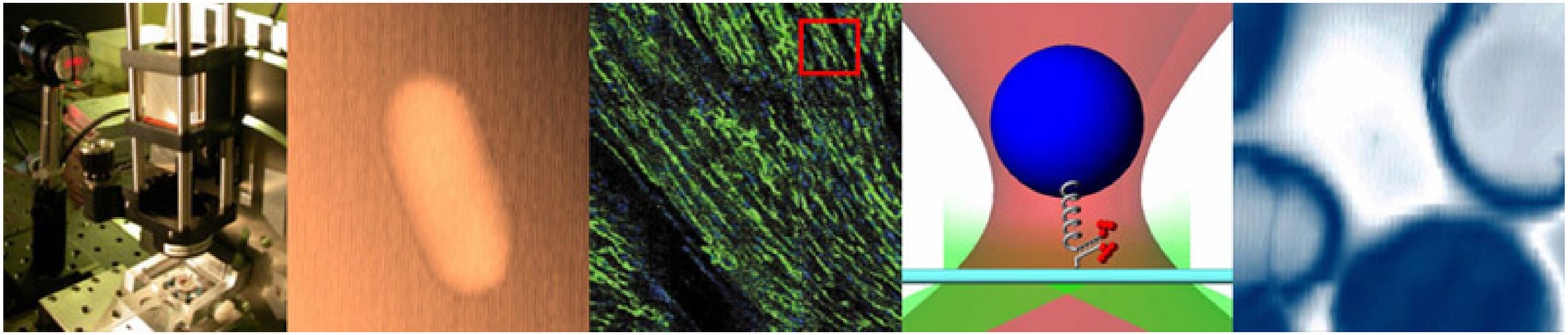
20.309: Biological Instrumentation and Measurement



<u>Instructors</u>: Scott Manalis and Peter So

<u>Laboratory Instructor</u>: Steve Wasserman

<u>Teaching Assistants</u>: Jaewon Cha
Heejin Choi
Rumi Chunara
Yuri Matsumoto

Lectures:
12-1 pm Tuesday and Thursday

Recitation:
12-1 pm Friday

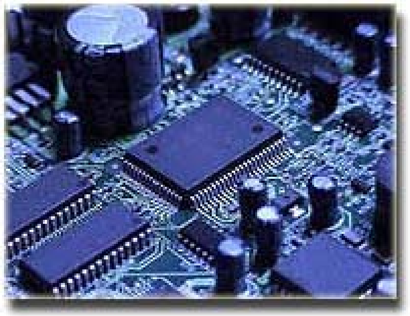
Labs:
Open lab format! Rm 16-342 open from 10-6pm MRF and 1-9pm TW. Sign up on class website for 6-8 hrs per week.

http://www.openwetware.org/wiki/20.309

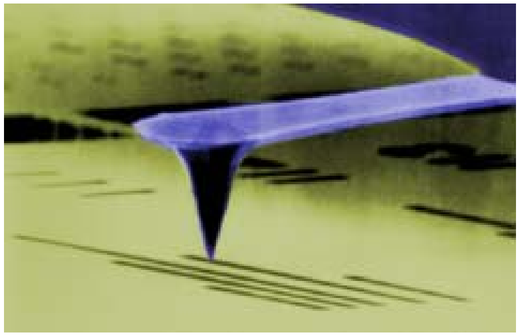
Prerequisite:
18.03 (differential eq.)

Textbooks:
PDF downloads from website and books in 16-342

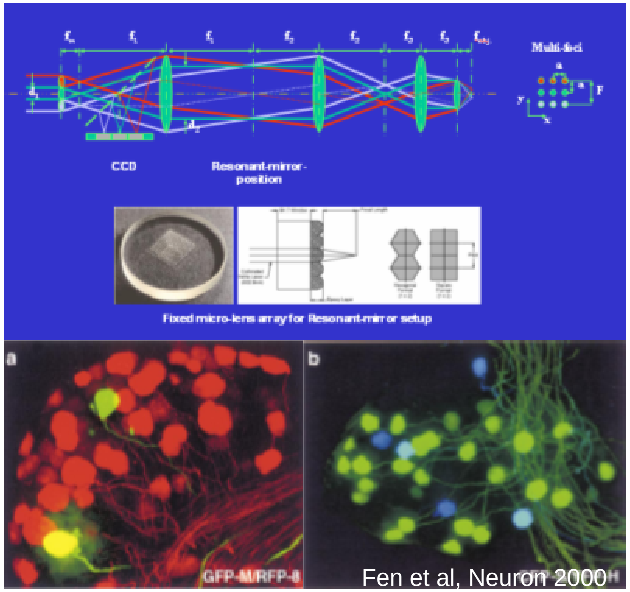
Course Outline



Electronics



Atomic Force Microscopy



Optical Microscopy

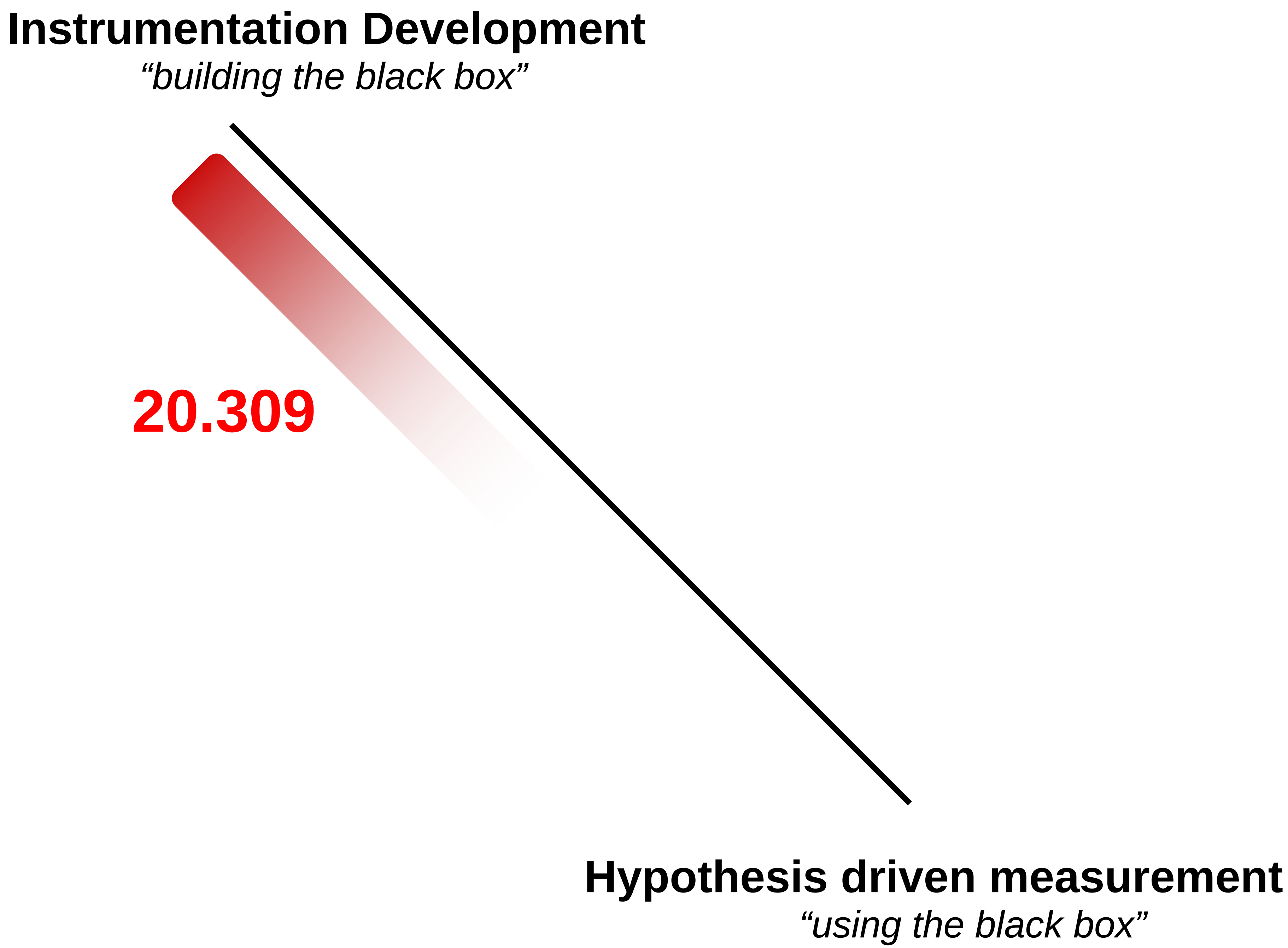
<u>Course objectives</u>:

1. Learn how to design and build instruments for laboratory measurement.

2. Understand fundamental principles of operation.

3. Understand methods for signal processing and data analysis.

4. Understand how instrumentation can advance biological engineering.



Instrumentation Development
“building the black box”
20.309
Hypothesis driven measurement
“using the black box”

Key concepts of 20.309

DNA Melting	*AFM*	*Microscopy*
Electronics	**Micromechanics**	**Optics**

Electronics and Micromechanics

Signals and systems (***time/freq domain***)

- Fourier transforms
- Correlation and Convolution

Thermal fluctuations and fundamental limits of position/force detection

Optics

Signals and systems (***spatial domain***)

- Fourier optics
- Image processing

Fundamental limits of resolvability

Lectures and laboratory sessions do not always correlate

Grading

Written reports from lab modules	50%
Student presentation	15%
Homework assignments	15%
Lab quizzes	10%
Oral participation during lectures and laboratory modules	10%

Student Presentations

Sept 28: Nucleic acid technologies [edit]

1. J. W. Hong, *et al.* "A nanoliter-scale nucleic acid processor with parallel architecture," Nature Biotech. **22**(4): pp. 435-439 (2004).
2. L Warren, *et al.* "Transcription factor profiling in individual hematopoietic progenitors by digital RT-PCR" Proc. Nat. Acad. Sci. 2006. OR E.A. Ottesen *et al.* "Microfluidic Digital PCR Enables Multigene Analysis of Individual Environmental Bacteria" Science 2006.
3. J. M. Nam, C. S. Thaxton, C. A. Mirkin "Nanoparticle-based bio-bar codes for the ultrasensitive detection of proteins," Science **301**(5641): pp. 1884-1886 (2003).
4. E. Winfree, *et al.* "Design and self-assembly of two-dimensional DNA crystals," Nature **394**(6693): pp. 539-544 (1998). AND P. W. K. Rothemund "Folding DNA to create nanoscale shapes and patterns," Nature **440**(7082): pp. 297-302(2006).

Oct 12: Scanning probe microscopy I [edit]

1. A. Engell and D. J. Muller "Observing single biomolecules at work with the atomic force microscope," Nature Stuct. Biol. **7**(9): pp. 715-718 (2000).
2. F. Schwesinger *et al.* "Unbinding forces of single antibody-antigen complexes correlate with their thermal dissociation rates" PNAS **97**(18): pp. 9972-9977 (2000).
3. D. Rugar *et al.* "Single spin detection by magnetic resonance force microscopy," Nature **430**(6997): pp. 329-332 (2004).
4. 20.309 Lab Module 1 -- measuring DNA melting curves

Oct 16: Scanning probe microscopy II [edit]

1. G. E. Fantner *et al.* "Sacrificial bonds and hidden length: Unraveling molecular mesostructures in tough materials" *Biophys. J* **90**(4): pp. 1411-1418 (2006).
2. SY Lee *et al.* "Chemomechanical mapping of ligand-receptor binding kinetics on cells" PNAS 104: pp. 9609-9614 (2007).
3. MJ Rosenbluth, WA. Lam, and DA Fletcher, "Force Microscopy of Nonadherent Cells: A Comparison of Leukemia Cell Deformability" Biophysical Journal 90: pp. 2994-3003 (2006).
4. I. Rousso *et al.*, "Microsecond atomic force sensing of protein conformational dynamics: Implications for the primary light-induced events in bacteriorhodopsin," *PNAS* **94**, pp. 7937-41 (1997).
5. 20.309 Lab Module 2 -- AFM Lab

http://www.openwetware.org/wiki/20.309:Presentations

Registering for 20.309

Class size is limited to ~24 students due to limited resources

<u>If you're not a senior in Course 20, you must:</u>

Register for 20.309 by emailing the following to be309@media.mit.edu:

1. Your background and research interests.
2. Why you are interested in 20.309 and what you hope to get out of it.

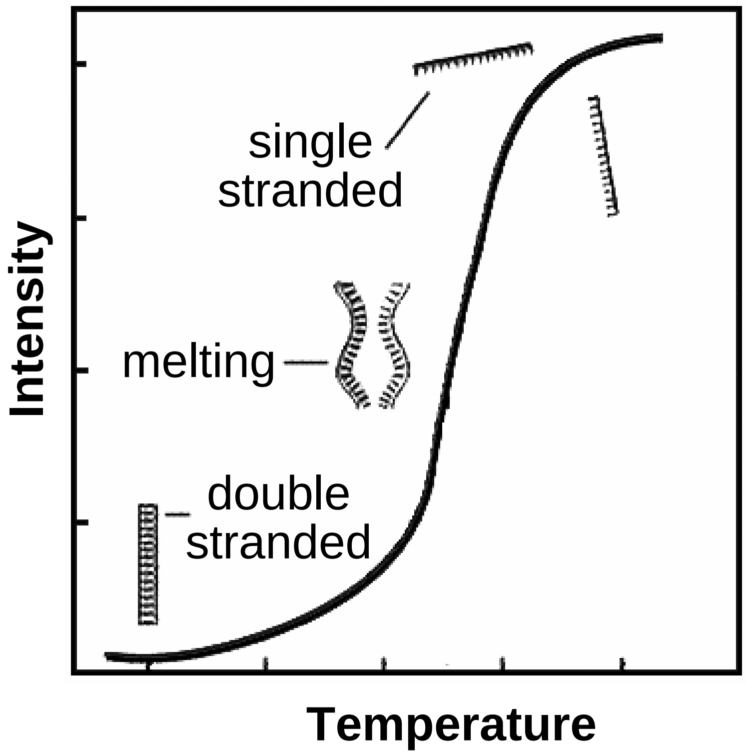
by <u>5pm Thursday (*today*)</u>

We will finalize the class list by Friday noon

Dropping 20.309 is not allowed

Questions?

