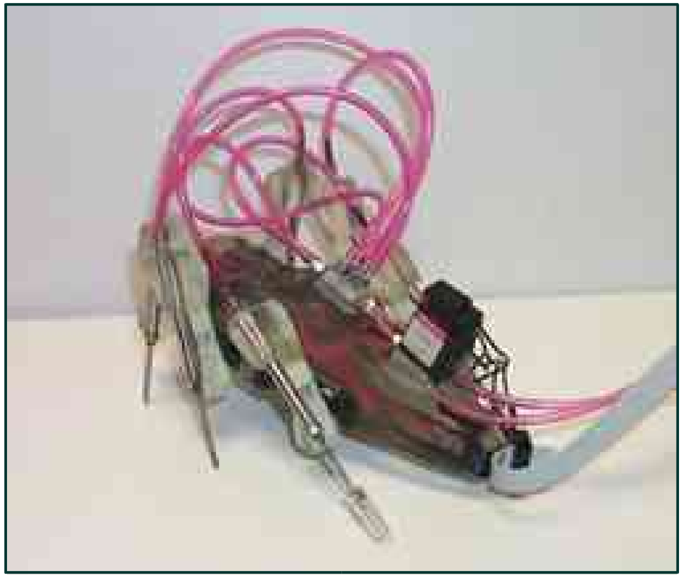
- The rover has completed its descent from "Half Dome"

Day 66

- Rover driving forward after backing up to analyze rocks

Robotic Cockroaches?



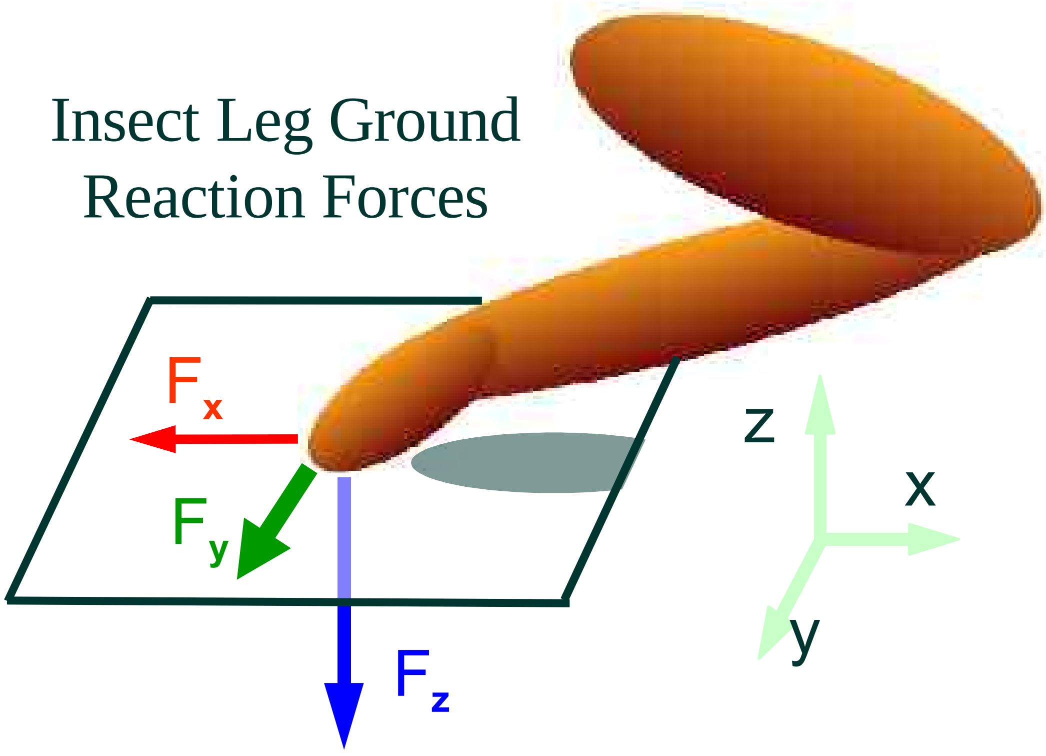


Sprawlita - Sean Bailey & Jonathan Clark, Stanford Biomimetics

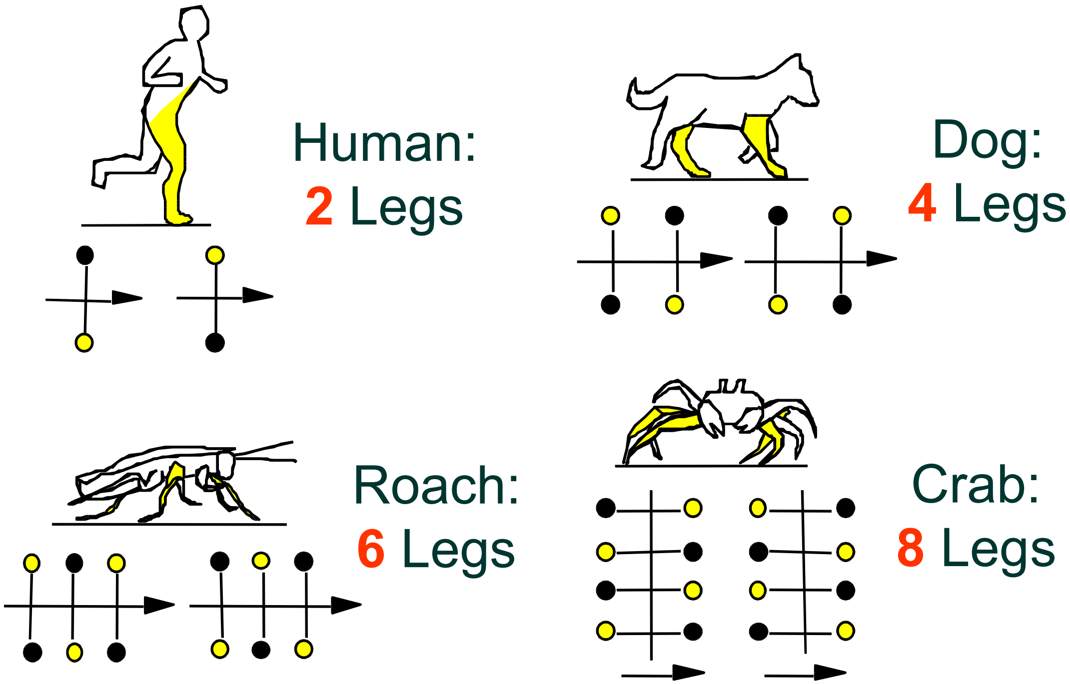
- **Biomimetic robots mimic morphology or function observed in nature**
- **Cockroaches identified as a model system for legged robots**
- **Biomechanical measurements yield lessons for robot design**

Ground Reaction Force Measurement

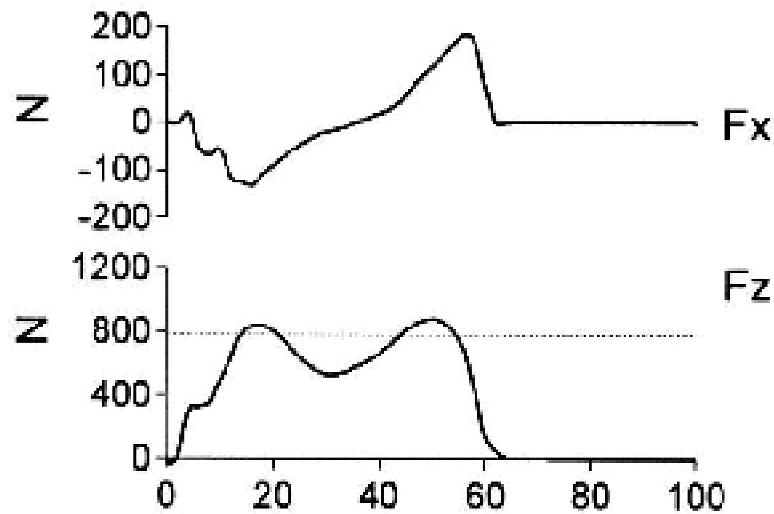
- **Ground reaction forces show**
  - » **How animal propels and stabilizes itself**
  - » **Distribution of body weight during various phases of locomotion**
  - » **How the animal deals with obstacles and perturbations**
  - » **Transmission of muscle forces and torques through the skeleton or exoskeleton**
- **Our Goal: to measure both in-plane and normal ground reaction force components**



