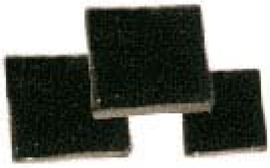
DNA in Nanotechnology

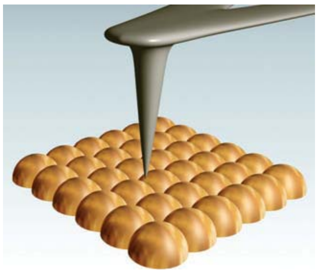
There is an avalanche-like increase of reports, where molecules of nucleic acids (DNA and RNA) appear as an object of nanotechnology research and/or as material for nano-sized devices. In many cases scanning probe microscopy (SPM) is the most powerful and informative research tool. Examinations as well as precise manipulations can be performed this way. What is important when SPM is applied to molecular level experiments? Three facets are illustrated further.

- Appropriate probes
  see the next page

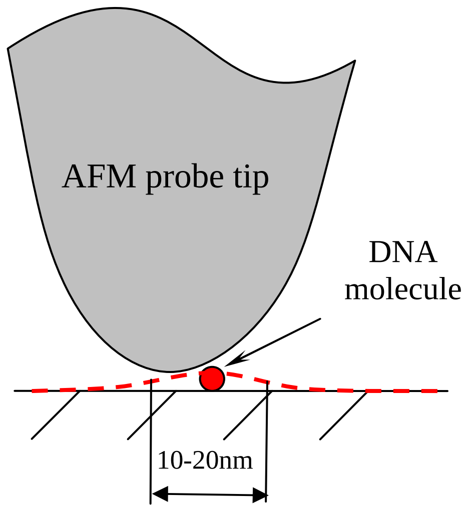
- Substrates and deposition protocols
  see page 3



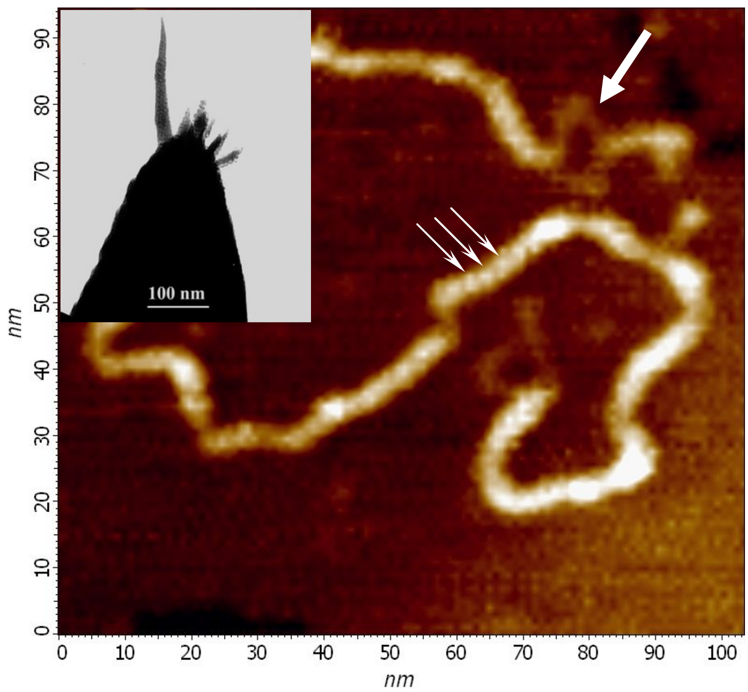
- AFM long-term stability
  see page 4



Probe sharpness determines resolution



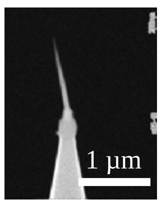
Strand width is usually
seen in AFM image



Tiny features of the relief can not be detected if the probe tip radius is too large. When imaged with conventional probe, the width of the DNA molecule is 10-20 nm usually, while real strand diameter is about 2 nm. Here are shown short poly(dG)–poly(dC) DNA fragments deposited on modified HOPG (see below). Small unwound single-strand fragments can be seen (bold arrow on the scan) and even helical pitch of the DNA molecule can be resolved (thin arrows) with a sharp enough tip (like DLC probe tip shown on the inlet). See comprehensive discussion on sub-molecular imaging in “High-resolution atomic force microscopy of duplex and triplex DNA molecules” Klinov D. et al. *Nanotechnology* (2007), V18, N22, p.225102.

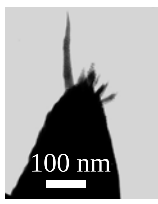
Related info:

Whisker-type sharp AFM probes



1 micron-long Whisker tip grown on silicon probe apex provides extremely high aspect ratio, tip radius is about 10 nm.

