Single-Molecule Recognition and Manipulation Studied by Scanning Probe Microscopy

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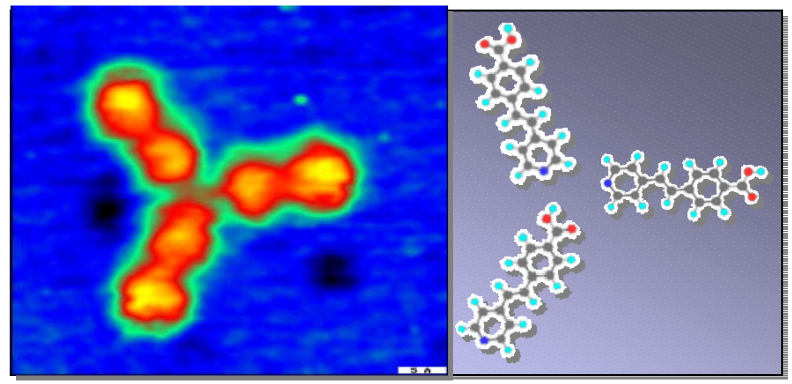
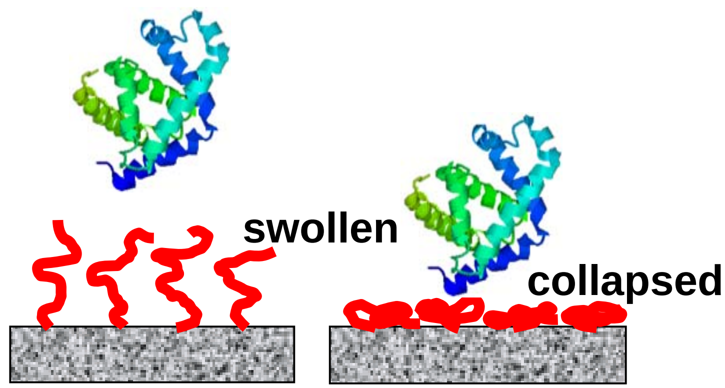


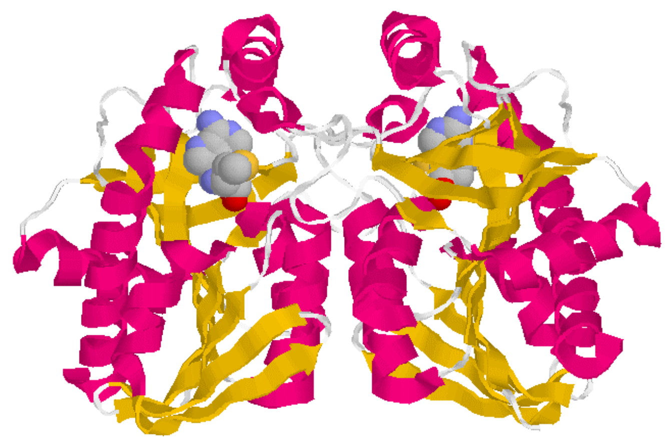
Langmuir (in press, 2006)



Hydrophilic → non-sticky

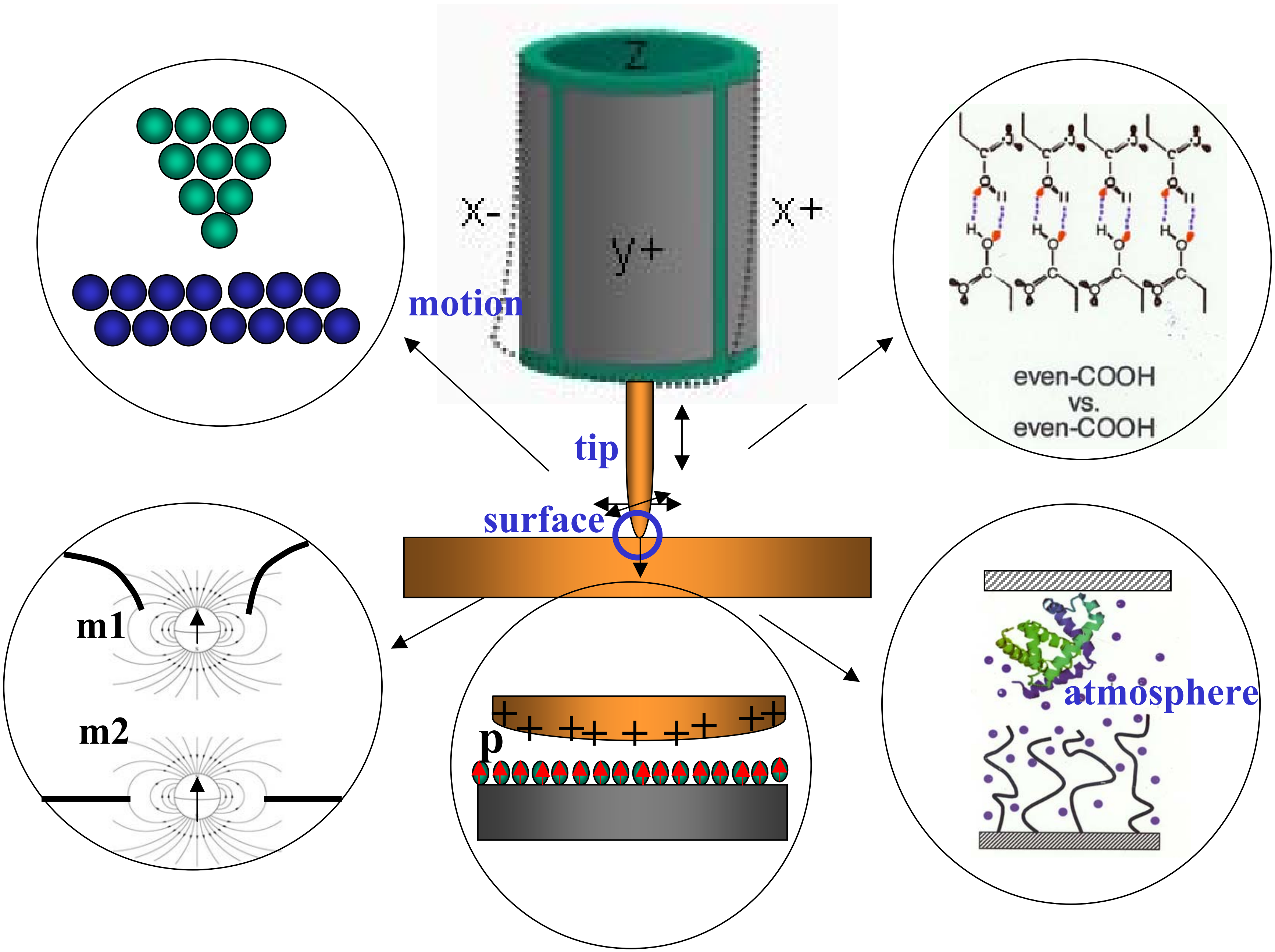
Hydrophobic → sticky

:Science, 301, pp.352-354(2003)

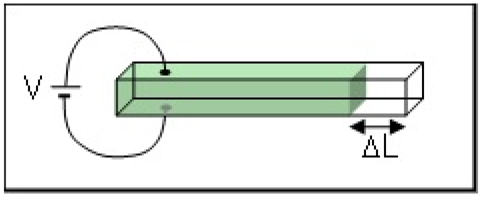


MTAN-inhibitor

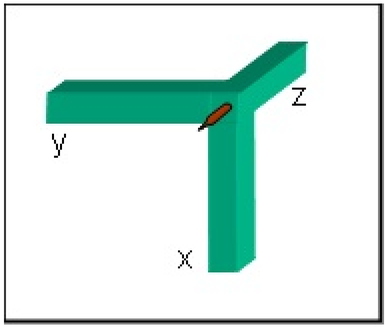
Scanning Probe Microscope (SPM) : Basic aspects



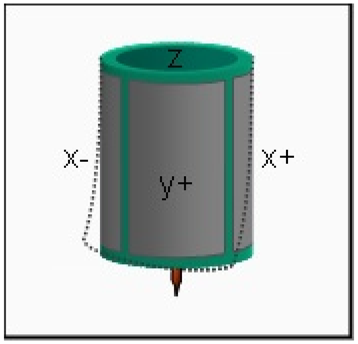
Scanning



•Principle of piezo element.
The applied voltage makes the element longer or shorter.



- *The combination of three piezo elements makes it possible to move the STM tip in the X-, Y-, and Z-directions.*



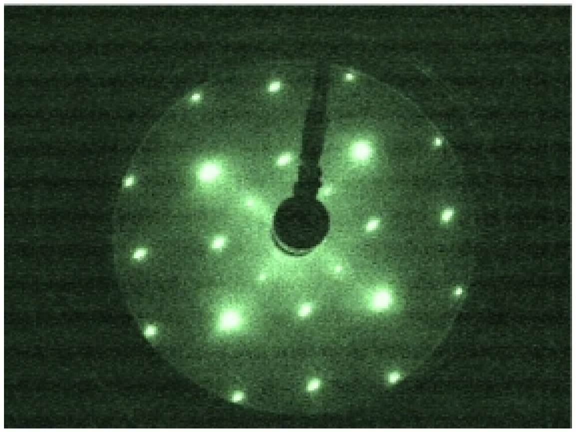
•In most modern scanning probe microscopes, one uses a tube geometry. .