Scaling & Comparative Biomechanics



Empirical Results: Human Walking

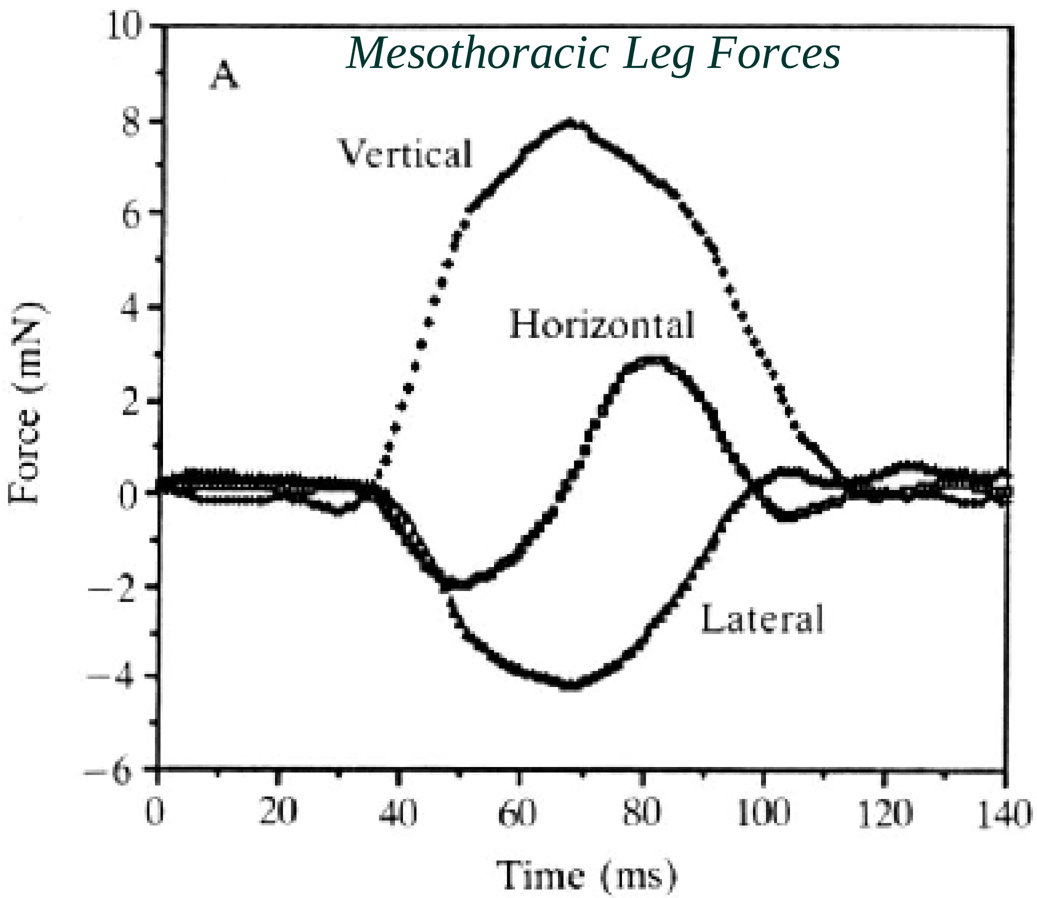


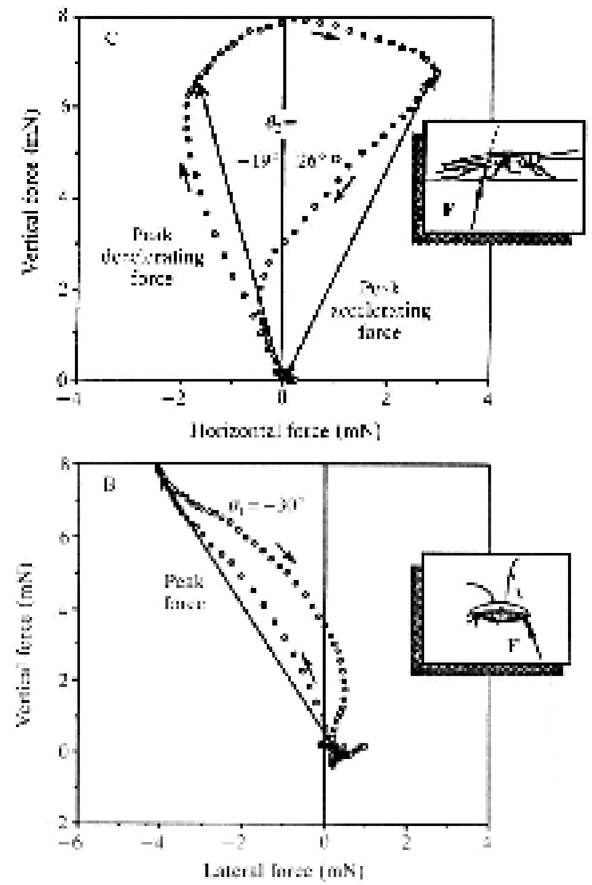
Grasso – 1998

Spring-Loaded Inverted Pendulum model is a generally applicable single-leg model for organisms of all sizes:
ELEPHANT to COCKROACH

Cavagna – 1975, Full – 1989

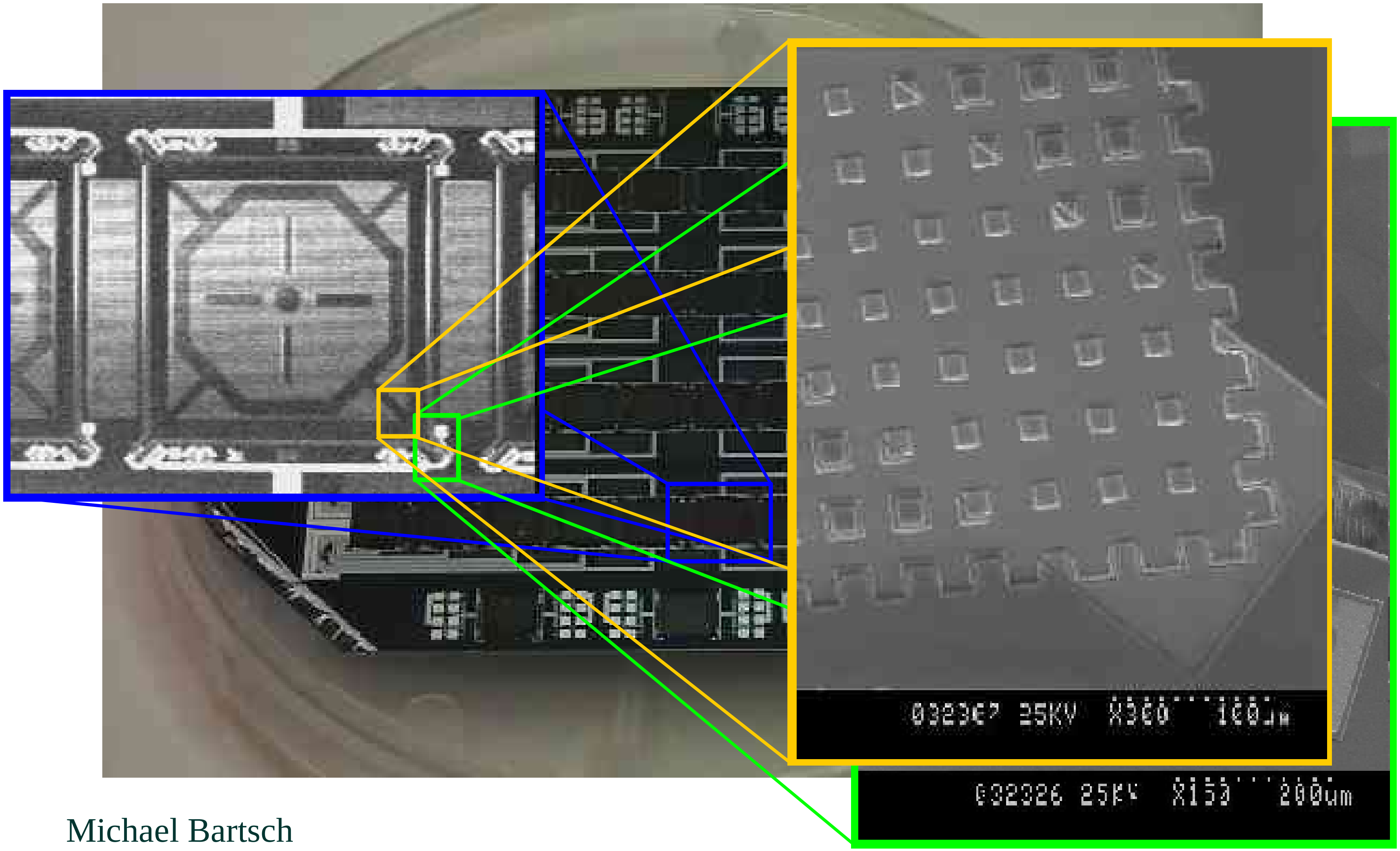
Early Cockroach Data





ull, R.J., Blickhan, R., Ting, L.H., "Leg Design in Hexapedal Runners." *J. Experimental Biology* 158, 369-390. 1991.