20.309 Instrumentation Lab:
Electronics Module



Goal

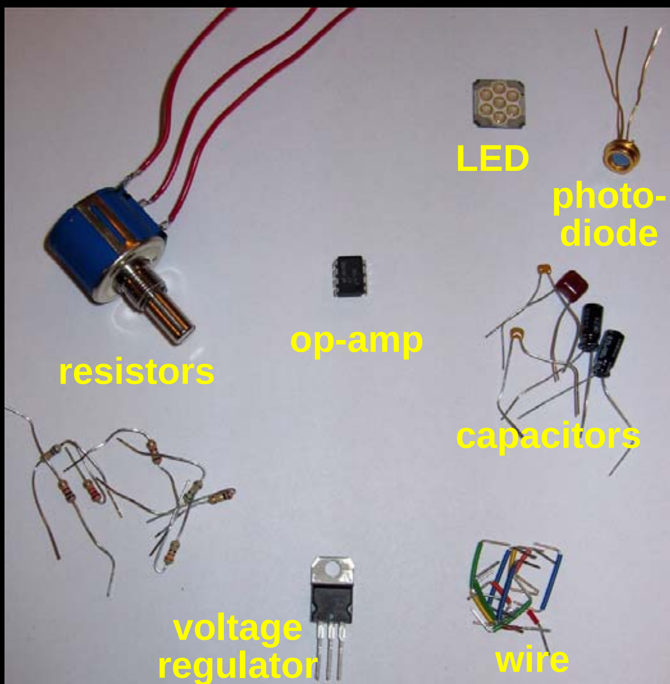
Measure DNA melting curves

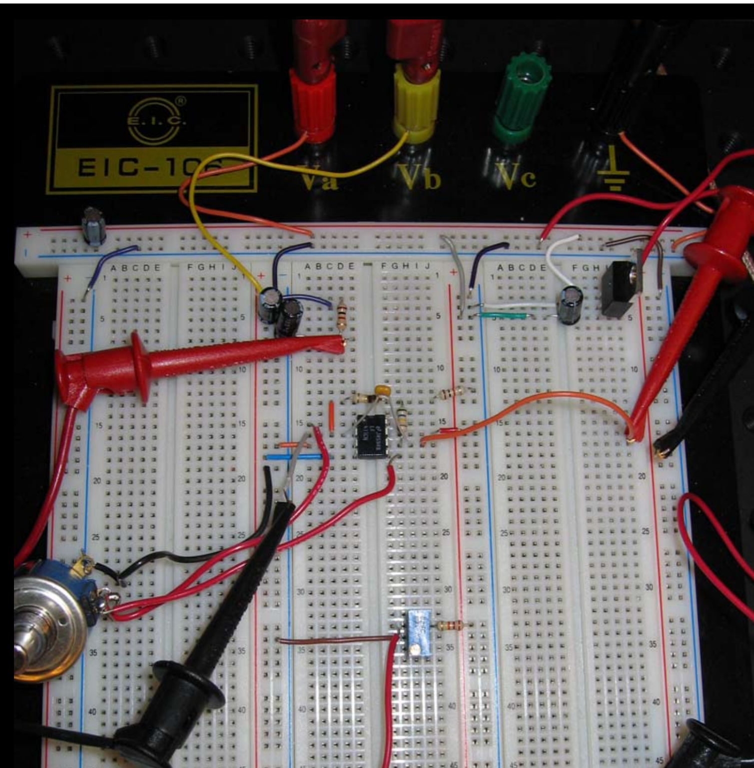
Topics

- Resistive dividers
- RC Filters
- Op-amp circuits
- Labview and Matlab

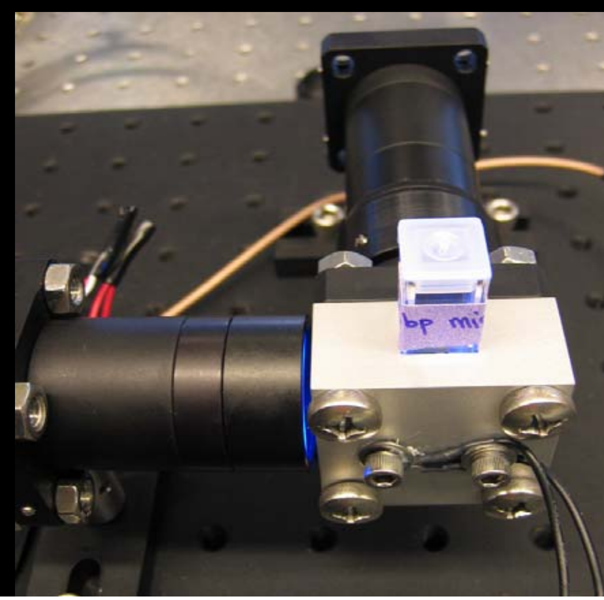
September 10 – October 5

From parts…

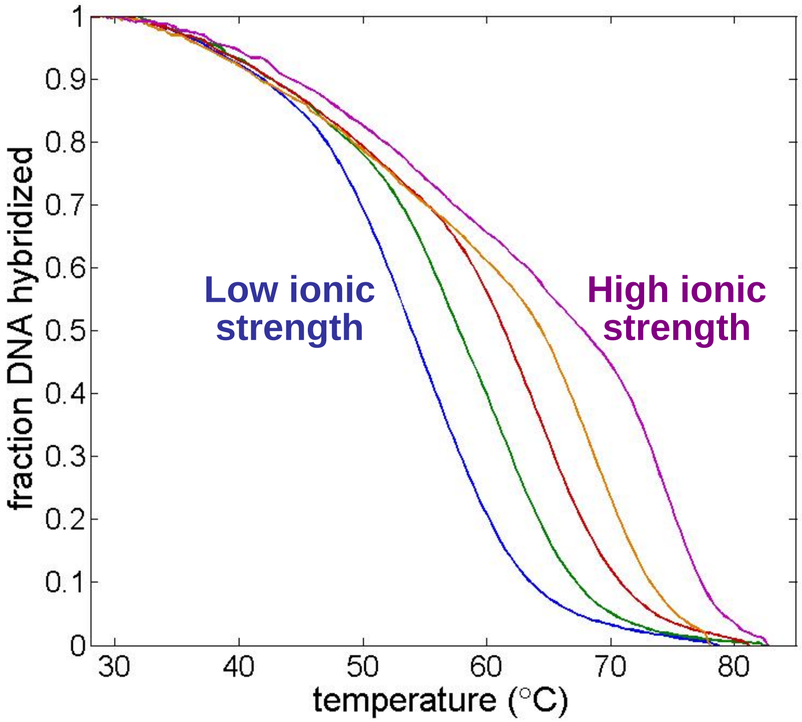


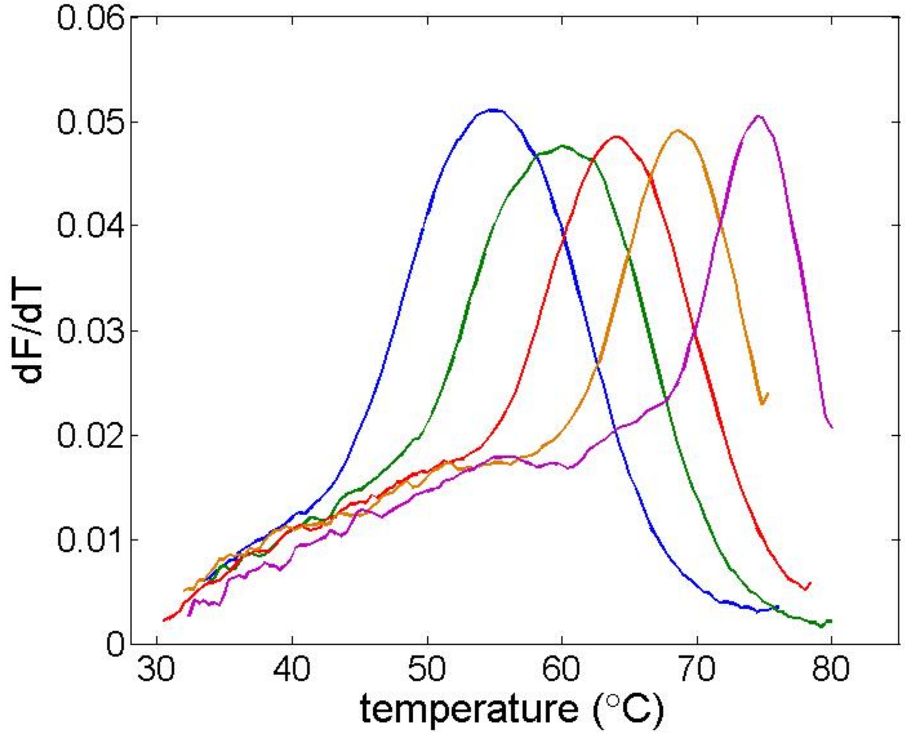


…to final instrument

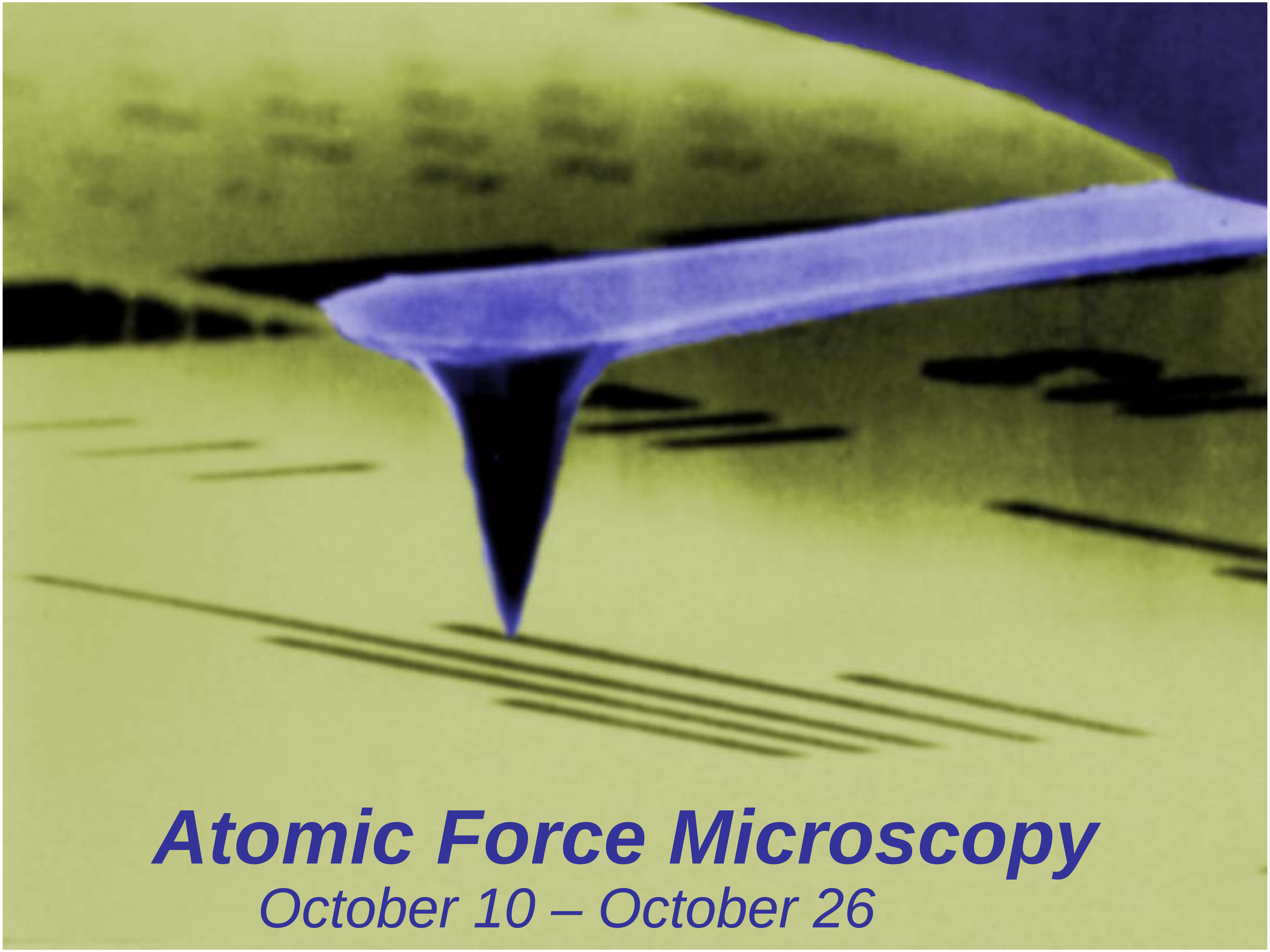


DNA Melting curves from 20.309