Reciprocal Space vs Real Space

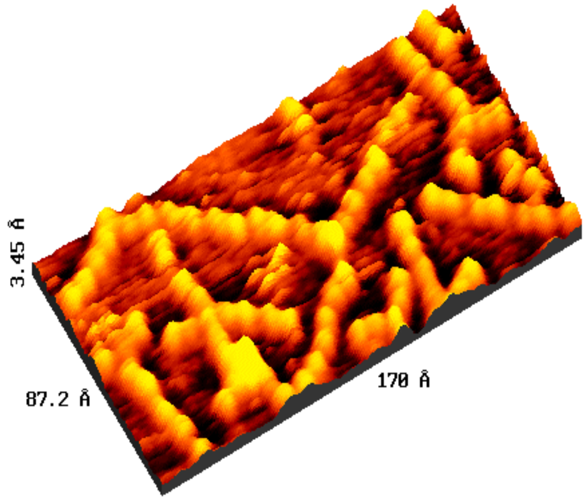
• Low Energy Electron Diffraction

•Scanning Probe Microscopy

Periodic system



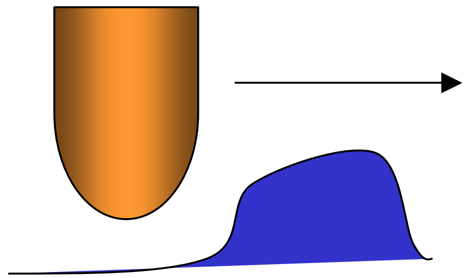
VC(100)

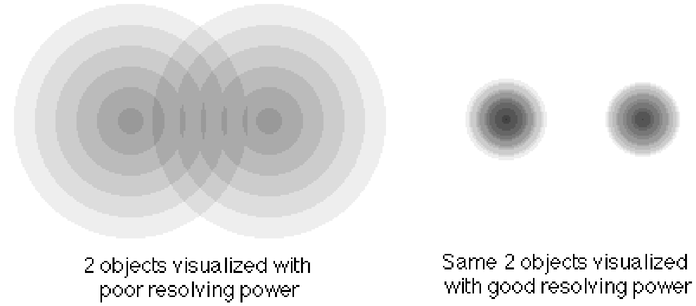


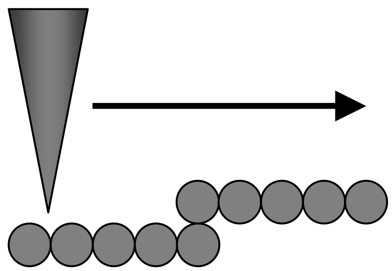
Self-assembly
of rod-like molecules on Pd(111)

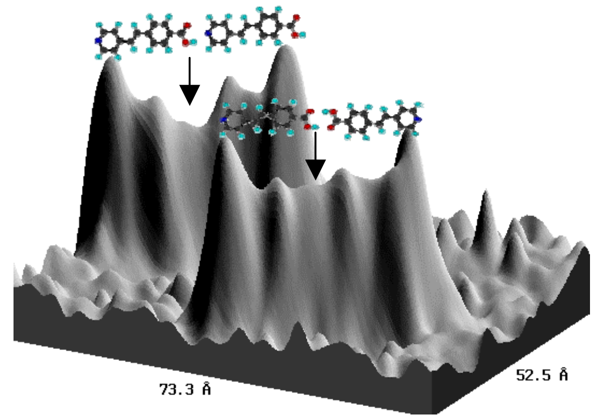
Local structures without periodicity can be understood only by scanning probe microscope.

Resolution









Instrument	depth resolution	lateral resolution
Mechanical Profiler	0.5 nm	0.1-25 μm
Optical Profiler	0.1 nm	0.35 - 9 μm
Atomic force microscope (AFM)	0.01nm	0.1nm
Scanning tunneling microscope (STM)	0.001nm	0.1nm

Scanning Probe Microscope (SPM)

General experimental approach-
Monitor a physical quantity which is dependent on separation between a probe tip and a sample surface.
→ Use Current (I) and Force (F)

- **Scanning Tunneling Microscope (STM)**
- **Atomic Force Microscope (SFM)**

SPM techniques provide unique information-

Local - probes topographic and electronic structure
on an atomic scale
Real space - information is collected through
a direct measurement

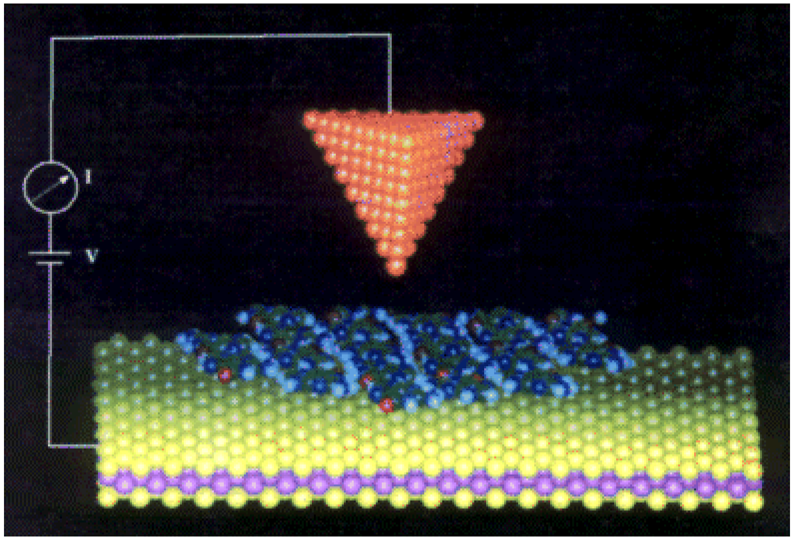
STM-**monitors a tunneling current.**

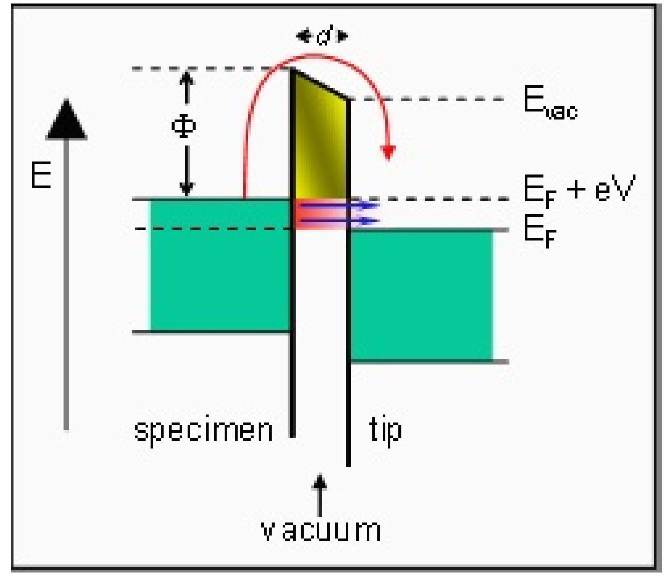
$$I \propto U e^{-(kd\sqrt{\Phi})}$$

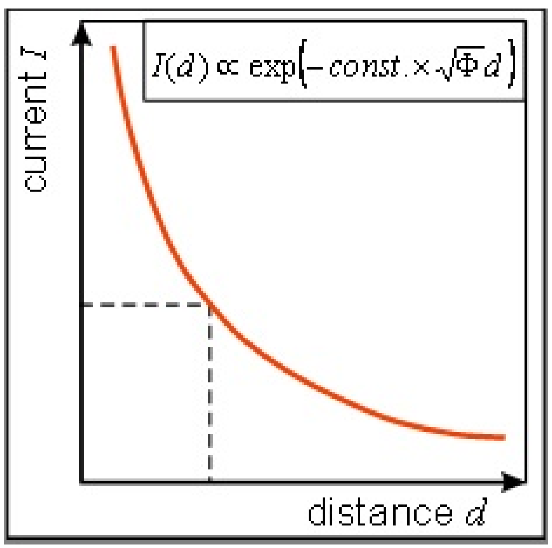
I-tunneling current
U-sample bias
k -transmission coefficient
d -tip sample separation
Φ-average work function

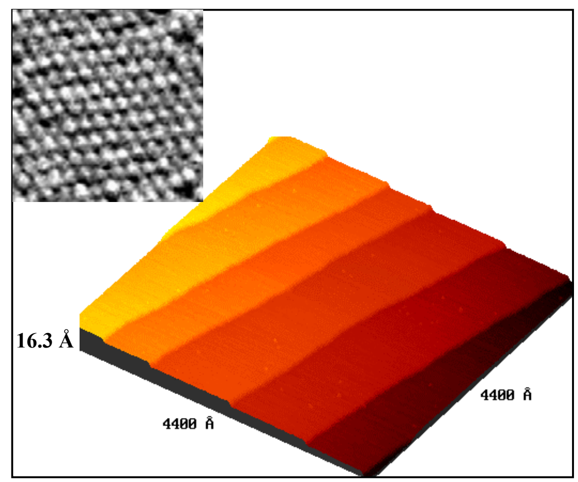
- **conductive sample**
- **tunneling current : pA~nA**
- **lateral resolution : 0.1nm**
- **depth resolution : 0. 001nm**

