

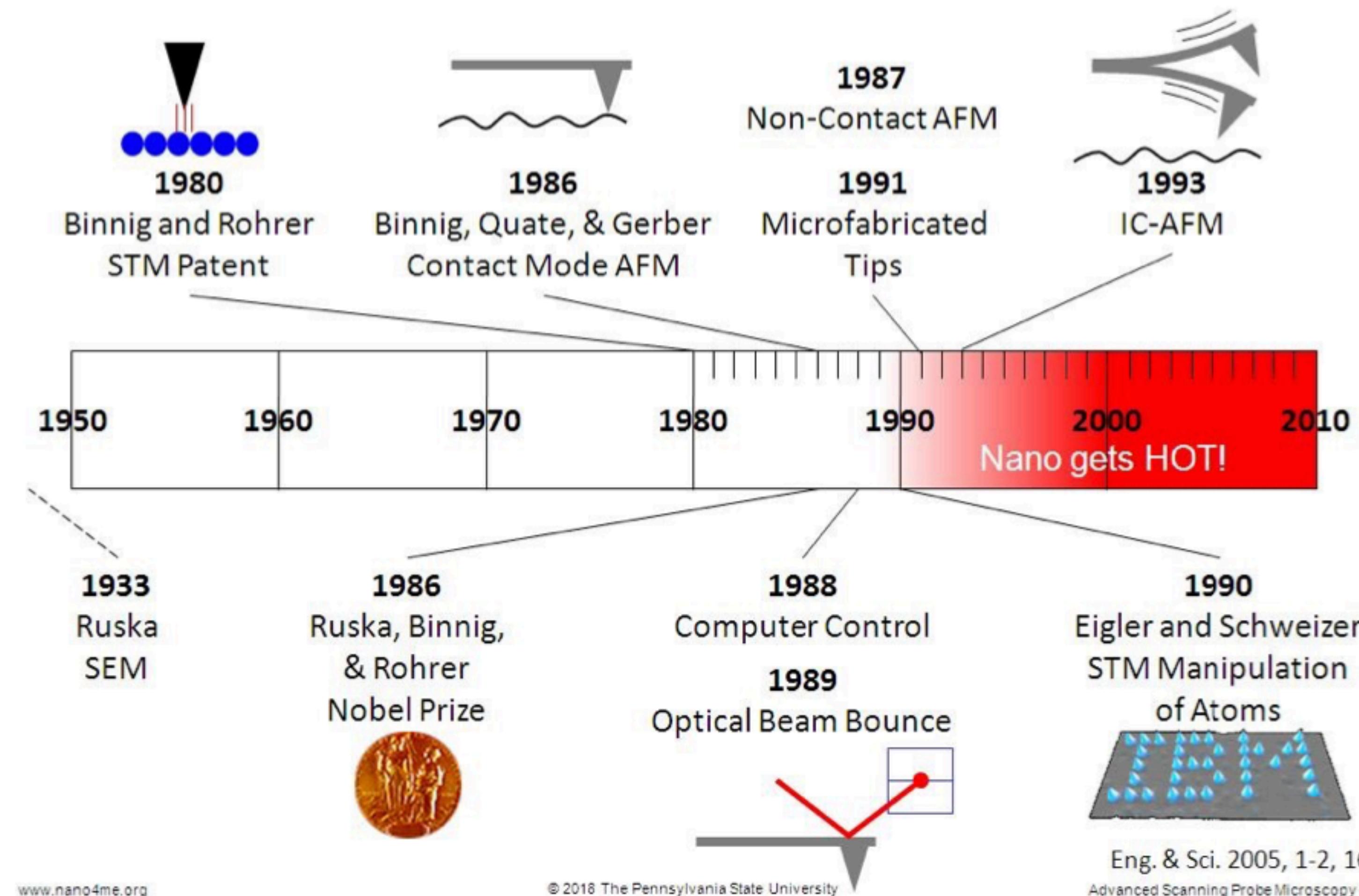
Module II: Single Molecule Mechanics

26.3	Tue (6)	Discussion, outlook: Structure Introductory unit: Single molecule mechanics	Read PBoC 8.3
28.3	Thu (GT)	Open discussion, Q&A	Ask questions
9.4	Tue (7)	Paul Hansma	Read paper
11.4	Thu (GT)	Discuss paper analysis	Bring completed worksheet
16.4	Tue (8)*	Carlos Bustamante	Read paper
18.4	Thu (GT)	Discuss paper analysis	Bring completed worksheet
23.4	Tue (9)	Steven Block	Read paper
25.4	Thu (GT)	Discuss paper analysis	Bring completed worksheet
30.4	Tue (10)	Discussion, outlook: Single molecule mechanics Introductory unit: Collective/emergent properties	Read pdf

Module II: Single Molecule Mechanics

- 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 Block: Study of bimolecular complexes for DNA, RNA and intracellular transport (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)

