HACETTEPE JOURNAL OF BIOLOGY AND CHEMISTRY
Review Article
Hacettepe J. Biol. & Chem., 2007, 35 (3), 157-161

Nanotechnology for Preparation of Array Platforms

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Abstract

The design and production of advanced array technologies, referred also as “biochips”, have attracted tremendous interest of the scientific community due to the broad application possibilities of these materials especially in the life sciences. It is especially useful in detection of multiple targets of biologic origin. Patterning of substrate surfaces is one of the major steps in the preparation of the arrays. Several techniques for the preparation of array platforms have been developed. Here, the basic information on nanotechnological approaches using atomic force microscope (AFM), i.e., dip-pen lithography, conducting AFM lithography, nanoshaving and nanografting, are briefly described.

Key Words: Array platforms, nanotechnology, AFM based techniques.

INTRODUCTION

Thousands of genes and the products they encode (i.e., proteins) function in a complicated and orchestrated way that creates the mystery of life of all organisms. In “genomics”, genes of organisms, their functions and activities are investigated. Genomics is naturally linked to “proteomics” the study of the proteins encoded by the organism’s genome. Genomics in combination with proteomics resulted in fascinating biomedical research however it requested large scale and high throughput methodologies [1-3].

Array technologies offer a number of advantages for the screening of a large number of analytes including speed, convenience and high throughput analysis. Array platforms consist of patterned surfaces and probe molecules immobilized onto these patterns. There are two main approaches: (i) surfaces are first patterned and then different probe molecules are selectively immobilized onto different locations on the surface (a two step process); and (ii) different probe molecules are delivered to different locations on the surface to form a patterned surface design probe molecules (two steps together). Nanotechnology is a rather new fashion attracting a lot of scientific and technological interest in the recent years. DNA and protein array platforms with feature sizes smaller than 100 nm have been fabricated by novel techniques of nanotechnology, including dip-pen nanolithography, conductive AFM nanolithography, nanoshaving and nanografting, which are briefly described here [4,5].

AFM in Lithography

Atomic Force Microscope (AFM) is one of the most widely used nanoscale imaging techniques [6-11]. AFM has a molecular or atomically fine tip attached to bottom of a flexible/reflective cantilever. As the tip scans the surface of the sample, the laser beam is deflected off the cantilever; therefore its position and

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the extent of deflection of the cantilever can be monitored. Both, the lateral position of the cantilever and the distance of the tip to the sample are controlled by piezoelectric crystal tubes. It is possible to change the direction and scanning rate of the tip on the surface. One may also apply a specific voltage to the substrate surface using conductive AFM tips.

AFM can be used to deliver molecules loaded on the tip in the desired patterns. Mirkin et al. in 1999 was the first to use AFM in lithography. They named it "dip-pen nanolithography" (DPN) [12]. The concept of DPN is that the printing of molecules is paralleled with nanoscale writing. As seen in Figure 1, the AFM tip, carrying the probe is moved in pre-programmed defined patterns. The tip will be in contact with the surface, either allowing the tip to dwell at a certain location or simply by rastering the tip close to the surface at a particular speed. As such, different shapes and sizes (i.e., dots, lines) can be created ("patterned") allowing molecules to diffuse onto the solid surface by means of capillary forces. Resolution of Dip-pen patterning with AFM is down to line widths of about 15 nm, in function of, type of substrate, contact time (between the tip and substrate), scan speed, relative humidity, and the relative solubility of the molecules in the water-meniscus [13].

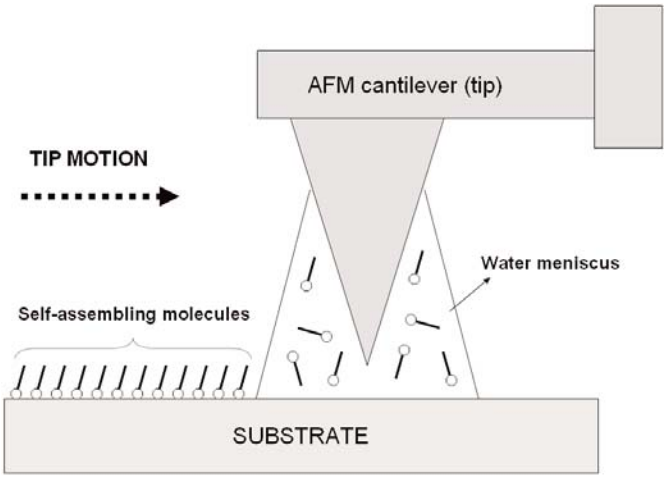

Figure 1. Schematic description of the dip-pen nanolithography.