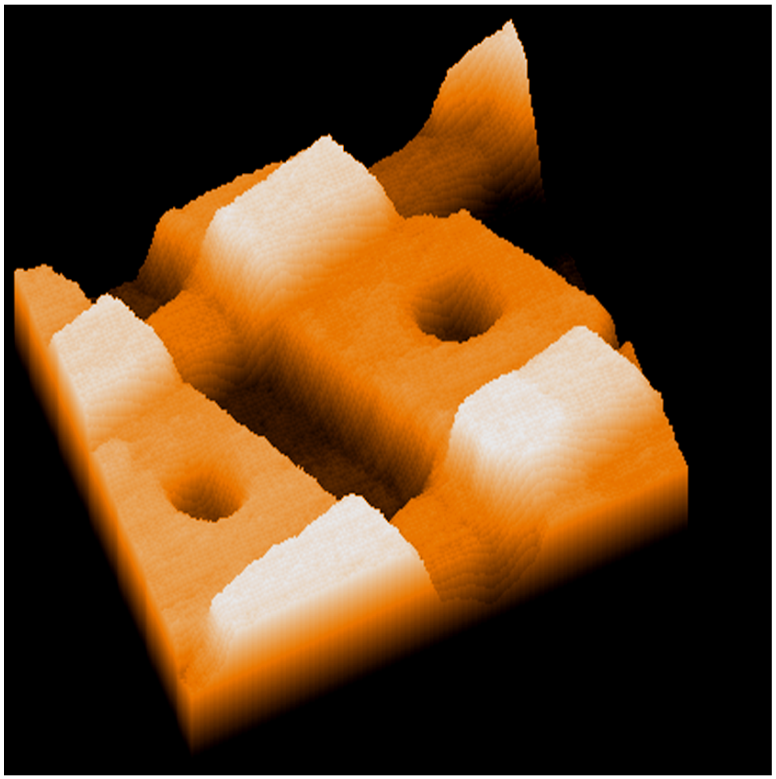


Justin Lo and Andrzej Wojcieszynski


Atomic Force Microscopy
October 10 – October 26

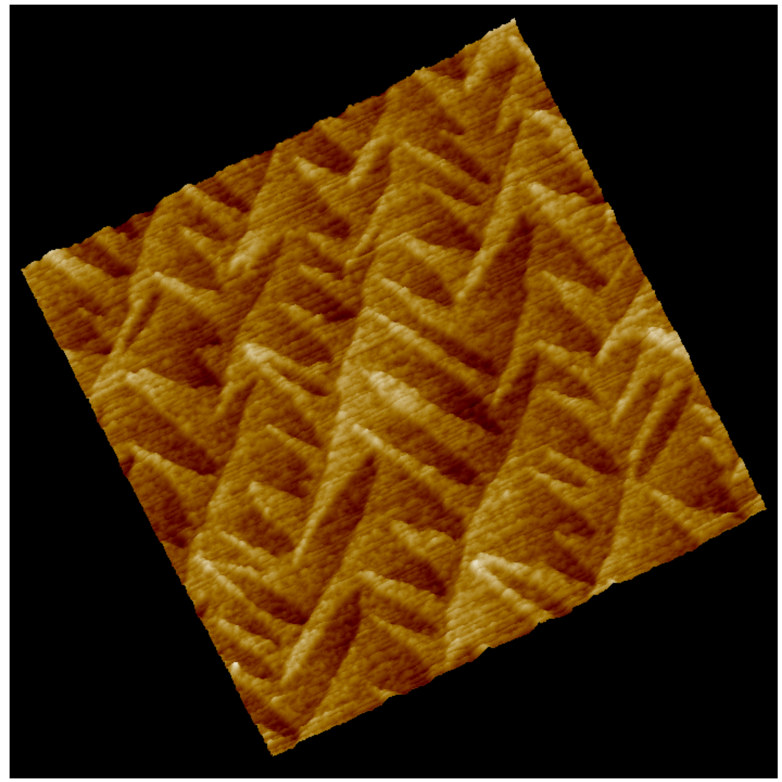
Semiconductor Imaging

Integrated Circuit



vertical scale: 4 µm

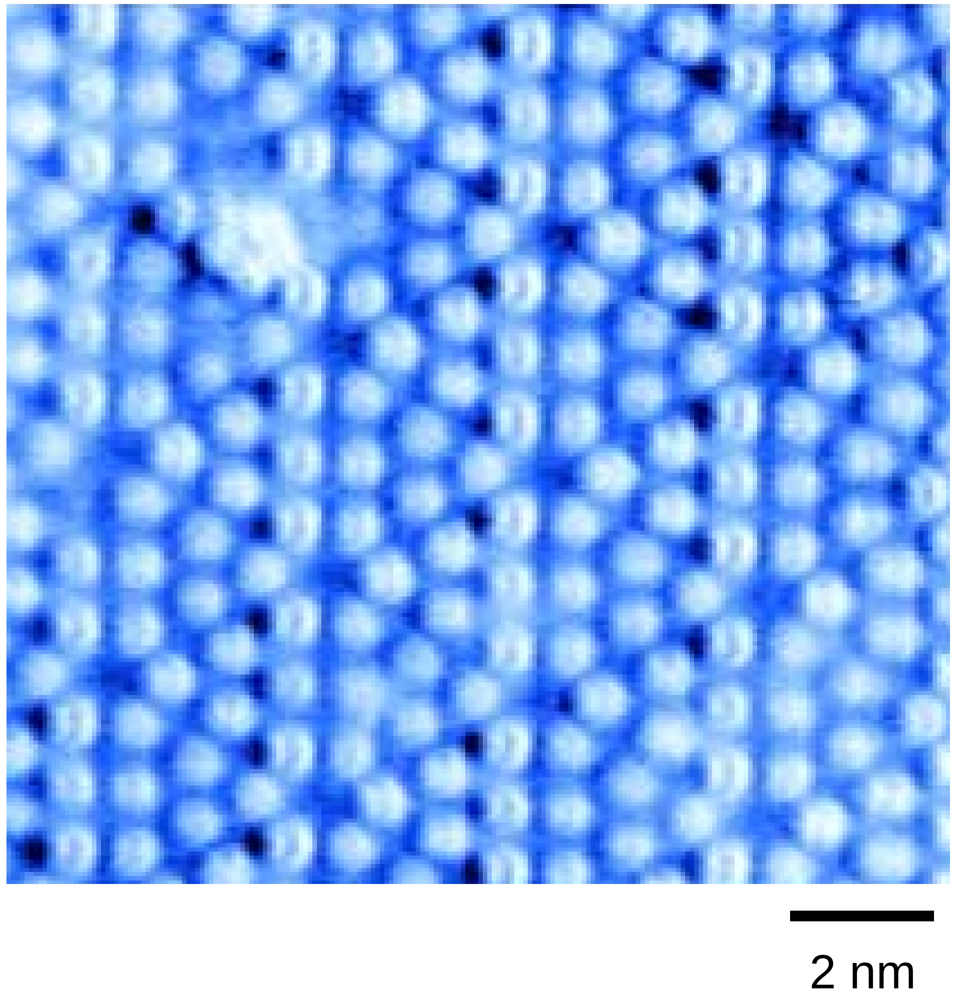
Epitaxial Silicon



vertical scale: 10 angstroms

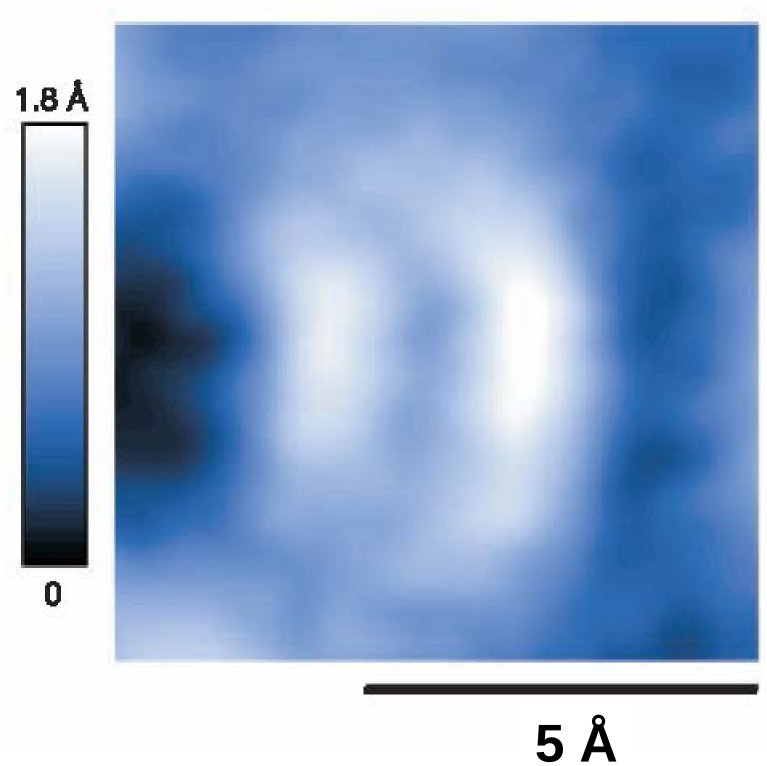
Digital Instruments, Santa Barbara CA

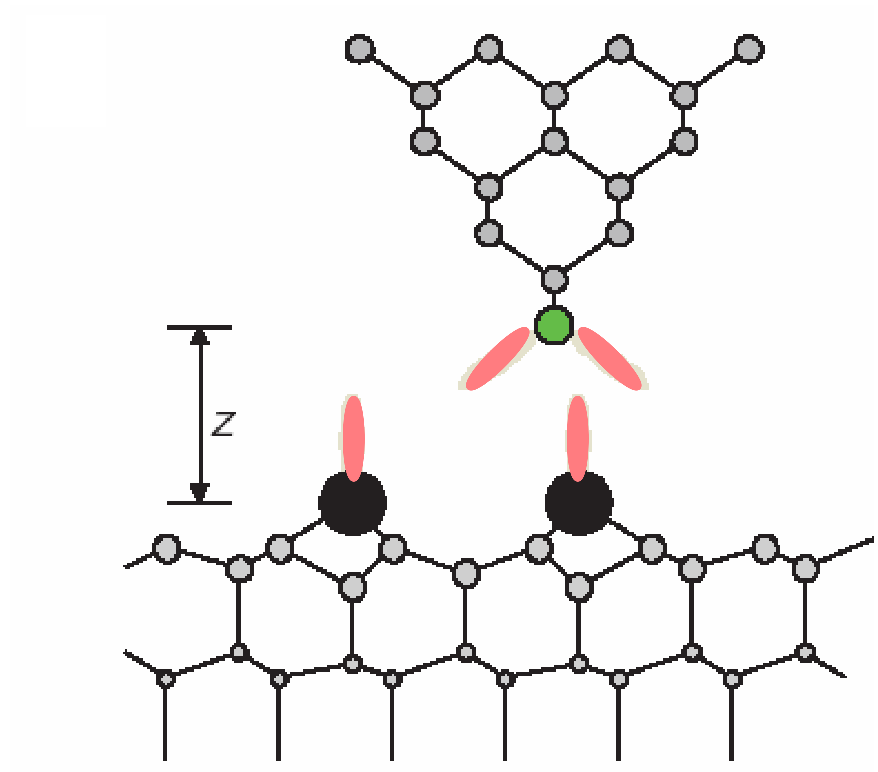
Atomic Resolution of Silicon (111) Surface by Atomic Force Microscopy



