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A Virtual Presence Interface for a Scanning Probe Microscope

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A Virtual Presence Interface for a Scanning Probe Microscope

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NanoManipulator™ System

A Virtual-Environment Interface
to a
ThermoMicroscopes™ SPM

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Agenda

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- About 3rdTech
- NanoManipulator System Overview
  - Components
  - Features/Functions
- What Science has the NanoManipulator Enabled?
  - Adenovirus
  - Carbon Nanotubes
  - DNA
  - Fibrin

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About 3rdTech

3rdTech is a foundry for new companies. Located in Chapel Hill, NC, directly across the street from the University of North Carolina, 3rdTech is working to turn the most advanced technologies into leading edge products.

The Computer Science Dept. at UNC-CH has one of the world's best computer graphics and virtual environments research efforts. The department also enjoys a world-class reputation in medical image analysis, networking, and hardware systems design, and has significant strengths in other areas. And there are many other technology development groups within the University with similar reputations and potential.

3rdTech is driven by the opportunities to build new businesses around these world-class technologies and this exceptional talent pool. We are leveraging these resources by creating a channel and a culture to enable the rapid development of new products and new businesses.

About 3rdTech

- New Kind of High-Tech Incubator
  - Working with researchers at UNC-CH
  - Creating a channel to bring advanced technology from the university to the marketplace
  - Productize technology; develop sales/distribution channels
  - Enable spin-off of independent companies

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Ideal Microscopy: Virtual Environment Interface to SPM

In Scanning Probe Microscopy, we are working with objects a million times smaller than everyday objects. How can we make it intuitive and easy to manipulate them? With the NanoManipulator system, an environment with the computer is created where it seems like the viruses and molecules are sitting on the table in front of you, and you can see, feel and move them.

Ideal Microscopy: Intuitive Merging of User and Sample

A virtual environment interface to SPM

The Goal:
- Remove boundaries between user and sample
- Can we make experiments on the molecular scale as easy as rolling a pencil or pushing a golf ball?

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NanoManipulator System

The Computer Science Dept. has been working to build tools to help the Physics Dept. do SPM microscopy for about seven years. 3rdTech has worked with the researchers in both departments to develop a commercial version of these tools – the NanoManipulator System. The components of the NanoManipulator make manipulations and experiments easier, more intuitive and more efficient.

Three-dimensional display of the sample during the experiment enables new interpretation of the shape of the sample.

Force feedback gives you information about the sample location and surface features during a manipulation.

Automatic recording of the entire experiment session enables new discoveries and analysis on recorded data.

What is the NanoManipulator System?

- Real-time Control for ThermoMicroscopes SPMs
  - Integrated software and hardware
- Virtual-Environment Interface
  - See, feel, manipulate your sample
- 3D Graphics
  - Improved visualization during the experiment
- Force Feedback to Guide Manipulations
  - Real-time position information
- Virtual Tips
  - Oscillating/contact switch
- Automatic Lab Notebook
  - Store/replay/re-analyze data

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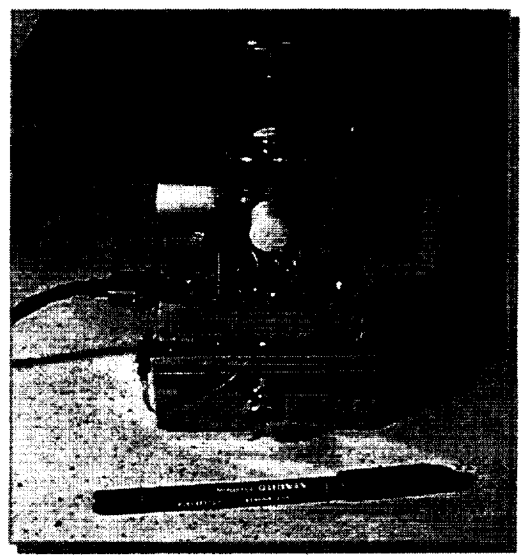
NanoManipulator System Components: SPM

We provide an interface to these ThermoMicroscopes SPMs. The Explorer is pictured. The NanoManipulator communicates to the SPM control software through a standard network connection.

NanoManipulator System Components

- A ThermoMicroscopes™ SPM
  - Explorer™
  - Discoverer™
  - Lumina™
  - Observer™



