Lectures 7, 8, 9

- Paul Hansma: Development of AFMs to monitor individual protein molecules, in liquids (1990-2000)
"*For pioneering contributions to the development of biological scanning probe microscopy and for the molecular resolution imaging of biological molecules in aqueous solutions.*" (2000)

- Carlos Bustamante: Study of DNA, RNA, and protein molecular mechanics (1990-2000)
"*For his pioneering work in single molecule biophysics and the elucidation of the fundamental physics principles underlying the mechanical properties and forces involved in DNA replication and transcription.*" (2002)

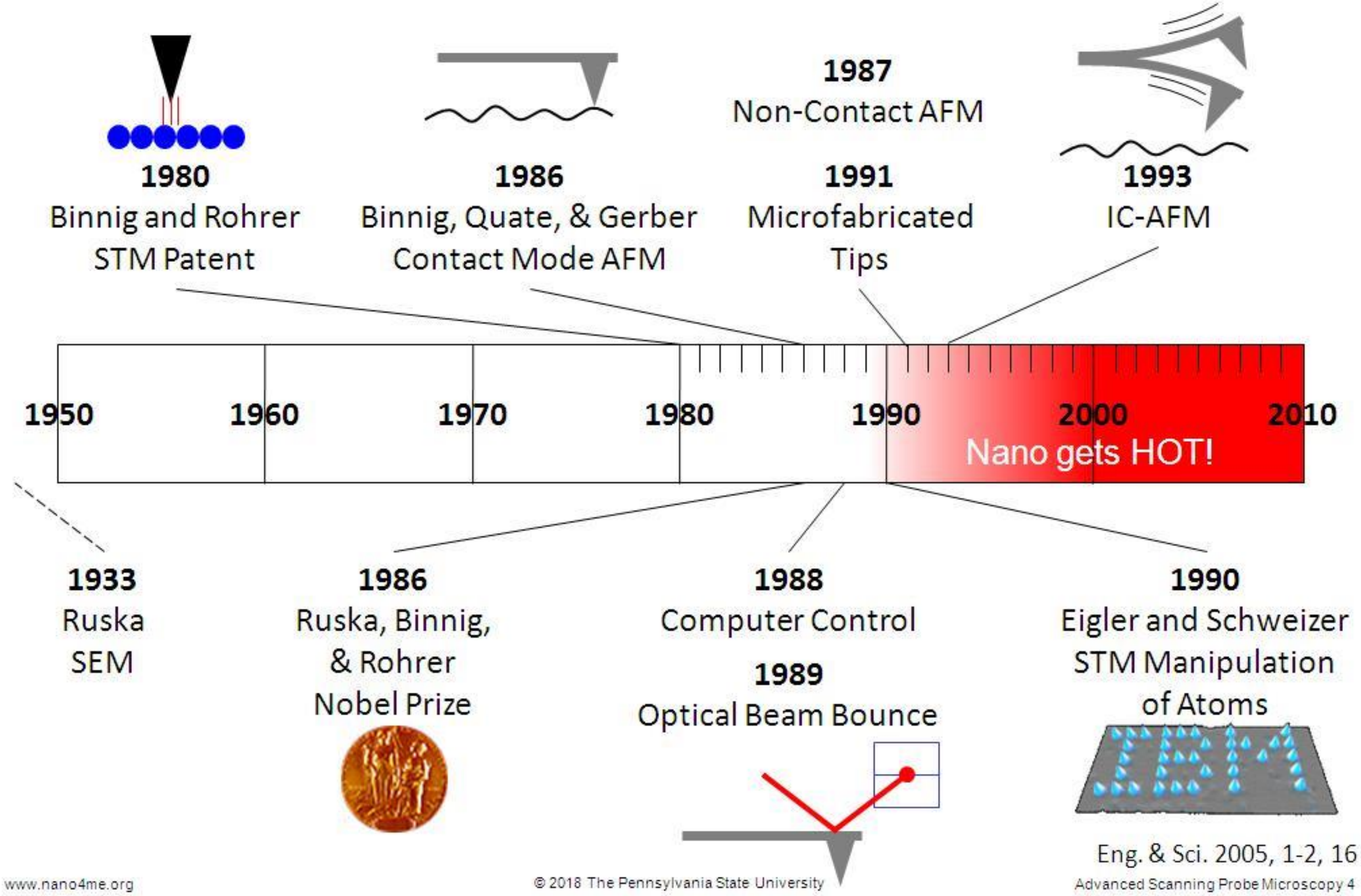
- Steven M. Block: Optical tweezers, molecular motors (kinesin, RNA polymerase) (1990-2000)
"*For his originality in the direct measurement of forces and motions in single biomolecular complexes undergoing the nucleoside triphosphate hydrolysis reactions that drive intracellular transport, cell motility, and DNA and RNA replication.*" (2008)

Guiding questions

- Pay attention to the sources, their attributes and “genre”
- What was the scientific breakthrough?
- Can you identify a key insight(s) needed for the breakthrough?
- How do the findings align with or challenge existing models?
- Can you put this work in the context of others in the course? Compare/contrast.
- What are some potential implications of their findings?