History of nanocharacterisation



The scanning tunnelling microscope

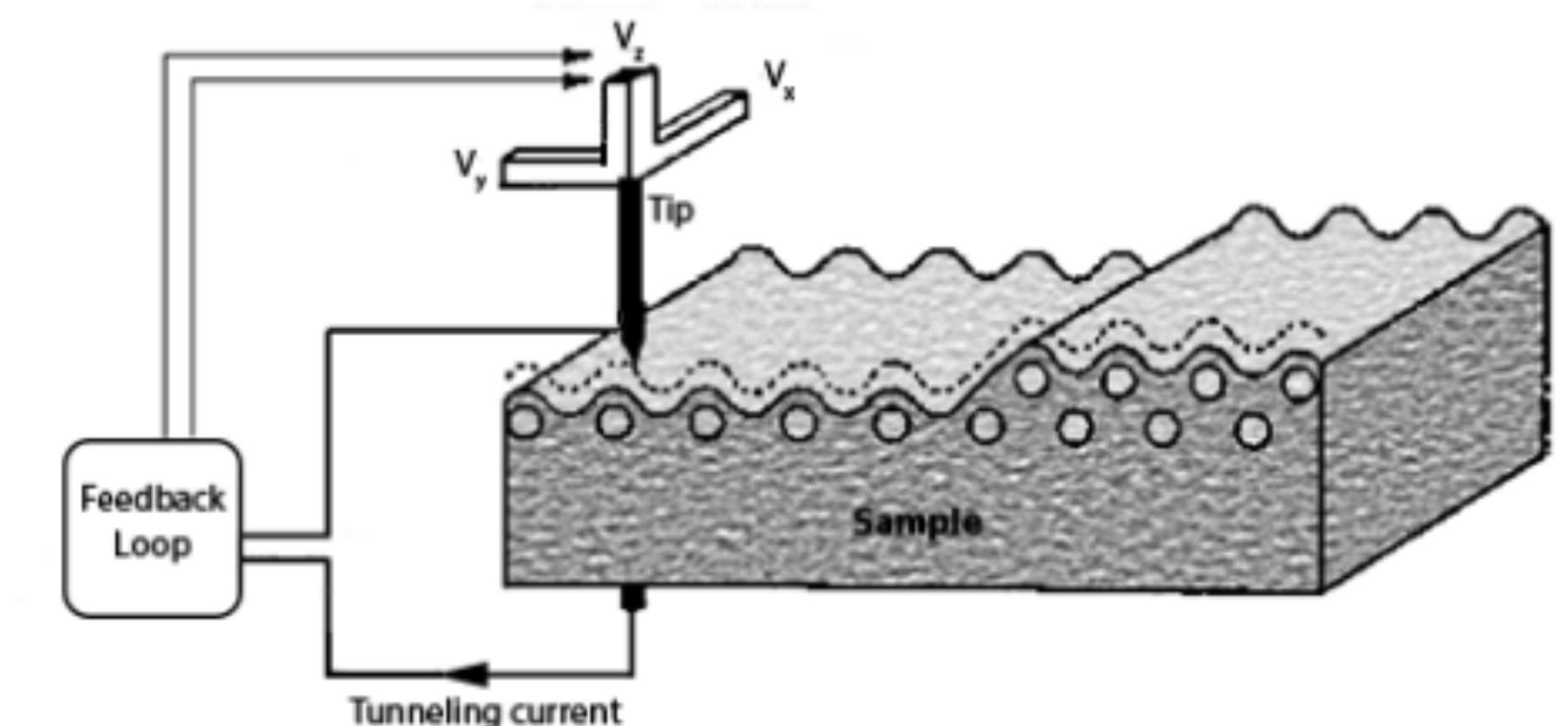
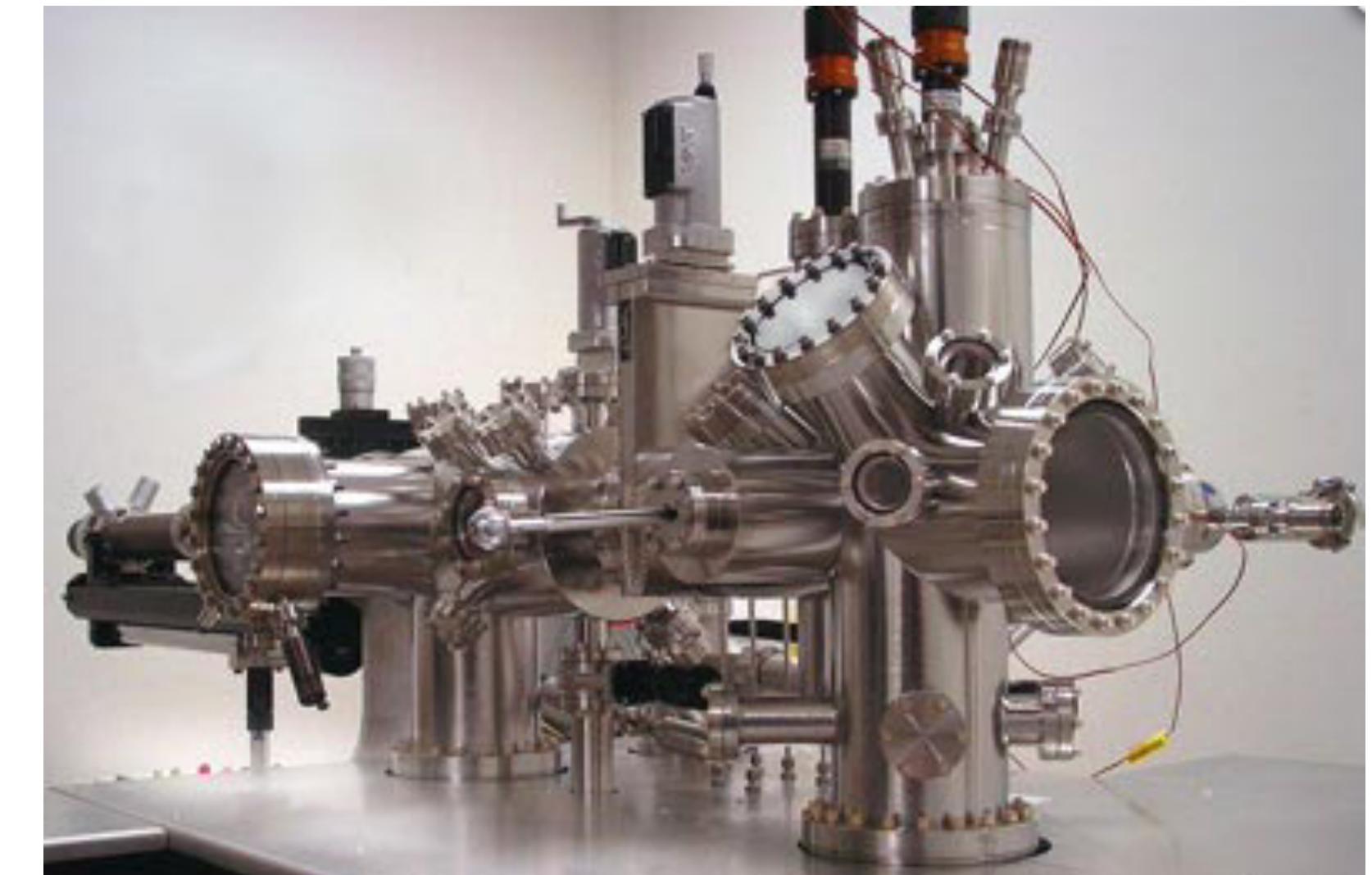
The Nobel Prize in Physics 1986