Giessibl et al., Science 2000

Subatomic Resolution of Silicon (111) Surface

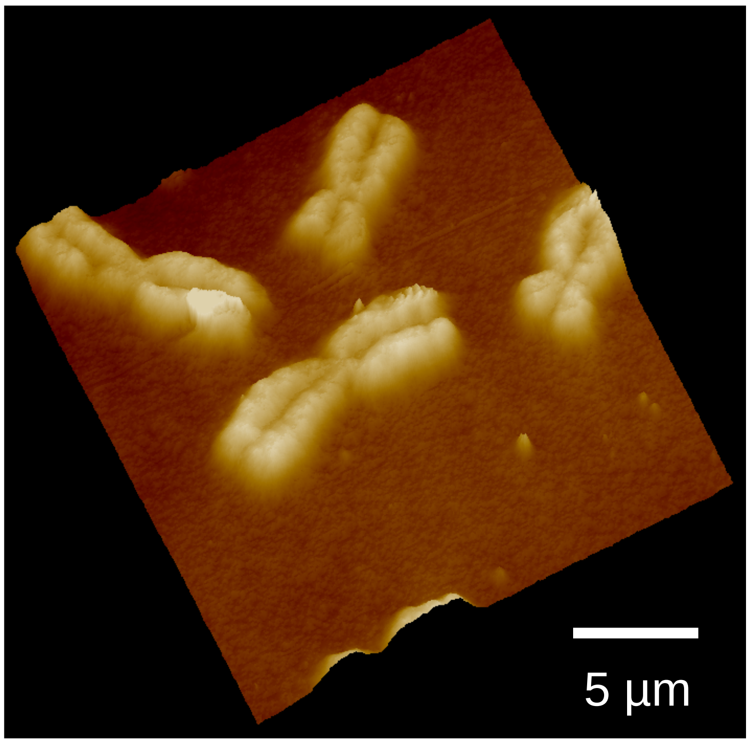




Giessibl et al., Science 2000

Biological Imaging

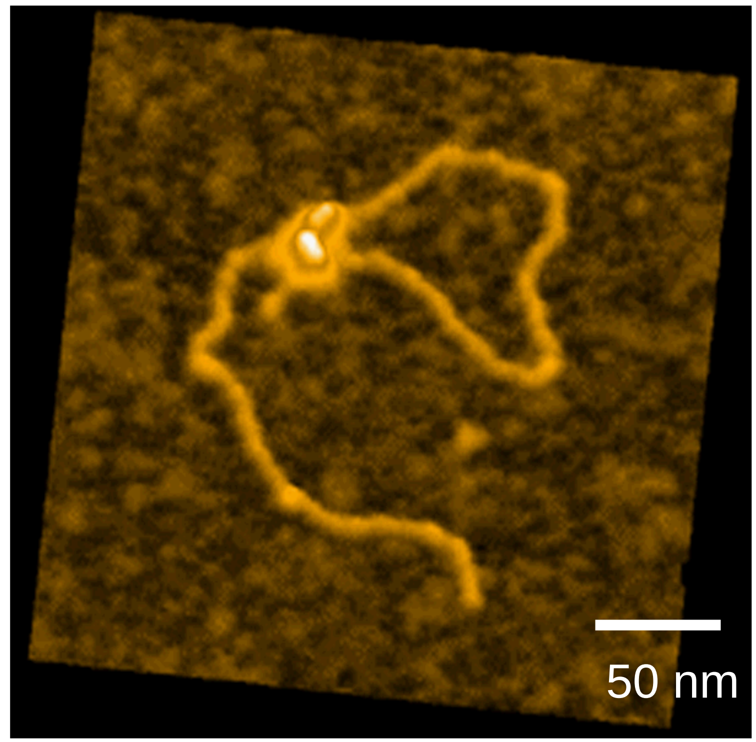
Human Chromosomes



vertical scale: 200 nm

Digital Instruments, Santa Barbara CA

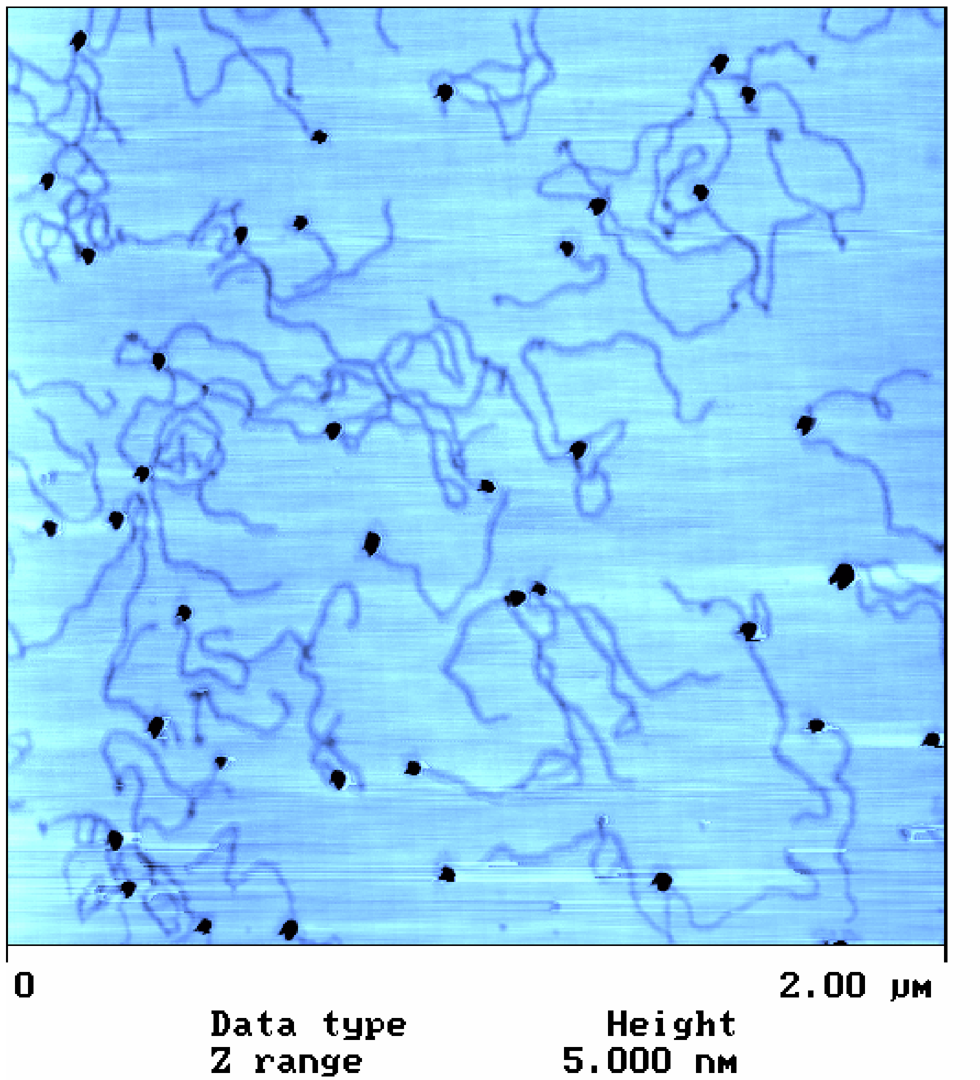
DNA



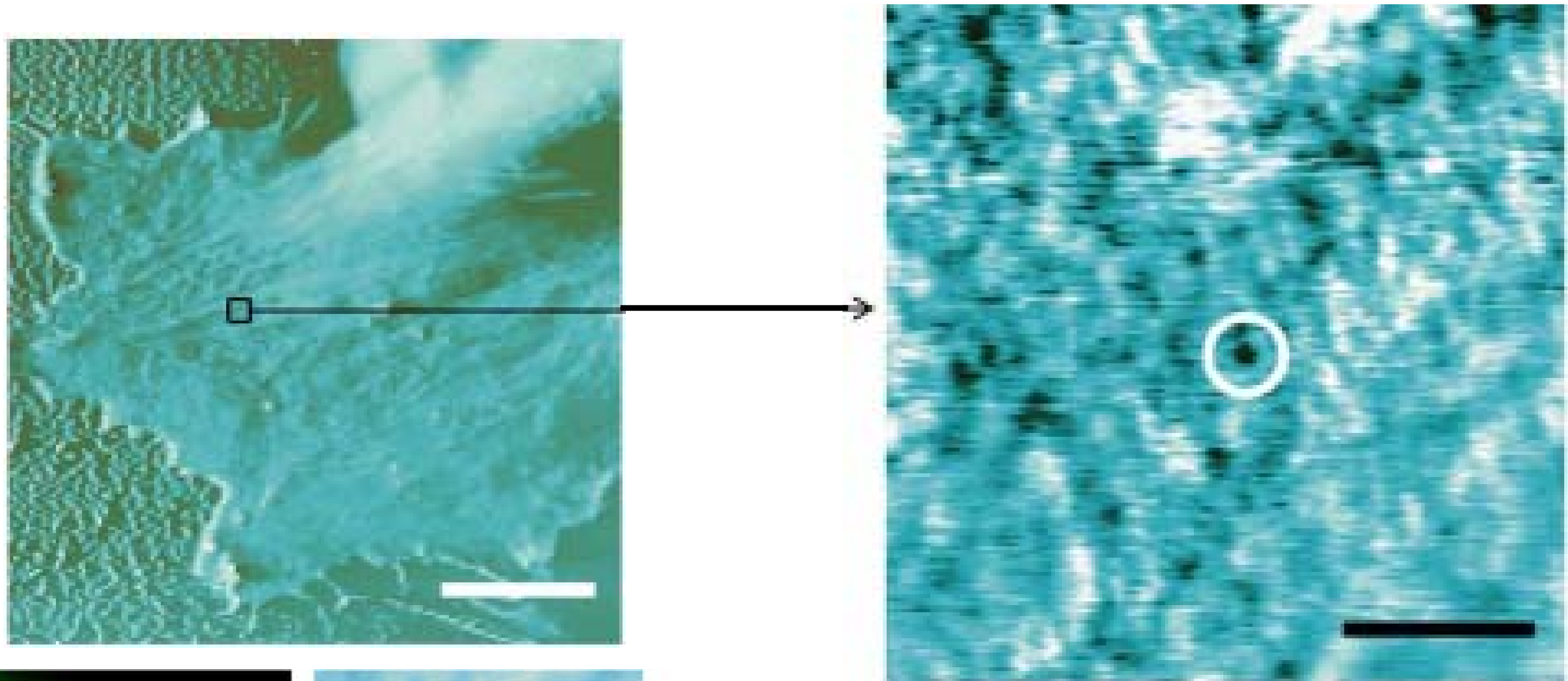
vertical scale: 5 nm

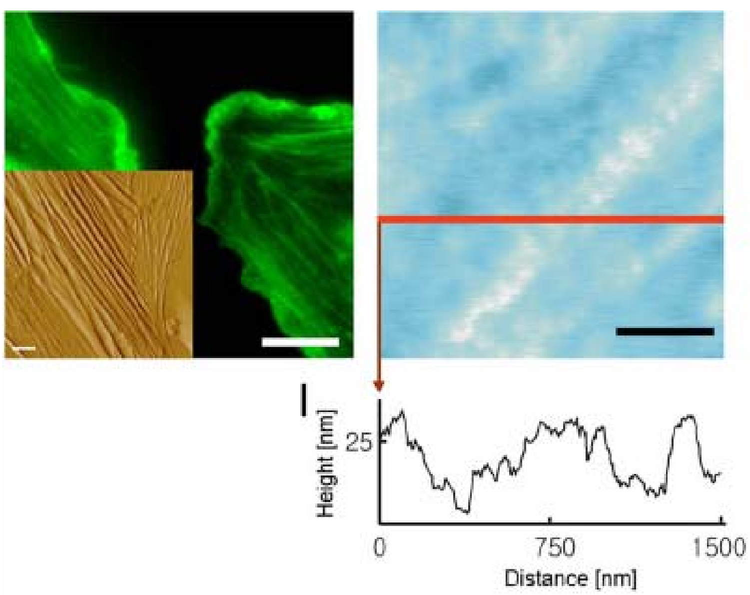
Bustamante Group, University of Oregon

AFM nanoparticles and DNA



with Ting Group, MIT Chemistry





Cytoskeletal bundles

VGEFR2 receptors on endothelial cell surface

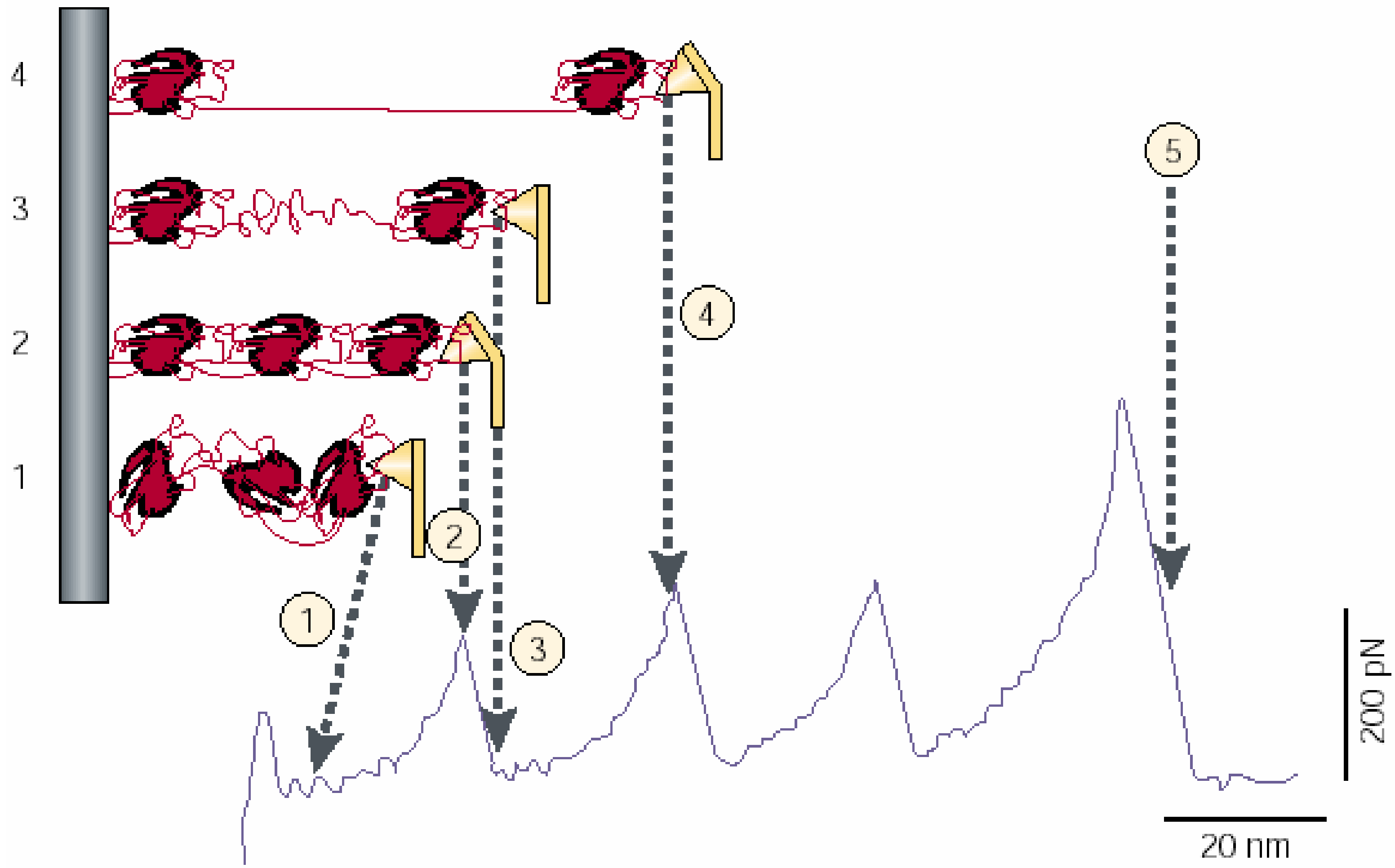
Chemomechanical mapping of ligand-receptor binding kinetics on cells