History of nanocharacterization

Last time:



Atomic force microscope

History

LAUREATES AND PRIZES / 2016 KAVLI PRIZE IN NANOSCIENCE

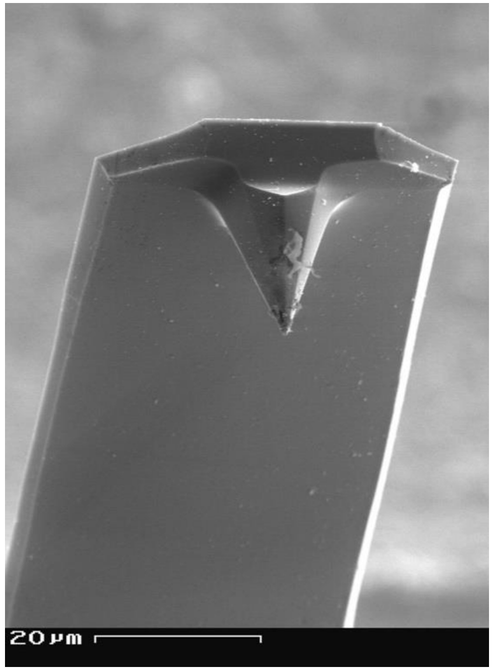
2016 KAVLI PRIZE IN *NANOSCIENCE*

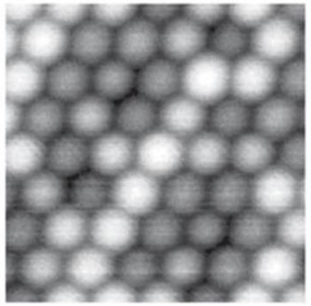
Gerd Binnig
Former Member of IBM Zurich Research Laboratory, Switzerland

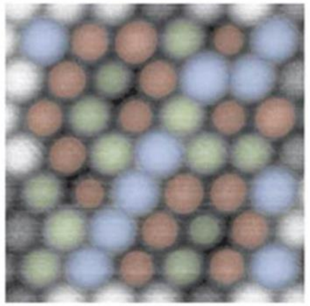
Christoph Gerber
University of Basel, Switzerland