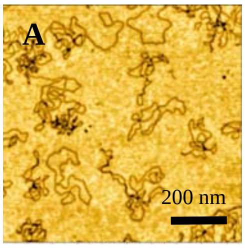
Super-sharp DLC AFM probes

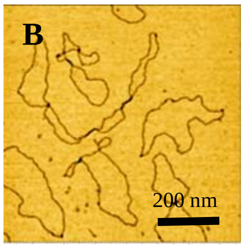


Tip from diamond-like carbon (DLC) grown on the probe apex is shorter and much sharper (tip radius ~1 nm).

DNA deposition: substrates and procedures

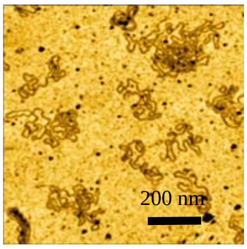
- Binding to mica surface via inorganic cations





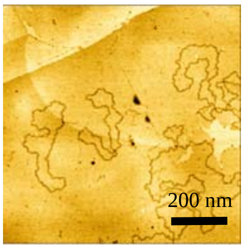
DNA molecules (plasmid) were deposited onto mica surface from solution containing Mg^{2+}. Pre-treatment of mica by pure water increases density of surface negative charge (because of cations loss). Binding of DNA in this case is fast and strong, circular plasmid becomes compacted (A). Freshly cleaved surface has lower density of the negative charge, thus DNA binding is slower and lateral diffusion occurs during deposition (B).

- Binding to mica surface via organic molecules



Plasmid DNA deposited onto mica surface pre-treated with APTES. The attachment occurs relatively fast.

- Binding to HOPG



Plasmid DNA deposited onto HOPG surface pre-treated with organic modifier $(CH_2)_n(NCRH_2CO)_m$–NH_2. Attachment occurs relatively slow.

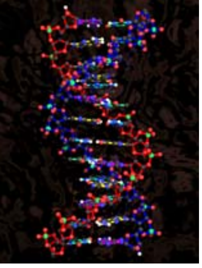
Related info:

HOPG for SPM applications

Highly oriented pirolytic graphite has atomically smooth surface and can be cleaved many times like mica. In contrast HOPG surface is hydrophobic.

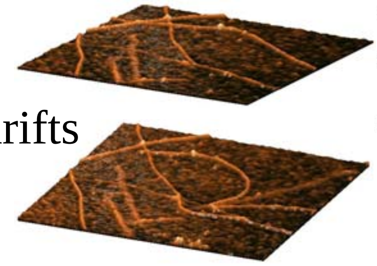
DNA molecules on mica

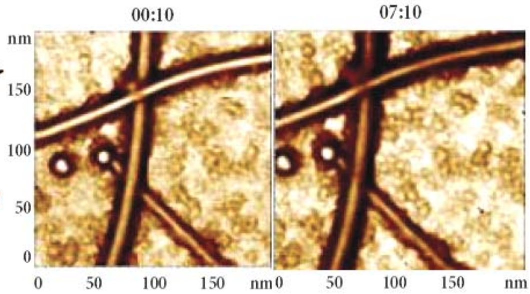
Test sample to be used in calibration of SPM device. Can be imaged both under liquid and in air.



AFM stability is essential for precise and long-term manipulations

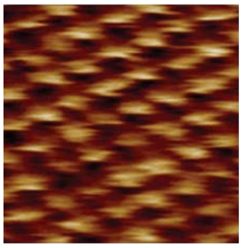
- Manipulations on small fields: low temperature drifts





Temperature drifts are serious obstruction for long-term experiments on small fields. Typical drifts values are 10-15 nm per hour in best commercial AFM devices. Due to this effect objects with sizes of tens of nanometers can be lost during long observations. On the left images it is shown how carbon nanotube (that is similar to DNA in terms of its dimensions) can be moved by AFM probe. Right pare of scans show this object in long-term experiment. Displacement for 7 hours is small enough and the same particles remains in field of view. Sample courtesy of Dr. H.B.Chan, Department of Physics, University of Florida, USA.

- Manipulations on small fields: closed loop correction



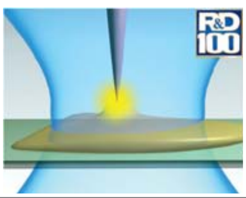
Closed loop (CL) sensors are essential for correct probe re-positioning and manipulations. Because CL sensors put some electronic noise they usually are not available below 100 nm. NTEGRA Therma allows CL correction even below 10 nm. Here is atomic lattice of mica imaged with CL sensors.

Related info:

NTEGRA Therma

The only commercial AFM system that provides drifts <3 nm/h. CL correction available below 10 nm.

NTEGRA Spectra



SPM-combined Raman spectroscopy system for single molecule experiments (in-plane resolution for spectroscopy is ~50 nm). Tip enhancement of Raman allows detecting signal from single molecule.