Tip Based Lithography for Biocompatible Materials

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The last decade has witnessed an explosion of interest in miniaturization technologies for life science applications. To begin with, these methods were based on instrumentation developed for the semiconductor industry, but as limitations of these techniques became apparent, new methods and instrumentation have been developed specifically for biological sciences. The advantages of miniaturization have already been realized in genomic analysis and to a certain extent in proteomics.

Reducing the domain sizes has some distinct advantages in several bioscience areas. In the field of protein detection, smaller feature sizes will have the benefit of drastically reduced sample size requirements, potentially higher detection sensitivity, reduced assay time, and better compatibility with lab-on-a-chip technologies. In addition construction of sub-cellular scaled features of biological and biocompatible materials enables the interrogation of cellular processes at single cell levels.

Tip based lithography is a powerful platform capable of creating high-quality patterns of biocompatible materials at nanometer to micron scales. The advantages of this novel technique include working at ambient conditions on laboratory benches in biologically friendly conditions and the ability to maintain the biomolecules in a hydrated state during the entire process.

This fabrication technique is applicable to a wide range of materials. For example proteins can be printed to a chemically functionalized surface and be retained at the printed location without loss of activity. The ability to precisely place biological material at defined positions can be utilized to develop biomarker detection assays and to functionalize microelectromechanical systems (MEMS) based sensing elements. It can also be used to investigate the cellular activity at single cell levels.

Another application is the patterning of hydrogels. Hydrogels have been used extensively for tissue engineering scaffolds and other biomedical applications because of their unique three-dimensional cross-linked polymer network that provide structural support while endowing an environment similar to natural tissue. Fabrication of hydrogels at submicron scales is greatly desirable; however structures with well-defined organization and high uniformity are not easily achievable by using traditional methods. We have demonstrated that sub-cellular scales of hydrogel patterns can be easily generated by tip based lithography.