Force Feedback Joystick as a low cost haptic interface for an atomic force microscopy nanomanipulator

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Abstract. In order to manipulate material at the nanometer scale new methods and devices have to be developed. A nanomanipulator interface was designed and implemented into a commercial atomic force microscope (AFM) system. With the aid of a positioning joystick, direct positioning of the AFM probe with nanometer precision is possible. A commercial force feedback joystick serves as haptic interface and provides the user with real-time feeling of the tip-sample interactions. Due to the open design the manipulator interface can be used with other microscopes of the SPM family using tip-sample interactions like tunnelling current, interatomic magnetic force or electrostatic forces as haptic feedback signal. In addition, the nanomanipulator and a 337 nm nitrogen UV-laser microbeam for photoablation were combined on an inverted optical microscope. To test the nanomanipulator, human metaphase chromosomes were dissected using both techniques, photoablation and mechanical AFM manipulation. The experimental results show that by combining both methods biological material can be manipulated on different size scales in one integrated instrument. The effects of manipulation on human metaphase chromosome were studied in detail by atomic force microscopy. Sub-400-nm cuts were achieved by photonic ablation. Chromosomal fragments of a size less than of 500 nm could be isolated. By means of mechanical microdissection different cut size ranging from 80 nm to 500 nm can be easily obtained applying different load forces.

Much research has been performed regarding the application of scanned probe microscopes (SPM) [1] in the field of material processing taking advantage of its high-resolution and alignment accuracy. Examples range from semiconductor processing [2] and polymer modifications [3] to microdissection of biological specimens [4], where SPM techniques are used for surface structuring, to name only a few. By indenting the tip of an atomic-force microscope (AFM) onto the sample, patterning below the light diffraction limit can be realized [5]. Only the mechanical dimensions of the AFM tip restrict the width of the patterns. However, standard AFM systems are designed to obtain high-resolution images and their application to material processing is difficult without modifications of the standard AFM instrumentation. The integration of haptic interfaces into AFM control systems helps to overcome these limitations and allows for an intuitive nanomanipulation as it was successfully demonstrated earlier [6] [7]. With the aid of a haptic interface real-time control of the tip-sample interaction by the user is possible. Recently, force feedback devices have jumped from the academic and military research to the entertainment industry [8]. These devices add realism to video games. Thus, a great range of force feedback devices is available at low cost offering high sensitivity performance and easy to program developer tools. A commercial force feedback joystick (FFJ), originally designed for computer games, is appropriate to transmit the tip-sample interaction directly in the hand of the user.

Physical dissection of metaphase chromosomes is a straightforward approach for the isolation of DNA sequences from specific chromosome regions. The dissected material can be used for various applications including the generation of probes for fluorescence *in situ* hybridisation (FISH), physical mapping for cytogenetic analysis[9] and the generation of chromosome band-specific libraries [10]. The AFM has recently been proposed as microdissection tool for the generation of genetic probes [11] [12] since it provides higher precision for the dissection of the region of interest and subsequent nanoextraction of DNA material as compared to other techniques. Due to the irregular shape of chromosomes, it is convenient for the user to have a real-time feedback when the AFM is used for manipulation.

Laser ablation is another powerful tool in micro patterning. Laser techniques are suitable for hard, brittle and heat-sensitive materials [13]. Pulsed ultraviolet lasers have been applied for ablation of biological samples due to their precision (±2000 Å) with which the depth of the cut can be controlled as well as the lack of thermal damage[14] [15]. “Non-contact” isolation of DNA by laser micromanipulation was successfully demonstrated earlier [16].

The aim of this work was the development and test of a nanomanipulator stage that combines light microscopy, AFM and UV-micro laser beam ablation in a single instrumentation system (Figure 1). The AFM was modified in order to use it as a tool for nanomanipulation. For imaging, the standard commercial AFM system was used. For manipulation, a specific system was developed. During manipulation, the user takes control of the AFM tip using a positioning joystick. A commercial force feedback joystick (FFJ) is used as a low-cost haptic interface that transmits the forces at the AFM tip to the user. In this paper we present the nanomanipulator design, the experimental set-up and its experimental test with human metaphase chromosomes. Chromosome regions can be isolated by means of photonic ablation as well as by mechanical microdissection controlling the system with the joysticks. The results of the manipulation are analysed *in situ* by AFM directly after manipulation.