Conductive AFM Lithography

Scanning probe techniques, including "Conductive Atomic Force Microscopy (c-AFM)", to form nanometer scale patterns of organic molecules on silicon substrates have attracted much interest for their potential applications in chemical and biological sensors and molecular electronic device structures including DNA and protein arrays [14-16]. In c-AFM, a voltage is applied to the AFM tip, while AFM is performing its normal scan. The tip acts as cathode and the water meniscus formed between tip and surface serves as electrolyte. As demonstrated by Hou et al., the strong electric field near the tip causes electrochemical reactions in the water column as water decomposes into hydroxyl ions (OH^-) and radicals (H•) [17]. This results in breakdown, including field-induced ionization, of the water molecules yielding electrons, protons and free radicals (OH•). The OH• molecules can be consumed in three ways: (i) they may formed hydrogen peroxide (H_2O_2) molecules; (ii) they may couple with H• radicals to produce water, or (iii) they could be electrochemically reduced to hydroxyl ions at the tip-surface area (Figure 2) [18,19].

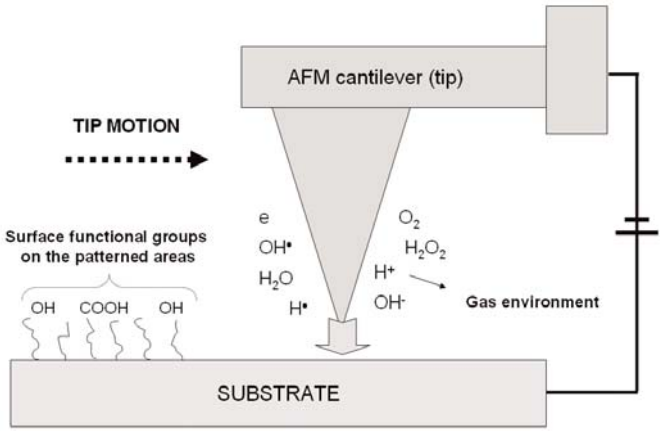

Figure 2. Schematic description of c-AFM nanolithograpy.