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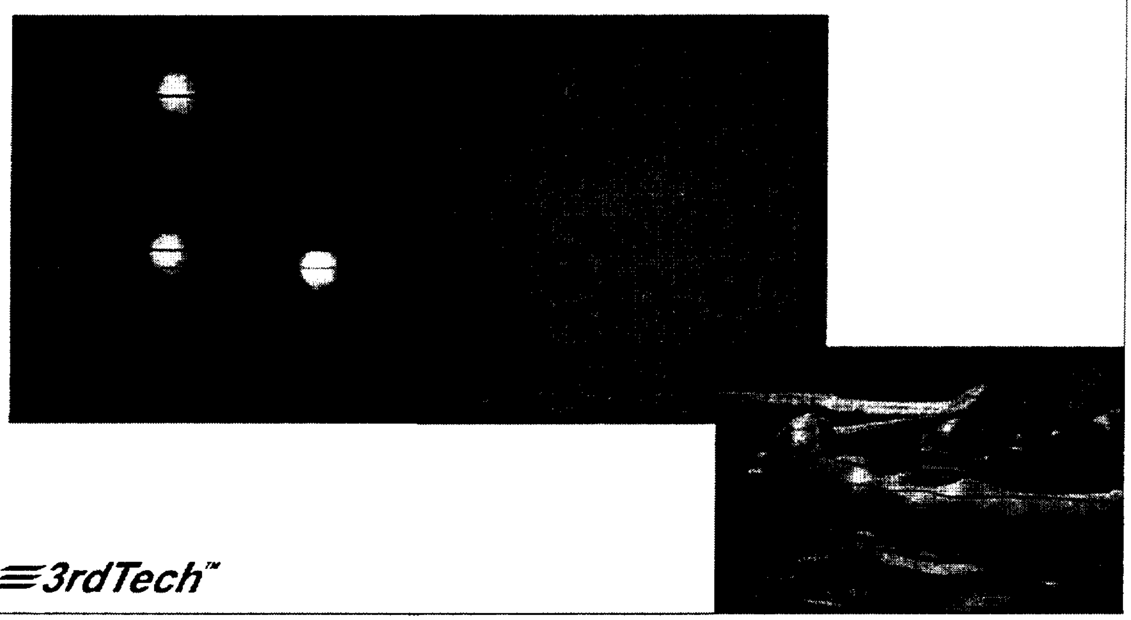
NanoManipulator System Components: 3D Graphics

A key component of the NanoManipulator is real-time display of the sample surface with 3D graphics. Here is a side-by-side comparison of two views of adenovirus. One of the adenoviruses is leaking DNA on the surface, and you can see how the highlights from the light on the right is picking out the DNA on the surface. It is also showing some subtle shape changes on the tops of the adenoviruses which are lost on the left. The user has interactive control of the view and lighting, which means one can zoom and rotate in any direction, getting views like this during the experiment.

NanoManipulator System Components: 3D Graphics



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NanoManipulator System Components: Force Feedback

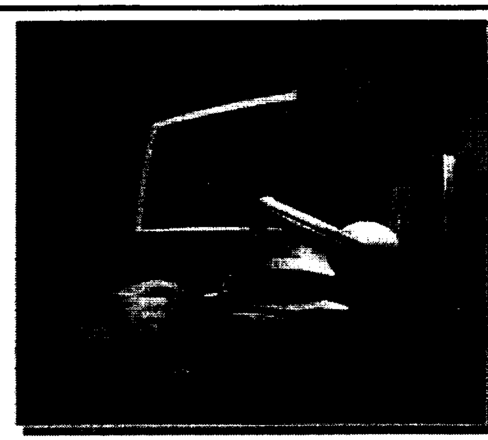
The Phantom Desktop from SensAble Technologies is the other key component. It is a 6D input tool, which makes it easy to interact with the 3D environment of the NanoManipulator. It also is a 3D force-feedback tool enabling one to "feel" the sample surface. This provides additional data about the surface topography of the sample.

It is also particularly valuable during a sample modification because it lets you feel the shape of your sample as you guide the SPM tip while it is modifying your sample. Hysteresis and drift have no effect on the tactile feedback – you can find exactly the right spot to modify, and feel what is happening during a modification. This is unlike the visual feedback which is not current and accurate during a modification.

This results in the ability to do modifications which would otherwise not be possible – or would be extremely difficult.

NanoManipulator System Components

- Haptic/force feedback output
  - A SensAble Technologies PHANTOM™ Desktop
  - Continuous, real-time location identification
  - Find the right spot to modify; feel it during manipulation



"It was really a remarkable feeling for a chemist to be running his hand over atoms on a surface," R. Stanley Williams, UCLA Chemistry

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NanoManipulator System: Virtual Tips

The NanoManipulator software has been developed over the years to enable a number of different techniques for sample modification.

The simplest is to move the Phantom over the surface, and have the SPM tip follow, pushing down into the sample as it goes.

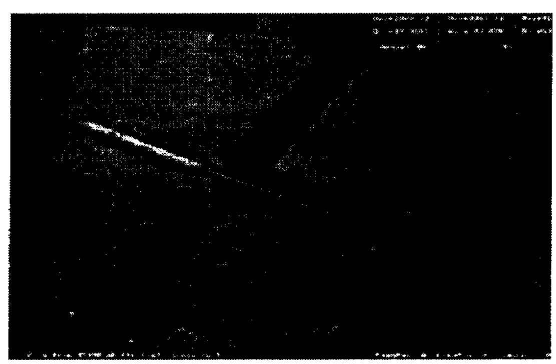
A second simulates a "Virtual Tip" shape. For example, to clear out an area of photoresist, to etch and separate electrical contacts, as pictured here, SPM tip can simulate a broom or scraper by moving side-to-side as you move forward.