PRINCIPLE of STM



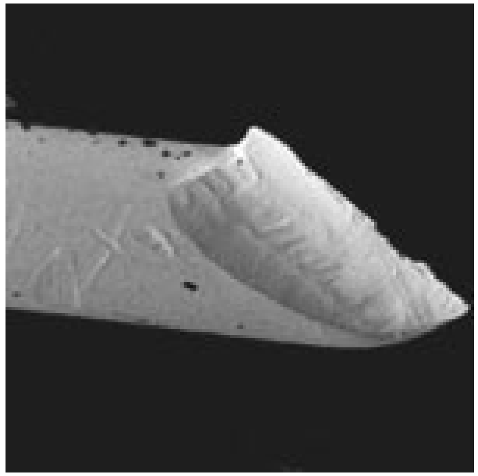


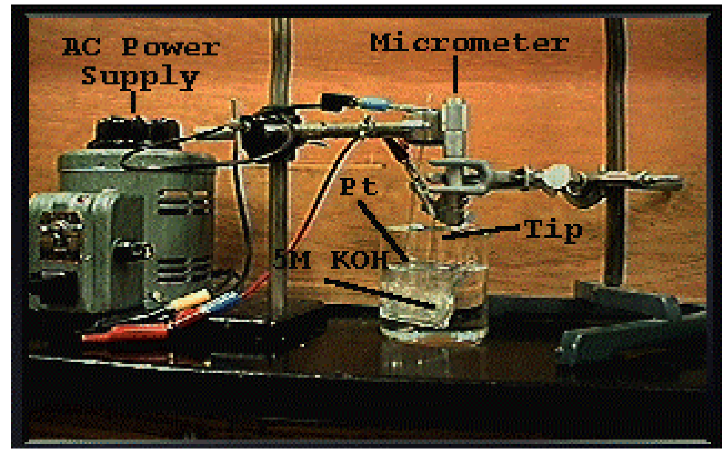


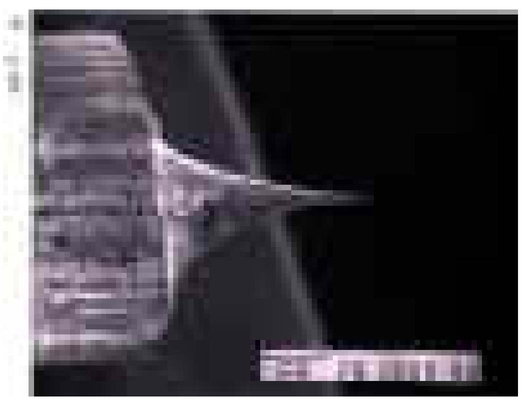


Pd(111)

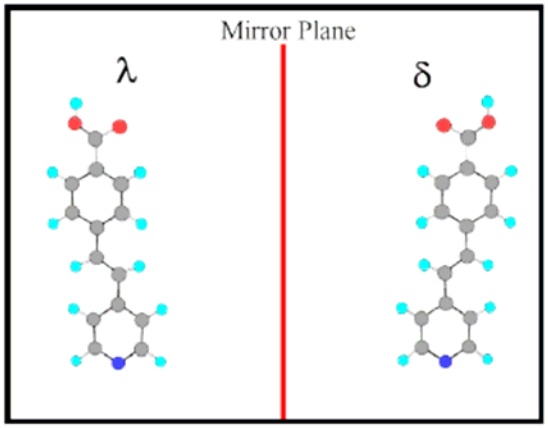
STM Tip



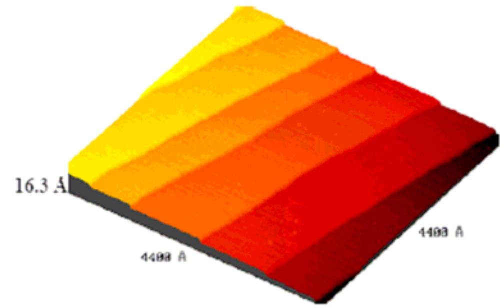




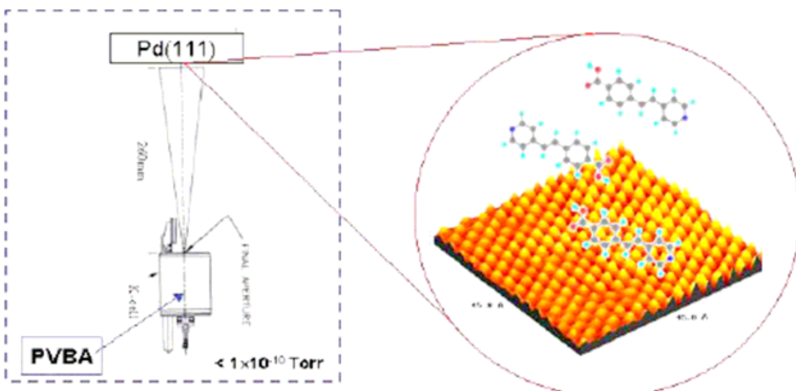
PVBA/Pd(111)



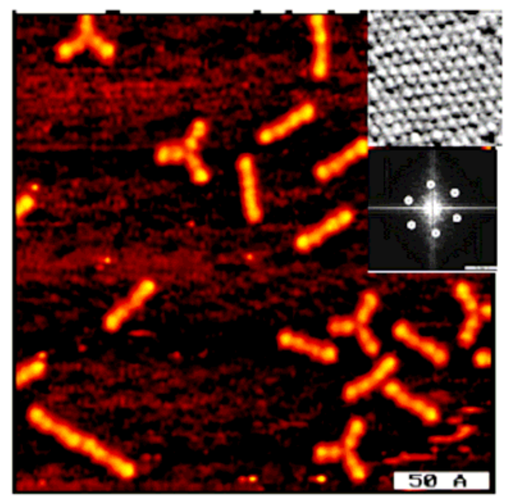
(a)



(b)

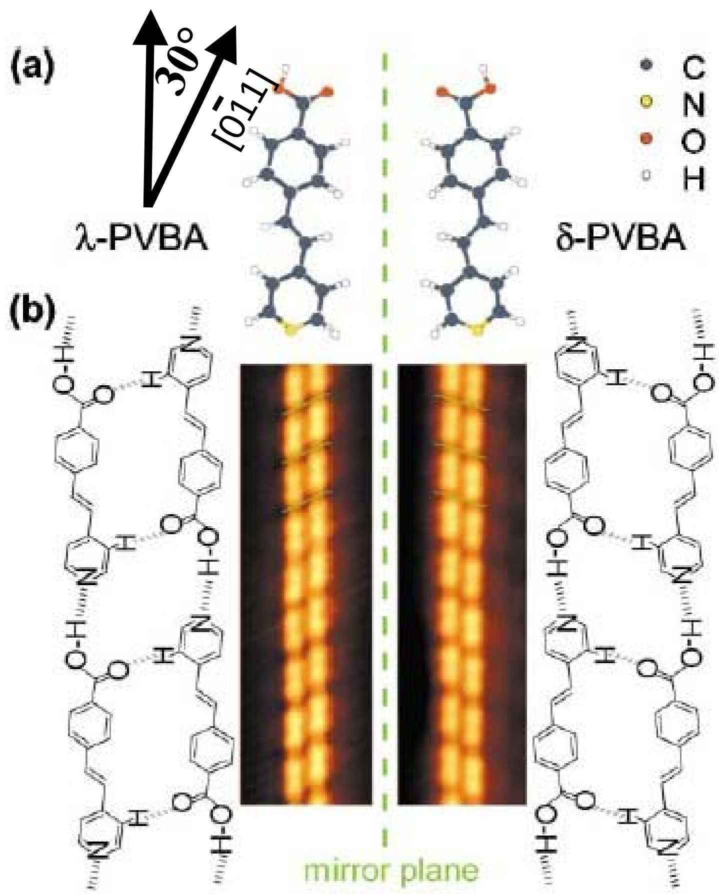


(c)



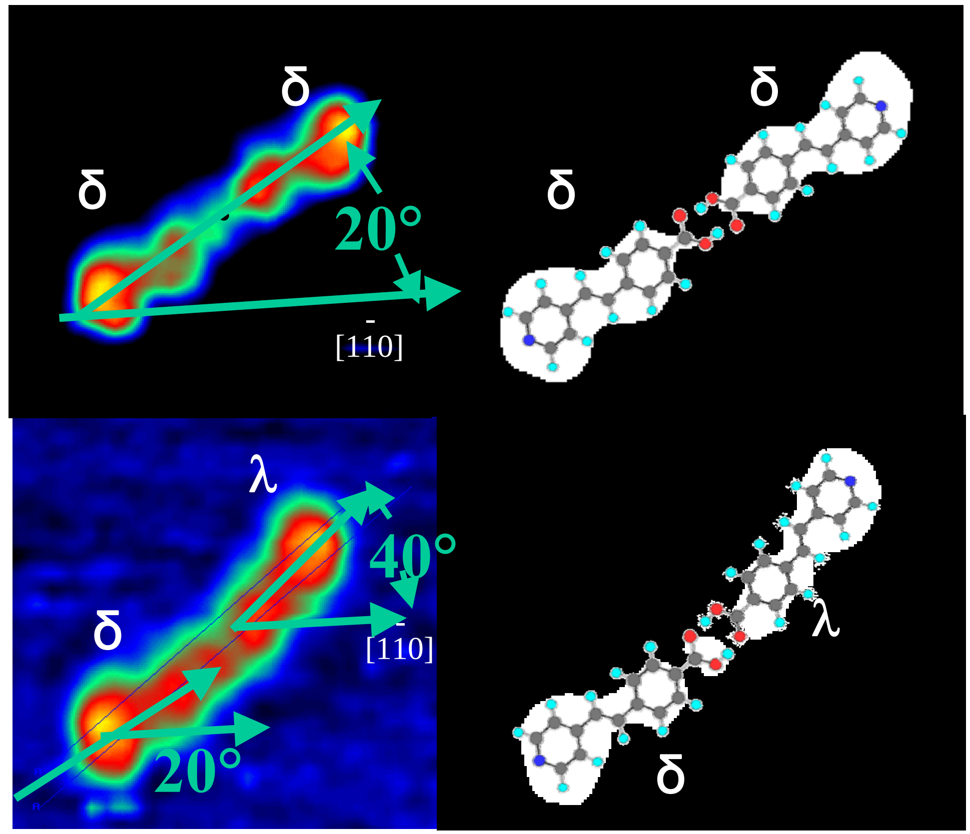
(d)