Van Vliet Lab, MIT

Lee et al. PNAS 2007

Single molecule force-spectroscopy

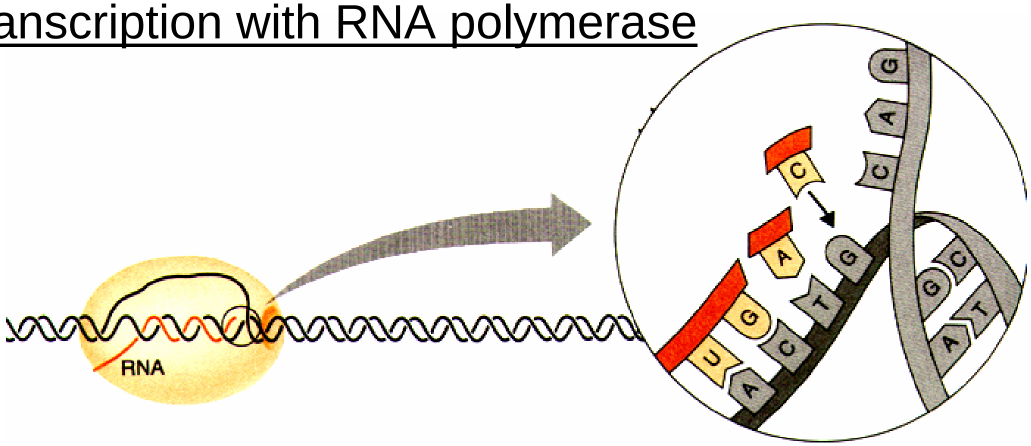
protein folding and unfolding



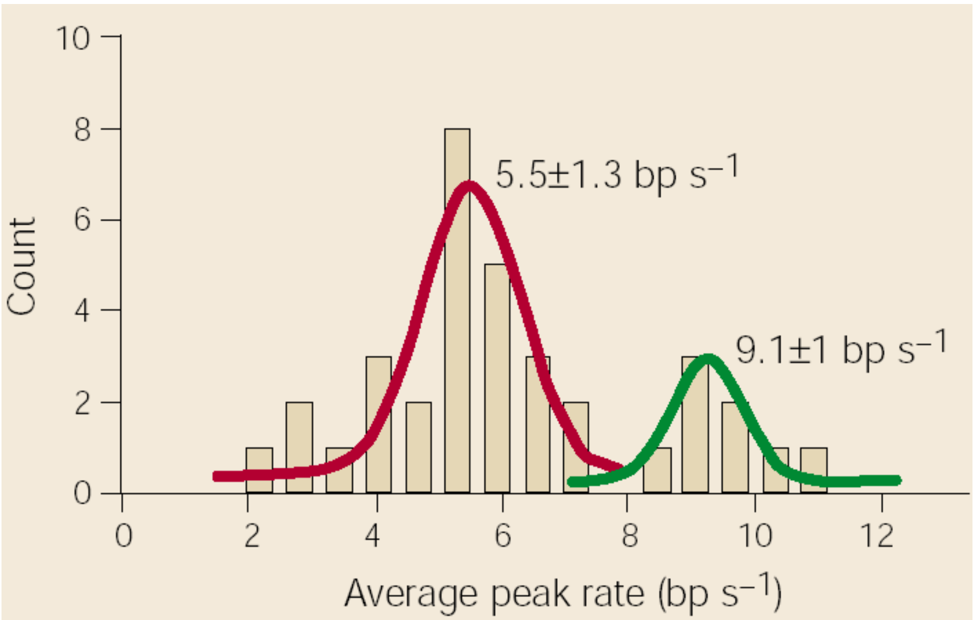
Rief et al., Science 1997

What can single molecule manipulation tell us about biology?

Transcription with RNA polymerase

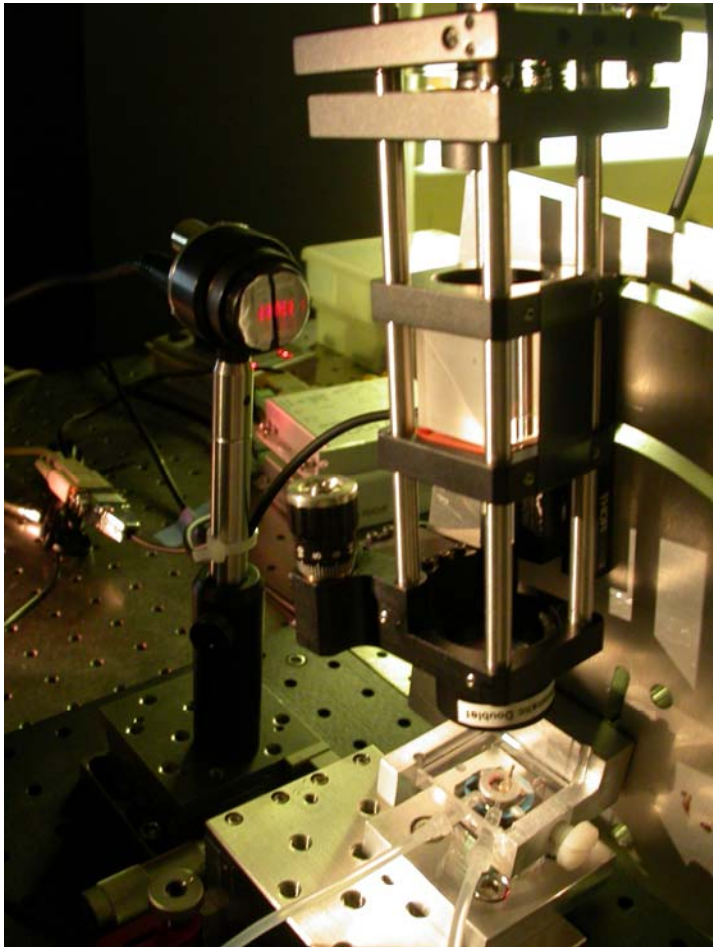


Transcription Rate

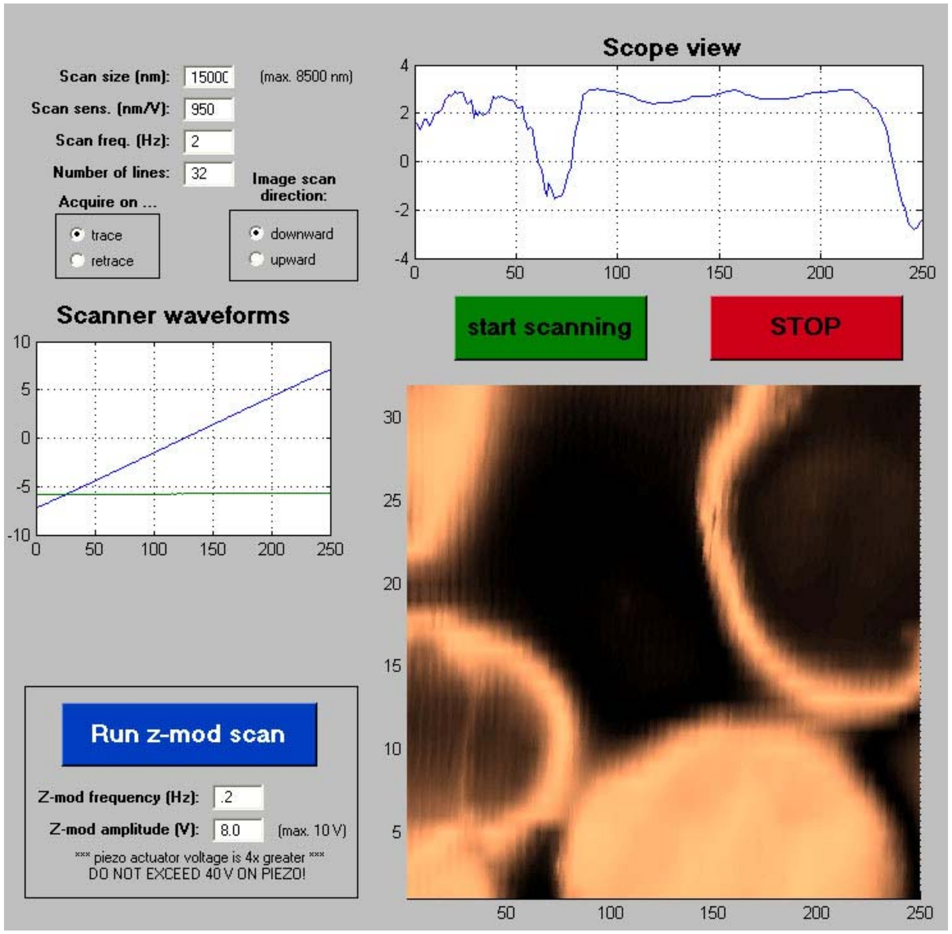


Bustamante et al. Nature 2000

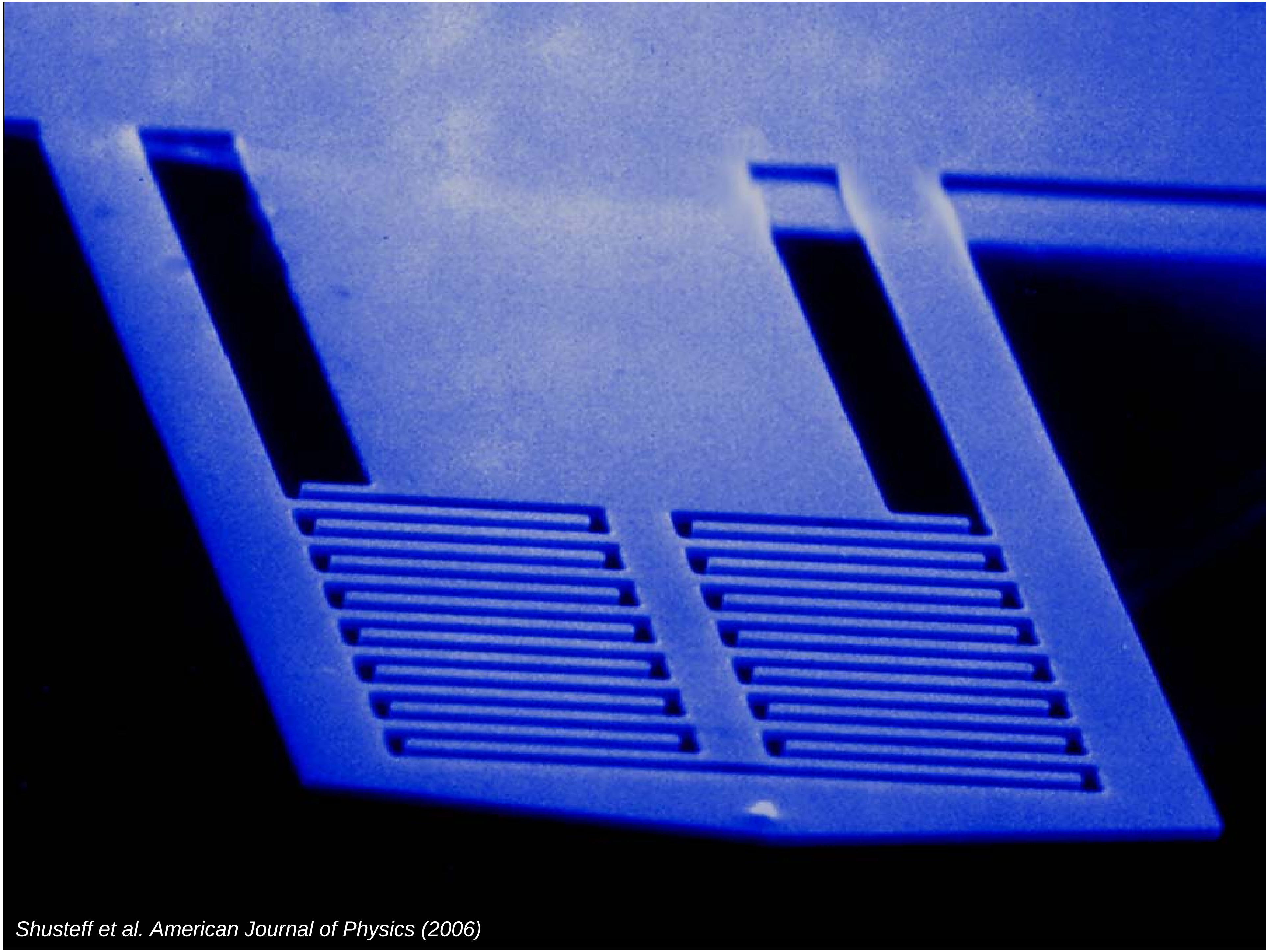
BE309 Instrumentation Lab:
Force Measurement Module