In addition, one can specify movements across the surface to move freely, to be constrained to a line, or to automatically have the SPM tip follow a pre-planned path.

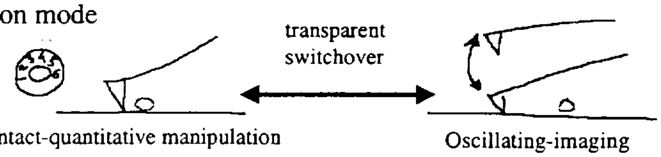
Finally, the NanoManipulator provides an automatic switch-over from oscillating imaging mode to contact mode, so one can scan and feel the sample with the light touch of oscillating mode, but modify and measure lateral forces using contact mode.

NanoManipulator: Virtual Tips

- Whisk broom
- Freehand, constrained or automatic
- Oscillating/contact



Touching, Modifying: need to switch quickly between imaging mode and manipulation mode



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NanoManipulator System: Store/Replay

A vital feature of the NanoManipulator is the "automatic lab notebook," which records a complete record of all the data obtained during an experiment. This file can be replayed and reviewed at any later time, at the speed of the original experiment or it can be "fast forwarded" to locate specific data more rapidly. This enables new analysis of data that might not have been understood while the experiment was taking place. One clear example of its value was the discovery, days after an experiment was performed, that a nanotube was rolling and not sliding. This had not been noted at the time of the experiment.

NanoManipulator: Store/Replay

"If it's not in the lab notebook, it didn't happen."

- Store data for the entire experiment
- Enables replay from different points of view
- Playback at different speeds
- Perform new analysis on old data
- Results:
  - tube slid on top of another
  - tube rolling, not tip artifact

All the best science seems to happen at 3 AM

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Science Enabled by the NanoManipulator

Let's look at four areas of science that members and collaborators of the NanoManipulator Project at UNC Chapel Hill have investigated.

Science

- What science has been enabled by the NanoManipulator System?
  - Adenovirus
  - Carbon Nano Tubes
  - DNA
  - Fibrin

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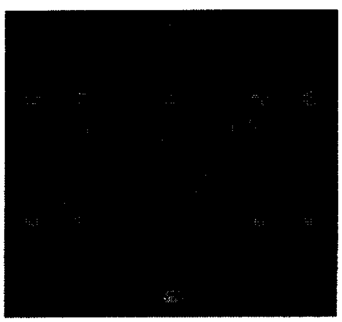
Application 1: Adenovirus

Adenovirus causes the common cold, and can be used as a vector in gene therapy. Scientists would like to understand how the adenovirus infects a cell in detail. Using the NanoManipulator, scientists have found out more about how they work.

Application 1: Adenovirus



Icosahedral Virus
85 nm diameter

Why are they interesting?

- Responsible for common human illness
- Model virus for understanding basic virology
- Vector for gene therapy

Questions:

- Can we correlate shape (form) with function?
- How does virus bind to cell?
- How do virus capsid mechanical properties relate to infectivity?

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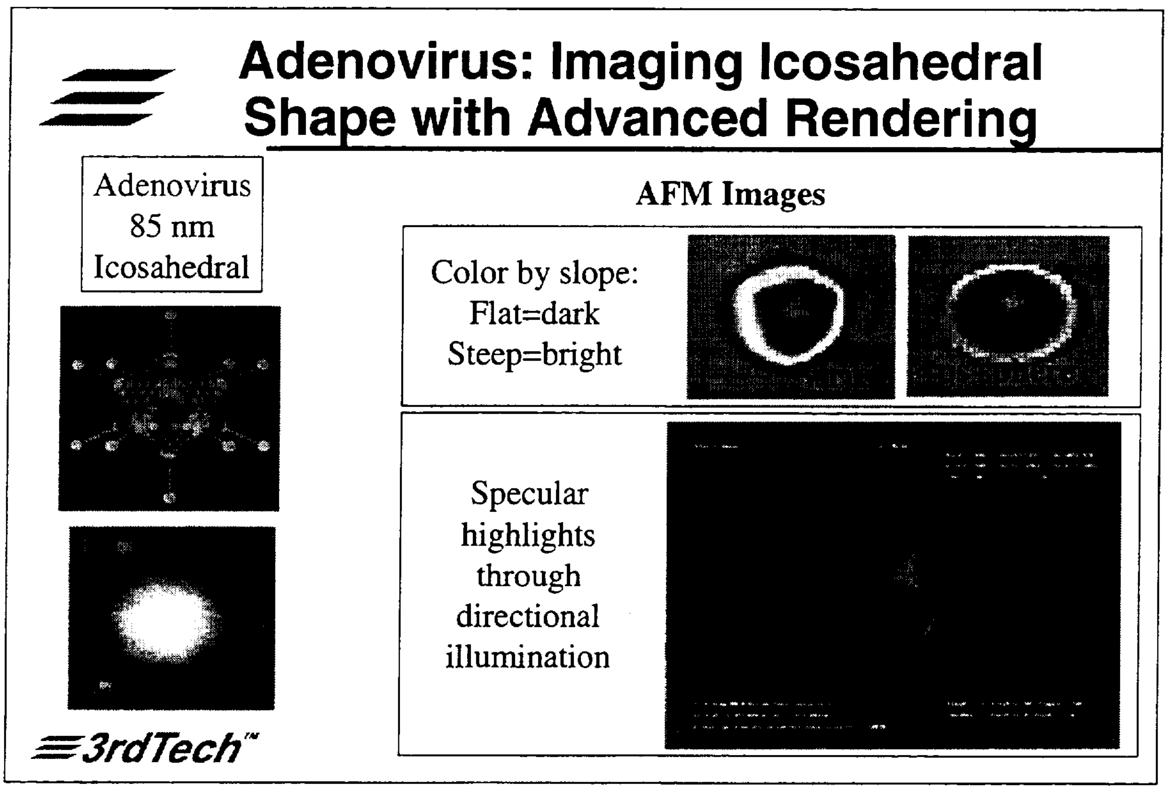
Application 1: Adenovirus Icosahedral Shape