Molecular Orientation and Chiral Recognition of a Single Chiral Molecule



PVBA/Ag(111)

Weckesser et. al. PRL 87, 096101(2001)

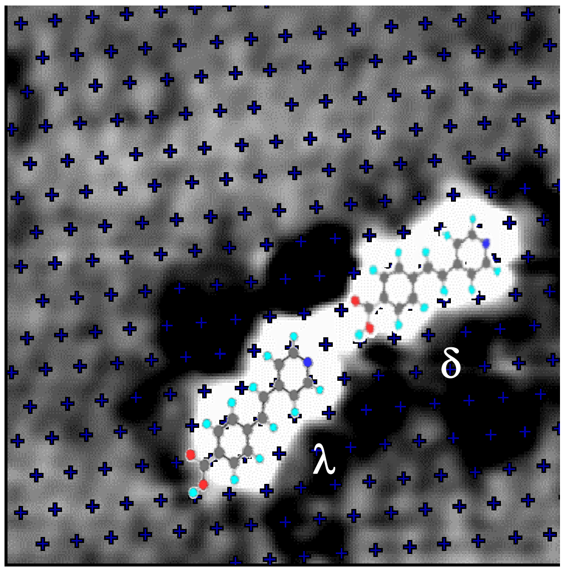


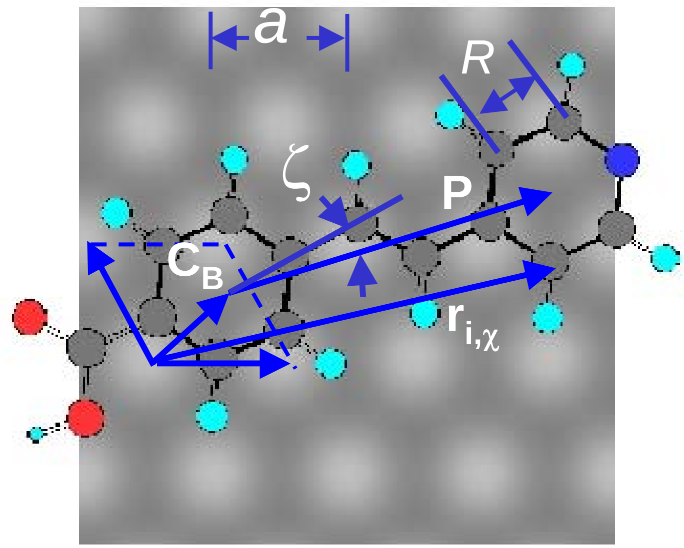
PVBA/Pd(111)

Kim et. al. Surf. Sci. 538, 45(2003)

Adsorption Preference of PVBA on Pd(111)

(Submitted to PRL, July 2003)





Model Potential V(r) between a Carbon Atom and fcc(111)

V(r) = 0 at a top-site, V(r) = 1 at a hollow site

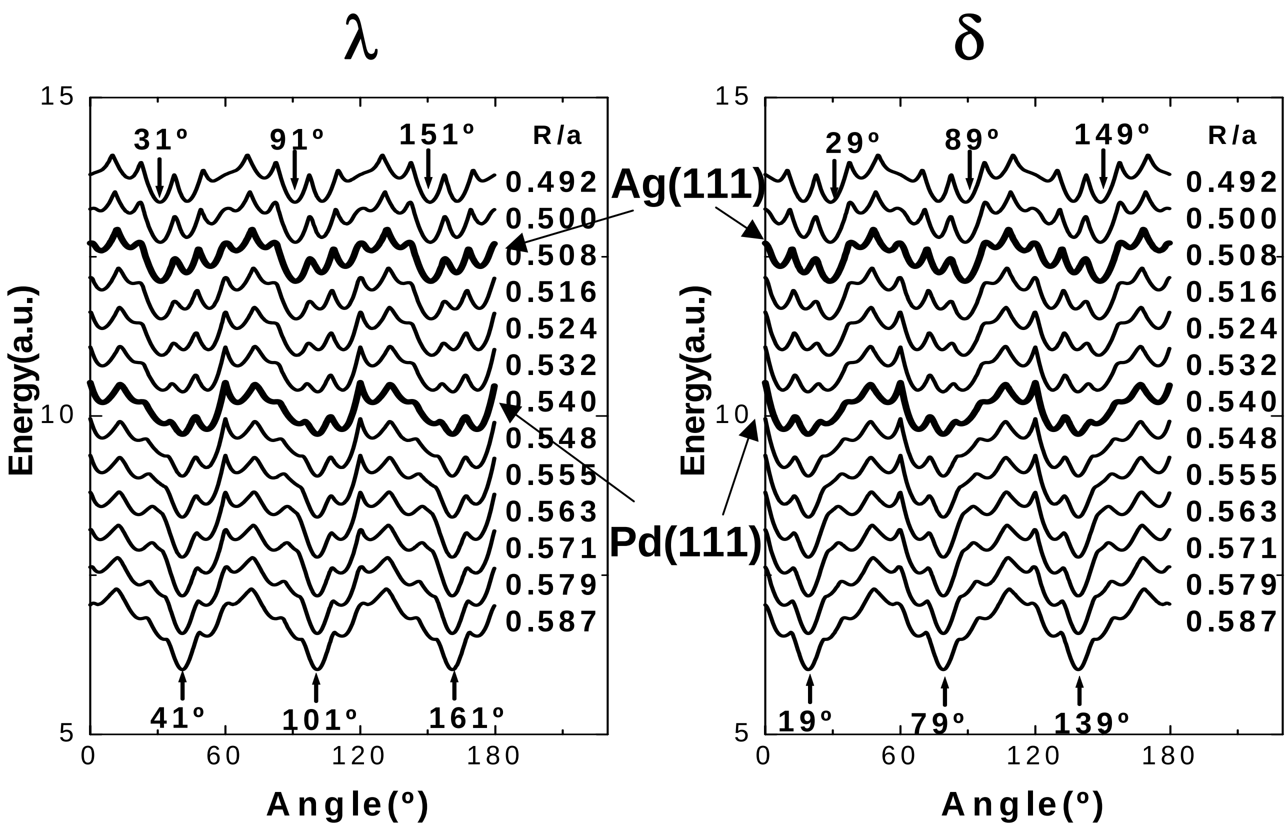
(Fourier Expansion of Surface Reciprocal Lattice)

$$V(\mathbf{r}) = 2/3 - 2/9\, \Sigma_{n=0}^{2} \cos \omega_n \cdot k\mathbf{r}$$

r : position coordinate, ω_0=(0,1), ω_1=(-√3/2, -1/2), ω_2=(√3/2, -1/2), $k = 4\pi/\sqrt{3}\, a$.

Binding Energy

Summation of each potential value for all atoms of two rings as a function of angle for each chirality(χ)

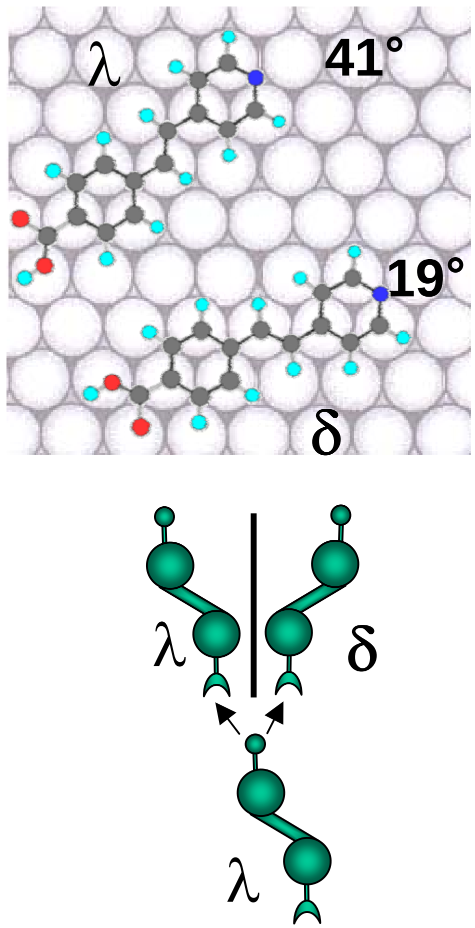


Orientation and Chiral Recognition of PVBA on fcc(111)

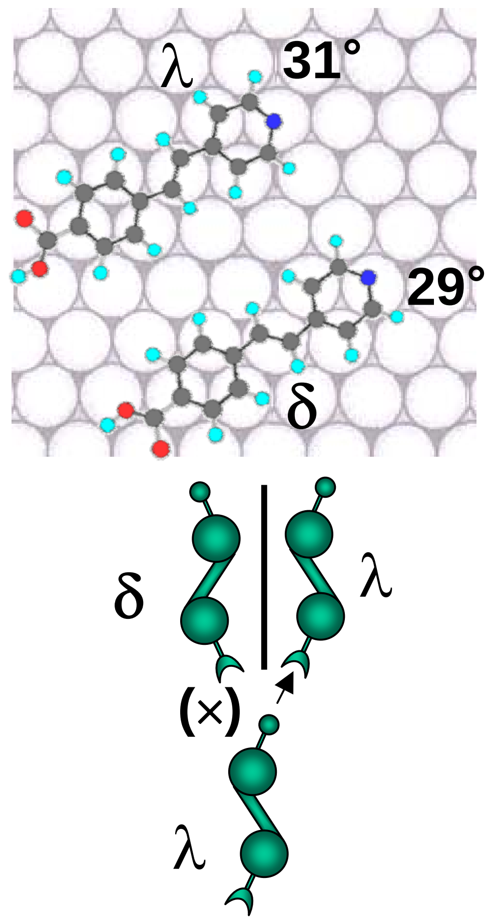
Pd(111)

