

# Nanomanipulation by Atomic Force Microscopy\*\*

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*The linking of our macroscopic world to the nanoscopic world of single molecules, nanoparticles and functional nanostructures is a technological challenge. Researchers in nanobiotechnology face the questions “How extract and analyze a single nano-object?”, “How to pick and place nano-objects?” and “How to prototype a functional nanostructure?”. Here, nanomanipulation by an atomic force microscope (AFM) in combination with optical manipulation by a microbeam laser offers a practicable solution. In such a system, the AFM can be operated as a nanorobot for manipulation purposes allowing for nanometer precision. A contact free manipulation is achieved by the laser microbeam.*

## 1. Introduction

Technologies to control and manipulate objects on the nanometer scale are thought to be key technologies for the upcoming decades or even century. The problems we are currently confronted with were already foreseen by Richard Feynman in 1959 as he described the challenges of small scale manufacturing in his famous and visionary talk ‘Plenty of Room at the Bottom’ at Caltech. Nearly fifty years later, there are two fundamental questions that are not yet fully answered: “How do we write small?” and “How do we manipulate and control things on a small scale?”. Science and technology have made tremendous progress in providing us with various methods to write on a small scale. Manipulating and controlling things on the nanometer scale, however, turned out to be far more difficult. Handling nanoscale objects includes finding these objects, tracking and moving them. Technologies are sought after that allow one to pick and place or cut and fuse in a completely alien environment. Thus, there are two important lines of investigation towards nanoscale manipulation: nanopatterning, where strategies are developed that allow us to generate arbitrary nanostructures, and nanotelerebotics, where the nanoworld is translated into a virtual reality that allows us to interact with smallest objects.

Current research towards nanopatterning includes nanostructured surface functionalization and directed self-assembly of nanoscale objects. Surface properties such as wettability, adhesion, friction and specific chemical interaction can be controlled with nanometer resolution.<sup>[1]</sup> Controlled positioning of particles, clusters or single molecules allows for the investigation of new chemical processes, predefined molecule interaction and the direct assembly of new chemical compounds.<sup>[2]</sup>

Although various nanomanipulation methods have been developed, systems based on scanning probe microscopes offer the most versatile approach.<sup>[3]</sup> Among the other instruments of the scanning probe microscope family the AFM has the widest range of application, both for imaging and for nanomanipulation. However, standard AFM systems are restricted to small working areas and operating speed efficiency is quite limited. To enhance and expand the capabilities of the AFM for manipulation we have developed a combined system. In this system, we conjoin an AFM for high resolution imaging and manipulation with video microscopy and non-contact ablation by a ultraviolet (UV) microbeam laser for large scale manipulation of biological specimen.<sup>[4]</sup> This laser ablation method relies on a locally restricted ablative photodecomposition process without heating.

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## 2. AFM as a Nanorobot

The main elements of an AFM are depicted in Figure 1a. The AFM probe consists of a high aspect ratio tip attached to the end of a micromachined cantilever. To obtain high-resolution images, the tip is brought into mechanical contact with the sample surface and the cantilever is deflected by the tip-sample loading forces. The deflection of the cantilever can be measured with high accuracy (about 0.1 Å), the lateral resolution is limited by tip radius to less than 1 nm depending on the imaging conditions. The relative position between probe and sample is adjusted by three orthogonal piezo actuators. A laser beam is focused on the cantilever and reflected onto a quadrant photodiode in order to detect the deflection. The electronic control unit reads the photo diode signal and runs a feedback loop to control the tip deflection. Data are transmitted to a personal computer for graphical representation of the sample surface.

Unfortunately, the performance of the open loop controlled piezo actuator is limited in an AFM. The dynamic response restricts the operation speed of the microscope and nonlinearities such as hysteresis and creep limit the position reproducibility. These issues severely affect the microscope's nanomanipulation performance. A straightforward solution to compensate for the nonlinearities is to operate the AFM in closed-loop in all three dimensions. However, this does not suppress the mechanical resonances of the actuator. Recently it was demonstrated that modern control feedback designs can dramatically increase the imaging speed of the AFM.<sup>[5]</sup> The operation of several cantilevers in parallel is another promising approach to increase the manipulation speed.<sup>[6]</sup>

A simple and straightforward manipulation procedure includes the localisation and imaging of the area of interest, followed by the 'blind' feed-forward execution of the manipulation task as defined by the user. Finally, success or failure of the manipulation is determined by re-imaging the manipulated area. However, this procedure has some drawbacks. First, the state of the system may change during the manipulation process, mainly due to drift processes. Secondly, due to the strong non-linearities dominating the tip-sample interaction it is difficult to know *a priori* the manipulation results. Frequently, time-consuming trial-and-error experiments are required. Different elements of virtual reality can assist the human user to explore and manipulate nanoscale objects.