First, one can confirm the icosahedral structure of the virus from a three-dimensional rendering using a directional light which shows the triangular facets. Above that is a color map based on the slope of the surface.This clearly shows that the adenovirus has facets and that the polystyrene bead does not. Multiple rendering techniques like this enable one to show more than one kind of data on the surface at the same time.

Negishi, A., Matthews, W. G., McCarty, D. M., Samulski, R. J., Rohrer, D., Henderson, A., Taylor, R. M. and Superfine, R., "Three-Dimensional Icosahedral Structure of Adenovirus Using AFM," *Biophys. Journal* (submitted).



Adenovirus Surface Binding

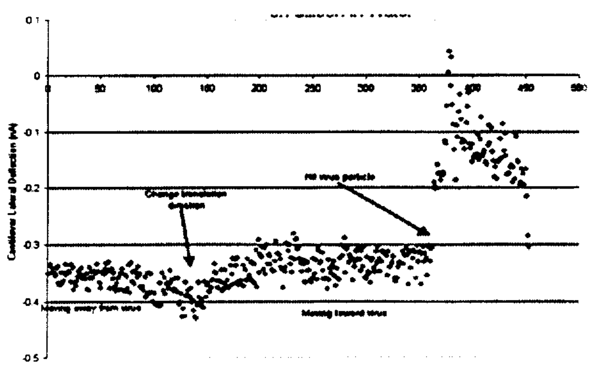
Here we investigated the stickiness of the adenovirus. By doing repeated contact mode manipulations, we can measure the lateral force it takes to slide a virus across the sample surface, which, in this case, is silicon. The graph shows an initial peak in the force which detaches the virus from the surface, and then shows a steady-state sliding force.

Negishi, A., Matthews, W. G., McCarty, D. M., Samulski, R. J., Rohrer, D., Henderson, A., Taylor, R. and Superfine, R., "Probing the Structural Properties of Adenovirus Using the Atomic Force Microscope," *Biophysical Society 43rd Annual Meeting, Feb. 13-17, 1999, Baltimore, MD, Biophys. Journal,* 1999, Vol. 76, A27.