The other half of this year's prize has been awarded to **Gerd Binnig** and **Heinrich Rohrer** for "their design of the scanning tunneling microscope". This instrument is not a true microscope (i.e. an instrument that gives a direct image of an object) since it is based on the principle that the structure of a surface can be studied using a stylus that scans the surface at a fixed distance from it. Vertical adjustment of the stylus is controlled by means of what is termed the tunnel effect – hence the name of the instrument. An electrical potential between the tip of the stylus and the surface causes an electric current to flow between them despite the fact that they are not in contact. The strength of the current is strongly dependent on the distance, and this makes it possible to maintain the distance constant at approximately 10^{-7} cm (i.e. about two atom diameters). The stylus is also extremely sharp, the tip being formed of one single atom. This enables it to follow even the smallest details of the surface it is scanning. Recording the vertical movement of the stylus makes it possible to study the structure of the surface atom by atom.

The scanning tunneling microscope is completely new, and we have so far seen only the beginning of its development. It is, however, clear that entirely new fields are opening up for the study of the structure of matter. Binnig's and Rohrer's great achievement is that, starting from earlier work and ideas, they have succeeded in mastering the enormous experimental difficulties involved in building an instrument of the precision and stability required.

"Work hard to meet all the fabulous challenges in science and to overcome the abundant difficulties. But do not forget to enjoy life."