Orientation

Ag(111)



No Chiral Recognition



Chiral Recognition

AFM-Monitors interfacial forces

$$F \propto (1/d)^x$$

F-interfacial force
d-tip sample separation
x-power law of acting force

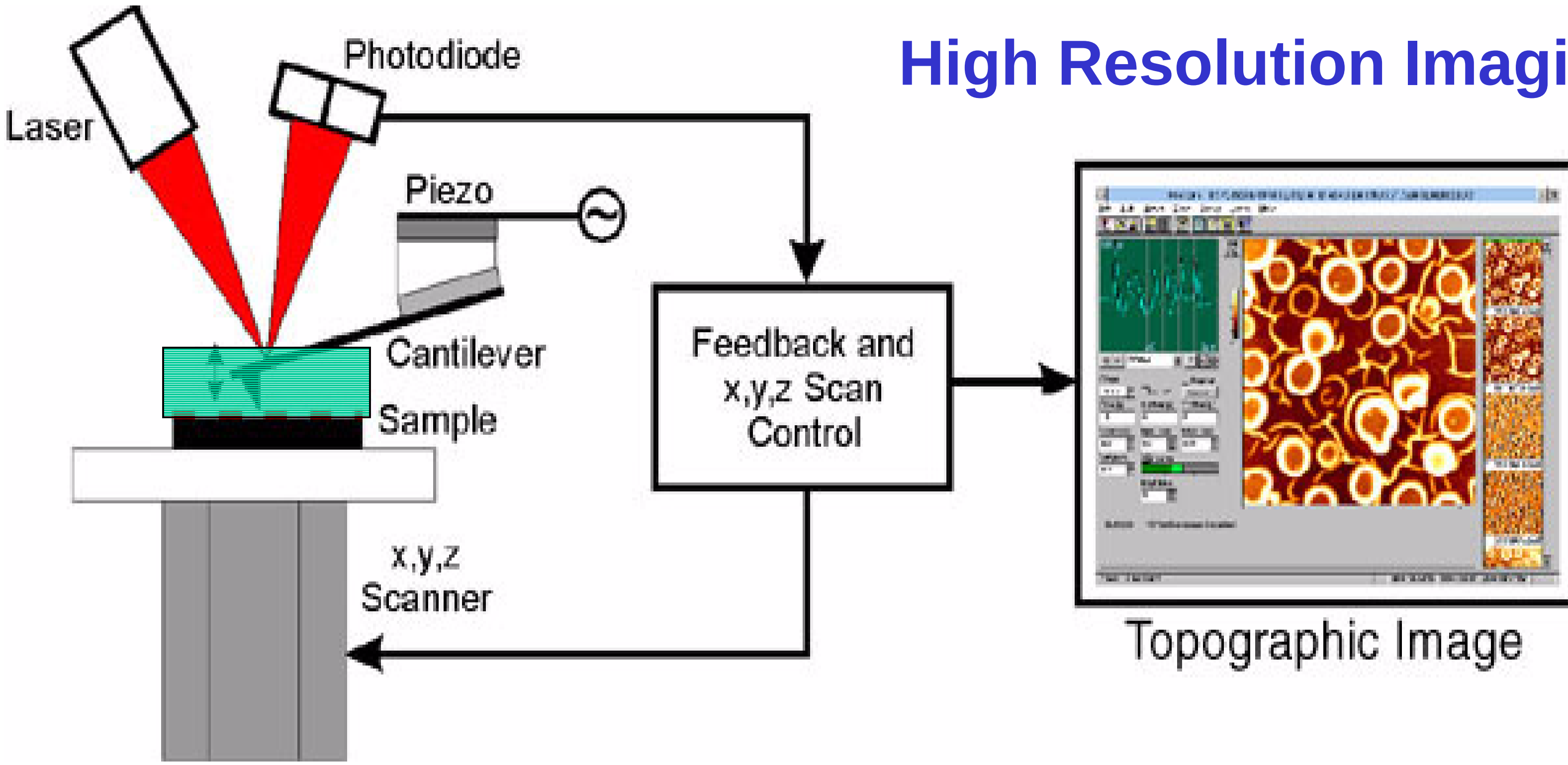
Interfacial forces include:

repulsive forces (contact AFM)
van der Waals forces (noncontact AFM)
electrostatic forces (EFM)
magnetic forces (MFM)
chemical forces (CFM)

- **interfacial forces : pN –nN**
- **lateral resolution : 0.1- 10nm**
- **depth resolution : 0.01 – 0.1nm**

Atomic Force Microscopy (AFM)

High Resolution Imaging



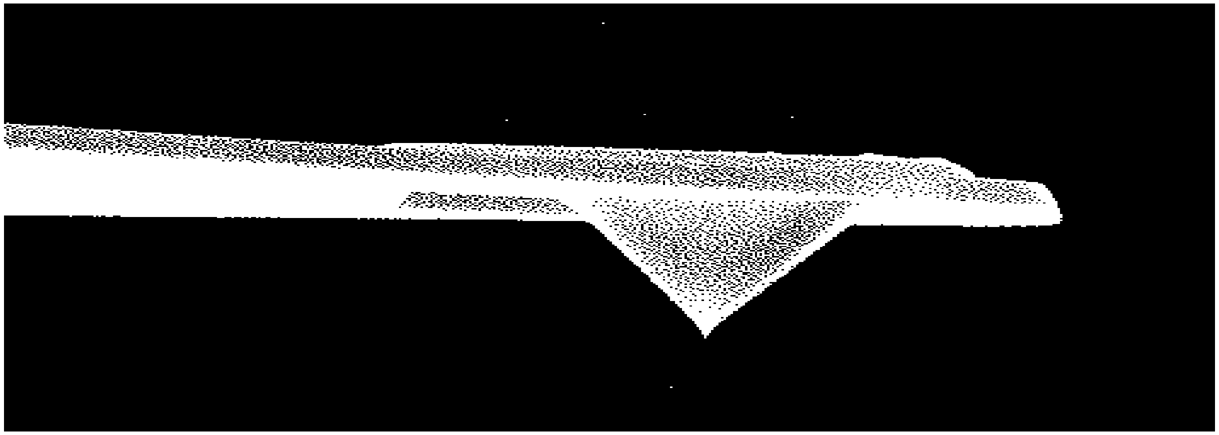
AFM has made it possible to view living biomolecules with atomic resolution in physiological environment

AFM Tip and Cantilever

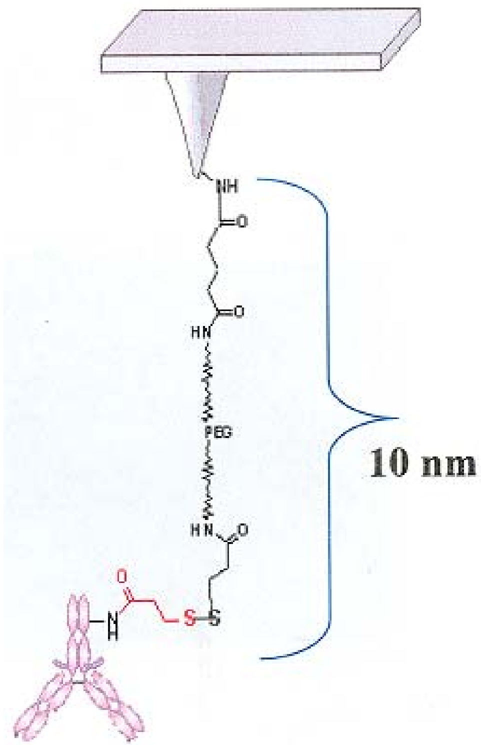
•Tip radius : 4 nm

I.

I.