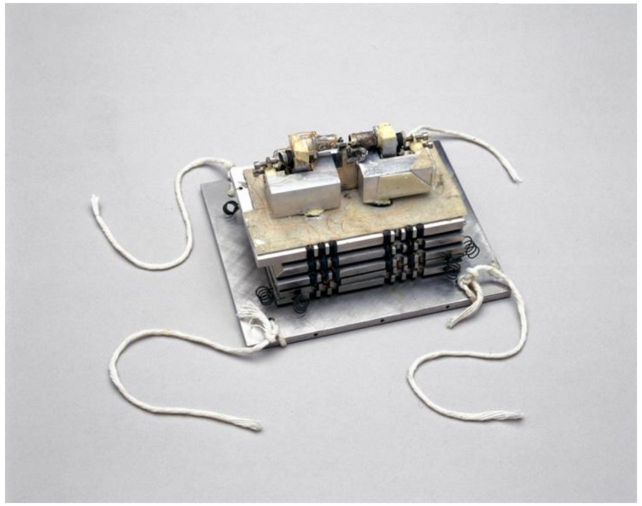
Calvin Quate
Stanford University, USA

https://www.kavliprize.org/prizes/nanoscience/2016









Atomic force microscope

State of the art

Atomic Force Microscope

G. Binnig, C. F. Quate, and Ch. Gerber
Phys. Rev. Lett. **56**, 930 – Published 3 March 1986

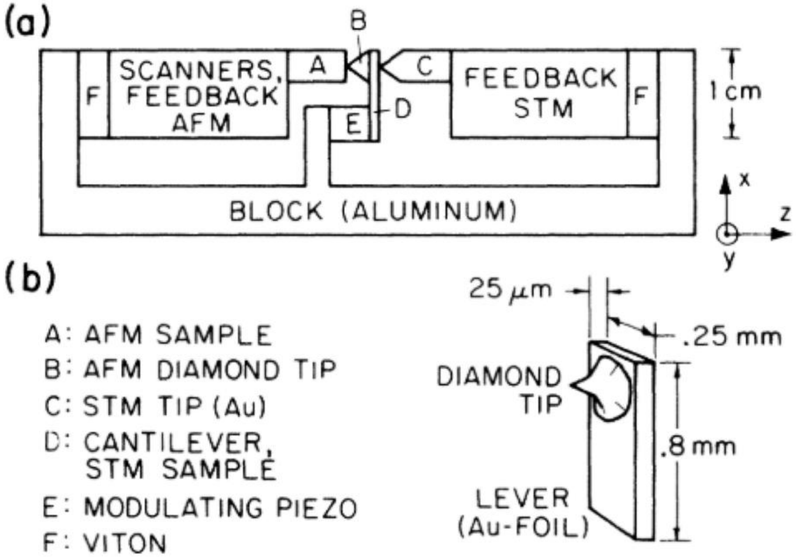


FIG. 2. Experimental setup. The lever is not to scale in (a). Its dimensions are given in (b). The STM and AFM piezoelectric drives are facing each other, sandwiching the diamond tip that is glued to the lever.

Despite its immense potential, the STM only works on conductive samples. Gerd Binnig came up with an idea to modify it and create an instrument that would provide images of all types of sample, conductive or insulating, and in 1985 filed a patent for an instrument that he called the atomic force microscope (AFM). The ingenious modification was to place a conductive cantilever, terminated by a tip, just under the tip of an STM. The current between the cantilever and the STM tip would therefore vary with the vertical movement of the cantilever. By scanning the cantilever over the sample's surface, the vertical movement of the cantilever, hence the profile of the sample, could be recorded by monitoring the changes in current.

The Atomic Force Microscope (AFM) can measure small forces in air, for conductors and non-conductors, but it can't work for samples in aqueous solution

Guiding questions

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Atomic force microscope

Paul Hansma

Imaging Crystals, Polymers, and Processes in Water with the Atomic Force Microscope

B. DRAKE, C. B. PRATER, A. L. WEISENHORN, S. A. C. GOULD, T. R. ALBRECHT, C. F. QUATE, D. S. CANNELL, H. G. HANSMA, AND P. K. HANSMA Authors Info & Affiliations

SCIENCE • 24 Mar 1989 • Vol 243, Issue 4898 • pp. 1586-1589 • DOI: 10.1126/science.2928794

The AFM now works in aqueous solutions, opening the technique to the investigation of biological materials.

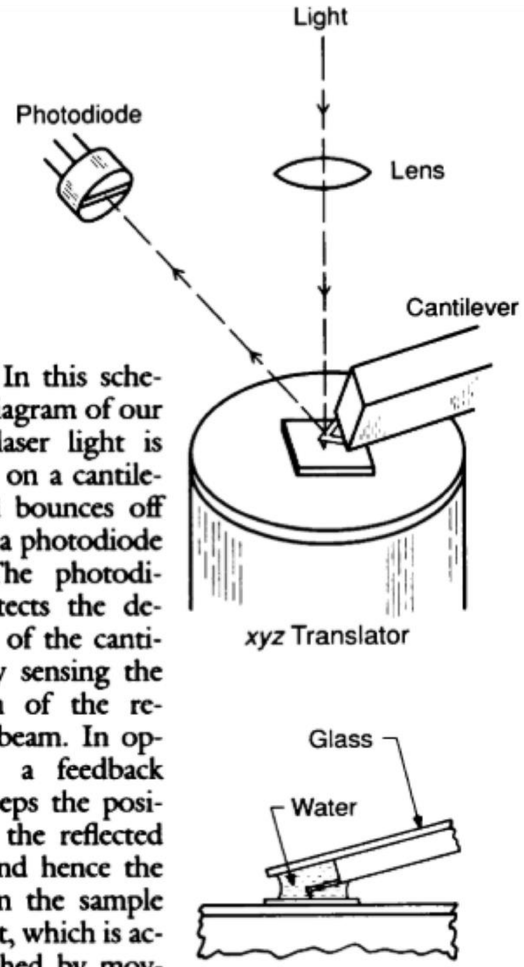


Fig. 1. In this schematic diagram of our AFM, laser light is focused on a cantilever and bounces off toward a photodiode (*11*). The photodiode detects the deflection of the cantilever by sensing the position of the reflected beam. In operation, a feedback loop keeps the position of the reflected beam and hence the force on the sample constant, which is accomplished by moving the sample up and down with the *z*-axis of the piezoelectric translator as the sample is scanned underneath it with the *x*- and *y*-axes. An optional small cell formed by the sample and a microscope cover glass can be filled with water to image samples in water.