1 Nanomanipulator

1.1 Hardware

The commercial AFM electronics and software for high-resolution imaging is based on a digital signal processor (DSP) universal SPM control system (Nanotec electronica, Madrid, Spain) [17], which generates the scanning waveform and processes the topographic data. A system of piezoelectric actuators attached to the sample holder (Triple O GmbH, Postdam, Germany) manage the scanning motion of the sample. Two piezo-elements that are in plane with the sample generate the movement in the X and Y direction. Three coupled piezo-elements in the direction perpendicular to the sample plane, (Z direction), adjust the probe-to-sample distance. The system has nanometer positioning capability of the sample in 100 µm range in the planar coordinates and 30 µm in the vertical. The scanning stage is placed on an inverted light microscope (Zeiss Axiovert 100S, Göttingen, Germany) that is equipped with a high-resolution CCD camera for visual control. The AFM head, based on the bouncing beam detection method [18], is placed on top.

An UV microbeam laser (P.A.L.M. Mikrolaser Technology GmbH, Bernried, Germany) is focused on the sample through the microscope objective using the fluorescence path by reflection from two high power beam splitters. A high power nitrogen laser with laser output of 337 nm , pulse width (FWHM) of 3 ns, pulse repetition rate between 0 and 60 Hz and maximum pulse energy of 300 µJ was used.

1.2 Manipulation system

The manipulation system (Fig. 1) generates the waveform necessary to take control of the previously described piezoelectric actuators. A 600 MHz Pentium PC running under Windows 98 generates the manipulation waveform using a DSP module (ADwin-Gold Jäger Computergesteuerte Meßtechnik GmbH, Lorsch, Germany) by reading the input of the joystick and the user interaction through a Graphical User Interface (GUI). It also sets the force at the FFJ.

An electronic switch couples the manipulation signal to the AFM hardware. In the electronic switch, the scanning waveform is fed into a sample and hold (S/H) stage controlled by a logic input. After the S/H stage, the scanning waveform is summed to the manipulation waveform. The logic input switches the signal controlling the piezoelectric actuators between imaging mode, when the scanning waveform is being sampled, and manipulation mode, when the scanning waveform is held.

For horizontal positioning of the sample, a precise two-axis joystick with auto-center spring was employed. The main program retrieves the joystick data and increments the corresponding voltage in the manipulation waveform every 10 ms. Thus, the sample is moved in the X and Y direction with a velocity proportional to the position of the joystick in each axis relative to its center. The maximal speed on each direction was set to 20 nm/s.

For vertical positioning of the sample a hat switch at the top of the FFJ is used. The conversion of the data retrieved by the joystick and the movement of the scanning stage in the Z direction is analog as in the positioning joystick.

The FFJ implemented in the system was a *Wingman Force* of Logitech. In the *Wingman*, a system of motors and magnetic coils communicates forces to the user hand. Using DirectX®, Microsoft programming interface designed to develop computer games, an interface was developed, which produces a force along the vertical axis of the FFJ. The magnitude and direction of the force can be changed with an acquisition time of 1 ms giving a real-time interactive signal to the user. To use the FFJ as a haptic interface between the AFM tip and the user, an interactive signal is A/D converted from the AFM electronics, scaled by the manipulator control system and returned in the FFJ. Therefore, the user feels a force proportional to the interactive signal. The delay between the returned force and the interactive signal is less than 2 ms. Two interactive signals can be given to the user through the FFJ:

- **Topography signal as interactive signal:**

  To give a real-time 3D feedback, the topography signal from the AFM is fed to the FFJ. The user “feels” a force proportional to the height of the sample point interacting with the AFM tip. The topography signal from the AFM electronics is pre-processed in the DSP and then scaled to perform the appropriate response on the FFJ. The topography signal can be used as an interactive signal as long as the proportional-integral (PI) loop of the AFM control system is working. The force set at the FFJ is proportional to the height of the sample. This proportionality is set in the GUI by the user in order to scale the increment of the height to the range of the feedback force.