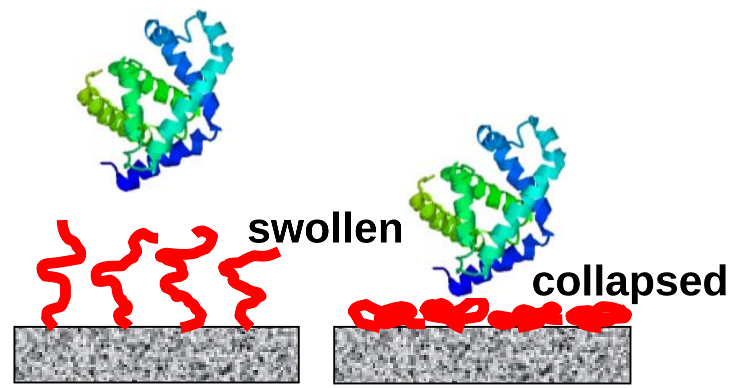


Surface Forces on Switchable Bioactive Surfaces Studied by Interfacial Force Microscope



Probing of Biomolecular Interaction

Thermally-Activated Surfaces: Tethered PNIPAM Films



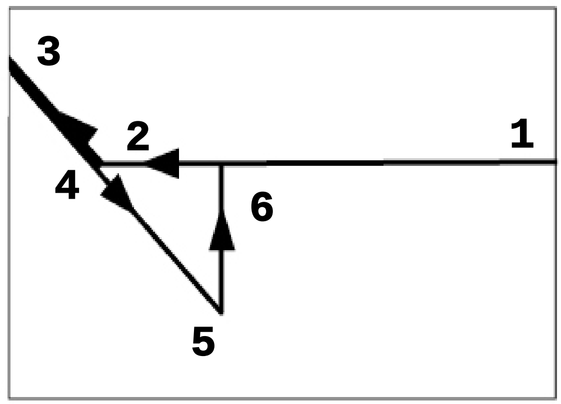
Hydrophilic
→ non-sticky

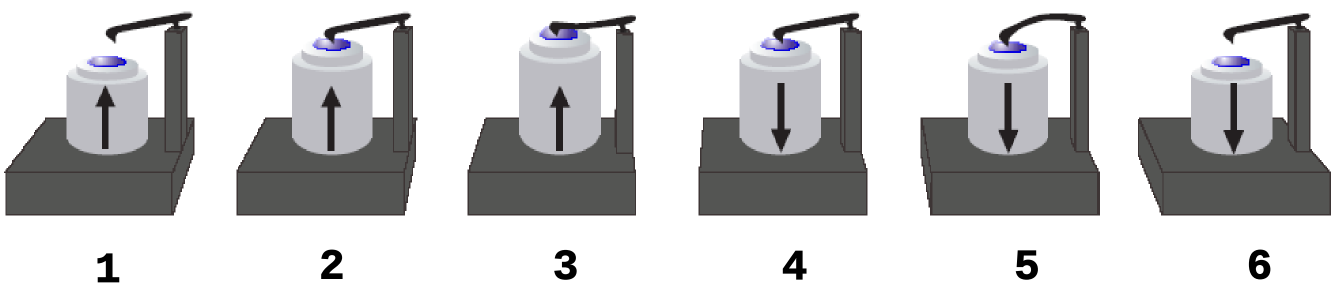
Hydrophobic
→ sticky

:Science, 301, pp.352-354(2003)

Sandia National Laboratories

Force-Distance Curve

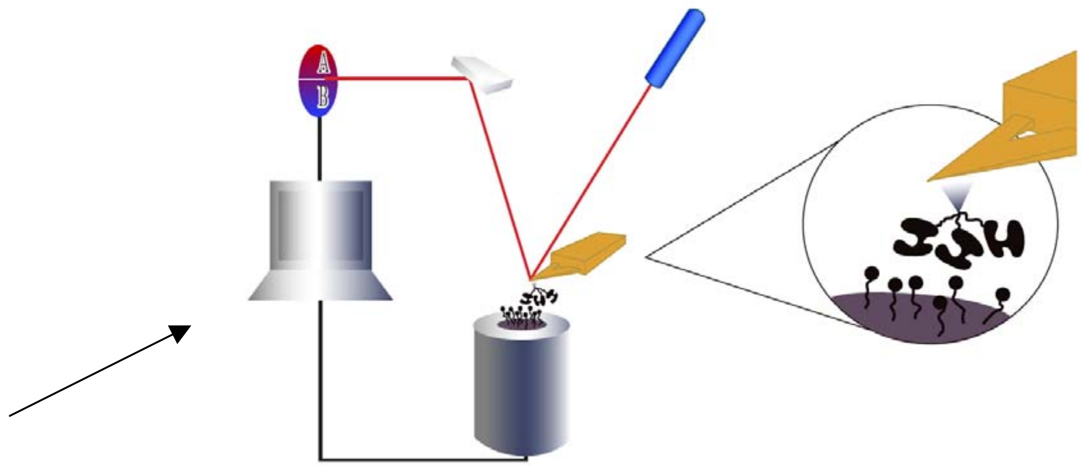




Single Molecular Force Spectroscopy
Enzyme-inhibitor interaction

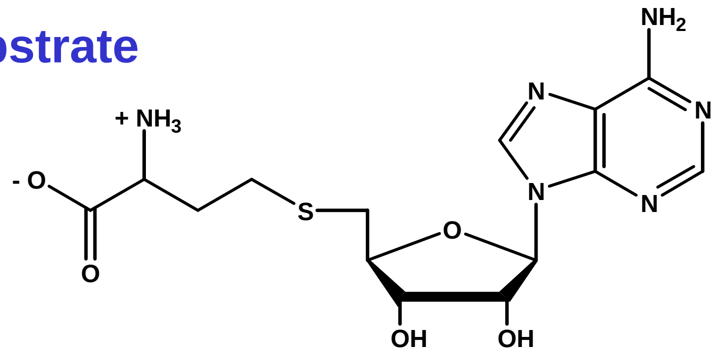
Bomb Fishing

Hook and Bait Fishing



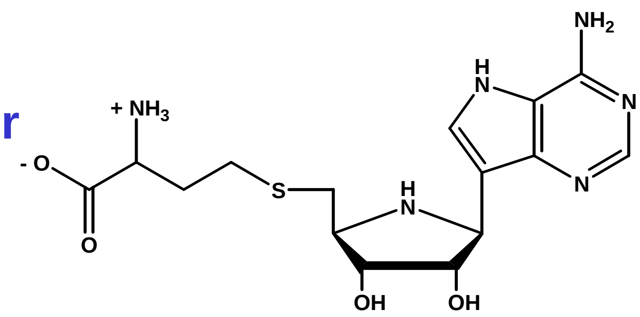
5’-methylthioadenosine/S-adenosylhomocysteine nucleosidase (MTAN)

Substrate

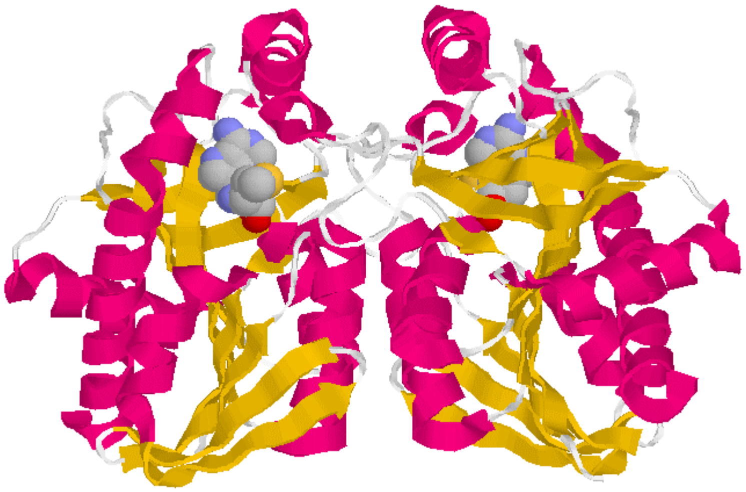


S-Adenosylhomocysteine (SAH)

Inhibitor



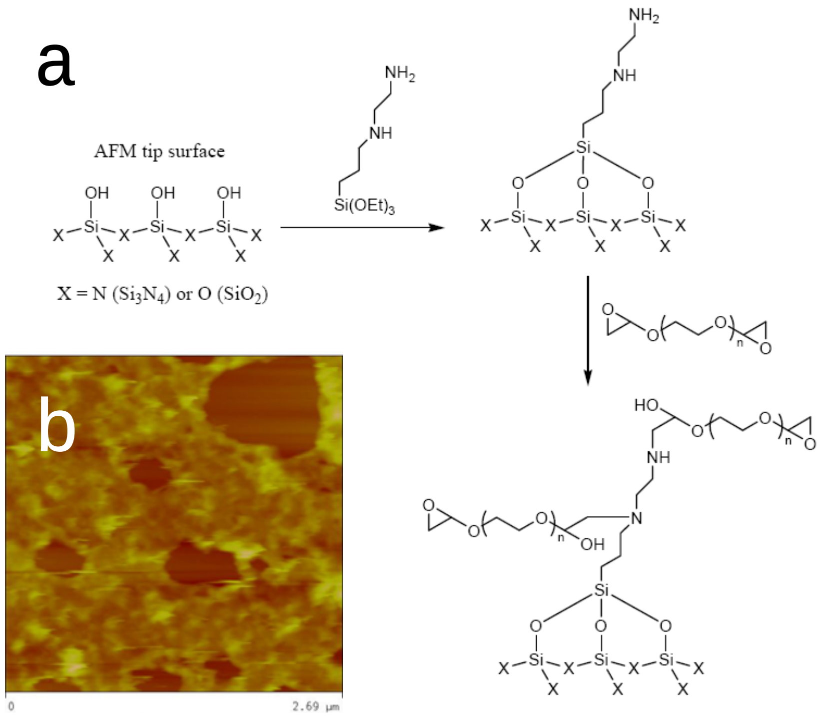
Homocystinyl Immucillin A (HIA)