Atomic force microscope

Impact

Reversible Unfolding of Individual Titin Immunoglobulin Domains by AFM

MATTHIAS RIEF, MATHIAS GAUTEL, FILIPP OESTERHELT, JULIO M. FERNANDEZ, AND , HERMANN E. GAUB Authors Info & Affiliations

SCIENCE • 16 May 1997 • Vol 276, Issue 5315 • pp. 1109-1112 • DOI: 10.1126/science.276.5315.1109

Published: 24 June 1999

Molecular mechanistic origin of the toughness of natural adhesives, fibres and composites

Bettye L. Smith, Tilman E. Schäffer, Mario Viani, James B. Thompson, Neil A. Frederick, Johannes Kindt, Angela Belcher, Galen D. Stucky, Daniel E. Morse & Paul K. Hansma

Nature **399**, 761–763 (1999) | Cite this article

Single Molecule Force Spectroscopy on Polysaccharides by Atomic Force Microscopy

MATTHIAS RIEF, FILIPP OESTERHELT, BERTHOLD HEYMANN, AND , HERMANN E. GAUB Authors Info & Affiliations

SCIENCE • 28 Feb 1997 • Vol 275, Issue 5304 • pp. 1295-1297 • DOI: 10.1126/science.275.5304.1295

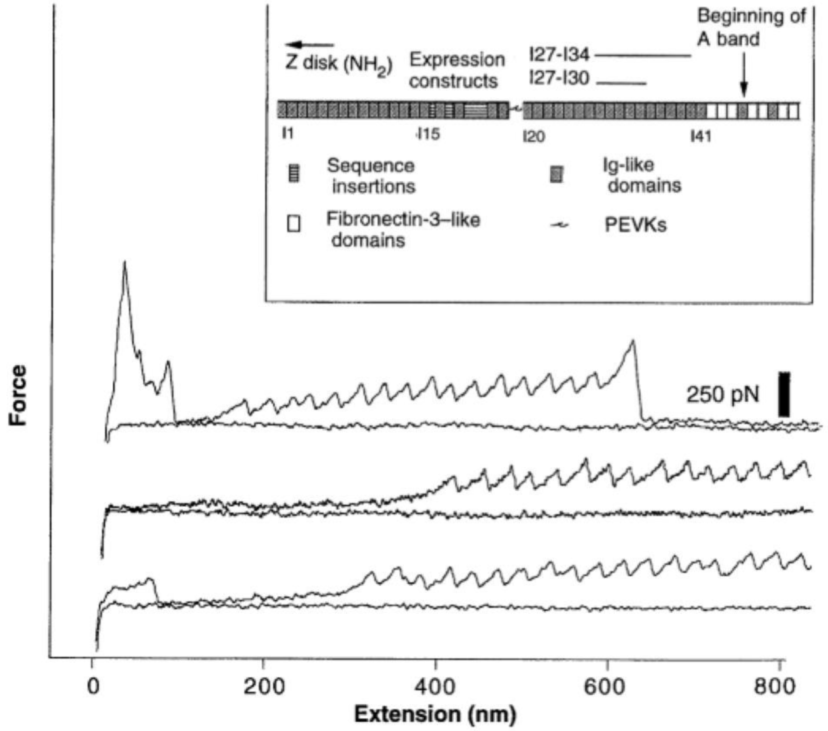


Fig. 1. Force extension curves obtained by stretching titin proteins show periodic features that are consistent with their modular construction. Native titin proteins (10 μg/ml in PBS) were allowed to adsorb onto a gold surface. Three typical approach and retract cycles are shown. The AFM tip approaches the surface covered with the protein (lower trace), and segments of the adsorbed titin are picked up at random by an AFM tip and then stretched (upper trace). We frequently observed a sawtooth pattern in the retraction curves, with as many as 20 force peaks that varied between 150 and 300 pN and were spaced between 25 and 28 nm. The sawtooth pattern was in most cases preceded by a spacer region of variable length, where the force extension curve was not well defined and varied widely. All experiments were done at room temperature. Titin is a large modular protein composed of 244 repeats of Ig-like and fibronectin-like domains (inset). These domains are 89 to 100 amino acids long. Each domain folds into a seven-stranded beta-barrel. The sawtooth pattern observed while stretching titin segments is consistent with the sequential unfolding of individual titin domains.

