Imaging a Biological Sample Using a Scanning Probe Microscope

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Scanning Probe Microscopy (SPM) has seen limited use in the field of biotechnology until recently due to problems arising from:

- ✓ Scanning under adverse conditions.
- ✓ Precise tip positioning.
- ✓ Extensive sample damage due to multiple scans.

The success of experiments such as the one described in this article have lead to the development of SPM instruments that address these and other issues, bringing nanoscale 3-dimensional imaging to the biological researcher.

In this experiment, fluorescently labeled polythene chromosomes acquired from a Drosophila salivary gland were absorbed to a glass slide. The slide was placed on a Zeiss Axiovert™ 35 inverted light microscope and the AFM was placed above the sample with the tip positioned in the center of the optical field (See Figure 1).

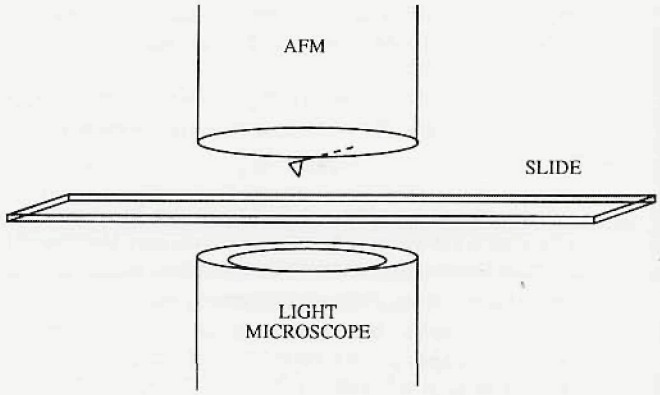


Figure 1

The inverted light microscope was used to position the AFM tip over a small cluster of chromosomes for AFM scanning. Due to the liquid environment, meniscus forces were eliminated and imaging could be done at much lower forces than when performed in ambient air.

A standard pyramidal AFM cantilever (200 micron cantilever arms, spring constant of .03 N/m) was used. As shown in Figure 2, the scanner configuration allowed simultaneous viewing of fully hydrated polythene chromosomes in the light microscope while imaging with the AFM without the use of an external fluid cell. Blue attenuator filters were used and all operations were performed at room temperature.

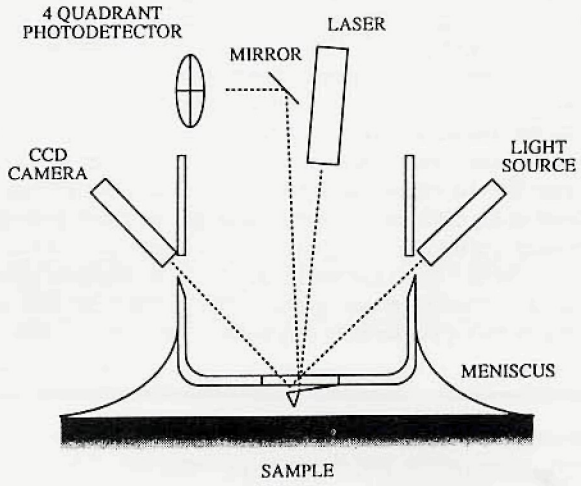
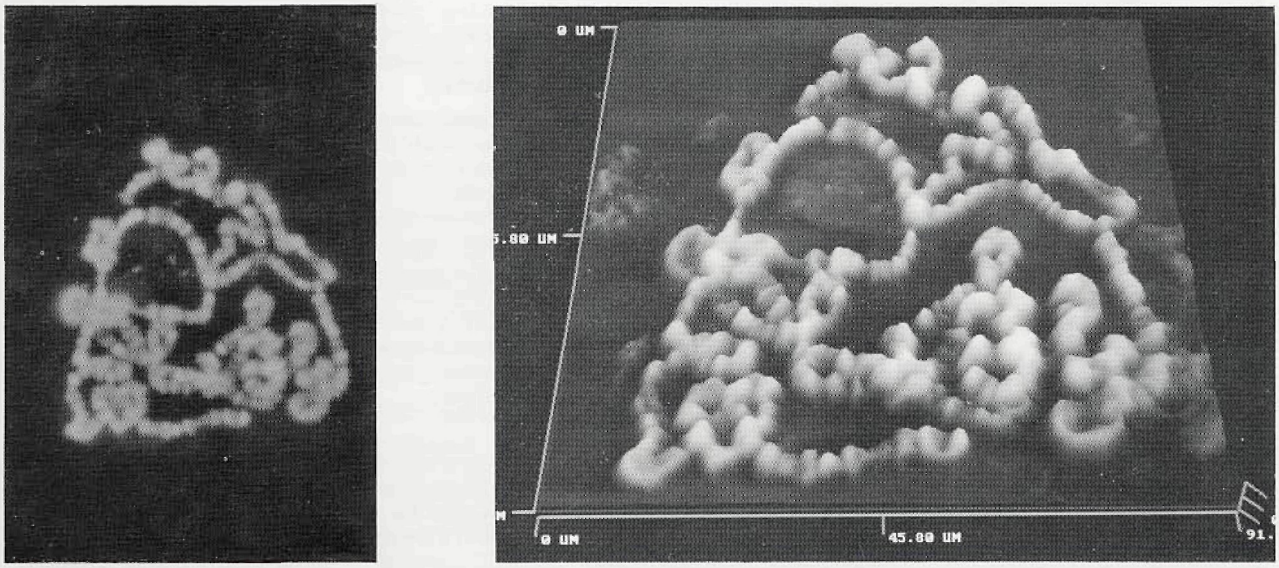


Figure 2

The light microscope allowed extremely accurate positioning of the AFM tip over the sample, which was then scanned in "contact" mode. A comparison of the light microscope image and AFM image in Figure 3 shows the data acquired using this technique. The chromosome bands and the fine structure of the interbands are clearly visible in three dimensions. Due to the unique abilities of the life sciences configuration of the TopoMetrix TMX 2000 Explorer™ SPM, lateral force, modulated force and non-contact images could be simultaneously obtained in a single scan.

The use of an inverted light microscope for sample location brings the AFM into the biotechnology laboratory, offering the entire continuum of tip modulation scanning techniques as well as conventional contact and lateral force imaging to the researcher. The ability to image under liquid allows AFM imaging of biological samples in a natural environment and allows the use of light forces, minimizing sample distortion. ■



Floursced Light Microscope Image

AFM Image

Figure 3

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