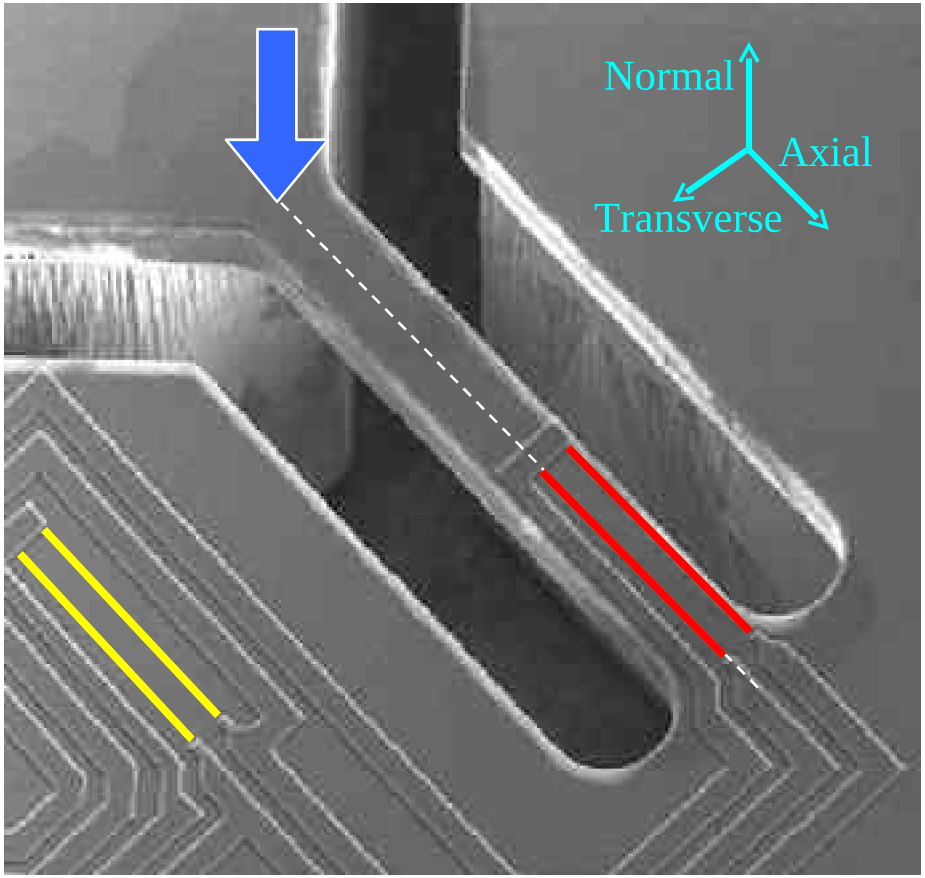
Sensor Geometry & Features



Michael Bartsch

Flexure Design

- Normal Load
  - Mid-flexure and edge piezoresistors strained equally
- Transverse Load
  - Edge piezo strain due to bending
  - Mid-flexure resistor lies along neutral axis



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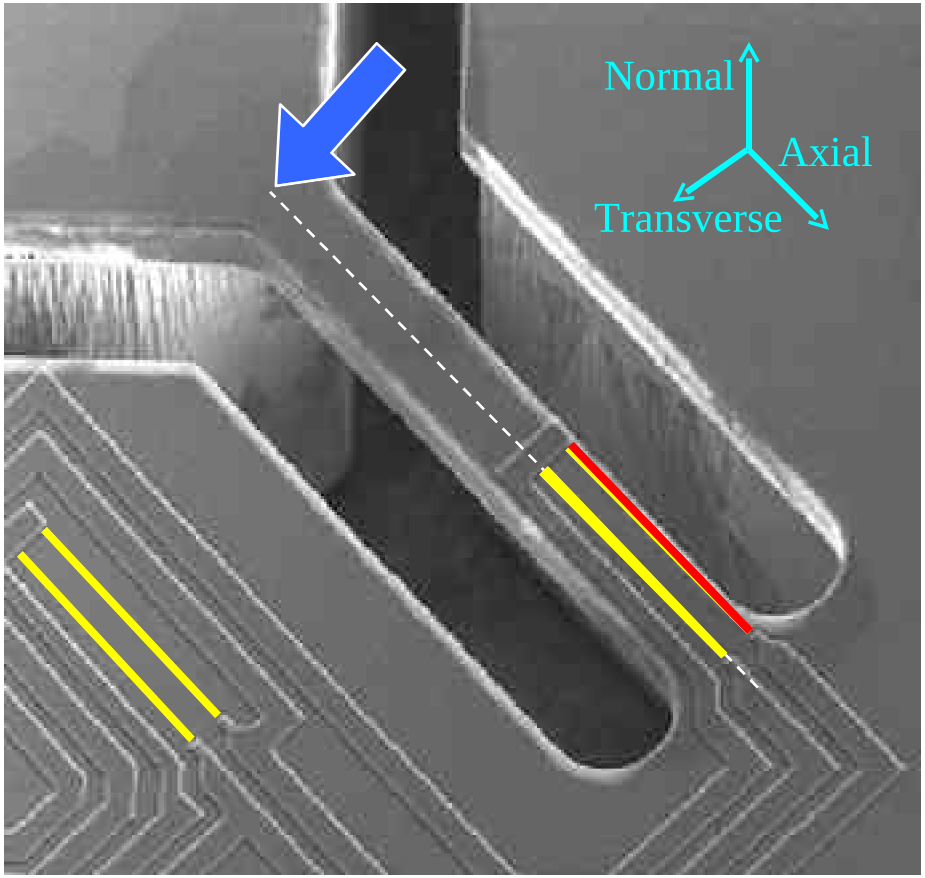
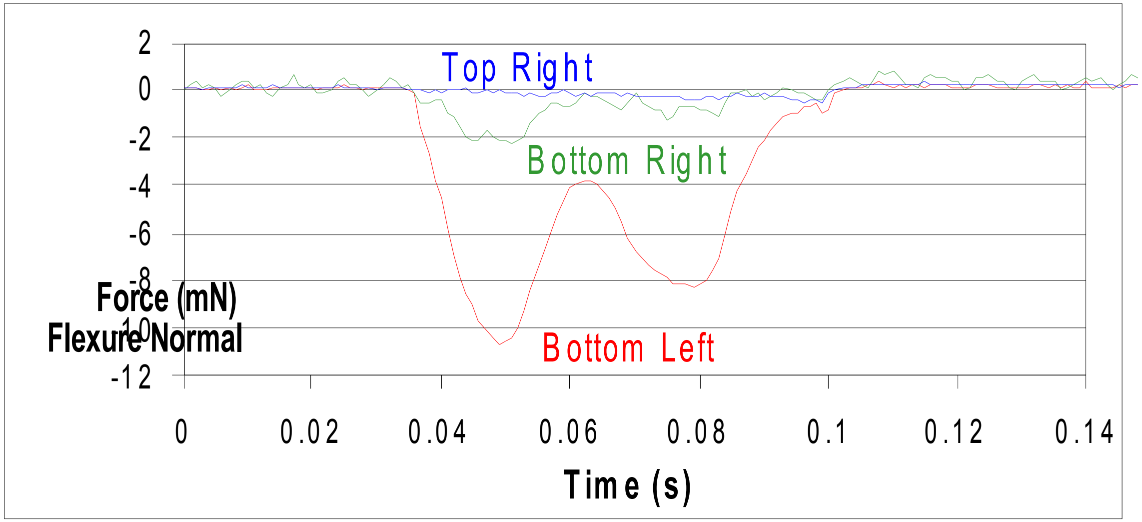
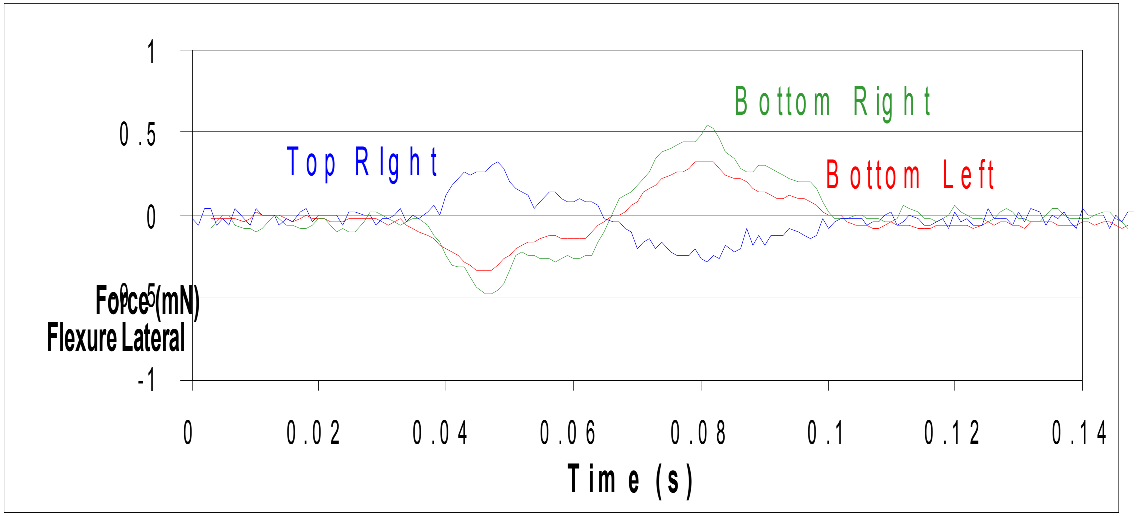