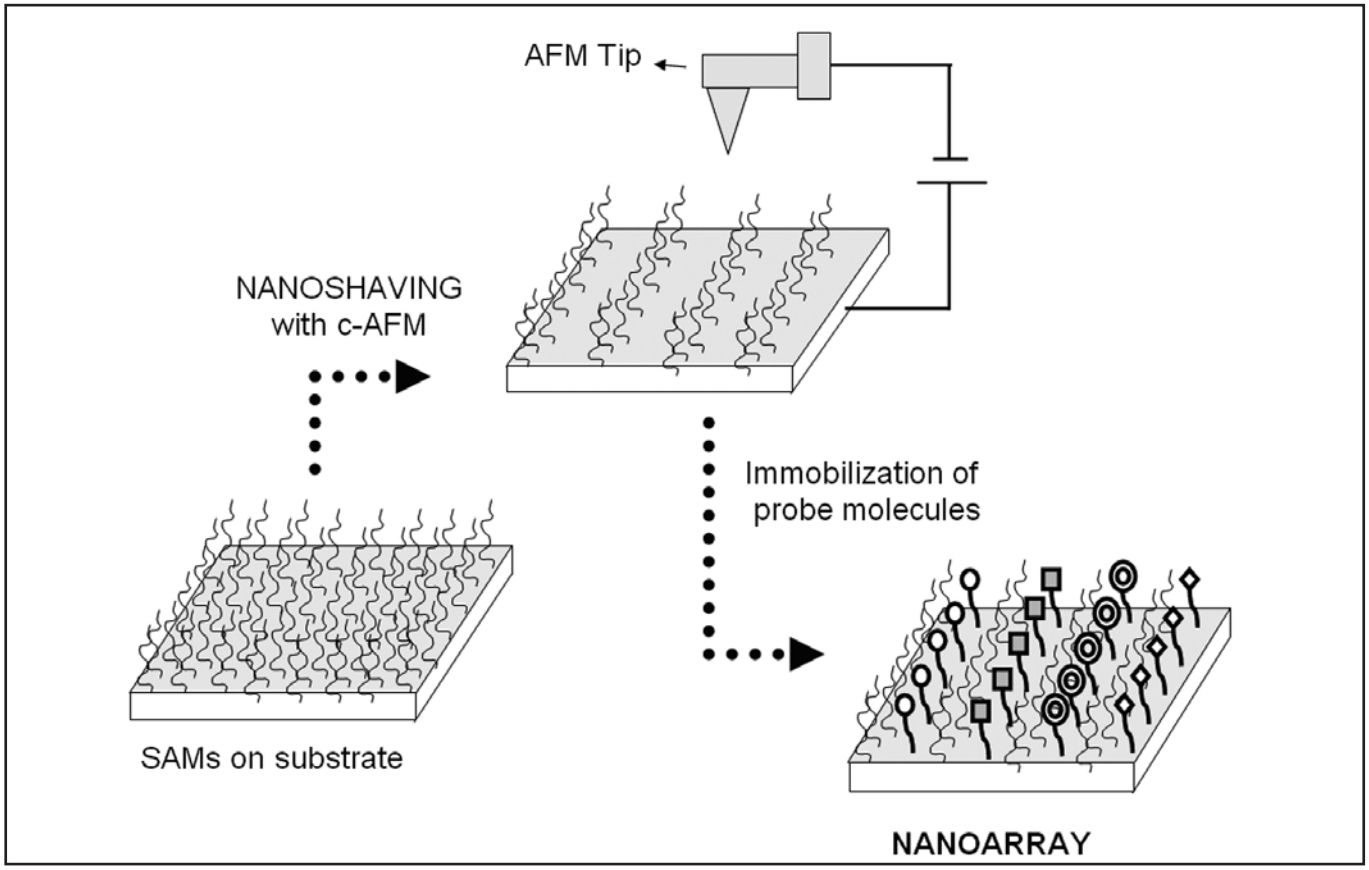

Figure 3. Schematic description of nanoshaving.