Adenovirus: Quantify Surface Binding Through Manipulation

Image/manipulation of Adenovirus in solution on silicon

Quantify lateral force recorded during manipulation: Adhesion and friction



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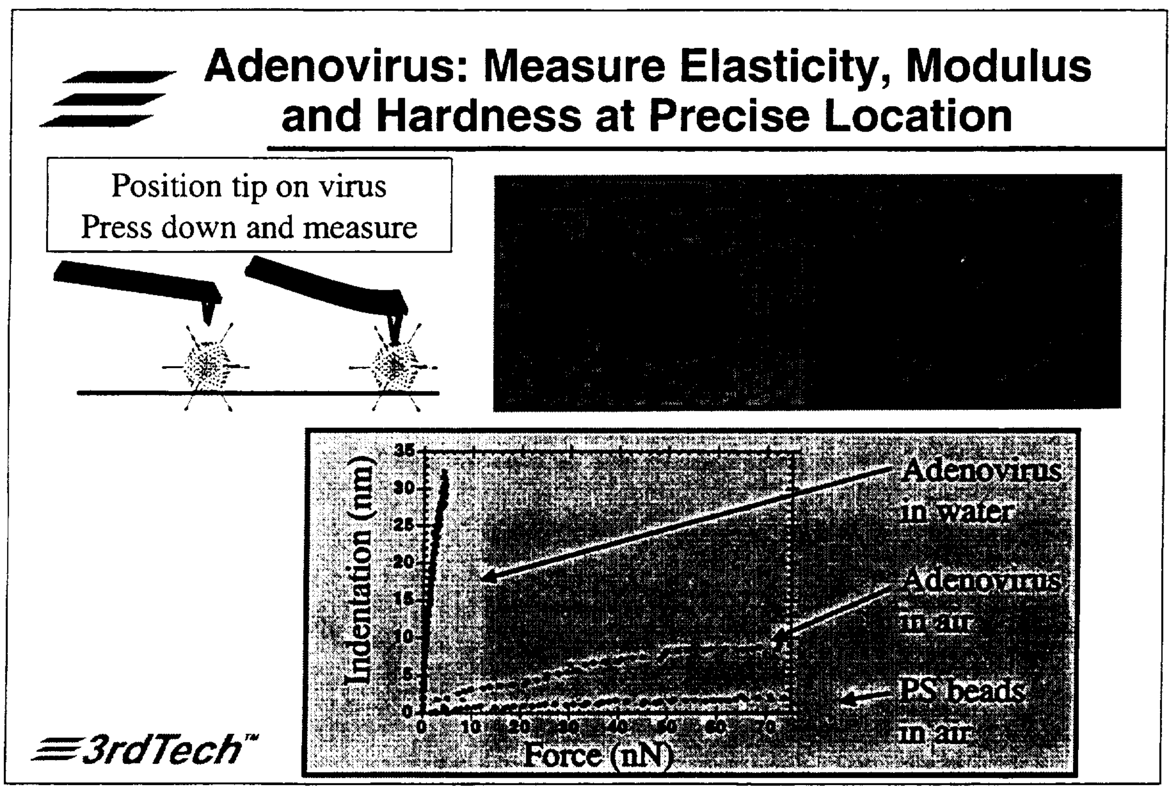
Adenovirus Elasticity

Scientists have also measured the "squishiness" of adenovirus using the NanoManipulator Interface. Because the scientists could feel their sample with the Phantom, they could position the AFM tip exactly on top of a virus. Then the NanoManipulator made an automatic switch to perform a force-spectrum. The image on the right shows an adenovirus with a dimple in the top from an AFM tip. They did this both in water and in air, and found that adenoviruses are much less rigid in water. The researchers' pathology collaborators had assumed that adenoviruses were always hard and had to force their way through cell structures. These measurements helped them realize the possibility that the viruses deform to get through those tiny spaces.

Matthews, W. G., Negishi, A., Seeger, A., Taylor, R., McCarty, D. M., Samulski, R. J. and Superfine, R., "Elasticity and Binding of Adenovirusin Air and in Liquid," *Biophysical Society 43rd Annual Meeting, Feb. 13-17, 1999, Baltimore, MD, Biophys. Journal, Vol.* 76, 1999, A265.



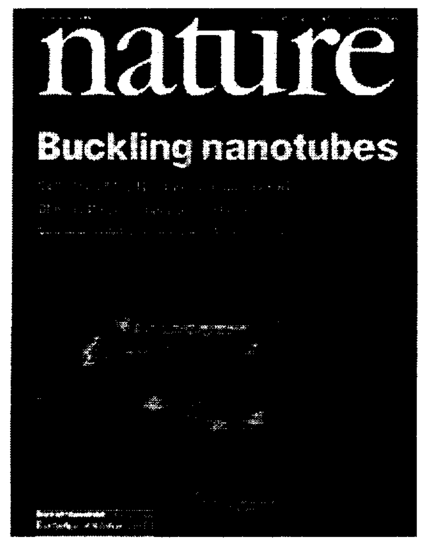
Application 2: Carbon Nanotubes

Another major area of research at UNC-CH is carbon nanotubes.

Application 2: Nanotubes

Size range from .8nm to >50nm diameter

- **Mechanical Properties:**
  Stiffest material in nature
- **Electrical Properties:**
  Ideal conductors, semiconductors, metals
- **Friction:** model system for basic science
- **NanoElectroMechanical Systems (NEMS)**
  Atomic scale gears
  Actuating devices



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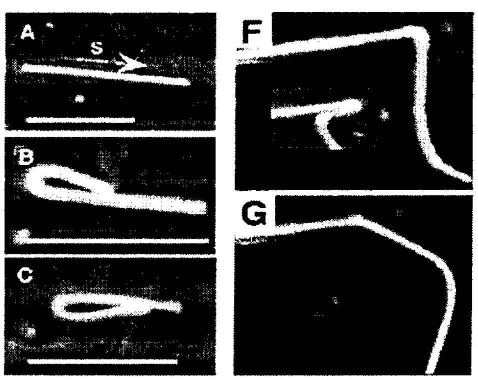
Nanotubes: Bending and Buckling