Atomic force microscope

History

https://www.aip.org/history-programs/niels-bohr-library/oral-histories/45465

Paul Hansma (36 min)

9:45-26:50 Bachelor degree, New College in Florida - PhD, UC Berkeley

29:24 - 32:26 UC Berkeley - moving to UC Santa Barbara

33:28 - 36:40 Do every experiment as poorly as possible

38:29 - 47:52 Finding research area that fit. Electron tunnelling -> surface science -> STM -> AFM -> liquid AFM

bio collaborations

patents ($10-20 M)

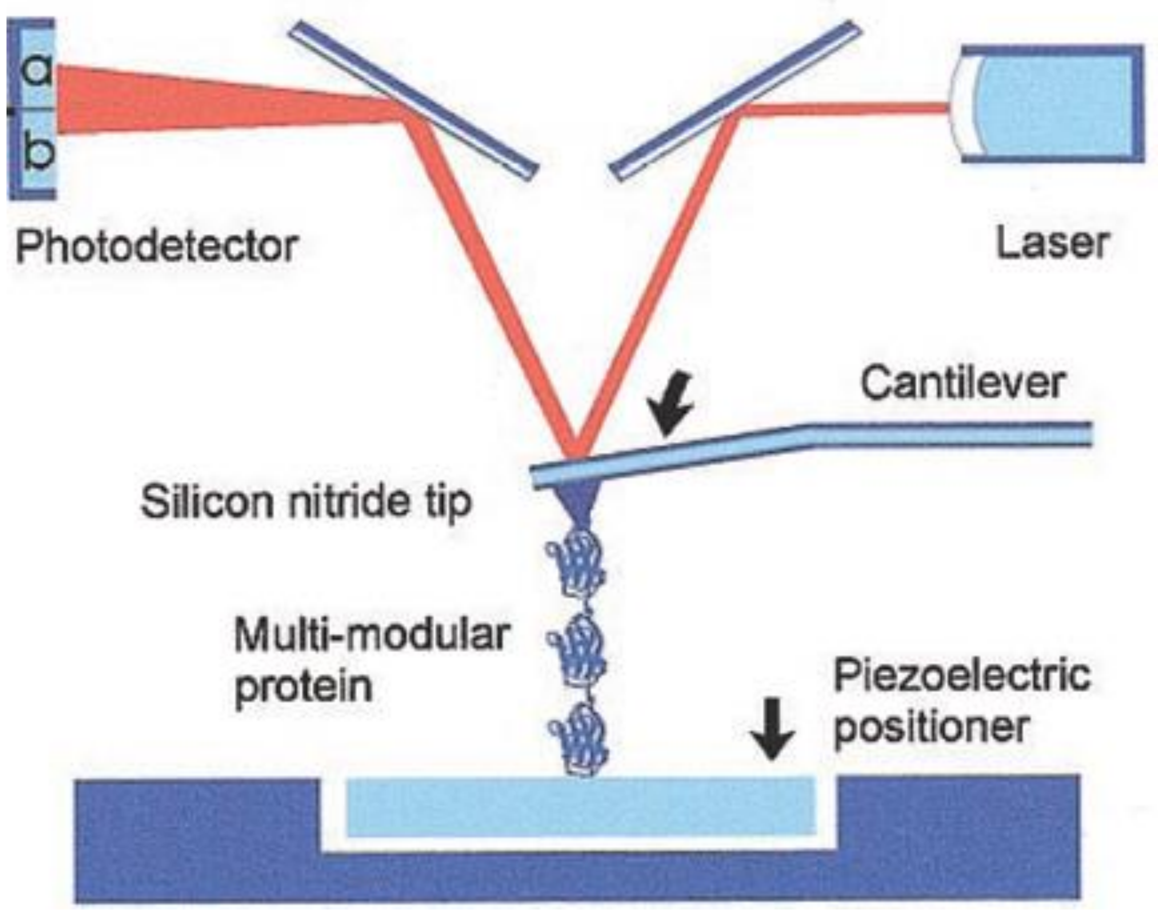
1:09:34 – 1:12:13 applications (+ EPFL Prof. Fantner)

bone mechanics

chronic pain

Atomic force microscope

Last time:



- AFM cantilever probes by moving its tip along surface, or pulling on a protein
- Cantilever movement is detected with a focused laser beam that refracts into a photodetector
- The deflection of the cantilever deflects the laser correspondingly and can map the surface
- In single molecule force spectroscopy, the cantilever is pressed against a layer of proteins attached to a substrate, the tip adsorbs a single protein molecule, which is then extended.
- Extension of the molecule by retraction of the piezoelectric positioner results in deflection of the cantilever.