Michael Bartsch

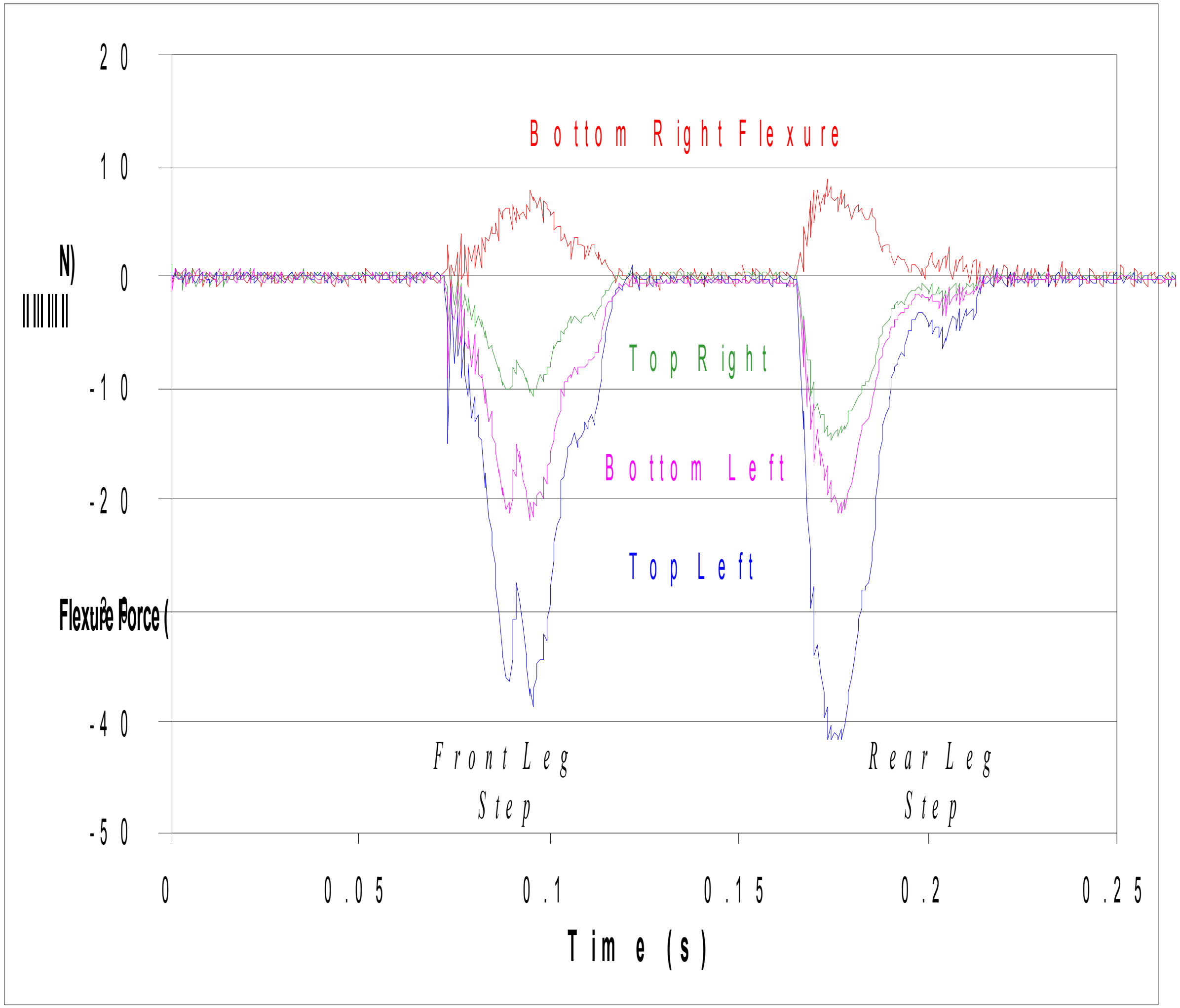
P. americana Front Leg Forces





- Dual peak in normal forces observed in other larger organisms, not previously observed for roaches.
- Possibly indicates flexing of “thigh muscles” in mid-stride
- Lateral forces consistent with clockwise leg twist followed by ccw.
- Many more sets of data to analyze, each illustrating different details

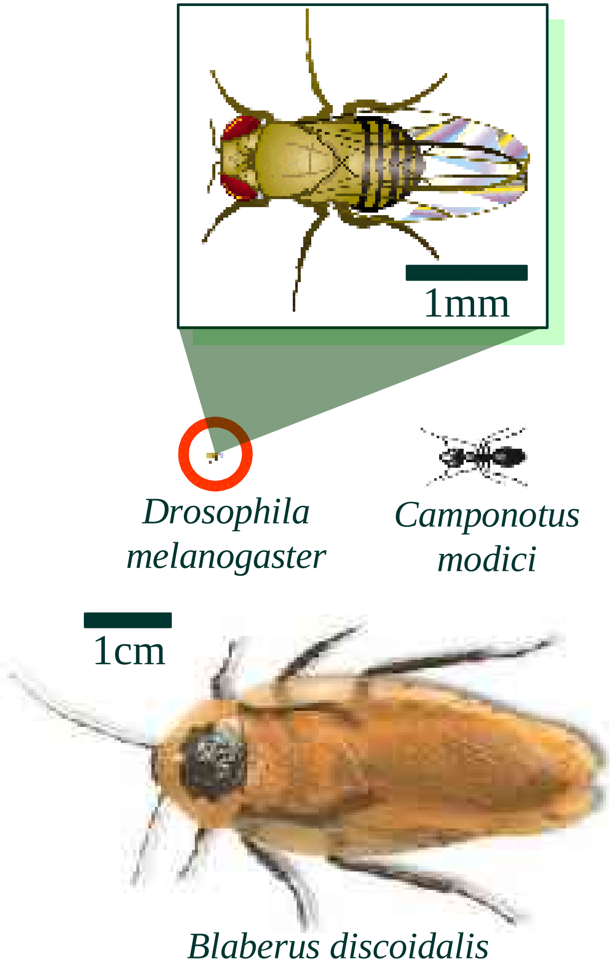
Ant Front & Rear Leg Forces



- Average flexure and piezo sensitivity: 670V/N unamplified
- Min theoretical resolution on a 3kHz bandwidth: 14nN
- Visible chart features
  - Spike at initial claw contact w. sensor
  - Dual peak in front leg force
  - Rear leg drag

Estimated Measurement Requirements

		Cockroach *Blaberus discoidalis*	Carpenter Ant *Camponotus modici*	Fruit Fly *Drosophila melanogaster*
Insect	**Animal Length**	5cm	10mm	2mm
	Animal Weight	30mN	350µN	3µN
Sensor Performance	**Sensor Element Area**	$(5mm)^2$	$(1mm)^2$	$(200\mu m)^2$
	Maximum Expected Force	300mN	3.5mN	30µN
	Minimum Resolvable Force (Typ/50)	100µN	1µN	10nN
	Required Sensitivity (0.1mV/Res.)	1V/N	100V/N	10000V/N
	Minimum Mechanical Bandwidth	300Hz	1kHz	3kHz



Michael Bartsch, Bob Full

Macroscopic Adhesion

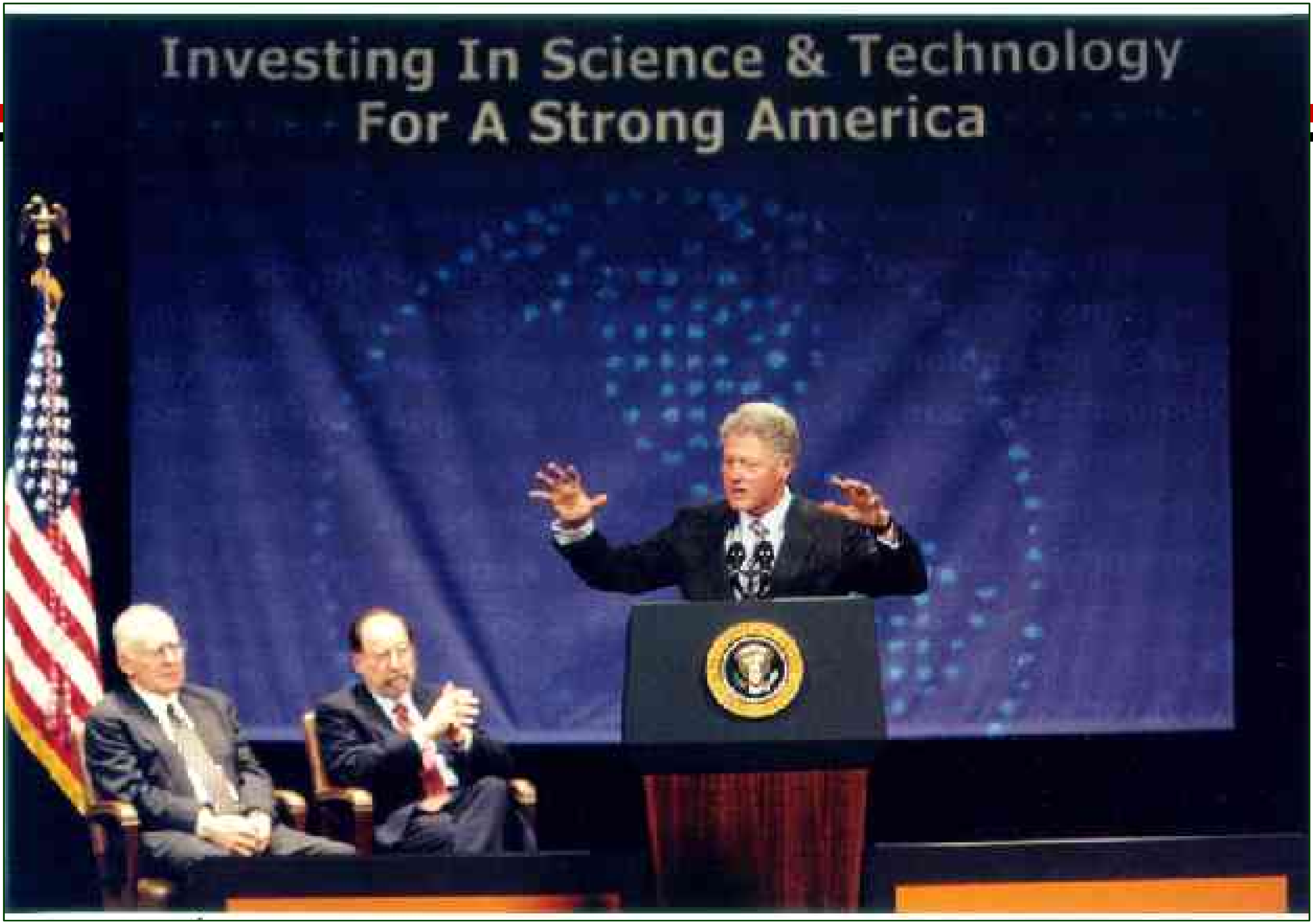
K. Autumn, Y. Liang, W.P. Chan, T. Hsieh, R. Fearing, T.W. Kenny, and R. Full

- Geckos are known for their remarkable wall-climbing ability.
- Mechanism for adhesion is not well established.
- Microscopic structures are responsible for adhesion.
- Understanding can lead to inspirations for new artificial dry adhesive.