Heinrich Rohrer



From current to force: the Atomic Force Microscope

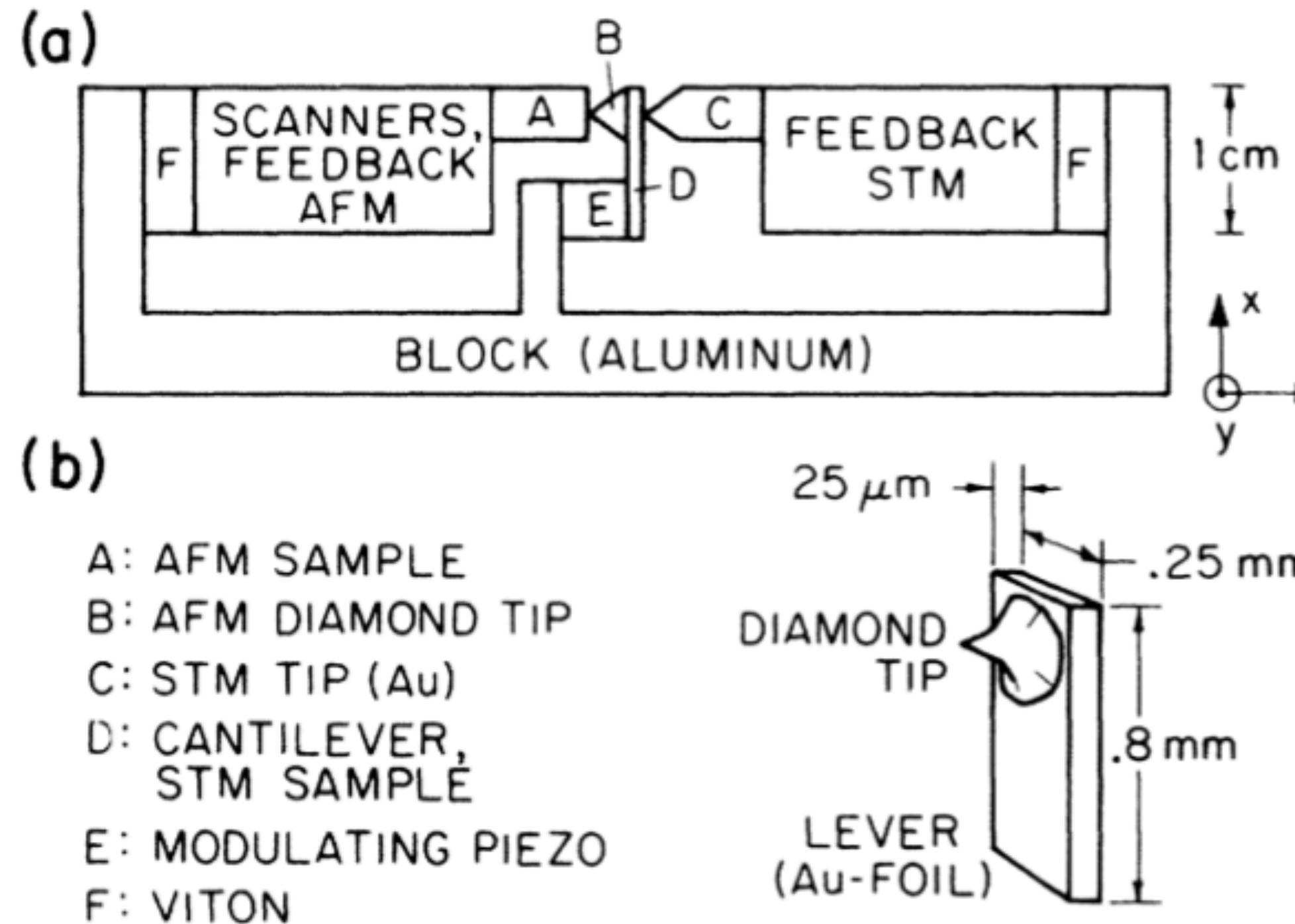