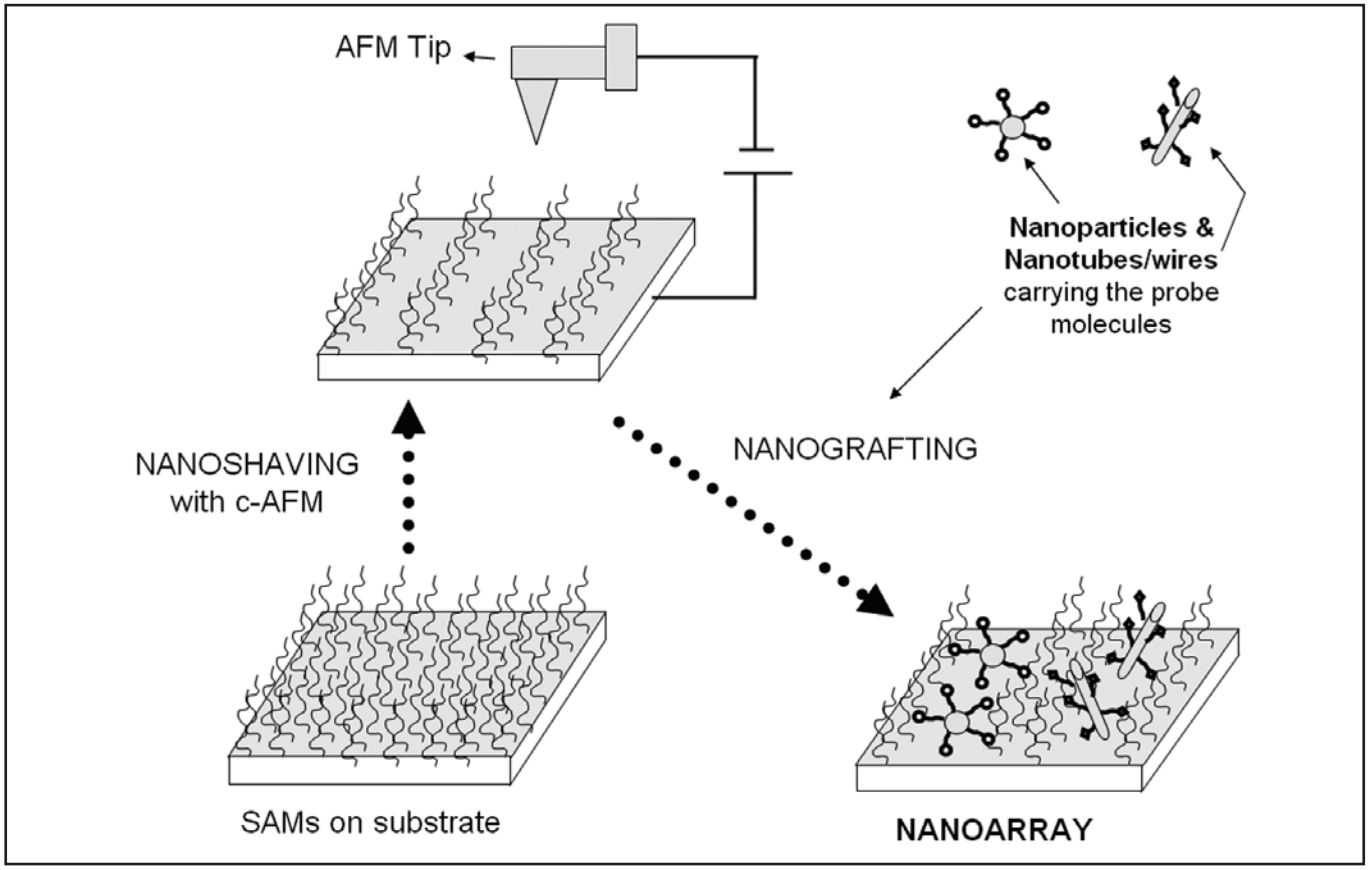

Figure 4. Schematic description of nanografting.

The organic monolayer composition and topography can be altered by using c-AFM. There are several factors affecting the physical (topology) and chemical changes on the nanopatterned areas with the use of c-AFM nanolithography such as, applied voltage, tip velocity, humidity, tip conductivity and tip diameter [18,19].

Nanoshaving and Nanografting

The recently developed AFM-based nano lithography "nanoshaving" and "nanografting", allowed the fabrication of nanoscale surface structures of alkane thiols, proteins, and DNA [14,20,21]. In nanoshaving, in a first step, self-assembled monolayers (SAMs) are formed. Usually long chain alkane thiols having ω-terminal functionality (or not) are used on substrate surfaces (usually coated with a gold layer) (Figure 3). Then, the desired nanopatterns are formed by nano-shaving by making trenches on the SAM using the AFM tip. Different probes ("bio-ligand") are immobilized on to different trenches and likewise, nanoarrays are formed.

Nanostructures (nanoparticles, nanowires, nanotubes, etc.) may be first functionalized for immobilization of probes on their surfaces. These functionalized nanostructures may then be grafted onto pre-patterned surfaces (e.g., nanoshaved). This is referred as nano-grafting (Figure 4). Note that, by this approach the surface area of substrate can be extended, and therefore resolution (sensitivity) can be increased significantly.

ACKNOWLEDGEMENT

Erhan Pişkin is supported by the Turkish Academy of Sciences as a Full Member.