Macroscopic Adhesion

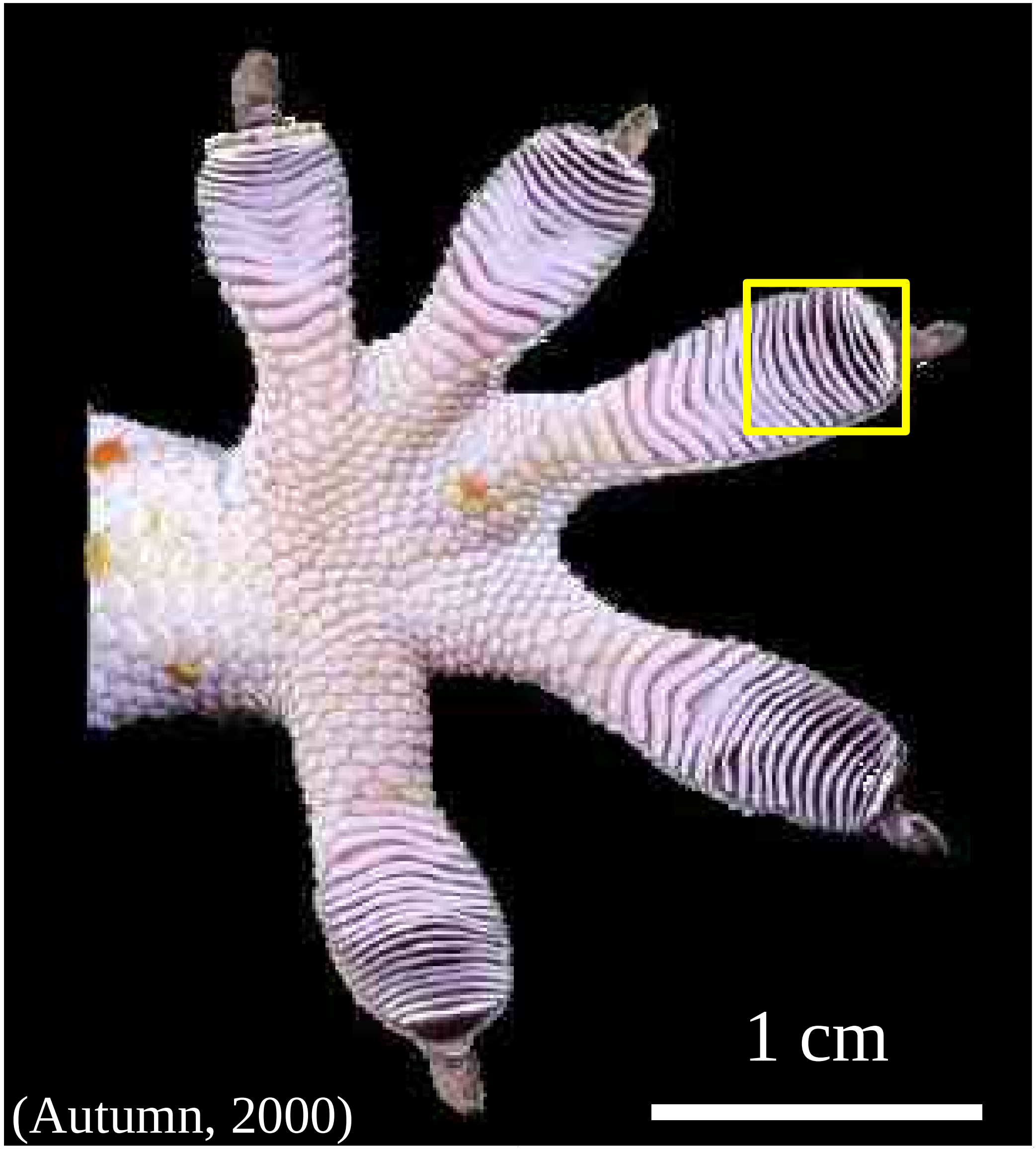
K. Autumn, Y. Liang, W.P. Chan, T. Hsieh, R. Fearing, T.W. Kenny, and R. Full

- **In fact, Geckos use NANOTECHNOLOGY for their adhesion capabilities**

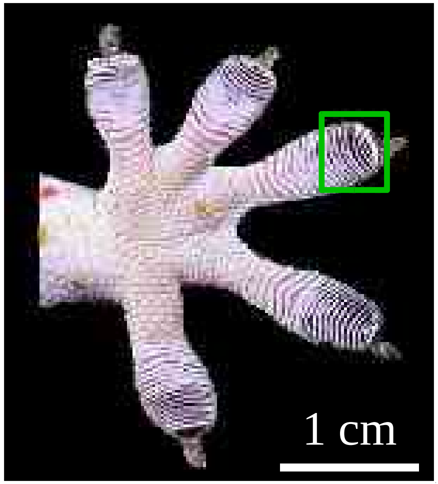


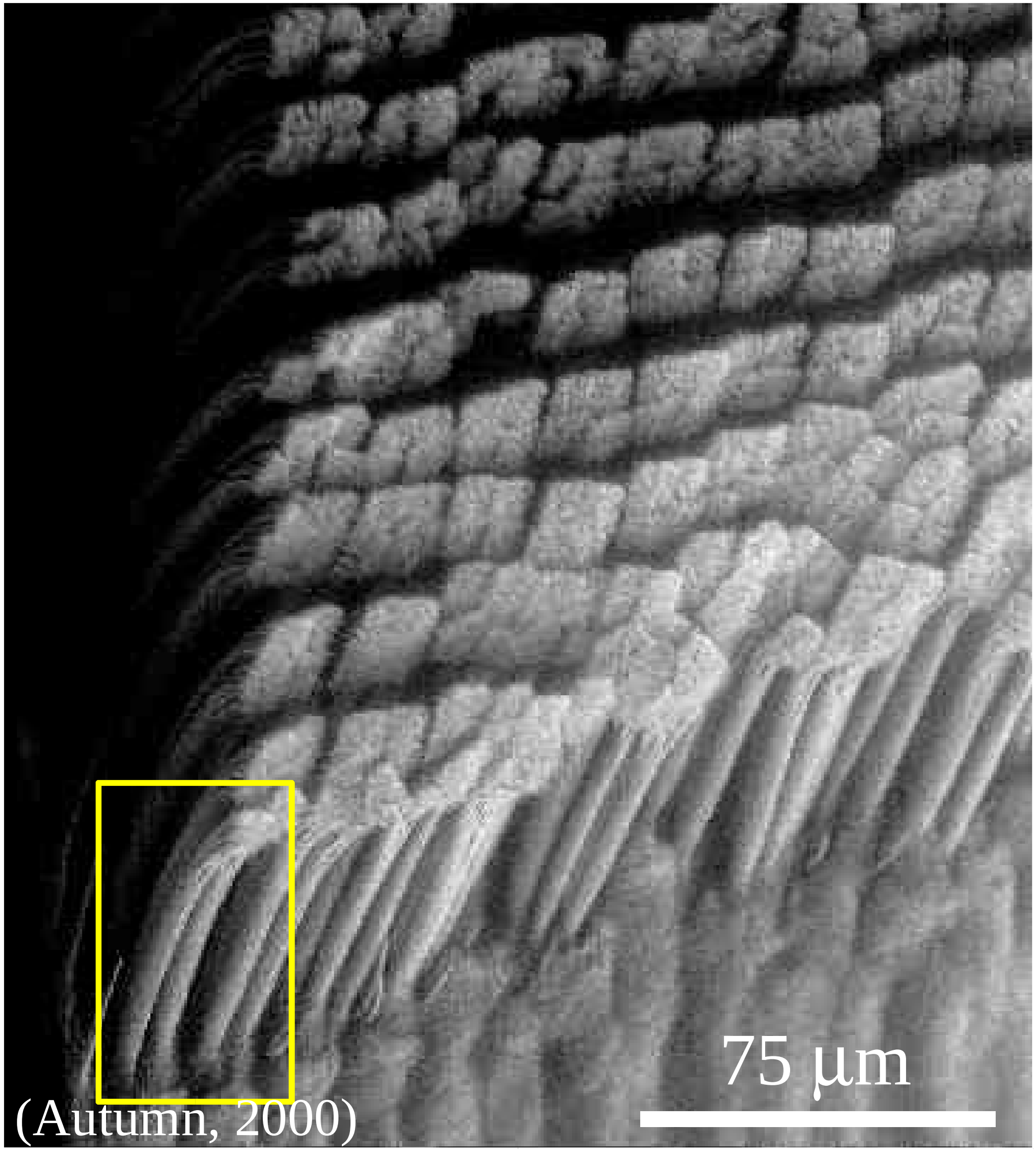
January 21, 2000 - President Clinton announces $500M initiative on "nanotechnology"