- **Cantilever deflection as interactive signal:**

  The normal force output from the AFM electronics, which is proportional to the normal deflection of the cantilever, can also be used as haptic signal. If the AFM system works in contact or tapping mode, the PI loop of the AFM control keeps the tip-sample force constant. Therefore, the PI loop has to be disconnected in order to provide full interaction to the user. During manipulation, the use of the normal force as interactive signal is quite appropriate. The force set at the FFJ is proportional to the photodiode signal. This proportionality is set in the GUI by the user in order to scale the photodiode signal to the range of the feedback force. This adjustment depends on the characteristics of the cantilever, sample properties and loading forces onto the sample.

The GUI was programmed using Visual C++ to allow the control of the whole system by the user. A cartesian graphic displays the position of the AFM tip on the sample and its velocity at every moment. A set of buttons allows the user to switch between manipulation and imaging mode. The manipulation can be arranged in manual mode, using the joysticks, or in automatic mode, tracing lines at a given angle and velocity.

1.3 System overview

The whole system and its data flow are schematically shown in Figure. The AFM computer generates X_s, Y_s and Z_s and processes the scanning information (F_N). The AFM electronics converts the input waveform (X_f, Y_f, Z_f) into a suitable signal (X,Y,Z) for controlling the piezoelectric actuators and amplifies the photodiode signal (f_n). The manipulation computer converts the input from the positioning joystick (V_x and V_y) and the FFJ (V_z) into analog signals and generates the waveform for manipulation (X_m, Y_m, Z_m). The computer also sets the returned force in the FFJ by D/A conversion of the interactive signal (F_n or Z_f) and manages the GUI. The DSP controls the communication process with the AFM system. The electronic switch allows imaging as well as direct control of the piezoelectric actuators by switching between a scanning signal and a manipulation signal as response to the logic signal (U_l)

2 Experimental results and discussion

2.1 UV laser ablation

Human metaphase chromosomes were prepared following standard protocols [12]. Spreads of chromosomes were easily located using the light microscope with a 10x achromat long distance objective. An AFM tip (0.17-0.45 N/m nominal force constant Nanosensors, Wetzlar, Germany) was placed on the spread and a high-resolution AFM image was taken in contact mode. Using the AFM image and considering the size of the chromosome and the centromer position, the chromosome number 2 in the standard classification of human metaphase chromosomes [19] was selected for photonic ablation. A 100x 1.20 Glyc Ultrafluar oil immersion objective was selected for photonic ablation. The sample was moved using the positioning joystick to place the UV laser focus at the beginning of each cut using the optical feedback of the CCD camera. Then, the automatic line tracing option on the GUI was selected and the laser was shot. Thus, six cuts with a fixed microdissection velocity of 0.3 µm/s, pulse energy of 0.68 µJ and pulse repetition rate of 60 Hz were realized. Immediately after the dissection, the chromosome was imaged by contact AFM. Figure 3 shows a 3D representation of the AFM image containing three of the cuts and its cross sectional analysis. The cross sectional profile reveals a full-width-at-maximum–height (FWHM) of about 360 nm for the microdissections. Chromosomal fragments of around 450 nm were isolated.

However, the width of the cuts is underestimated and the size of the isolated fragment is overestimated due to the so-called tip convolution [20] [21]. Assuming a tip radius of around 20 nm the measured size can be considered correct within an error margin of 5%.