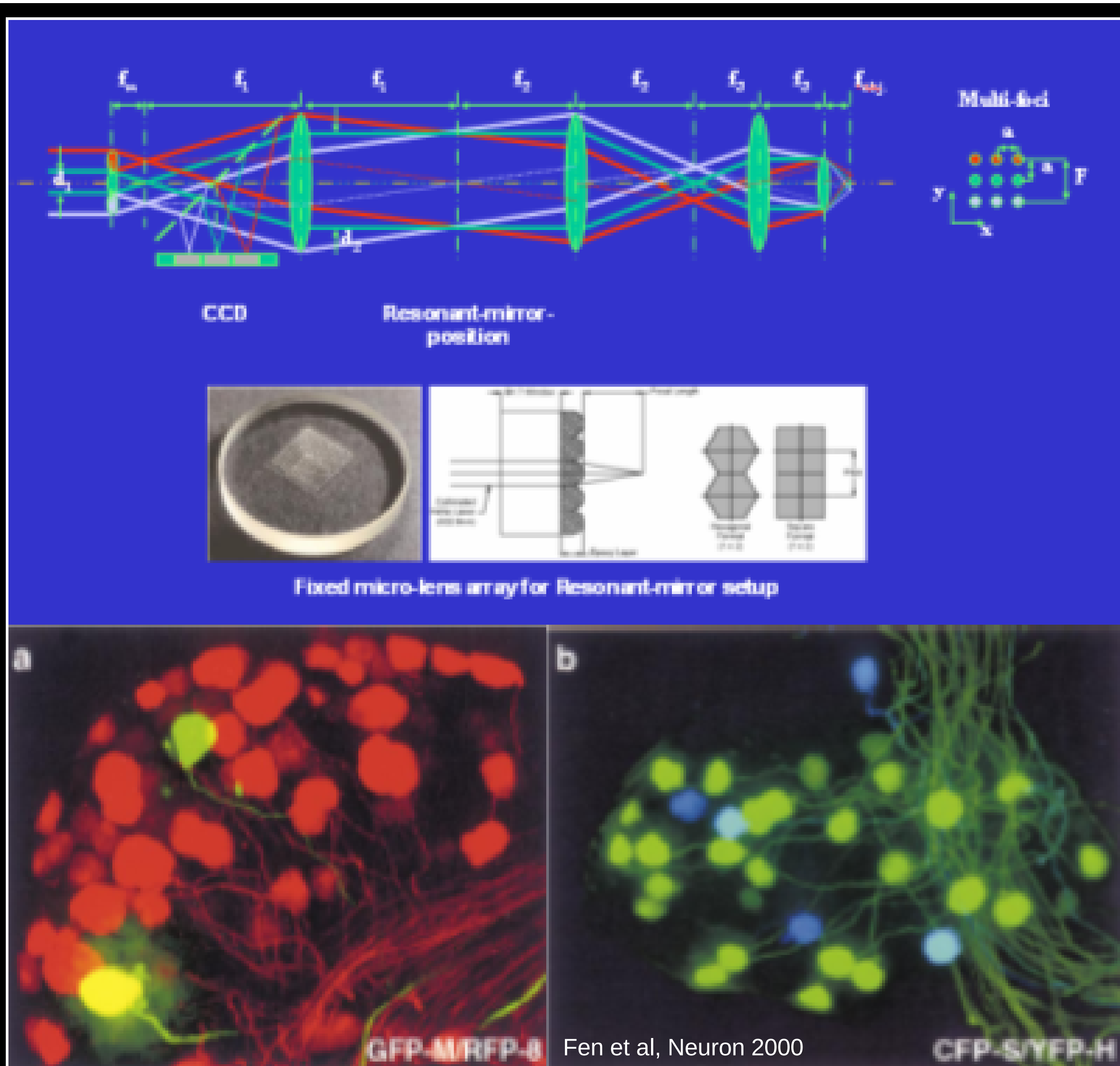
Homebuilt Atomic Force Microscope



Sample: Red Blood Cells



Shusteff et al. American Journal of Physics (2006)

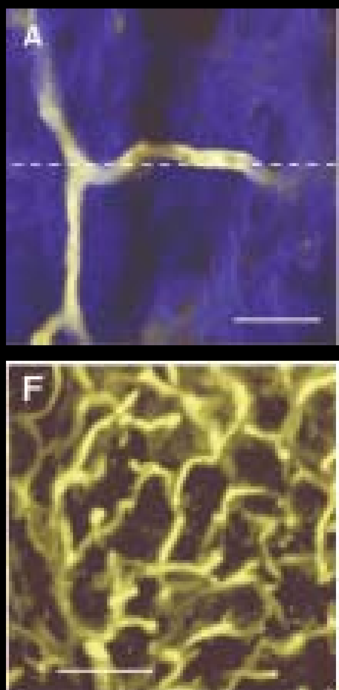


Optical Microscopy

October 30 – December 11

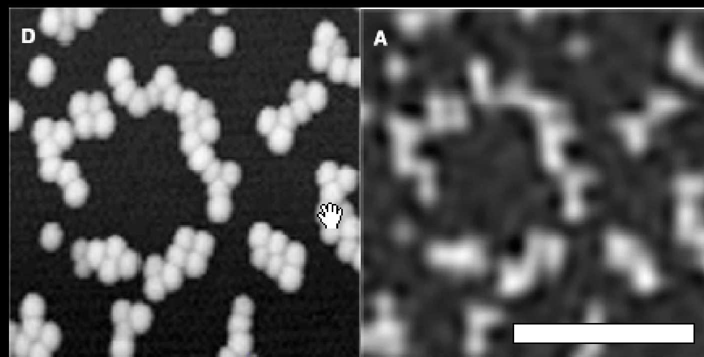
Optical Microscopy Can See Across Different Size Scales with Exquisite Sensitivity