REFERENCES

1. Eing, A. and Vaupel, M., Imaging Ellipsometry in Biotechnology, Verlag Axel Gierspeck, p. 1-10, 2002.
2. Zhu, H. and Snyder, M., Protein Chip Technology, Curr. Opin. in Chem. Biol., 7: 55, 2003.
3. Kim, J.H., Bioinformatics and Genomic Medicine, Genet. Med., 4: 62S, 2002.
4. Gu, J., Yam, C.M., Li, S. and Cai, C., Nanometric Protein Arrays on Protein-Resistant Monolayers on Silicon Surfaces, J. Am. Chem. Soc., 126: 8098, 2004.
5. Kramer, S., Fuierer, R. R. and Gorman, C. B., Scanning Probe Lithography Using Self-Assembled Monolayers. Chem. Rev. 103: 4367, 2003.
6. Binnig, G., Quate, C.F., Gerber, CH., Atomic force microscope, Phys. Rev. Lett., 56: 9, 930, 1986.
7. Hoh, J.H., Hansma, P.K., Atomic Force Microscopy for High-Resolution Imaging in Cell Biology, Trends Cell Bio., 2: 208, 1992.
8. Raab, A., Han, W., Badt, D., Smith-Gill, S.J., Lindsay, S.M., Schindler, H., Hinterdorfer, P., Antibody recognition imaging by force microscopy, Nature Biotechnology, 17: 901, 1999.
9. Kim, J.M., Ohtani, T., Sugiyama, S., Hirose, T., Muramatsu, H., Simultaneous Topographic and Fluorescence Imaging of Single DNA Molecules for DNA Analysis with a Scanning Near-Field Optical/Atomic Force Microscope, Anal. Chem., 73: (24), 5984, 2001.
10. Liu, M., Liu, G., Hybridization with Nanostructures of Single-Stranded DNA, Langmuir, 21: 1972, 2005.
11. Van der Heijden, T., Moreno-Herrero, F., Kanaar, R., Wyman, C., Dekker, C., Comment on Direct and Real-Time Visualization of the Disassembly of a Single RecA-DNA-ATP S Complex Using AFM Imaging in Fluid, Nano Lett., 6: (12), 3000, 2006.

12. Piner, R.D., Zhu, J., Xu, F., Hong, S.H., Mirkin, C.A., Dip-Pen Nanolithography, Science, 283: 661, 1999.

13. Smith, R.K., Lewis, P.A., Weiss, P.S., Patterned Self-Assembled Monolayers, Progress in Surface Science, 75: 1, 2004.

14. Zhao, Z., Banerjee, I.A., Matsui, H., Simultaneous Targeted Immobilization of Anti-Human IgG-Coated Nanotubes and Anti-Mouse IgG-Coated Nanotubes on the Complementary Antigen Patterned Surfaces via Biological Molecular Recognition, J. Am. Chem. Soc., 127: 8930, 2005.

15. Kinser, C.R., Schmitz, M.J., Hersam, M.C., Conductive Atomic Force Microscope Nanopatterning of Hydrogen-Passivated Silicon in Inert Organic Solvents, Nano Lett., 5: 1, 91, 2005.

16. Maoz, R., Frydman, E., Cohen, S.R.,Sagiv, J., Constructive Nanolithography : Inert Monolayers as Patternable Templates for In-Situ Nanofabrication of Metal-Semiconductor-Organic Surface Structures - A Generic Approach, Adv. Mater., 12: 10, 725, 2000.

17. Hou, S., Li, Z., Li, Q., Liu, Z.F., Poly(methyl methacrylate) Nanobrushes on Silicon Based on Localized Surface-Initiated Polymerization, Appl. Surf. Sci., 222: 338, 2004.

18. Park, J., Lee, H., Effect of Surface Functional Groups on Nanostructure Fabrication Using AFM Lithography, Mater. Sci. Eng. C, 24: 311, 2004.

19. Lyuksyutov, S.F., Paramonov, P.B., Dolog, I., Ralich, R.M., Peculiarities of an Anomalous Electronic Current During Atomic Force Microscopy Assisted Nanolithography on n-type Silicon, Nanotechnol., 14: 716, 2003.

20. Wang, X., Zhou, D., Rayment, T., Abell, C., Systematic Manipulation of Surface Chemical Reaction on the Nanoscale: a Novel Approach for Constructing Three-Dimensional Nanostructures Chem. Commun., 4: 474, 2003.

21. Zhou, D., Sinniah, K., Abell, C., Rayment, T., Label-Free Detection of DNA Hybridization at the Nanoscale: A Highly Sensitive and Selective Approach Using Atomic-Force Microscopy, Angew. Chem., 115: 5084, 2003.