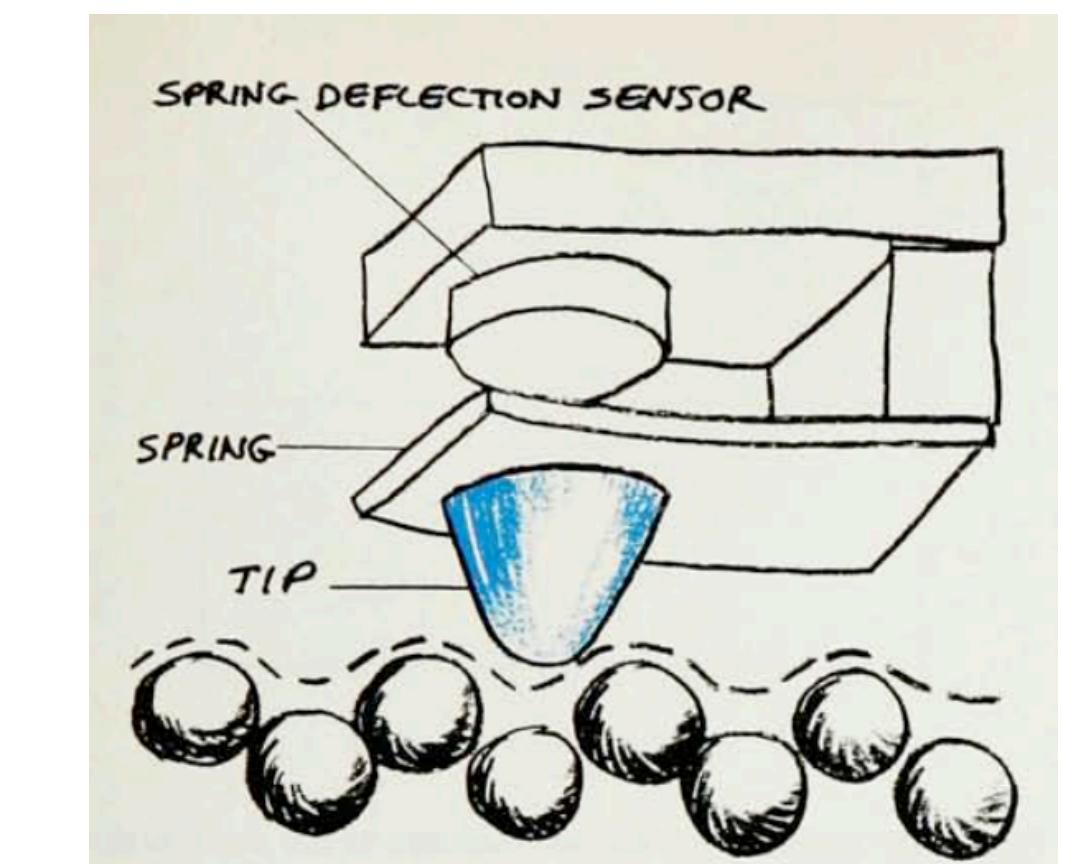
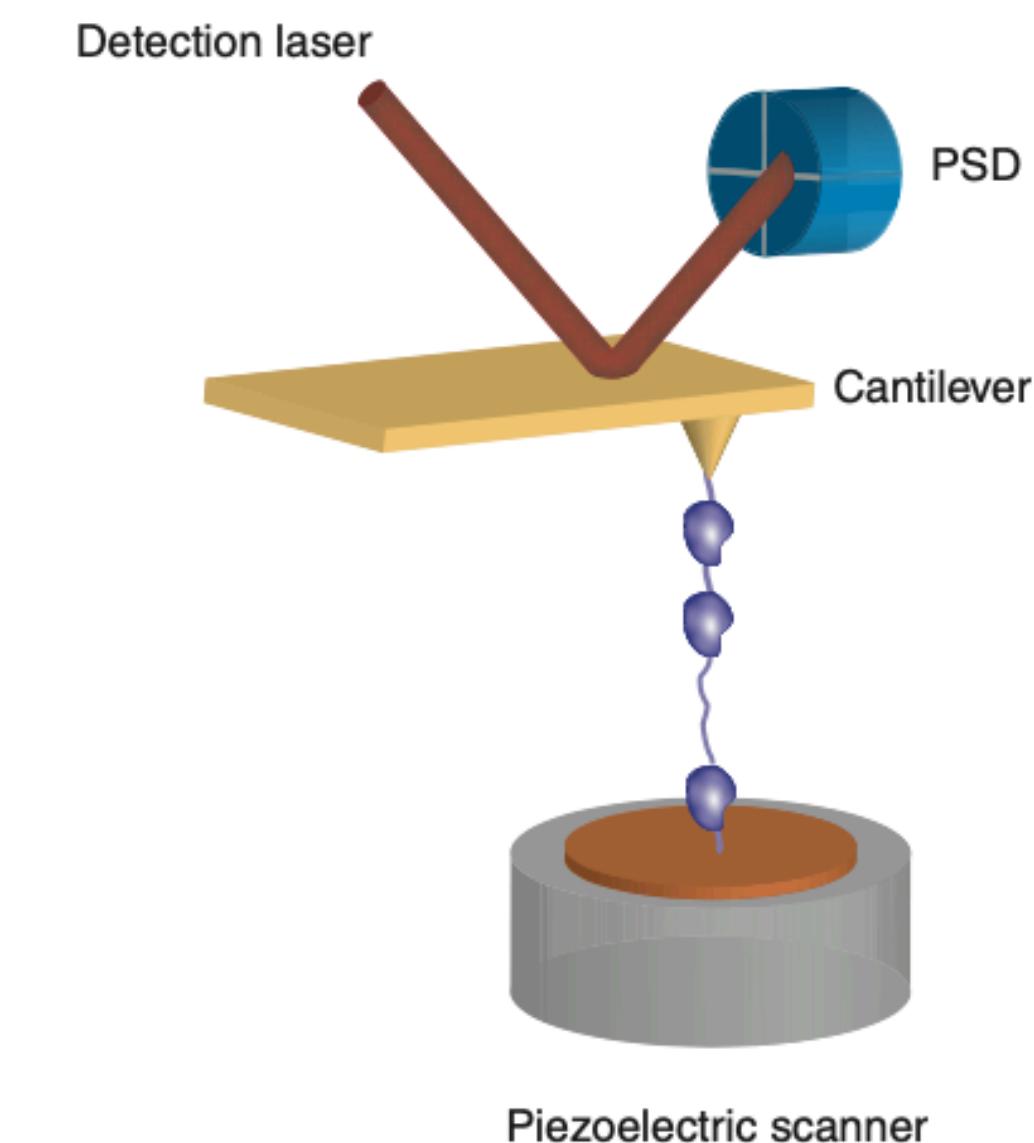