See Deeper

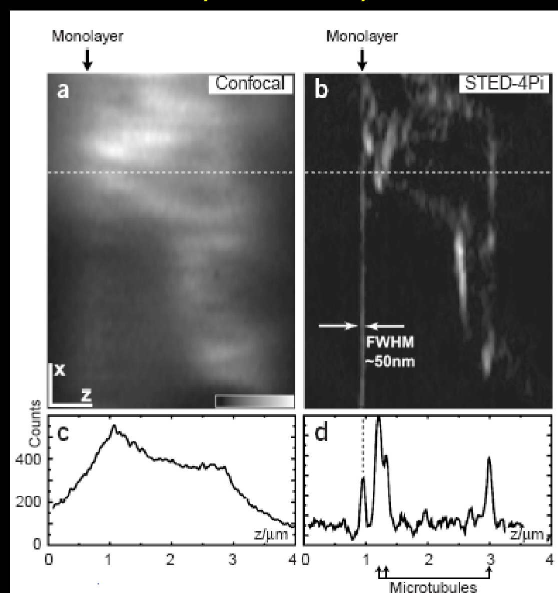


Larson, Science, 2003

See Finer

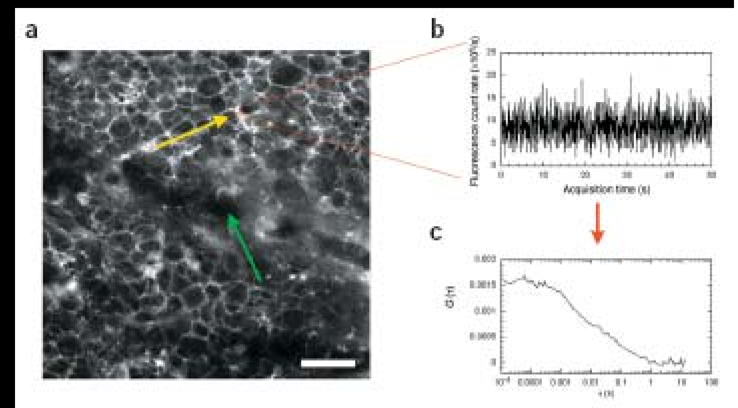


Frohn, PNAS, 2000

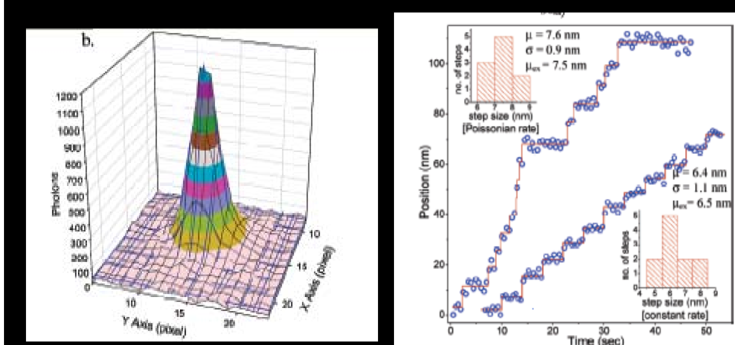


Hell, Nat. Biotech., 2005

Molecular Sensitivity

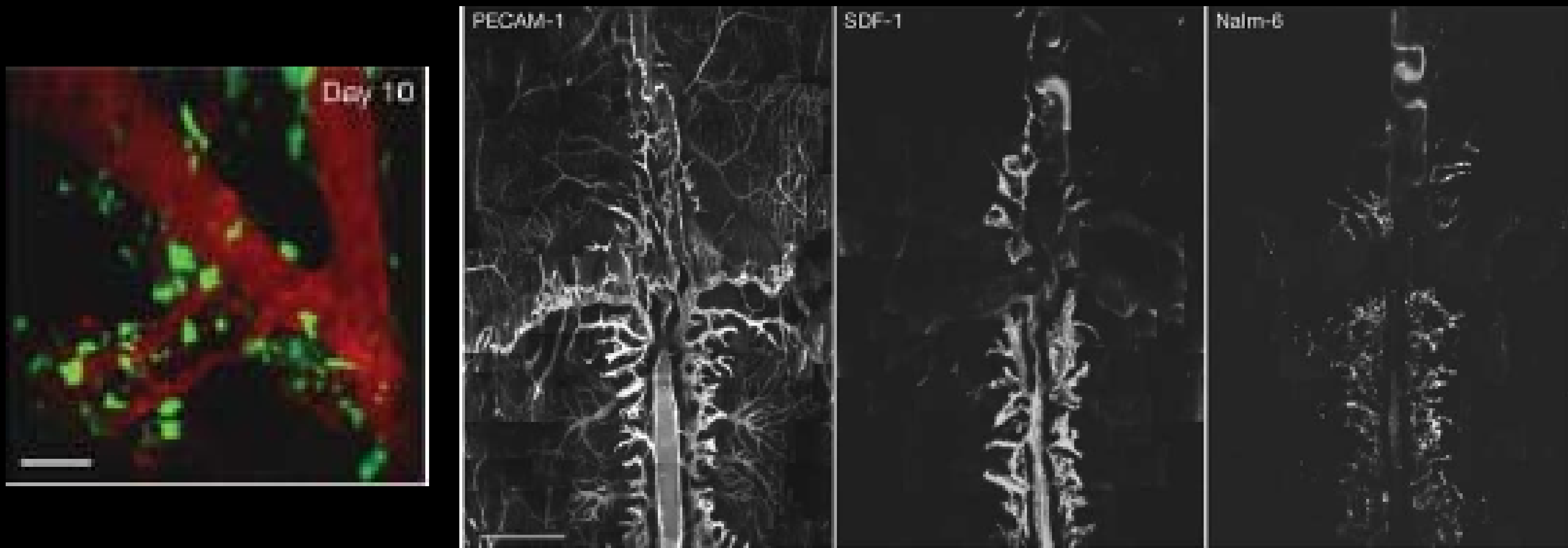


Alexandrakis, Nat. Med., 2004

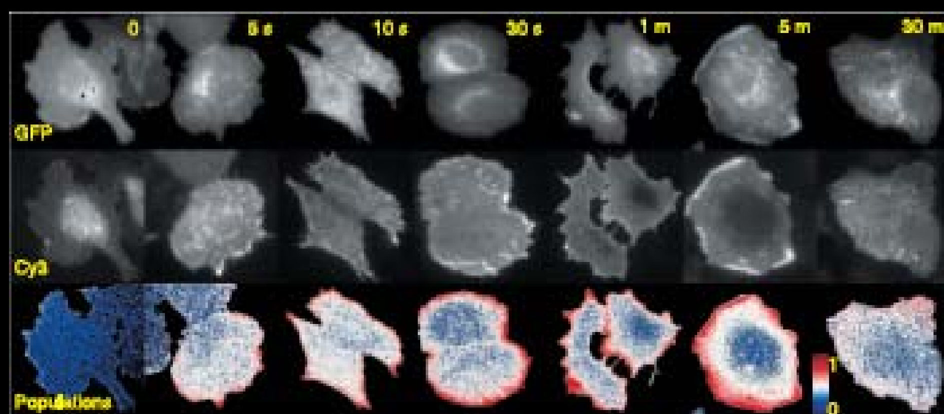


Yildiz, Acc. Chem. Res., 2005

Optical Microscopy Provides Imaging with Biological Specificity

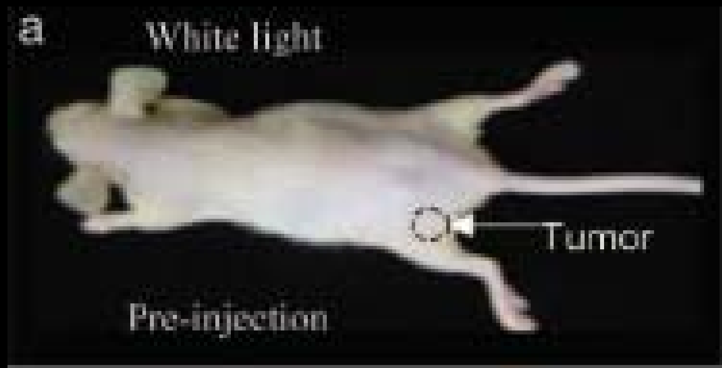


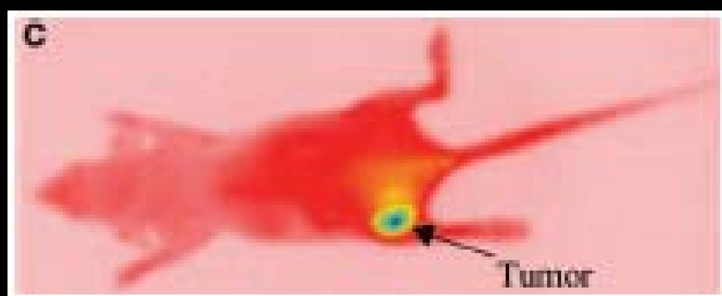
Spikins, Nature, 2005



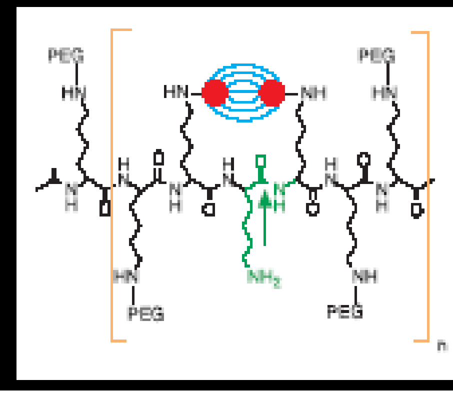
Verveer, Science, 2000

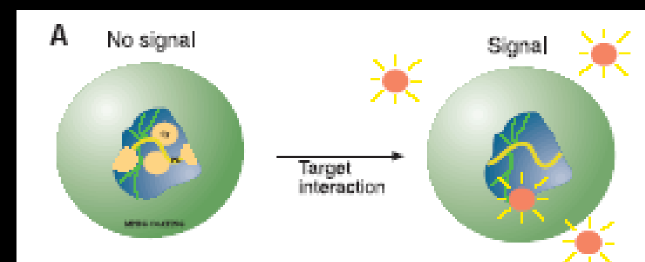
Optical Microscopy Impacts Medicine

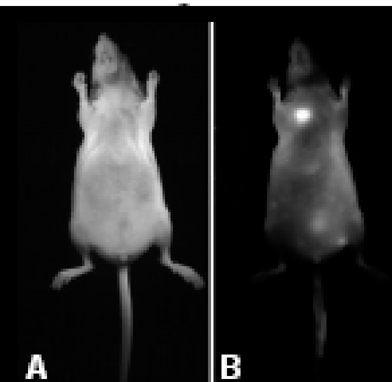




Achilefu et al, PNAS 2005

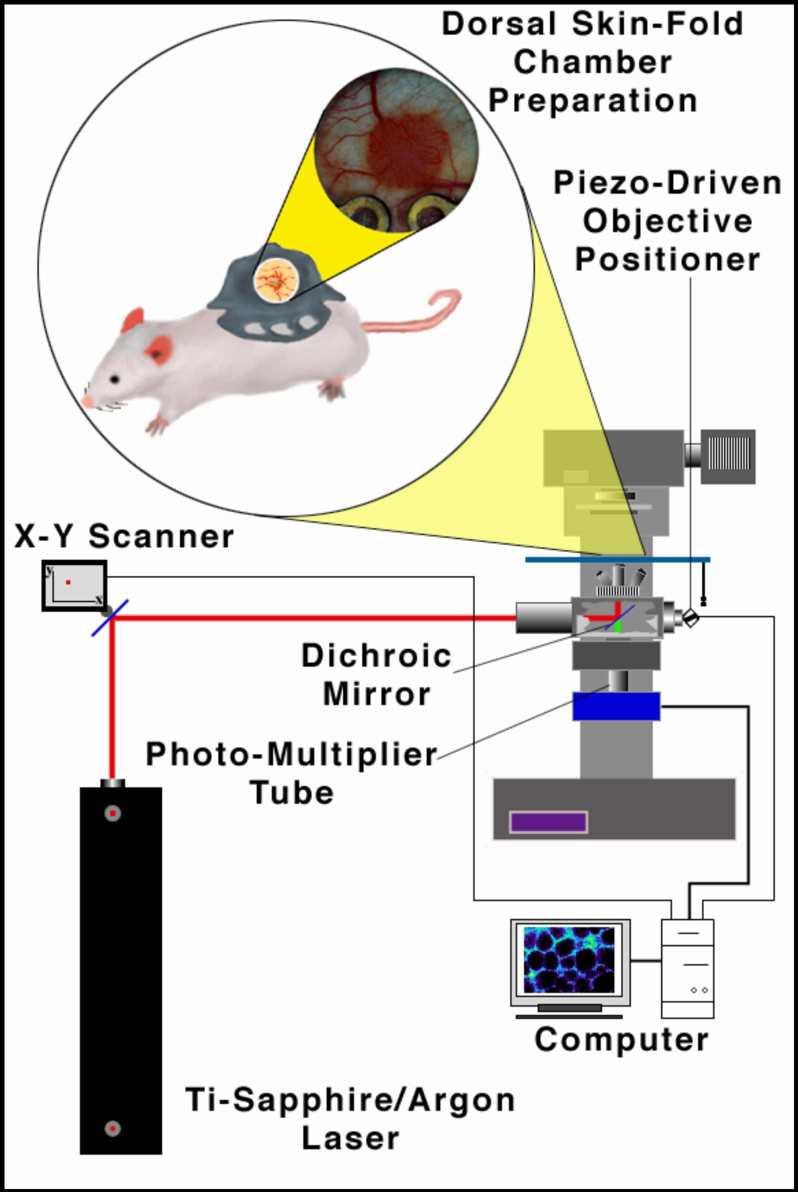


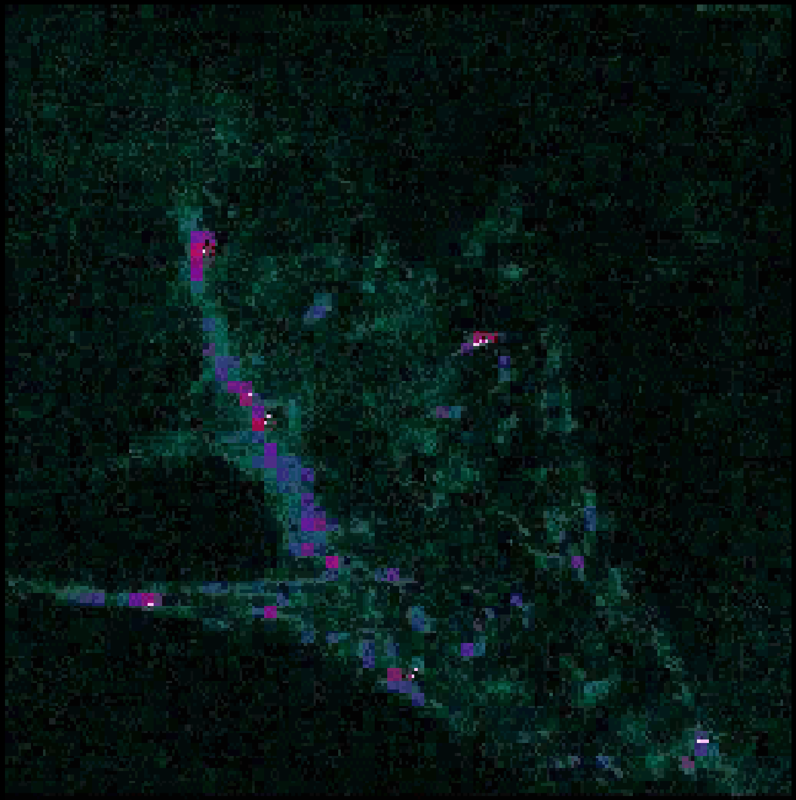




Weissleder, Nat. Biotech, 1999

Watch Blood Flow Inside Solid Tumor

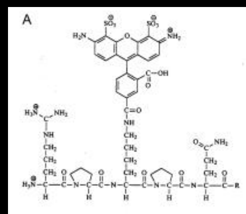




Optical Microscopy Can Utilize a Variety of Molecular Probes

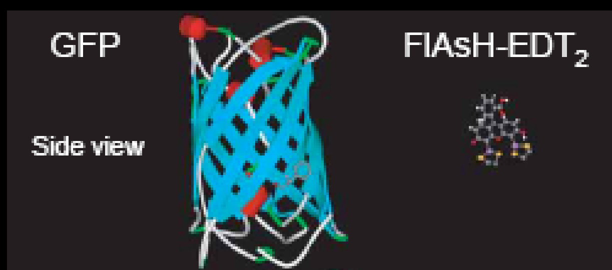
Fluorescent Probes

Organic Probes



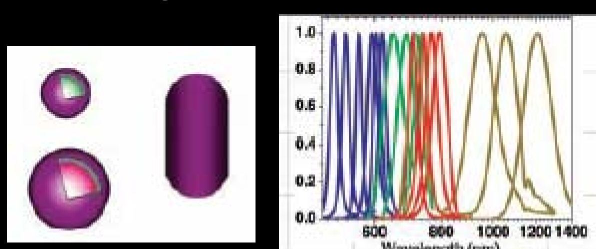
Molecular Probes, Oregon

Genetic Probes



Hoffmann et al, Nat. Meth, 2005

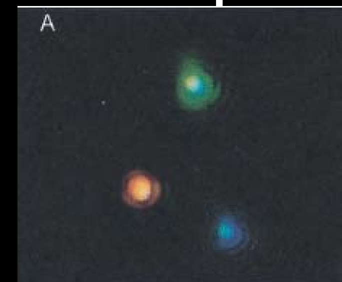
Quantum Dots



Michalet et al, Science, 2005

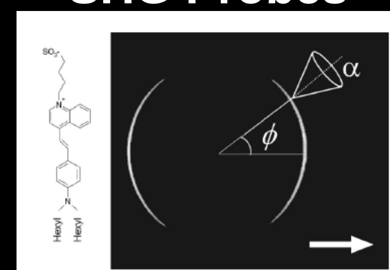
Non-fluorescent Probes

Metal Nanoparticles



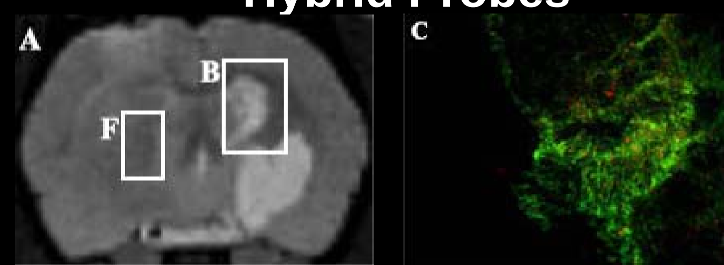
Schultz, PNAS, 2003

SHG Probes



Pons, JBO, 2003

Hybrid Probes

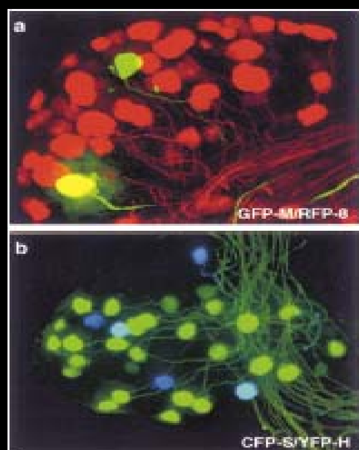


Modo et al, Neuroimage, 2004

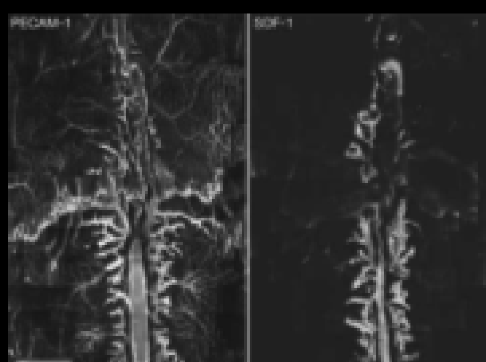
Biomedical Optics in The Age of Bioinformatics

A major challenge in the next few decades and century is the linking of gene/protein informatics with biological and medical imaging

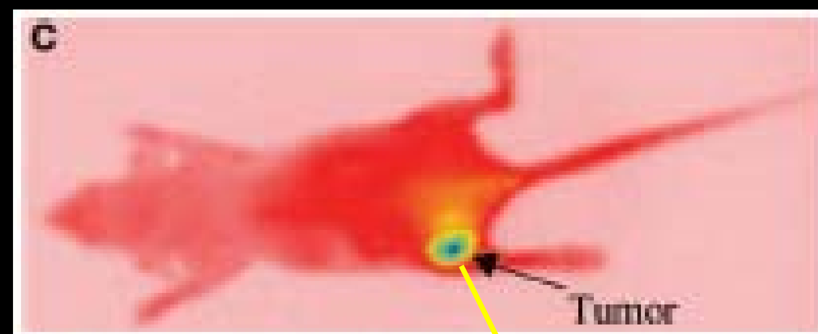
Imaging gene expression



Imaging Protein expression



What about mapping and modeling of many genes and many proteins throughout an animal?