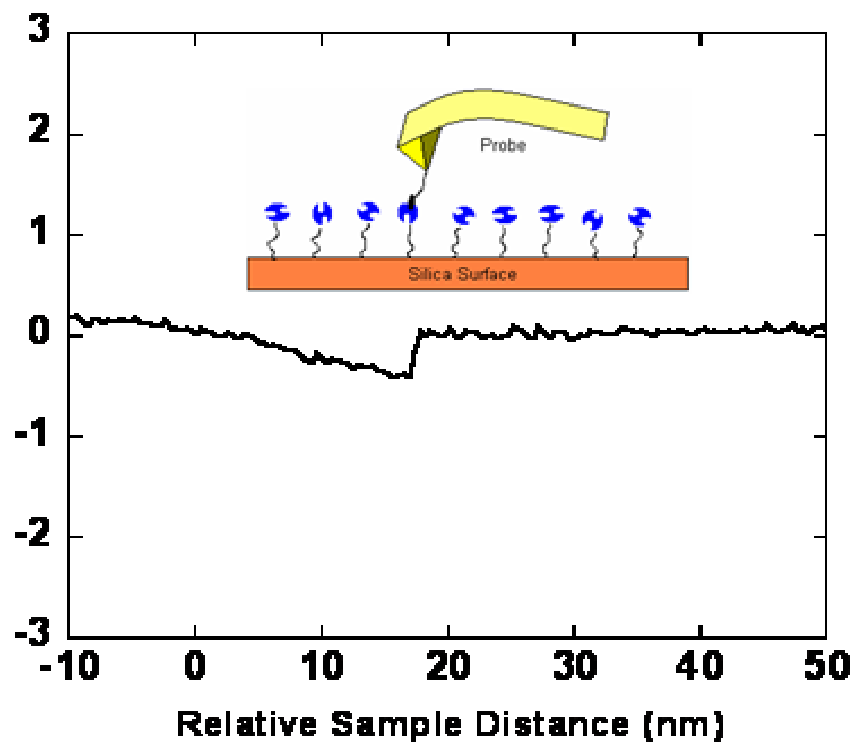


MTAN complexed with an inhibitor MT-ImmA

This enzyme-inhibitor pair is an important one, owing to its potential for antibiotic development.

MTAN-inhibitor interaction

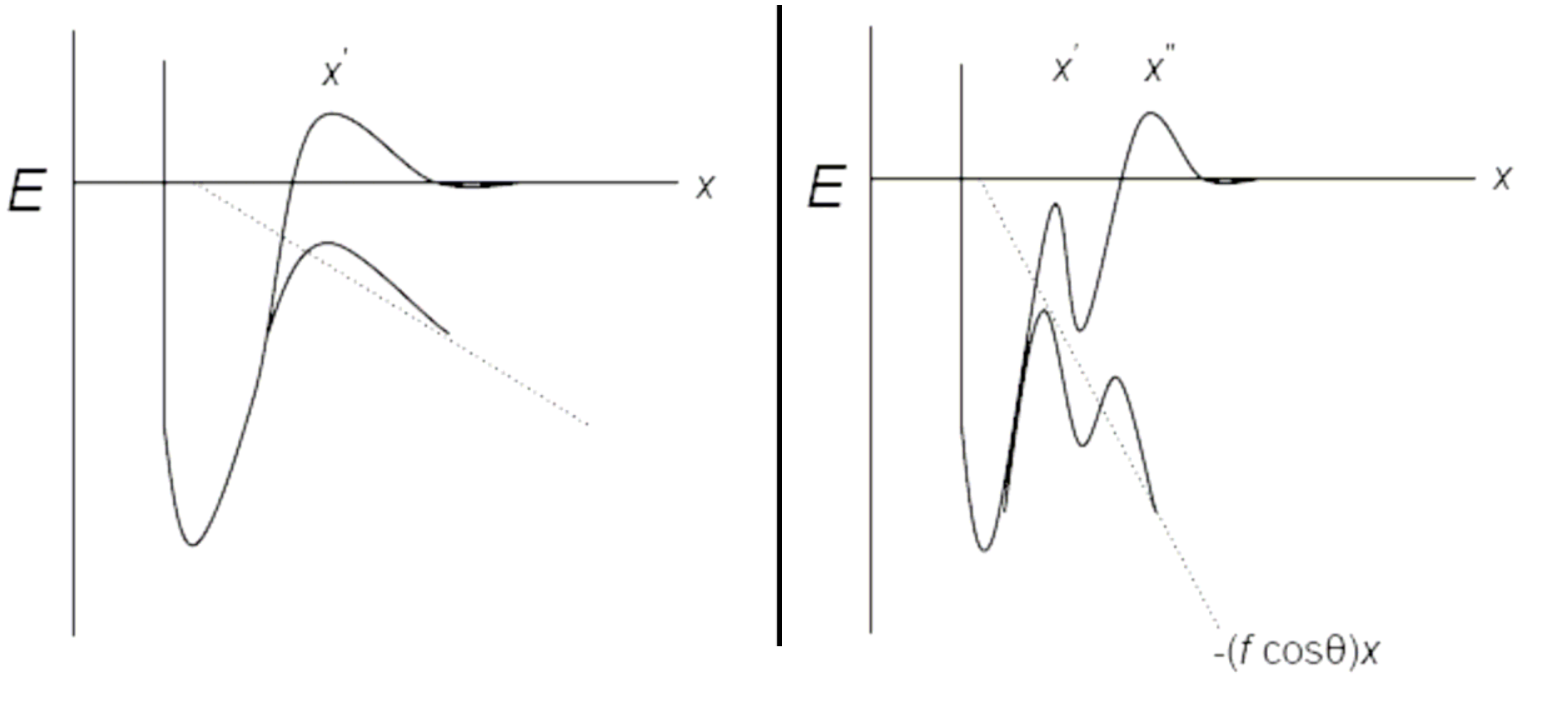




→ Epoxy group forms a covelanet bonding with -NH2 group

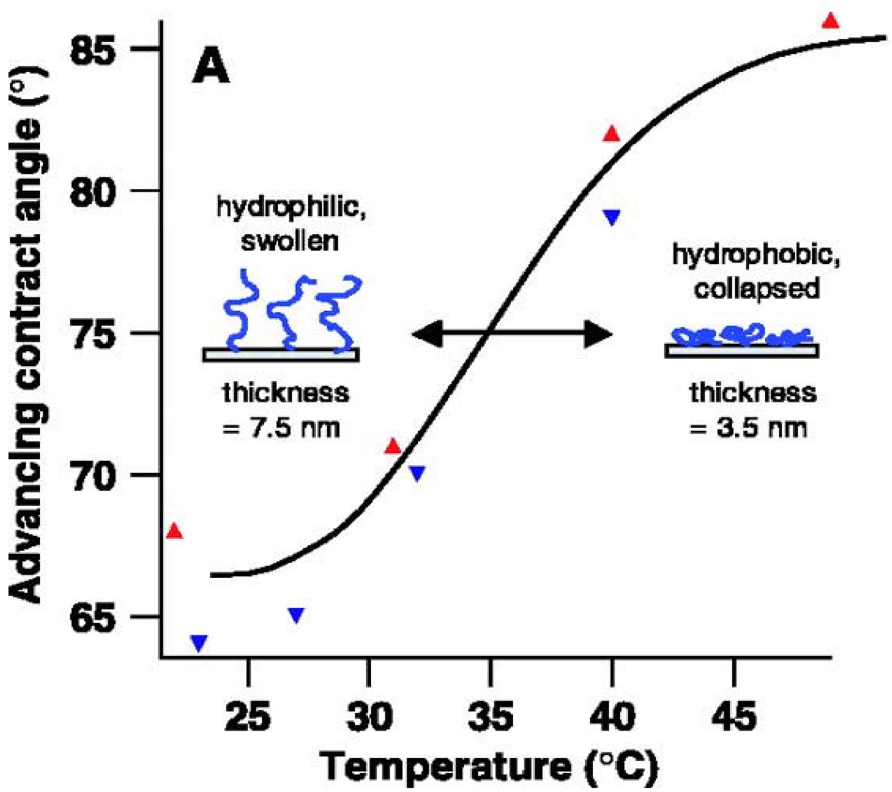
Single molecular interaction (enzyme-inhibitor)

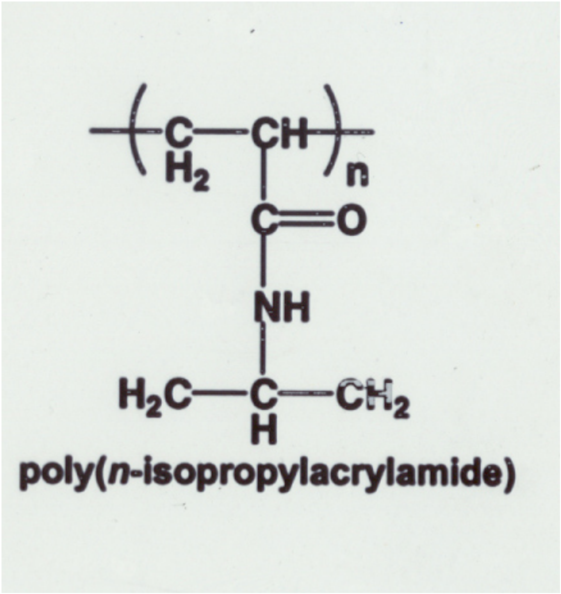
Force Induced Dissociation : Evans & Ritchie (1997)



→ **Statistical analysis enables to probe intermediate states between an enzyme and an inhibitor for a new drug design**

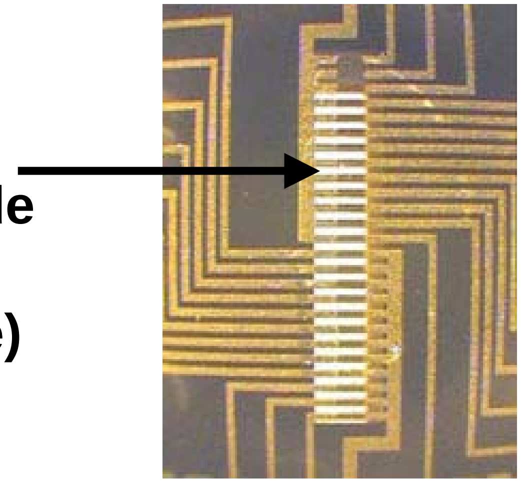
Temperature Controlled Reversible Switching in Tethered pNIPAM films