Haptic interfaces that generate a feed back of the tip-sample forces provide the user with a "feeling" for surface structure and forces during the manipulation process.<sup>[7-9]</sup> Entire synthetic worlds facilitate the orientation within the nanoworld.<sup>[10]</sup>

## 3. Nanoscale Modification Methods by AFM

Several methods have been proposed for the local modification of surfaces by AFM. One powerful patterning strategy is local anodic oxidation. The local growth of an oxide layer is induced by the application of an electric current between tip and sample surface. Under ambient conditions, the water meniscus acts as an electrolyte. Electronic devices such as nanowires, metal-oxide field effect transistors (MOSFET), single-electron transistors and quantum point contacts have been fabricated.<sup>[3]</sup> The control of the growth direction of organic molecule monolayers with conducting properties is a basic issue for the development of molecular electronics devices that could be solved using a silicon oxide template fabricated by means of local anodic oxidation.<sup>[11]</sup>

Chemical surface modification by AFM nanolithography can be achieved by adding molecules to the surface, e.g. by dip pen nanolithography,<sup>[12]</sup> or by substitution of surface components. In substitution lithography (nanografting and nanoshaving), self-assembled monolayers are removed by means of mechanical desorption by the AFM tip followed by in-situ replacement of a second component.<sup>[13]</sup>

Another prominent example for AFM nanomanipulation is mechanical nanomachining.<sup>[14]</sup> In this manipulation mode the loading force is increased beyond the limit for plastic deformation of the material. The main parameters influencing the machining process are the applied normal force and the patterning speed. For a better control of the machining process, the machining force can be modulated in the so-called dynamic plowing lithography.<sup>[15]</sup> AFM nanomachining was demonstrated on a wide variety of materials including metals,<sup>[16]</sup> semiconductors,<sup>[17]</sup> polymers,<sup>[18]</sup> and biomaterials.<sup>[19]</sup> Selective removal of superficial layers to study the internal structure of biological specimens has been achieved revealing the internal structure of collagen<sup>[20]</sup> or a bacterial cell wall.<sup>[21]</sup> Mechanical nanomanipulation was also used to extract small amounts of DNA from human metaphase chromosomes.<sup>[22]</sup>

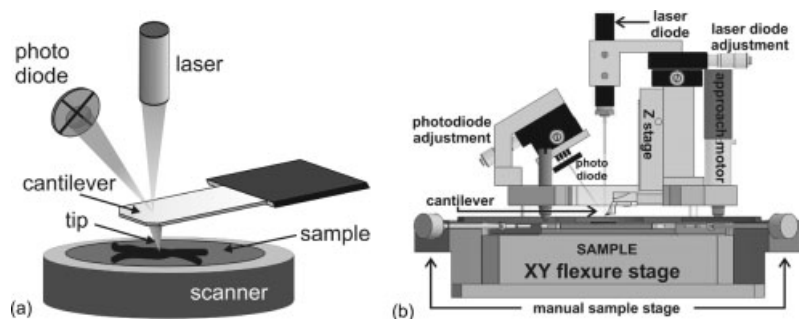


Fig. 1. (a) Scheme of an atomic force microscope (AFM). The sample is raster scanned and a small nanotip probes the sample surface. A light lever detection scheme is used to measure the deflection of the cantilever due to the surface topography. (b) Actual design of the AFM system placed on top of an inverted optical microscope.



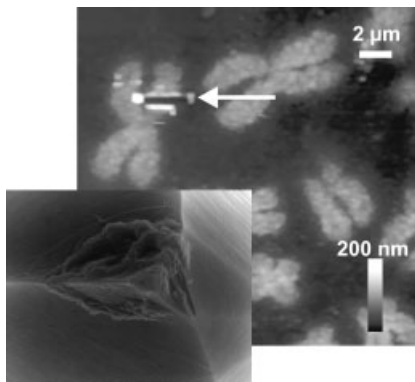


Fig. 4. Topographic AFM image showing the dissection of a single chromatid of a human metaphase chromosome (arrow). The insert shows a scanning electron microscope image of an AFM tip after manipulation on a human metaphase chromosome. Biomaterial adhered to the tip and could be used for subsequent biochemical analysis.

chromosome on the right was successfully dissected into seven different pieces. The minimal cut width (full-width-at-half-maximum-height) was 380 nm. The smallest isolated chromosomal piece had a width of 420 nm corresponding to a volume of approximately  $0.2 \mu\text{m}^3$ . This remaining isolated volume contains about 4000 DNA base pairs. The cut depth achieved by mechanical dissection depends on the applied loading force. The first two attempts did not completely dissect the chromosome. The third cut completely dissected the chromosome yielding a cut width of 280 nm. The dimensions of the cut correspond to the mechanical dimensions of the AFM tip. In the AFM image of Figure 4, a single cut was performed on a human metaphase chromosome by means of AFM dissection;<sup>[19]</sup> the cut was so precise that only one chromatid of the chromosome was dissected. After AFM dissection of chromosomes, usually some biomaterial adheres to the tip (inset of Fig. 4). DNA thus extracted by AFM nanomanipulation experiments has been biochemically analyzed by means of a degenerate oligonucleotide-primed polymerase chain reaction.<sup>[22]</sup> Thus, mechanical dissection of chromosomes by an AFM tip represents a straightforward method to generate genetic probes.

**Conclusions:** Nanomanipulation by atomic force microscopy provides a versatile technology for nanopatterning and nanomanipulation. For the extraction of DNA from human metaphase chromosomes an instrument that combines AFM nanomanipulation with UV laser surgery proved to be of high value. This experiment demonstrates that especially for applications in nanobiotechnology nanomanipulation devices are needed to provide additional feedback to the user. Haptic interfaces or even an entire virtual world help the human operator to explore and manipulate objects in an environment that is very distant in scale. Future developments in nanorobotics will certainly facilitate to bridge this distance leading to a deeper understanding of the nanocosmos.

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