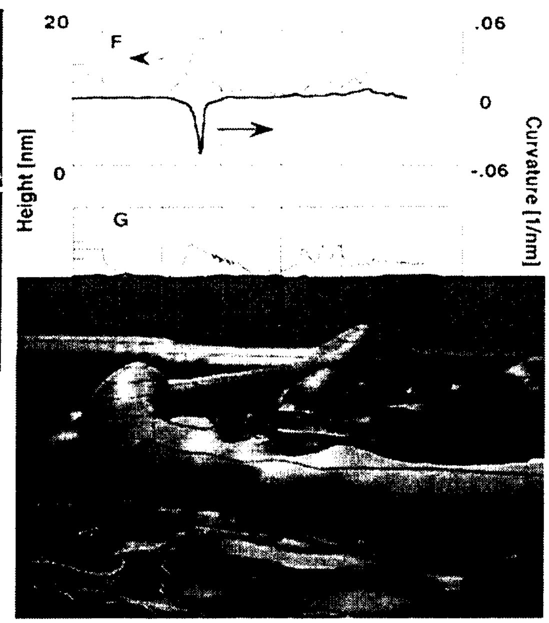
Using the NanoManipulator, it is easy to bend nanotubes. Researchers performed many manipulations of multi-wall carbon nanotubes and found that for small bends, the periodic ripples observed matched the behavior of a 1 cm aluminum tube, and of some theoretical simulations of single-wall tubes. They also found that small bends were completely reversible, but large bends or kinks caused a weak point that tended to kink again.

Falvo, M. R., Clary, G. J., Taylor II, R. M., Chi, V., Brooks Jr., F. P., Washburn, S. and Superfine, R, "Bending and Buckling of Carbon Nanotubes Under Large Strain," *Nature*, Vol. 389, No. 6651, Oct. 1997, pp. 582-584.

Nanotubes for Nanotechnology:

Reversible Bending/Buckling Through Manipulation





For small bends:
- Periodic buckles
- Reversible
- Move along tube according to bend

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Nanotubes: Slide or Roll?

Researchers also examined large multi-wall nanotubes on a graphite substrate. Most of the time, the nanotubes rotated in the plane of the substrate when pushed off-center. But in certain orientations, the tube required much more force to move, and it did not pivot. Instead, it maintained a specific orientation. The end of the tube pictured was originally thought to be an imaging artifact, but when the experiment file was later re-examined using the automatic lab notebook, they discovered that it was an indication that the tube was rolling. The periodic change in force also matched the circumference of the tube.

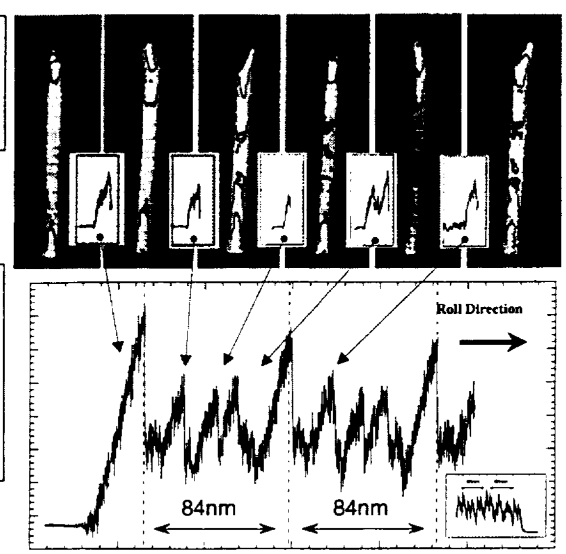
This is an example of a finding that might have been missed without the ability to re-analyze data.

Falvo, M., Taylor II, R. M., Helser, A., Chi, V., Brooks Jr., F. P., Washburn, S. and Superfine, R., "Rolling and Sliding on the Nanometer Scale," *Nature*, Vol. 397 , Jan. 1999, pp.236-238.

Push on a CNT: Slide, Rotate or Roll?

Results of AFM manipulation:
- Sliding with in-plane rotation
- Rolling!

How do we know it rolls?
- No in-plane rotation
- Tip end changes periodically
- Lateral force periodic with circumference of nanotube



Lateral Force

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Nanotubes: Graphite Lattice Interlocks

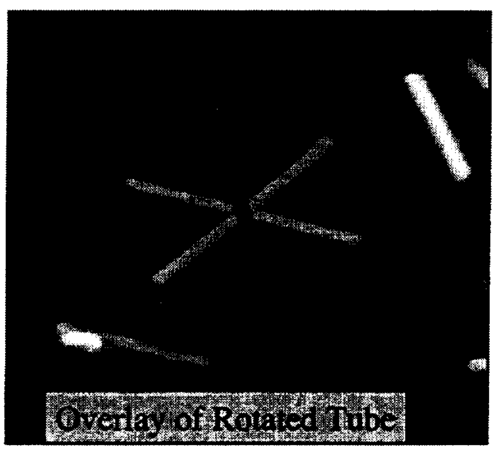
Further manipulations indicate that each tube locks in at three different orientations, 60 degrees apart, on a graphite substrate. This corresponds to the symmetry of the graphite lattice. The researchers also measured the increase in lateral force when the tube went into registry with the graphite lattice.