FIG. 2. Experimental setup. The lever is not to scale in (a). Its dimensions are given in (b). The STM and AFM piezoelectric drives are facing each other, sandwiching the diamond tip that is glued to the lever.



Scheme for an atomic force microscope. The tip is fastened to a cantilever spring that has a lower spring constant than the effective spring between two atoms. With sufficient sensitivity in the spring deflection sensor, the tip can reveal surface profiles with atomic resolution.



Adapted from: Neuman, K., Nagy, A. Single-molecule force spectroscopy: optical tweezers, magnetic tweezers and atomic force microscopy. *Nat Methods* **5**, 491–505 (2008)

An AFM needs:

- ▷ A sharp tip mounted on a soft cantilever spring
- ▷ A way of sensing the cantilever's deflection
- ▷ A feedback system to monitor and control the deflection (and, hence, the interaction force)
- ▷ A mechanical scanning system (usually piezoelectric) that moves the sample with respect to the tip in a raster pattern
- ▷ A display system that converts the measured data into an image.

The AFM for soft biological samples

Contact mode

The tip is mounted onto the end of a flexible cantilever and raster scans the surface of the sample. The deflection of the cantilever due to tip-surface interaction reveals the sample surface.

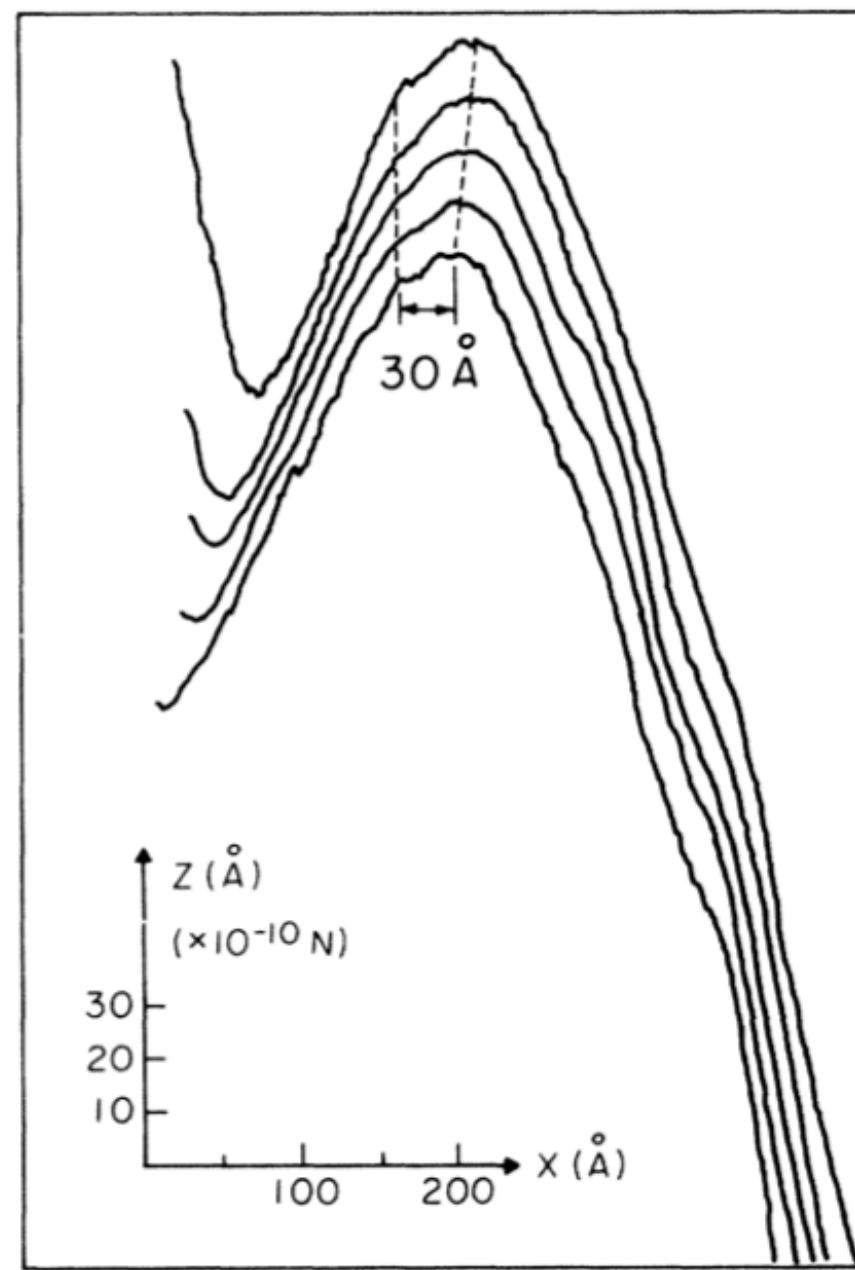


FIG. 3. The AFM traces on a ceramic (Al_2O_3) sample. The vertical scale translates to a force between sample and tip of $10^{-10} \text{ N}/\text{\AA}$. For the lower trace the force is near $3 \times 10^{-8} \text{ N}$. The stability of the regulated force is better than 10^{-10} N . The successive traces are displaced by a small drift along the y axis.