Foot of a Gecko

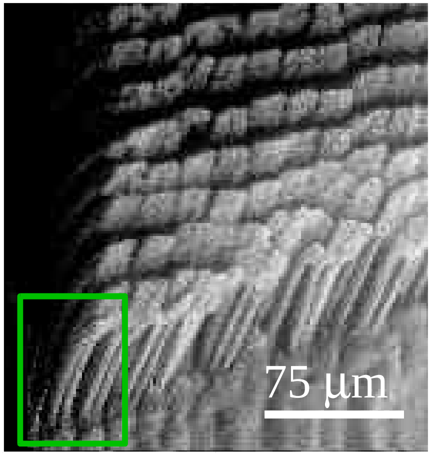


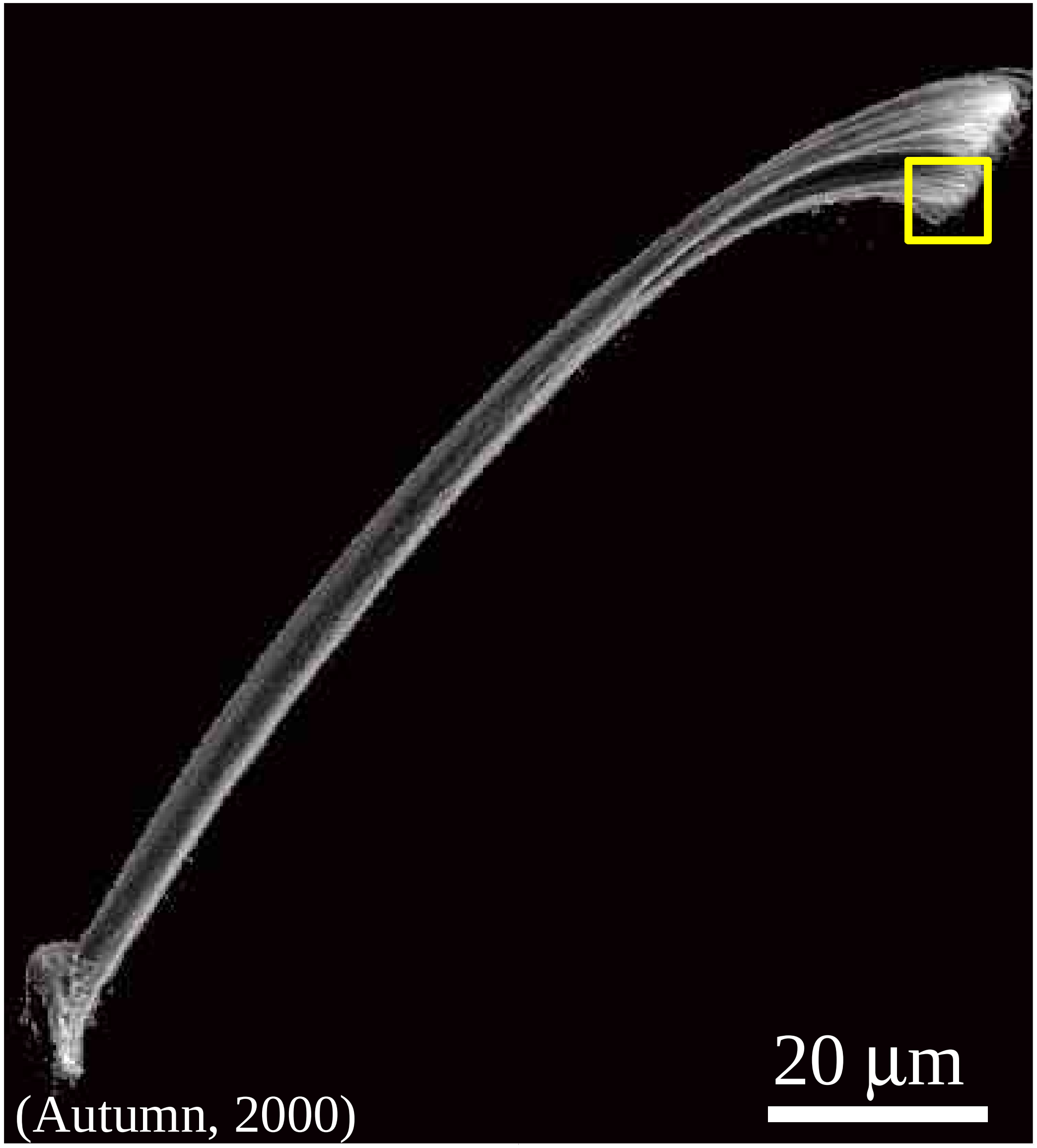
Array of Setae



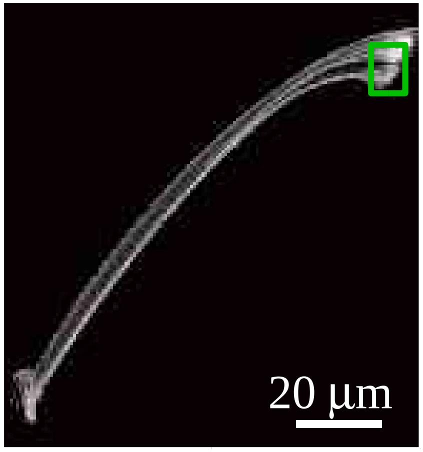


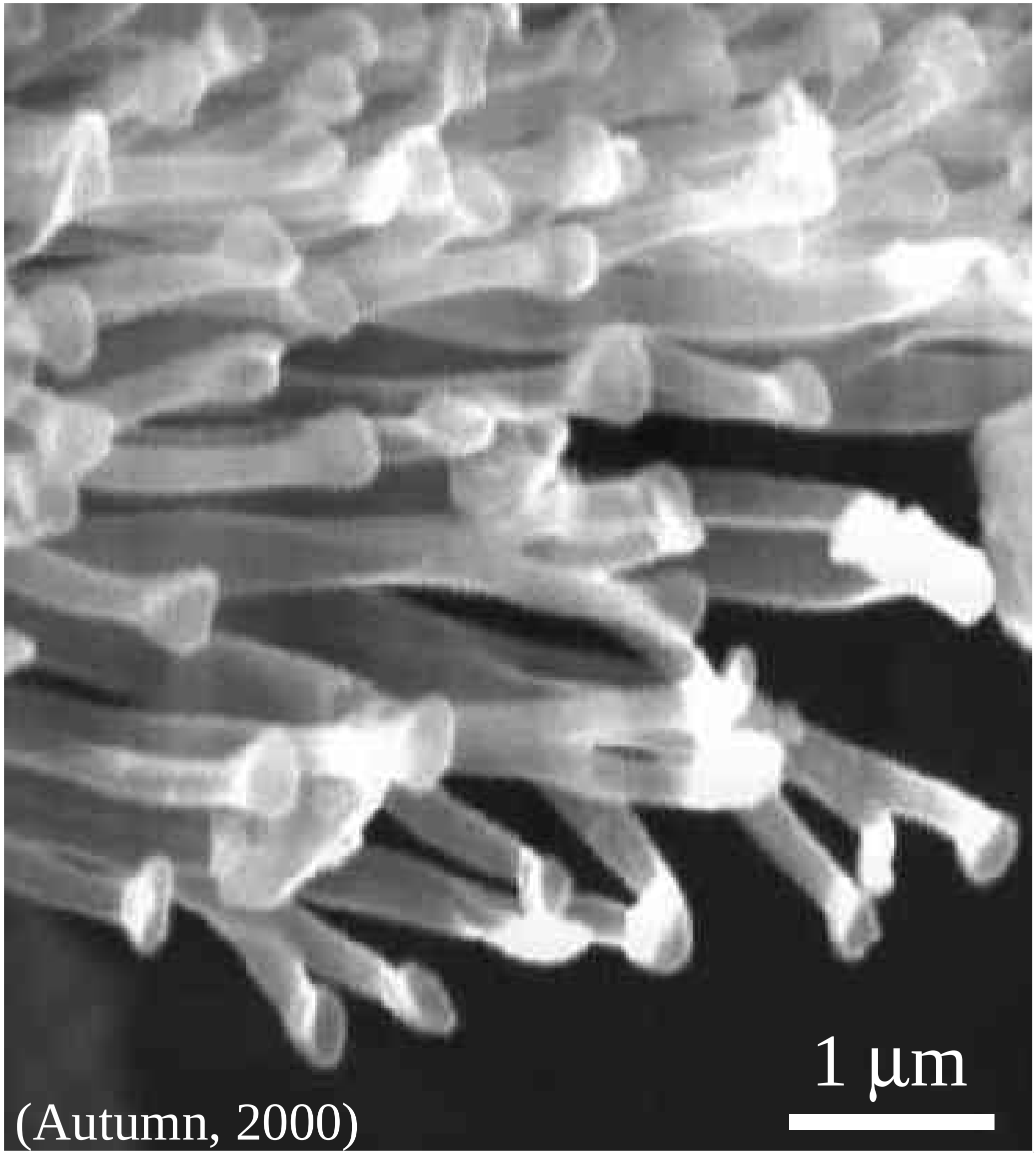
An Isolated Seta



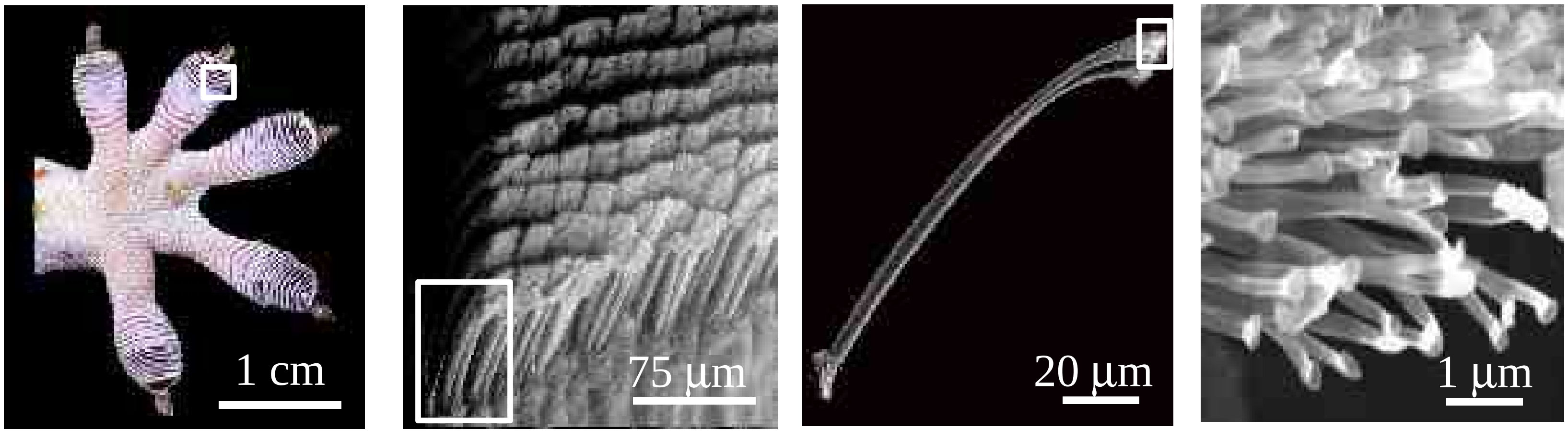


Spatula-Shaped Tips





Structure of a Gecko Foot



Kellar Autumn

(a) the foot of a Tokay gecko

(b) an array of tiny hair (setae)

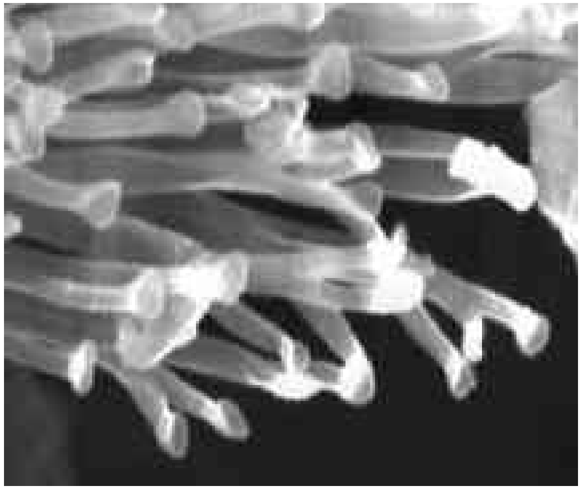
(c) an isolated seta (~ϕ5µm)

(d) spatula-shaped tips (~ϕ0.2µm)

Setae: [Ruibal, 1965]

- ~10^6 setae per animal
- Material: keratin
- ~100-1000 spatula-shaped tips per seta

Adhesion Hypothesis



Dense arrays of "spatulae" deform to match topology of opposing surface.

A small fraction actually are oriented to allow van der Waals adhesion.

If only ~2% of available spatulae is in real contact :

$$F \approx 800\text{nN/spatula} \approx 200\mu\text{N /seta}$$

Adhesive Development Opportunity