Falvo, M. R., Steele, J., Buldum, A., Schall, D., Taylor, R., Lu, J. P., Brenner, D. and Superfine, R., "Atomic Lattices Can Act Like Gears," *Nature* (submitted).

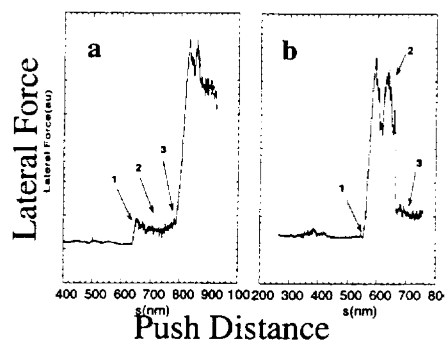
Nanotubes for Nanotechnology:

Manipulation Shows Energy Barriers for Rotation

AFM tip rotates tube to successive lock-in positions 60° apart



Atomic lattices interlocking - quantify the lateral force to rotate into and out of registry



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Nanotubes: Locking Orientations

Different tubes have different locking orientations. These tubes have different helicity, so when their lattices mesh with the graphite substrate, they have different orientations. Using the NanoManipulator, researchers could even roll one tube into the other and roll them both while the tubes maintained their orientations. This showed that the two tubes have different locking orientations on the same region of graphite.

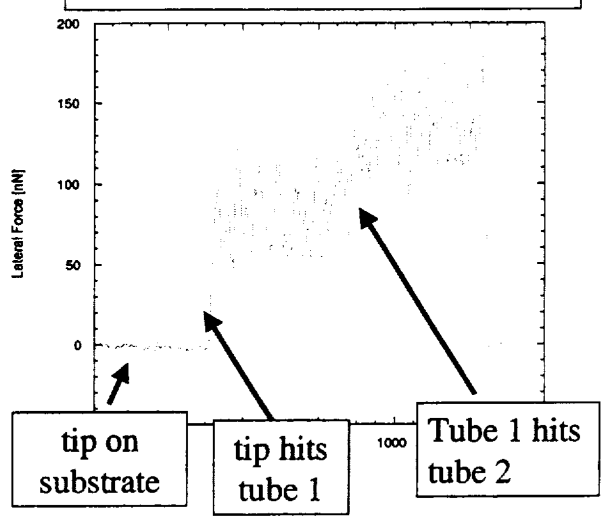
Scientists are still investigating why the force required to roll a tube in registry is much higher than the force to slide a tube which is not in registry.

Nanotubes for Nanotechnology:

Colliding Tubes Retain Their Locking Angles

- Different tubes
- Different registration
- Orientation maintained through collision

Lateral force measures collision



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Nanotubes: NEMS

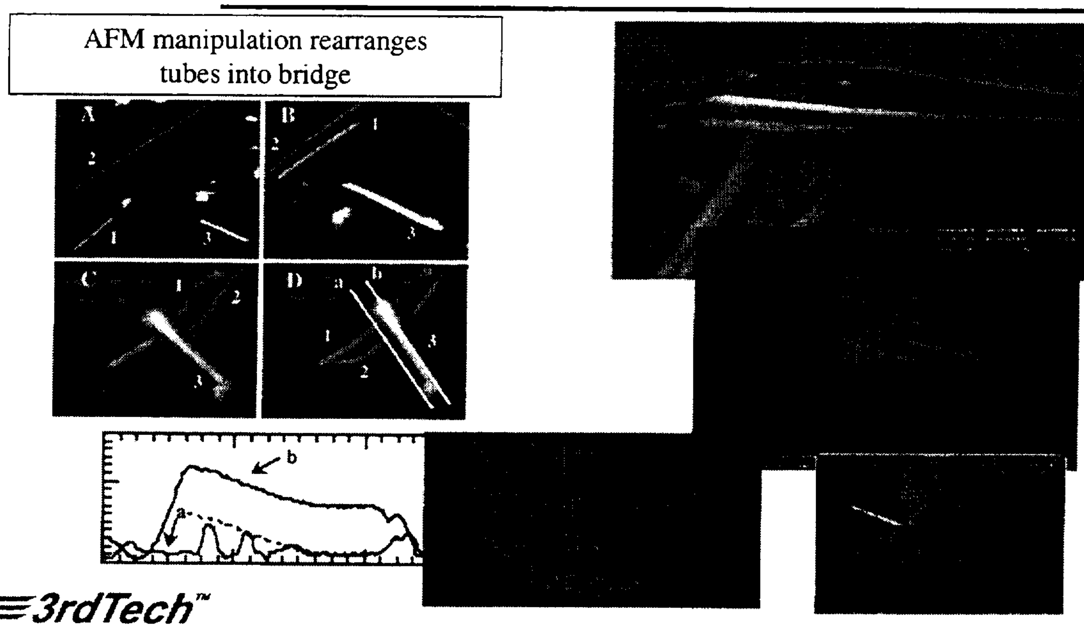
The UNC group has also experimented with arranging nanotubes to learn more in preparation for building nanotube structures. Here they push one tube on top of two others to form a bridge.