2.2 User guided mechanical dissection and nanoextraction

Next, a chromosome was mechanically dissected using a stiff cantilever and the manipulation interface. The cantilever (Nanosensors, Wetzlar, Germany) was calibrated using the method of Sader et al [22] yielding a spring constant of 59 N/m ± 5 N/m.. Tapping mode AFM was performed on a chromosome spread and the scan size was reduced to the selected chromosome. Manipulation mode was chosen in the GUI. Two cuts in opposite directions were made using the positioning joystick for sample positioning, and the FFJ for adjustment of the loading force. The user obtained an interactive feedback of the applied force through the FFJ. An average loading forces between 70 and 75 µN was applied for dissection. During the cutting process the cantilever was excited at its resonant frequency (360 kHz). After dissection, the cantilever was collected to further process the adhering DNA (nanoextraction). In order to obtain reliable metrological data of the arranged manipulation a fresh cantilever was used subsequently in tapping mode to image the manipulated chromosome (Figure 4a). Cross sectional analysis reveals the width and height of the cuts on both chromosomes (Figure 4b). In the AFM image of Figure 4 a progressively increased cut width within the direction of the cuts can be observed. A considerable amount of debris is accumulated at the ends of the cuts. The chromosome was totally microdissected and a chromosomal fragment was extracted.

3 Conclusions

Light microscopy, high-resolution imaging and nanometer precise sample positioning have been combined to achieve photonic ablation, mechanical manipulation and extraction of minimal samples. UV laser ablation can be easily achieved, using optical feedback and a friendly user interface. Mechanical manipulation below light diffraction limit was performed using a low-cost but highly intuitive haptic interface. In situ characterization of the cuts was directly performed.

The UV laser microdissection of metaphase chromosomes with this new experimental set-up yield a better cut resolution as compared to previous work [16]. Usually, systems for laser ablation move the sample using a system of stepper motors. The use of the piezo actuators to focus and move the sample during laser ablation optimizes the laser focusing and the energy deposited by the laser on the sample minimizing thermal effects.

Using the joysticks allows the user to easily manipulate specimens at a scale below the light diffraction limit. The FFJ intuitively indicates the user the applied force during mechanical manipulations. The force applied during mechanical microdissection plays a great role in the morphology of the produced cut. Different cut size can be obtained by mechanical dissection using the nanomanipulator by applying different load forces during microdissection. Thus, the force can be optimized for each sample to be manipulated.

Due to its open architecture, the manipulation control can be used with practically any commercial AFM system. With little modification it can be used also with other SPMs. Its application with the STM would facilitate the direct manipulation on molecules. Moreover, the haptic nanomanipulator can contribute in the future to develop minute tissue manipulation down to the field of molecular surgery, where a precise control of μm to nm movements should be complemented by the direct feedback feeling for the operator. In this way nanomanipulation and nanoextraction, as demonstrated recently for DNA by Thalhammer et al [11] becomes more reliable.

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Figures captions

Figure 1: Scheme of the experimental set-up.

Figure 2: Data-flow of the nanomanipulator system**.**

Figure 3: Close up of a human metaphase chromosome after UV laser ablation imaged by contact mode AFM. (a) 3D-representation showing three cuts. Two regions of the chromosome were isolated and remained intact after ablation. The line indicates the position of the cross section. (b) Cross sectional analysis reveals a cut widths (full-width-at-maximum–height) of 360 nm to 540 nm**.**

Figure 4: Human metaphase chromosome after mechanical microdissection imaged by tapping mode AFM. (a) Two cuts in opposite directions (arrows) were set at high loading forces using the FFJ (approximately 70 and 75 µN). White upheavals in the image corresponds to debris massively formed during microdissection. The chromosome appears with low contrast with respect to the background because of its low height difference to the accumulated debris. (b) Cross sectional analysis at the middle of the dissections revealing cut widths of 200 nm and 500 nm.