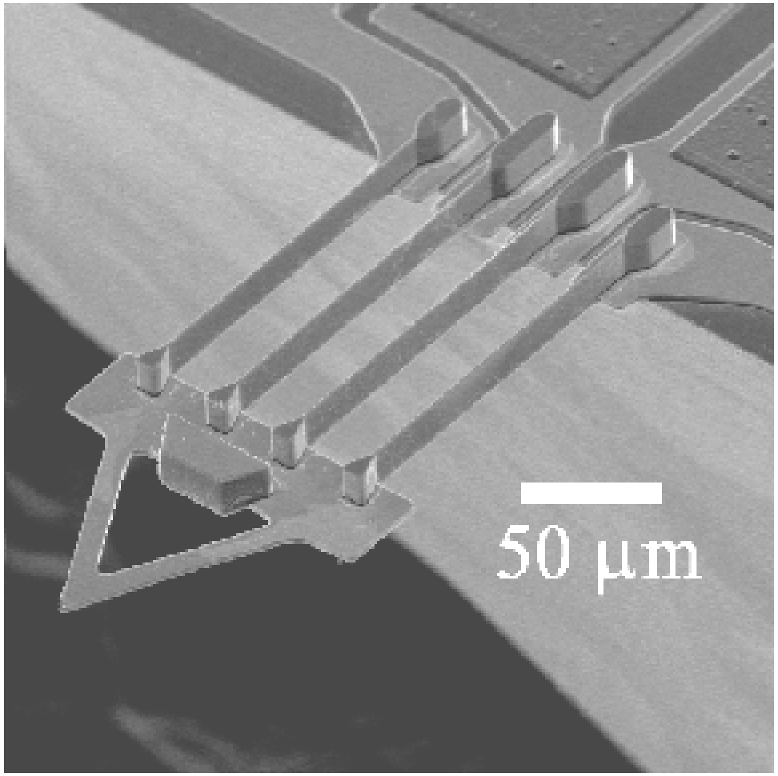
- Imagine an adhesive that can provide large attachment forces to all surfaces regardless of roughness, surface chemistry, or even moisture.
- Imagine that this adhesive can be easily cleaned after becoming dirty simply by pressing onto a clean surface a few times.

Goal - Identify the critical characteristics of the gecko adhesion structures, and explore ways to manufacture the same kinds of material.

Our Gecko Measurement Plans

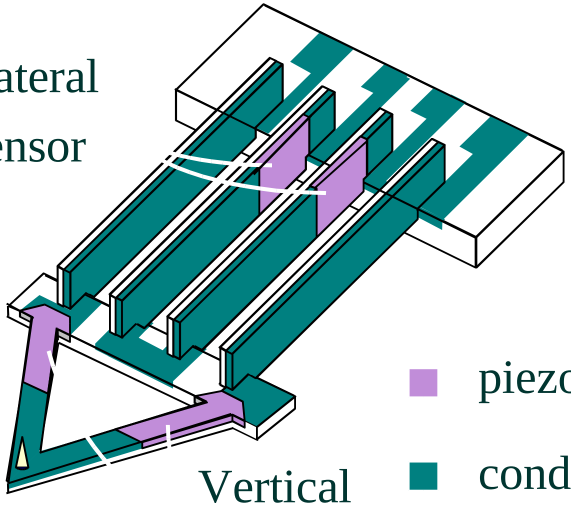
- Continue study of relationships between applied forces and adhesion force.
- Begin study of dynamics of adhesion.
- Identify critical features that enable/enhance adhesion.
- Begin to try fabrication experiments and measurements to develop an artificial adhesive.

2-D Piezoresistive Force Sensing



[Ben Chui, 1997]

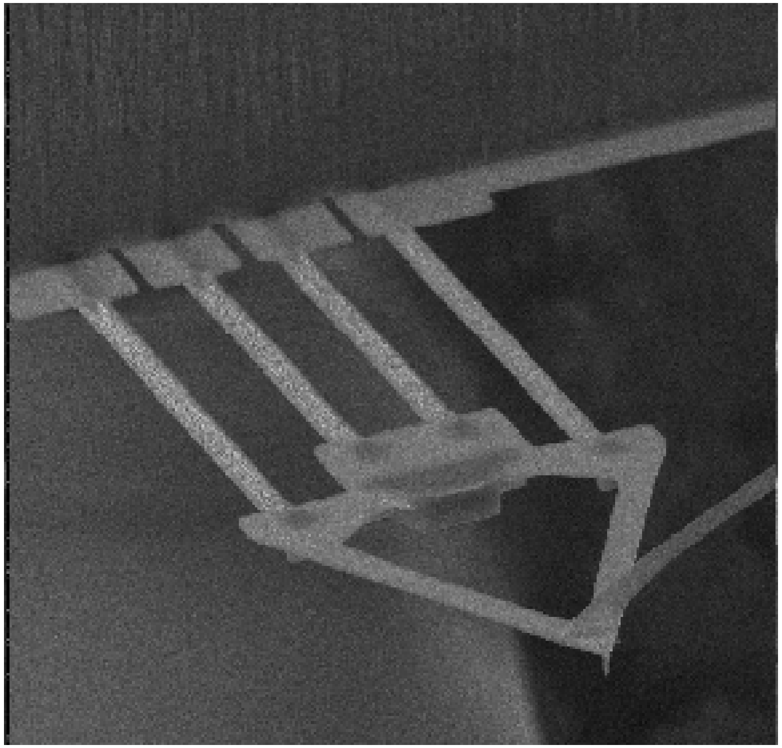
45° ion implantation to embed piezoresistors on horizontal and vertical surfaces.