Nanotubes can also be manipulated and connected to electrical contacts for electromechanical devices consisting of one or multiple tubes.

Paulson, S., M. R. Falvo, N. Snider, A. Helser, T. Hudson, A. Seeger, R. M. Taylor, R. Superfine, and S. Washburn, "*In situ* Resistance Measurements of Strained Carbon Nanotubes," *Applied Physics Letters*, Vol. 75, No. 19, Nov. 1999, pp. 2936-2938.

Nanotubes for Nanotechnology:

Next Step: 3D Structures and NEMS Devices



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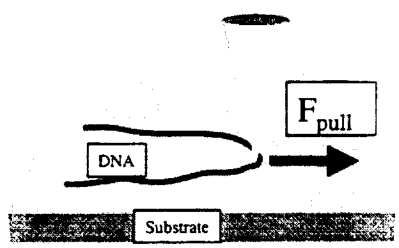
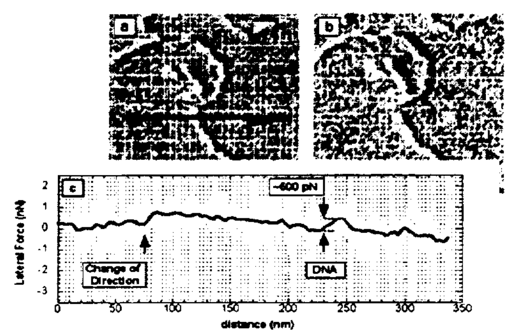
Application 3: DNA Manipulation

Here we have an example of a manipulation and a force measurement on a very small and delicate sample. The DNA is only a few nanometers high, and the lateral forces measured are very noisy. The average behavior of the force for this manipulation indicates a rupture force for the DNA of about 500 pico-Newtons.

Guthold, M., Matthews, W. G., Taylor, R. M., Erie, D., Brooks, F. P. and Superfine, R., "Quantitative Manipulation of DNA in Liquid with the NanoManipulator Scanning Force Microscope," *Biophysical Society 43rd Annual Meeting, Feb. 13-17, 1999, Baltimore, MD, Biophys. Journal, Vol.* 76, A351, 1999.

Application 3: DNA - Mechanical/Protein Interactions





Protein Nucleic Acid Complexes: High Resolution Imaging

DNA/Chromosome: Precision Selection and Dissection

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Application 4: Fibrin Manipulation

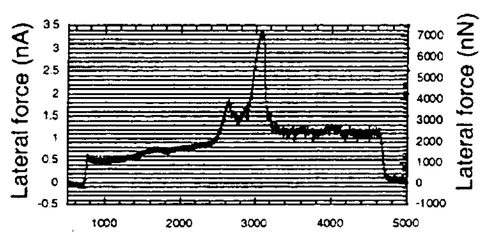
Fibrin is the fiber that forms when blood clots. The difference between fibrin from people with hemophilia, and from those without, can help scientists understand the disease. Researchers found that when a fiber is pushed with an AFM tip, it stretches and then ruptures. This particular manipulation shows that the fiber will also spring back towards its original position after the AFM tip passes.

Guthold, M., Falvo, M., Matthews, W. G., Paulson, S., Negishi, A., Washburn, S., Superfine, R., Brooks, F. P. and Taylor, R. M., "Investigation and Modification of Molecular Structures Using the NanoManipulator," *Journal of Mol. Graphics Mod.*, Vol. 17, 1999, pp. 187-197.

Application 4: Fibrin – Manipulation for Elasticity and Strength

•Diameter: ~ 180 nm

Lateral force measures:
- •Adhesion
- •Strength of fiber
- •Elastic properties



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Summary

The NanoManipulator combines 3D graphics, force-feedback, virtual tips and complete experiment recording to greatly increase the value of an SPM. The device has been used extensively by scientists at the University of North Carolina at Chapel Hill.

Now, with the commercialization of the NanoManipulator, scientists at other research centers and universities can have access to these same capabilities.

3rdTech, Inc. will be working with the researchers at UNC-CH on an ongoing basis – exchanging ideas and using their problems as driving problems for enhancing the NanoManipulator. 3rdTech will also be analyzing the needs of researchers in nanotechnology for the development of future interactive tools.

Summary

- The NanoManipulator System is a powerful new tool for research in nanotechnology
- It enables unique capabilities for SPMs
  - 3D visualization
  - Force-feedback
  - Record/replay/re-analyze
- Available commercially for the first time

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Further Information

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Further Information

- Come see, and feel, the NanoManipulator System.
- We are tool builders. What tools do you need?
- Company and product information:
  - http://www.3rdTech.com
- Previous research:
  - http://www.cs.unc.edu/Research/nano/
- Thanks: UNC-CH Physics and Computer Science for images and information.

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