The development of the Tweezers Nanoprobe Microscope

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Introduction

Technology to manipulate and measure at the nanometre scale is a fundamental requirement to stimulate the new era of single molecule research in the areas of material science, biology and medicine. In response to this, the Central Laser Facility in partnership with the Technology Department, the Central Microstructure Facility, the Medical Research Council (MRC) and Oxford University are developing the Tweezers Nanoprobe Microscope, funded through the STFC Technology Partnership programme. The project builds upon STFC's strengths in the areas of the optical tweezers, instrumentation and micro-structure fabrication.

The Tweezers Nanoprobe concept is to use optical tweezers to control a free floating needle-like probe. This will utilise the dexterity and finesse of the optical tweezers technique to measure forces at the pico-Newton level and for the first time provide a practical instrument capable of nanometre resolution of a nanometre scale probe.

The project has two key areas of innovation. The first uses custom-made, high-speed sensor and processing electronics to make dynamic measurements and adjustments to the position of the probe. This will provide dynamic force measurement at the probe tip. The electronics development is in collaboration with the Technology Department and the prototype is funded through the STFC Centre for Instrumentation [1] and the MI3 Basic Technology Programme [2].

The second, the nanoprobe concept, is a novel microstructure built by the Central Microstructure Facility (CMF). Uniquely, the nanoprobe has its force-sensitive tip outside the optical trapping fields. This means that the optical trapping beams do not interfere with the probe, reducing the risk of damage to the sample under study and disruption of the traps.

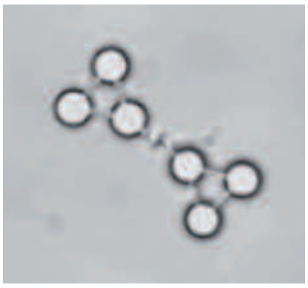

Figure 1. A Pair of Tweezers Nanoprobes held in Optical Traps.

The nanoprobe concept offers a potential breakthrough in nanoscale force-probe and imaging applications. The instrument aims to meet the requirements of life science researchers who seek to perform investigations at the molecular level to unravel the complex and dynamic properties of biomolecules that govern machinery within biological processes. Also, the instrument will be used for experiments in measuring the interaction between enzymes and DNA strands, aperture-less near-field microscopy and surface characterisation.

Optical Trapping

Optical trapping provides a powerful and dynamic method of manipulating multiple microscopic objects. However when the trapped objects are in solution, they are constantly subject to collisions with other particles undergoing Brownian motion. These collisions reduce the sensitivity of the trapped objects to the small displacements and forces that occur in single-molecule experiments. We propose to remove these unwanted movements by using a closed loop control system (see Figure 2) that will respond at high speed (10 kHz). The final instrument will enable feedback control of up to 6 objects in six independent optical traps using closed-loop feedback.

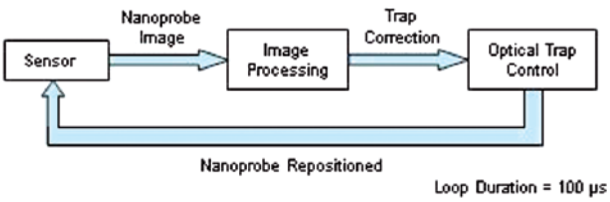

Figure 2. Closed Loop Control System.

Nanoprobe Design and Fabrication

Figure 3 shows an example of a probe, which consists of a transparent structure of several beads and a needle-tip. In this prototype, the tip is made from gold and has a tip approximately 50 nm wide.

The CMF uses production techniques such as electron beam lithography and chemical vapour deposition that allow thousands of repeatable and adaptable structures to be made. The triangular micro-structure is controlled with three separate optical traps.

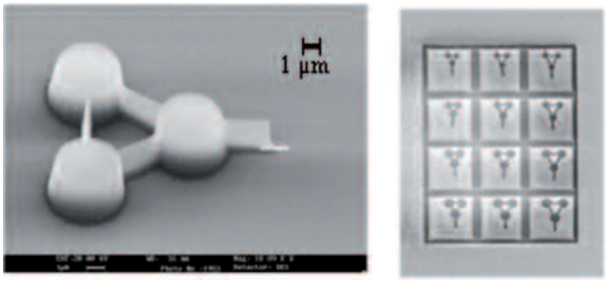

Figure 3. Scanning Electron Microscope Image of Prototype Nanoprobe (L) and Wafer-batch of Nanoprobes (R).