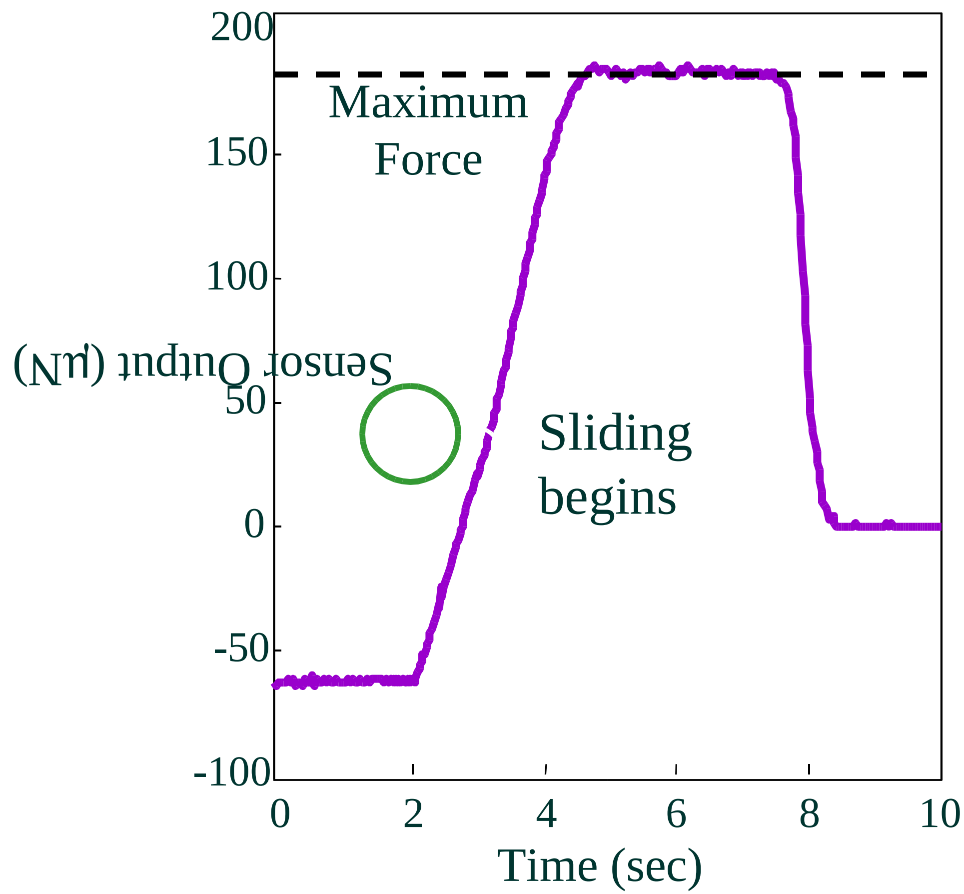
Forces resolved into 2 components

5 nN resolution, 5 kHz bandwidth

Force Curve With Sliding



Typical Lateral Force Curve



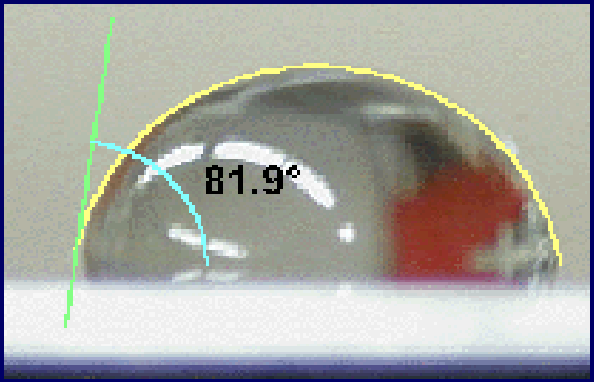
Yiching Liang

Consistent measurements of adhesion near 200 μN

Maximum is reached through sliding of the setae across the surface

Does Moisture Help Adhesion?

- Silicon (hydrophobic)



- Silicon oxide (hydrophilic)

Surface	Mean (μN)	σ (μN)	Sample Size
Hydrophilic	40.4	1.10	70
Hydrophobic	41.3	1.42	61

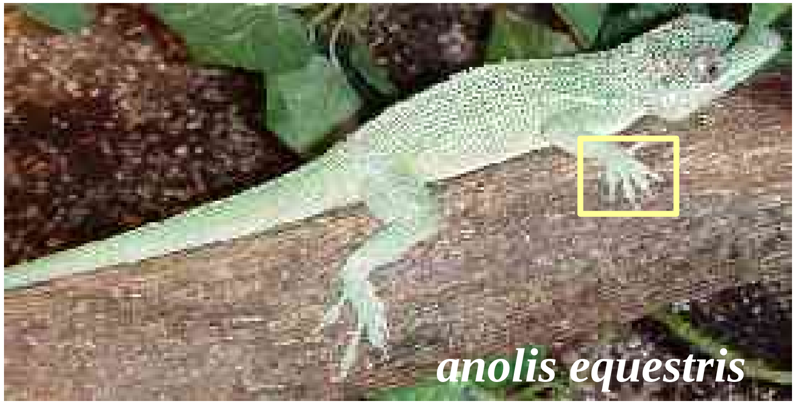
- Surface water does not affect adhesion.

Yiching Liang, Su-Wen Ueng

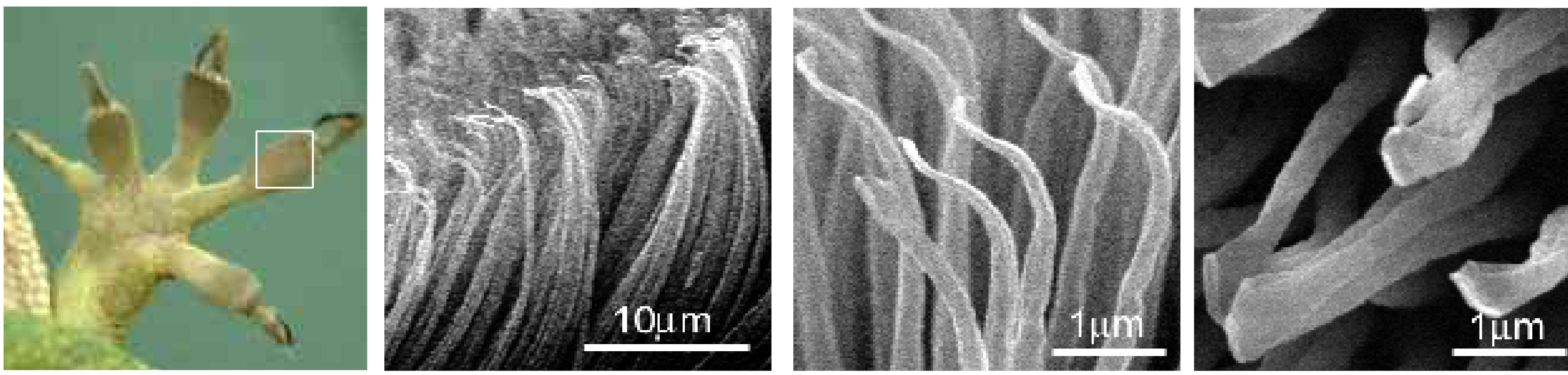
Preliminary Gecko Measurement Summary

- Adhesion Force consistent with vanderWaals effect.
- Adhesion enhanced by sliding, regardless of speed.
- Adhesion force mainly independent of humidity.
- Adhesion effective underwater.
- Adhesion not a strong function of surface hydrophobicity.
- Geckos walk through dirt - it normally takes about 5 steps for a gecko to recover adhesive capability after walking through graphite lubricant.

Other Geckos



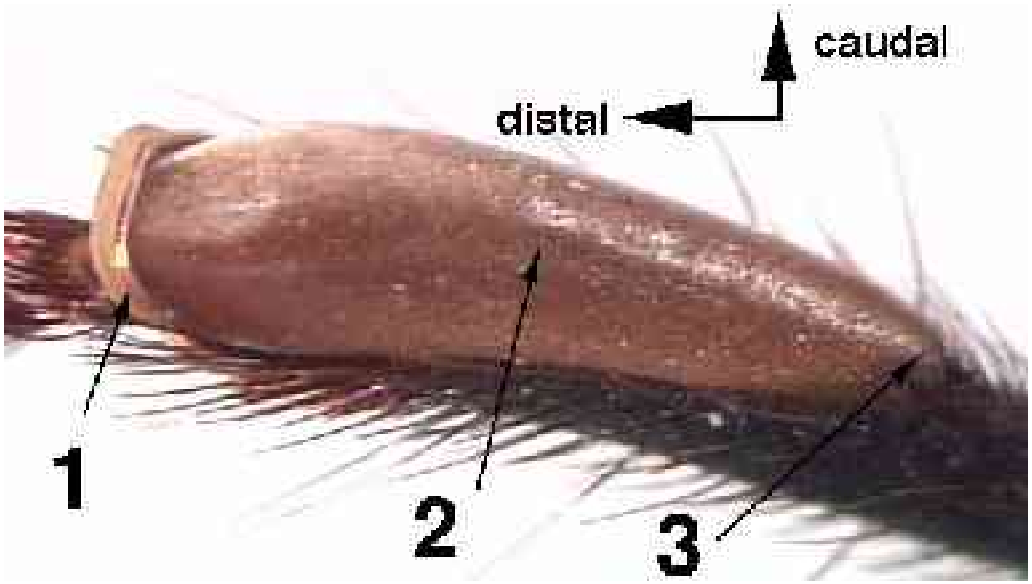
- **Anoles setae are smaller and simpler.**
  - » **Easier to study and compare to theoretical values.**



(Images by Kellar Autumn, Anne Peattie, and Juliann Chen)

- Length: ~ 20-30 µm; density: ~ 10^6 setae/mm^2.
- Each ends in a single tip.

Other Natural Adhesive Examples



QuickTimeª and a
Photo - JPEG decompressor
are needed to see this picture.

Assasin Bug - uses similar structures for manipulation

QuickTimeª and a
Photo - JPEG decompressor
are needed to see this picture.

Photos by Kellar Autumn, Lewis + Clark College

Overall Conclusions

- There are many opportunities for biological experiments with sensitive force measurements
- The applications range from opportunities for macro-scale bio-mimesis to the fundamental understanding of molecular biochemistry.
- It helps to be able to measure small forces, but there are many things that are very interesting at the larger scale.

Acknowledgements

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