Figures

Figure 1

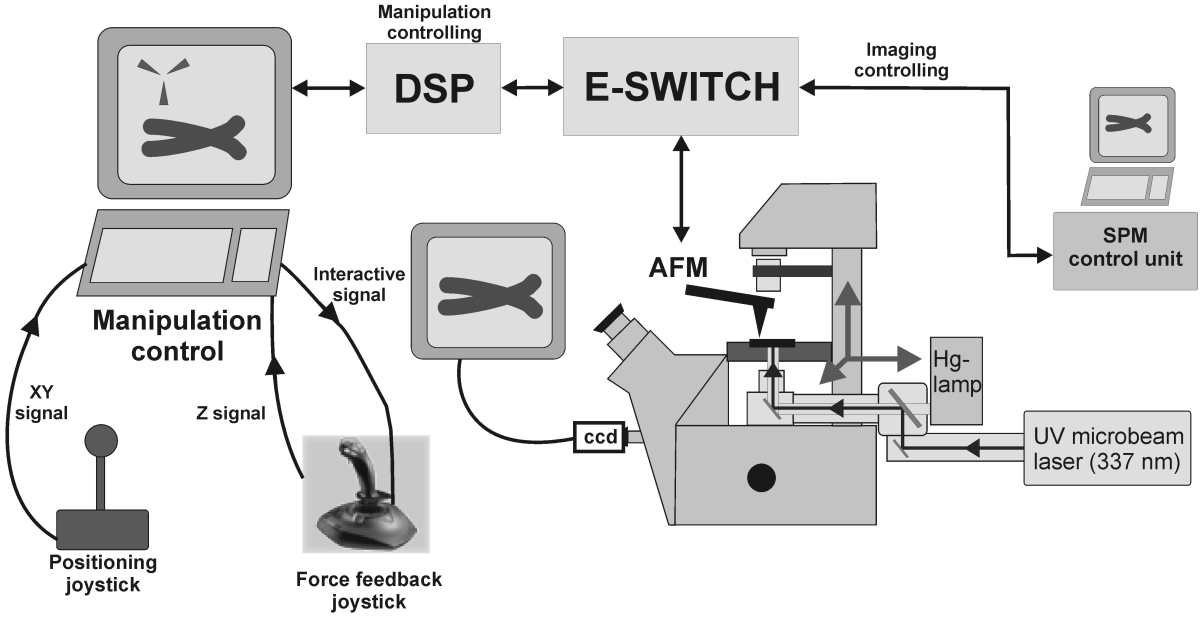

Figure 2

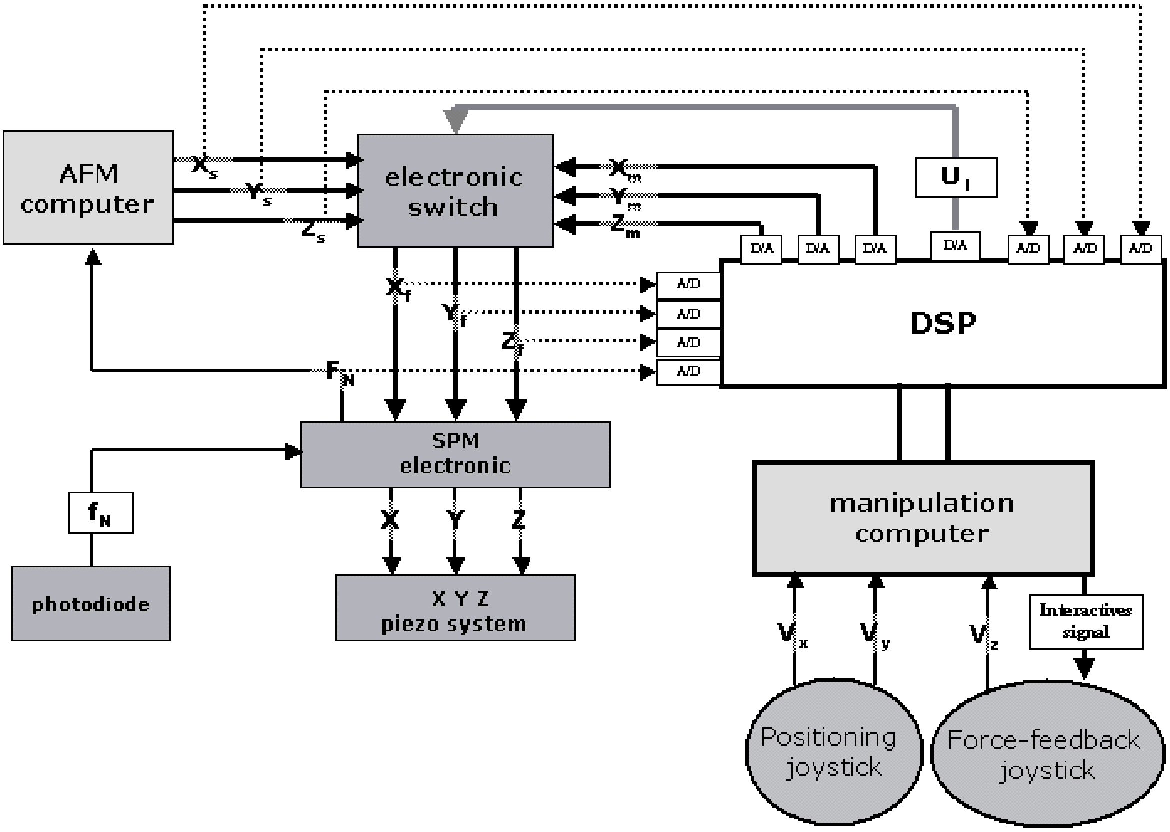
AFM computer
electronic switch
X_s
Y_s
Z_s
X_m
Y_m
Z_m
U_I
D/A
D/A
D/A
D/A
A/D
A/D
A/D
X_f
Y_f
Z_f
F_N
A/D
A/D
A/D
A/D
DSP
SPM electronic
f_N
photodiode
X
Y
Z
X Y Z piezo system
manipulation computer
V_x
V_y
V_z
Interactives signal
Positioning joystick
Force-feedback joystick