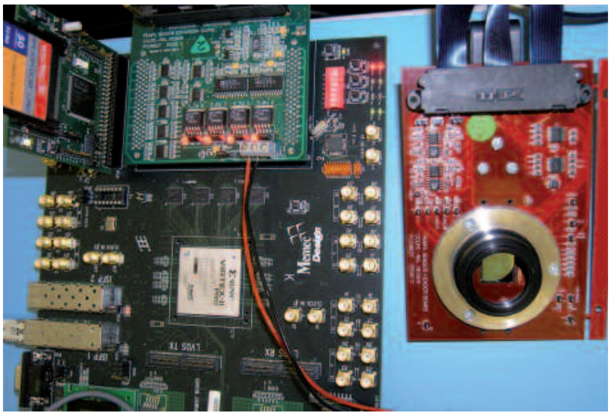

Figure 5. Photograph of FPGA Development Board (L) and Vanilla Sensor (R).

Vanilla Sensor

The position of the trapped objects will be measured using the Vanilla Monolithic Active Pixel Sensor (MAPS). Findings from previous collaborative experiments[1] between Lasers for Science Facility and the Technology Department were used in specifying the performance of this sensor. The sensor array consists of 520 × 520 pixels, each pixel having a dynamic range of 12 bits. Regions of Interest (ROIs) consisting of 36 pixels, will be read out from the sensor at high speed (20 kHz) with low noise (<2 bit noise per pixel). An example image of an optically trapped, 2 micron diameter bead is shown in figure 4. This image is from a stream of images acquired at >20 kHz.

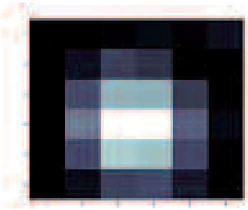

Figure 4. ROI Image of trapped bead.

Optical Trap Control

A single laser beam will be repositioned rapidly at 60 kHz using an Acousto-Optic Deflector (AOD) to produce 6 independent optical traps on a two-dimensional plane. An Electro-Optic Modulator will allow the traps to be moved by around one micron orthogonally to the plane, creating 3D control of the probe.

Processing, Readout and Control Electronics

The instrument will use dedicated electronics in the form of a Field Programmable Gate Array (FPGA) to control the readout of the Vanilla sensor, to reposition the optical traps and to implement the closed loop control. FPGAs are used widely in STFC for readout and control applications. They consist of reconfigurable electronic circuit elements that can be designed to carry out complex mathematical and control functions at high speed (10 – 100s MHz), which can outperform PC-based systems. As such, extensive electronic engineering skills are required to use the FPGA effectively.

Development Progress

An optical system has been setup in the Tweezers Nanoprobe lab which can optically trap and move microscopic objects. The Nanoprobes produced by the CMF have been successfully released from Silicon wafer into solution, and optically trapped.

The Vanilla sensor was delivered to the LSF by the Technology Department in June 2006. Single ROI images have been read out from the Vanilla sensor at approximately 20 kHz. These ROI images have been used in developing image processing algorithms in Matlab software. Initial results from these algorithms indicate that the position of a trapped sphere can be measured to within 5 nm.

The Technology Department has continued work on the multiple ROI, high speed readout system, which is now approaching completion.

A control system to drive the AOD has been produced, which consists of a commercial AOD system and an FPGA with a custom-designed control interface to allow dynamic repositioning of the optical traps at up to 60 kHz via PC (for experimental setup) or via FPGA (for closed-loop control). This work was particularly difficult to complete as this was the first time that the commercial AOD system had been controlled by an FPGA. Importantly, the fast working speed at which the FPGA controls the AOD-laser repositioning system is fundamental to the operation of the instrument.

The instrument with 2D nanoprobe control is on schedule to be completed in November 2007. The first experiments such as Aperture-less Near Field Microscopy and Restriction Enzyme-DNA interaction will commence shortly afterwards. Further work to allow 3D nanoprobe control will be completed before the project ends in November 2008.

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References

1. *"The Development of a MAPS Detector for Fast Position Detection on the Optical Tweezers Apparatus",* A. D.Ward et al, Central Laser Facility Annual Report 2003/4, pgs 188-189.
2. MI3 Consortium Website http://www.shef.ac.uk/eee/research/vie/research/mi3.html