Non-contact mode

The cantilever oscillates close to its resonant frequency at a small distance (1-10 nm) above the surface. Long-range attractive forces induce changes in the amplitude, frequency and phase of the cantilever and maintain a constant distance during scanning.

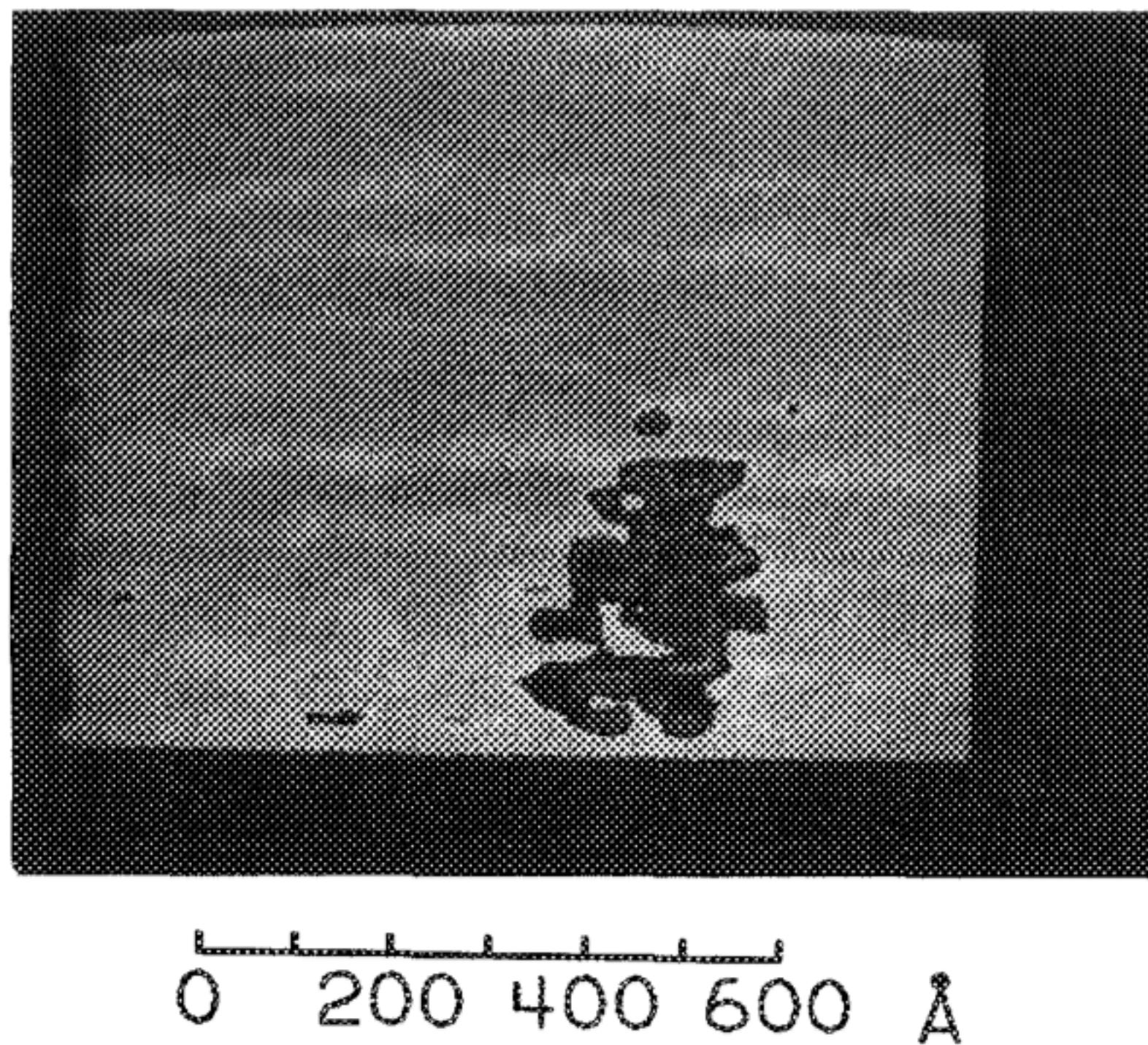


FIG. 4. Image of some contaminant on an atomically flat surface of graphite.

Tapping mode

The sample sits on a piezoelectric scanner, oscillates up and down and taps the tip at the apex of each oscillation cycle. The amplitude of the piezoelectric is set manually at the beginning of the run, and the tapping force is held constant by a feedback loop.