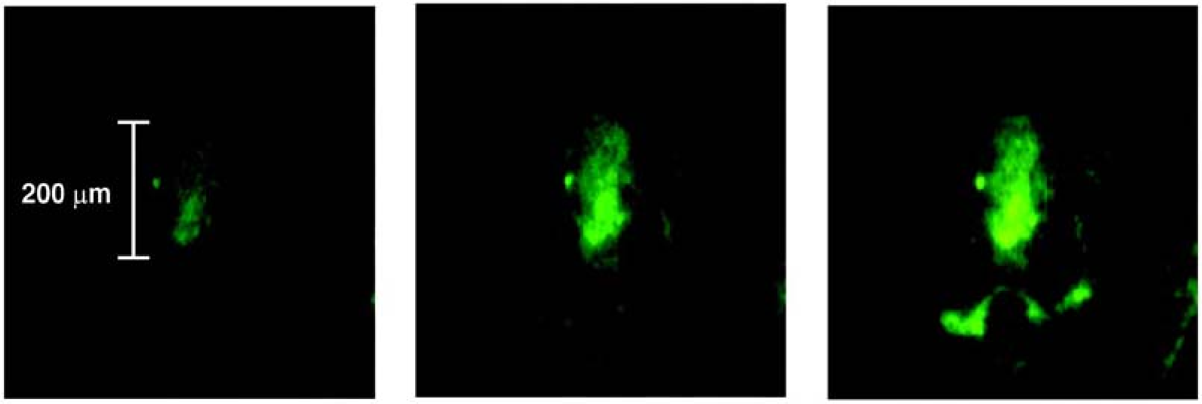
PNIPAM+Microhotplate = Reversible Protein Trap

PNIPAM coating on silicon nitride membrane (200μm wide)



Hot plate can be programmed to heat PNIPAM above transition

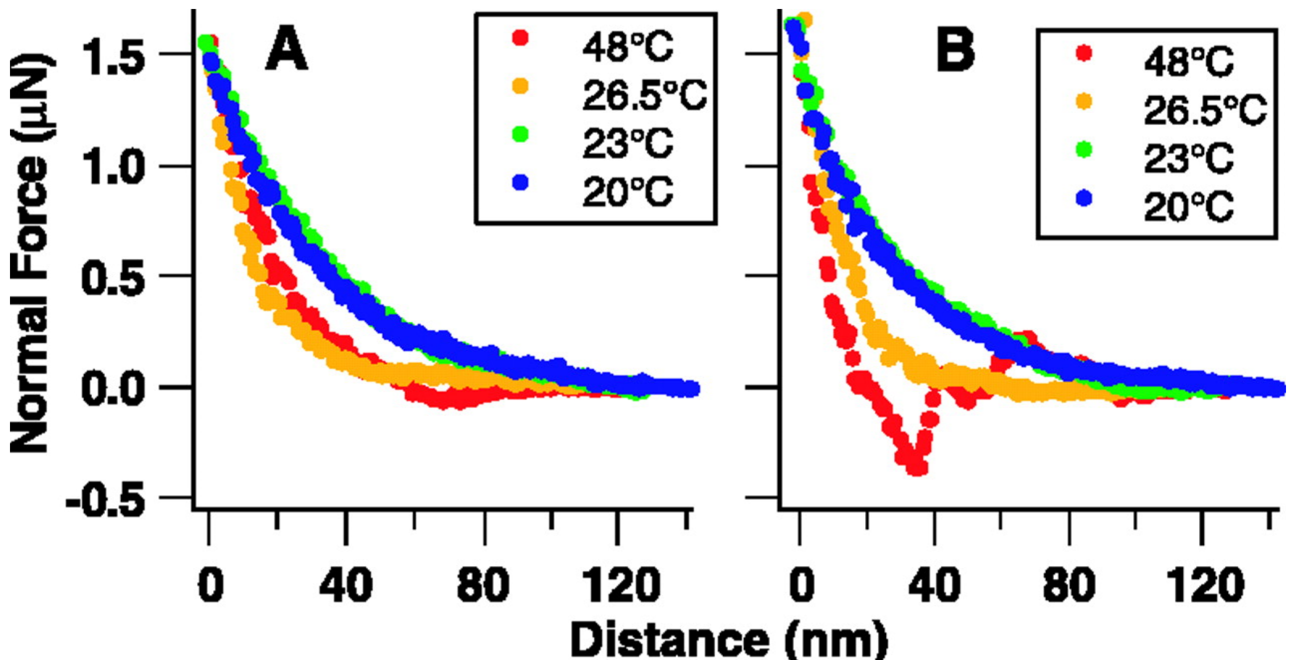
**Heating promotes protein adsorption.
Cooling promotes protein desorption**



T = 0.0 sec   T = 0.8 sec   T = 1.2 sec

Variable Temperature Studies Reveal Sharp Transition for PNIPAM

-ODTS Coated Tip

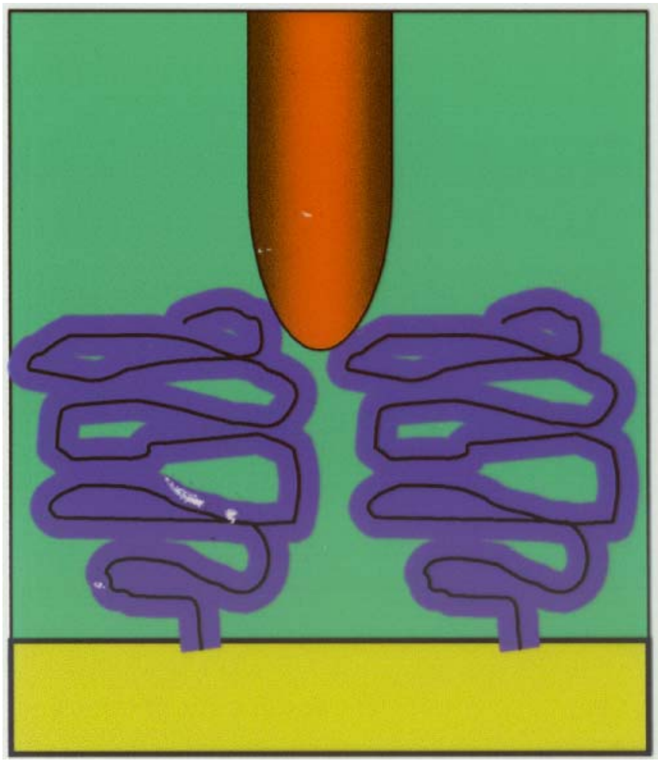


Behavior of PNIPAM under water

1) **All surfaces experience long-range repulsion→ consistent with "anti fouling" behavior**
2) **The repulsion collapses at a sharp transition temperature**
3) **Above the transition, PNIPAM surface become sticky after contact is made, consistent with protein adsorption.**

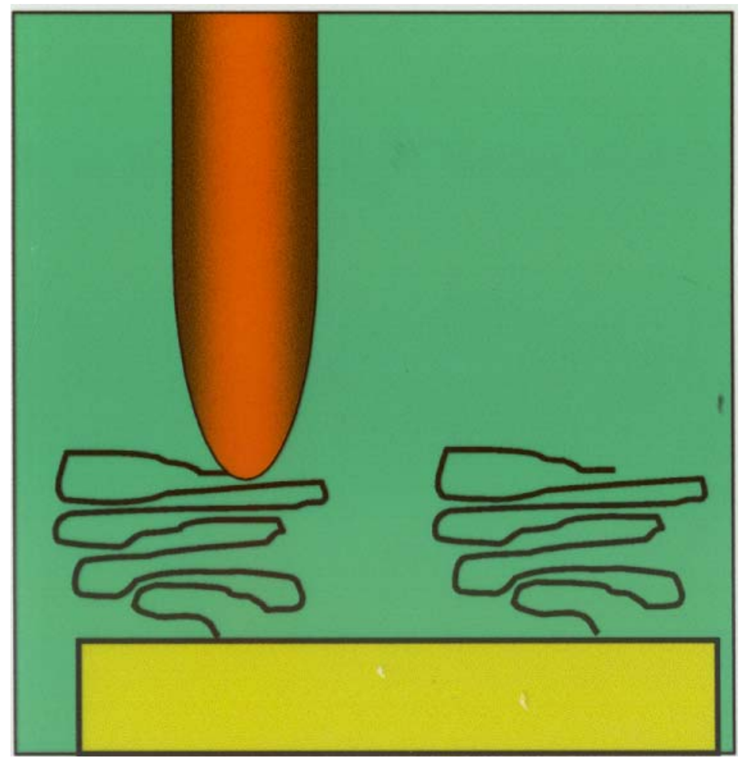
Tip-PNIPAM Interactions

Below Transition Temperature



Chain Hydration(2 nm thick)
1) **Promotes swelling**
2) **Inhibits adhesion**

Above Transition Temperature



Disruption of Hydration Layers
1) **Allows collapse**
2) **Promotes adhesion**

Acknowledgements

Prof. Ken Cornell (BSU Chemistry)

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Undergraduate Students: Jenny Rice (Biology), Joseph Holmes (Physics), Jeremy Bonander (Chemistry) and J.J. Durrant (Physics)