Figure 3

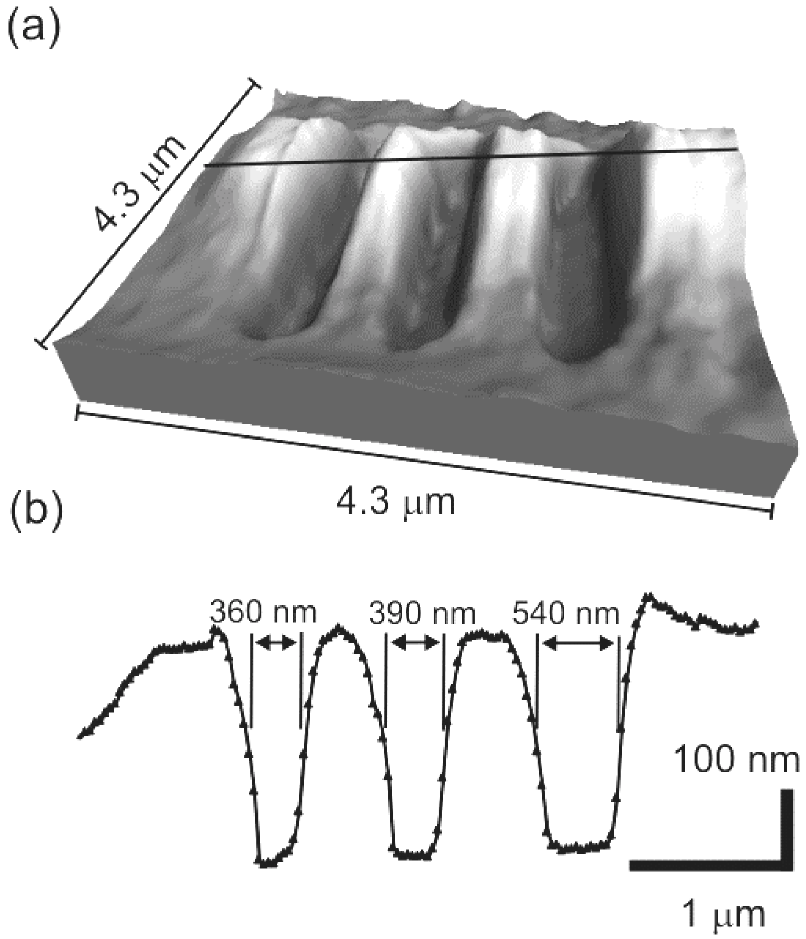

Figure 4