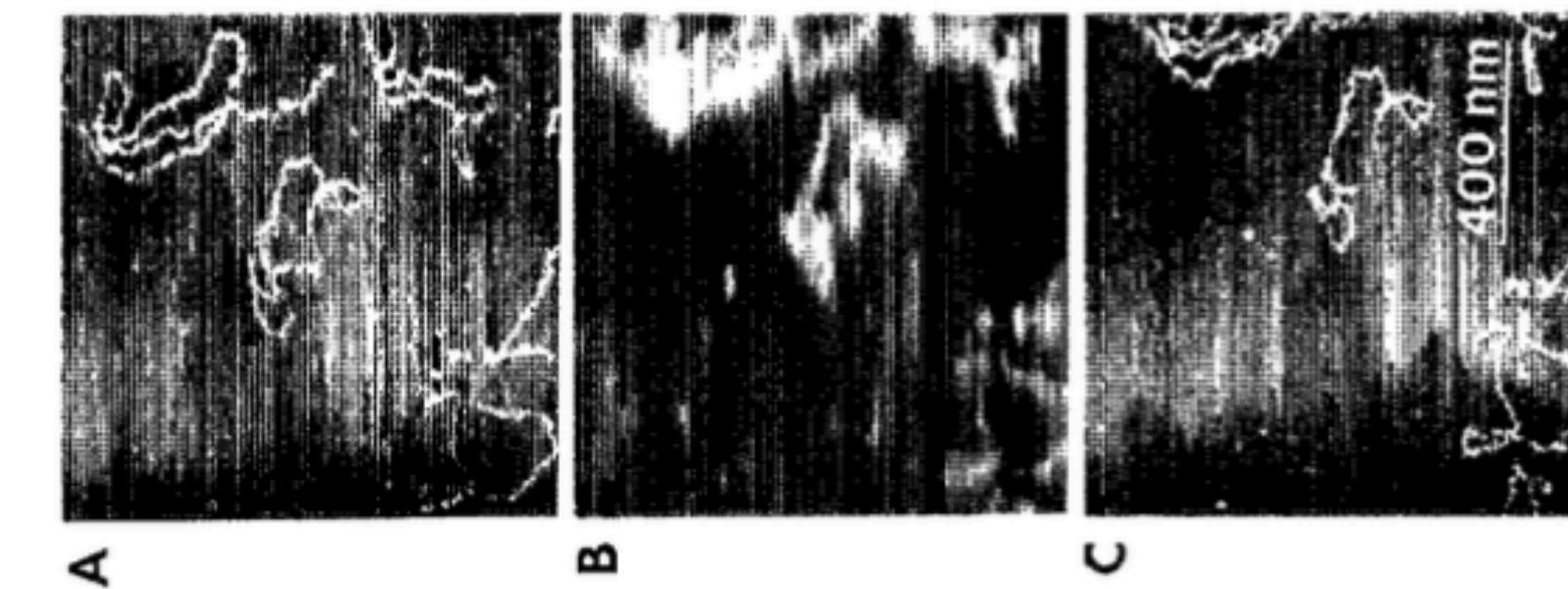


FIG. 3. AFM images of plasmid DNA on a mica surface in water obtained with the new tapping mode AFM before 2(a) and after 2(c) a conventional contact mode image 2(b). The image areas are $1 \mu\text{m} \times 1 \mu\text{m}$. The image acquisition time was 56 s for each image. The tapping mode images were obtained with approximately 0.5 V peak to peak ac voltage at 17 kHz applied to the z electrode of a piezo with a dc response of order 9 nm/V , giving a jump amplitude of about 4 nm. The black to white scale of each image is 2 nm. The height information in the tapping mode is calibrated just as for the height information in the conventional contact mode: by the voltage applied by the feedback amplifier to the z electrode to keep the deflection signal constant.

Interesting resources

- The 1986 Nobel Prize for the Electron Microscope and the Scanning Tunnelling Microscope:
[The Nobel Prize in Physics 1986](#)
- A brief history of the Scanning Tunnelling Microscope:
[IBM100 - Scanning Tunneling Microscope](#)
- Interviews with Heinrich Rohrer:
[kouroshziabari.com/2013/01/interview-heinrich-rohrer-1986-nobel-prize-laureate-in-physics/](#) and [Interview with Heinrich Rohrer, Nobel Prize in Physics 1986](#)
- Eureka moment for Gerd Binnig:
[Gerd Binnig Had a Eureka! Moment](#)
- IBM The World's Smallest Movie and the behind the scenes:
[A Boy And His Atom: The World's Smallest Movie](#) and [Moving Atoms: Making The World's Smallest Movie](#)
- A short history of the AFM:
[Paul Hansma's Website](#)
- A great introduction to the early AFM implementations, by Daniel Rugar and Paul Hansma:
[The Atomic Force Microscope](#)
- The paper introducing AFM:
[journals.aps.org/prl/pdf/10.1103/PhysRevLett.56.930](#)
- The paper introducing non-contact mode:
[Atomic force microscope-force mapping and profiling on a sub 100-Å scale | UScholar Works](#)
- The paper introducing tapping mode in liquids, by Paul Hansma:
[Tapping mode atomic force microscopy in liquids](#)