Surface Patterning using Attoliter Deposition by AFM Probes

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Surface patterning with different biological molecules is one of the critical steps in the complex procedure of combinatorial biochemical analysis used e.g. in proteomics or in diagnostics. High-density bioarrays can reduce the analysis time. The tiny dot pitches allow to diminish the array size and so the diffusion time, or to place more targets onto one surface. One approach to dispensing such high-density arrays is to use the sharp tip of an atomic force microscope (AFM) probe like a fountain pen, which, when combined with the nanometric resolution of the AFM scanner, permits the deposition of small droplets with a high positioning accuracy [1].

A commercially available AFM probe made of silicon nitride consists of a flexible cantilever with a downwards-pointing hollow pyramidal tip at its free end. This probe can be modified with a FIB. Firstly an aperture is milled at the apex of the tip to permit the transfer of liquid from the probe to the sample (Fig. 1). The diameter of such apertures can be as small as 200 nm. Secondly, the reflective gold layer covering the upper part of the cantilever is removed locally, in and around the hollow tip. The gold layer can be made hydrophobic by chemical treatment, while the bare cantilever remains hydrophilic. This hydrophilic area acts as a loading area for the liquid to be loaded manually onto this side of the probe tip (Fig. 2).

When a drop is deposited onto the loading area with a micropipette, the liquid fills the volume inside the hollow tip as well as inside the aperture by capillarity. By bringing the tip into contact with the sample, the liquid touches the surface and slightly spreads out. During the withdrawal of the probe, a liquid meniscus is stretched out between tip and sample, which finally breaks, leaving a small droplet on the surface. Repeating the dispensing process (contacting-withdrawing) several times at different locations leads to the creation of an array of liquid droplets (see Fig. 2). To achieve the deposition of a small volume of liquid, the dimension of the tip aperture, as well as the wettability of the surfaces must be taken into account. Small apertures combined with hydrophobic sample surfaces allow the deposition of droplets with volumes less than 5 attoliters (corresponding to 1/200 of a cubic micrometer).

An extension of this liquid dispensing method is to use the liquid as transport medium for other entities such as chemical or biological molecules (antibodies, proteins, DNA), nanoparticles, or generally any species that can be dissolved or suspended in the liquid. After the deposition and the evaporation of the solvent, only the non-volatile elements will remain on the surface, forming e.g. a bioarray or a pattern of nanoparticles as shown in Figure 3. The smallest spacing between two dots that could be achieved is in the sub-micrometer range, which corresponds to array densities of over 10^8 dots per cm^2.

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References:

[1] A. Meister, et. al., "Nanoscale dispensing of liquids through cantilevered probes", Microelec. Eng. **67-68**, 644 (2003).

Figures:

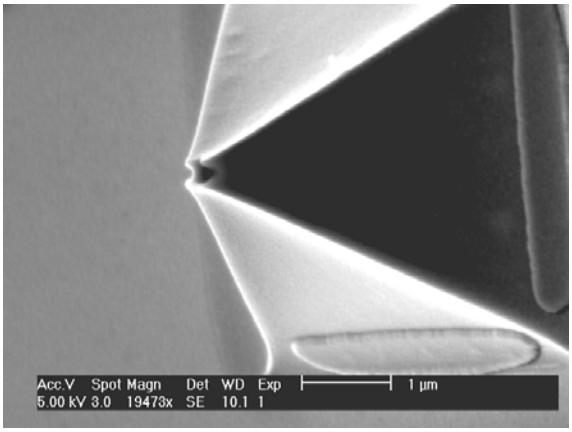

Figure 1: SEM micrograph of a 200 nm opening at the tip apex of an atomic force microscope probe. The aperture, made by focused ion beam milling, permits the transfer of liquid through the probe during the contacting of the tip with the sample surface.

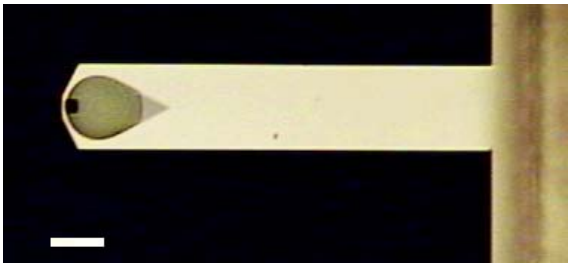

Figure 2: Optical micrograph (scale bar: 25 µm) of an atomic force microscope probe with liquid onto the loading area.

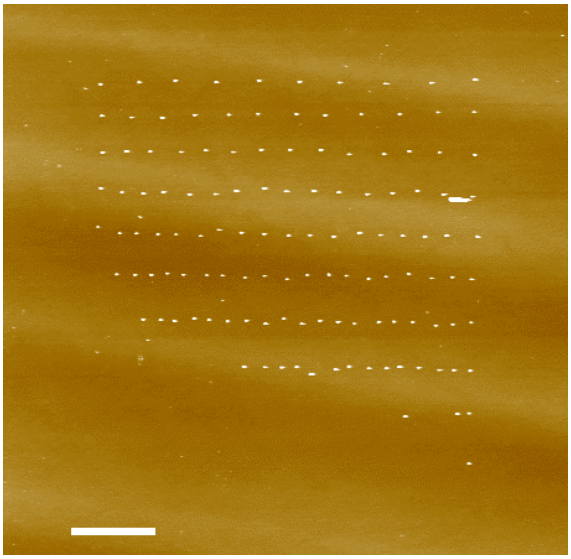

Figure 3: AFM micrograph (scale bar: 2 µm) showing an array of polystyrene nanoparticles (ø 20 nm). Glycerol, with the nanoparticles suspended in it, was dispensed to form an array of droplets. After the disappearing of the liquid by evaporation, only the nanoparticles remain on the surface.