BE309 Optics Module I

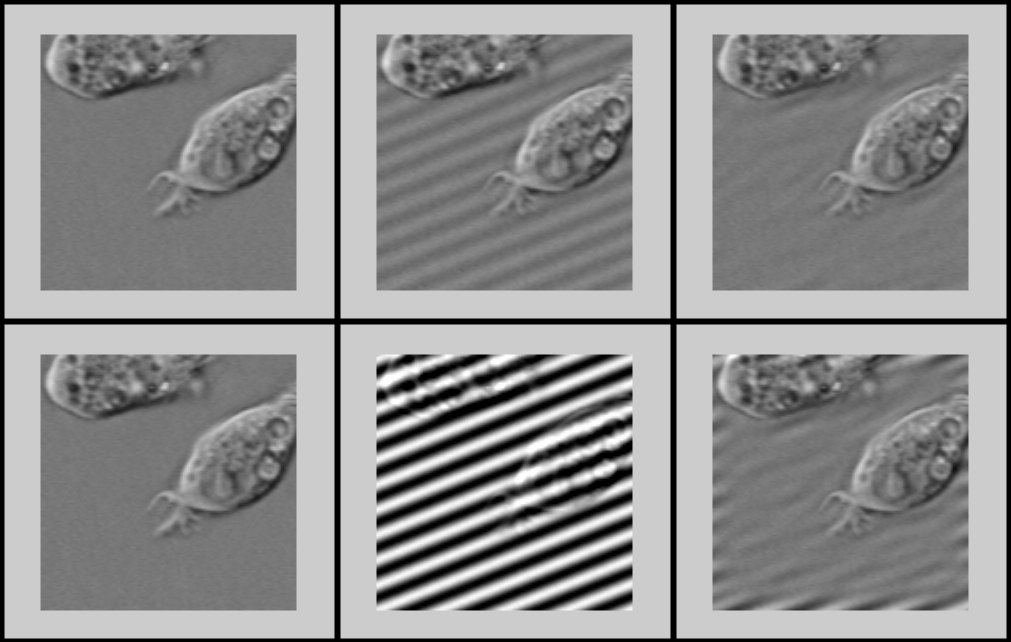
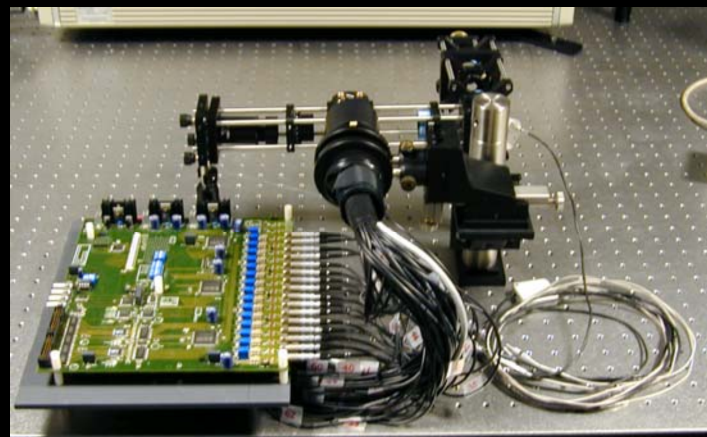
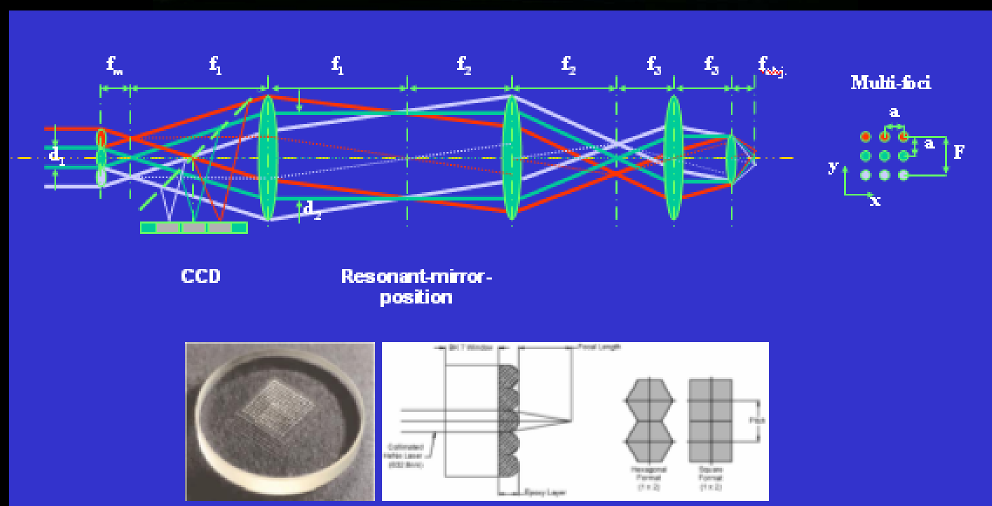


Image Processing and Analysis

BE309 Optics Module II

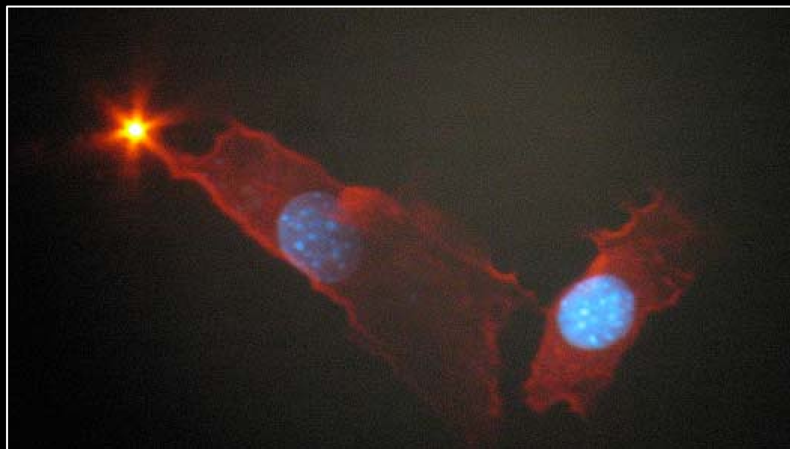




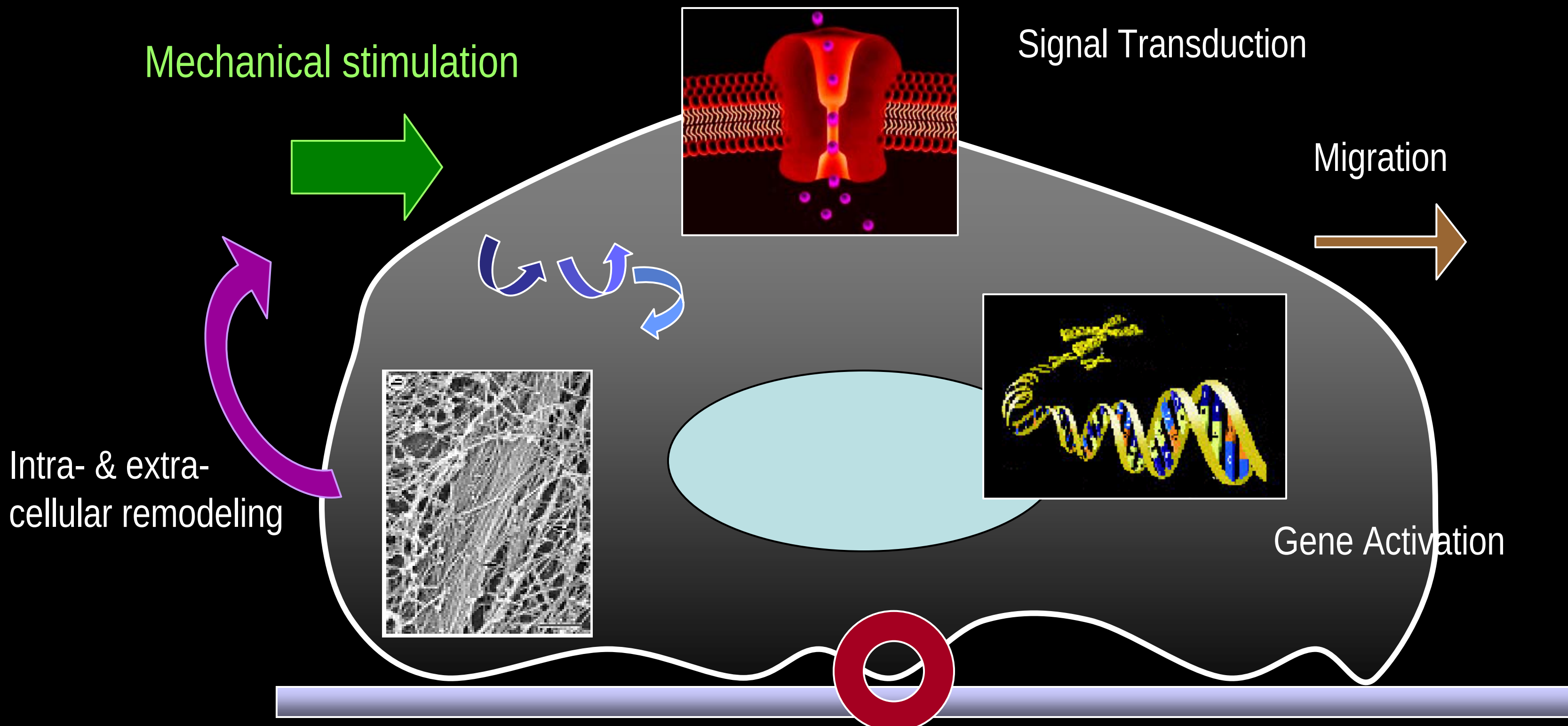
Fixed micro-lens array for Resonant-mirror setup

Build Your Own Microscope

BE309 Optics Module II



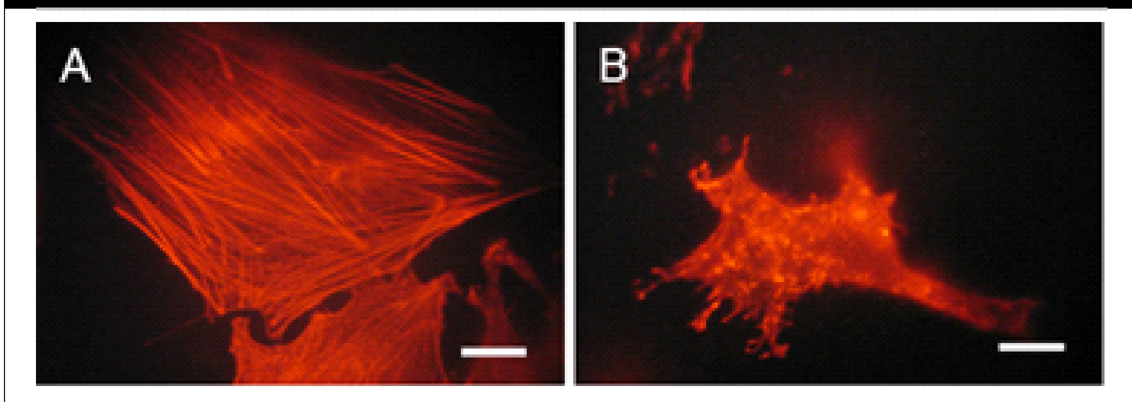
Apply 2D Wide Field Microscopy and Image Processing to study Mechanotransduction



BE309 Optical Module II

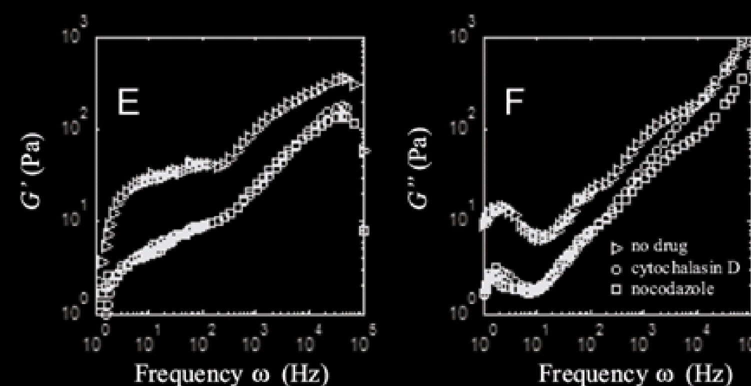
No drug

Cytochalasin D



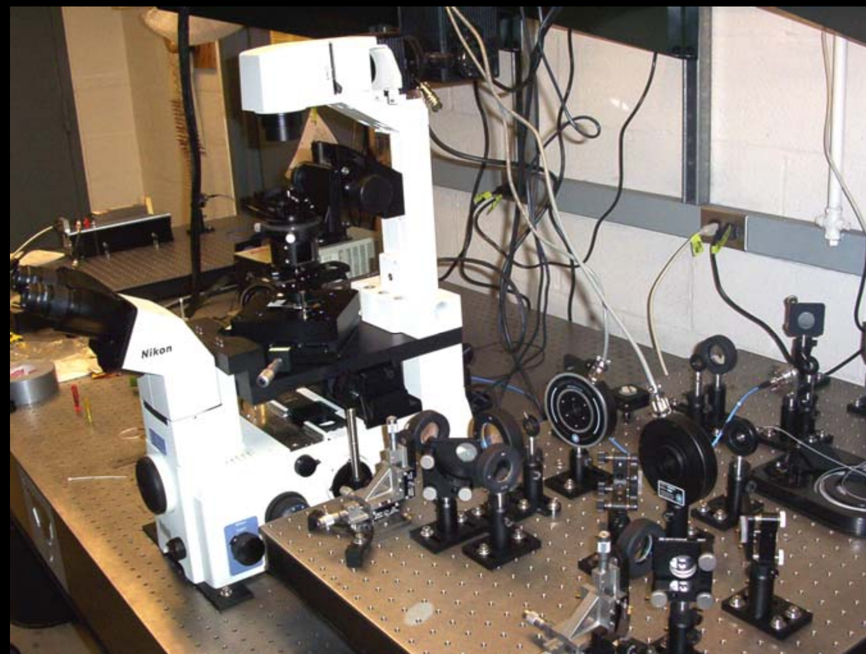
Visualize cytoskeleton disruption by CytoD

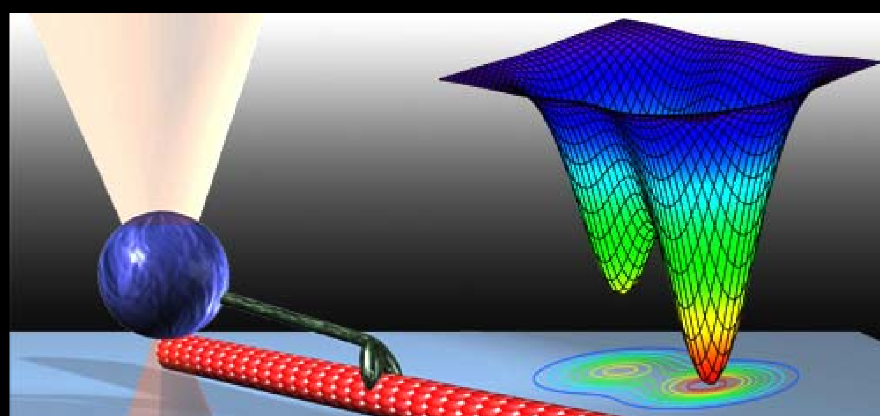
Multiple particle tracking to measure diffusive transport and cellular microrheology



BE309 Optics Module III

Apply Optical Trap to study Bacterial Propulsion





Developed by Guest Lecturer Prof. Matthew Lang

BE309 Optics Module IV

Apply Confocal and Two-Photon Microscopy to Study Heart Histology