

Bio Applications of Dip Pen Nanolithography

NanoInk markets instrumentation specifically designed for Dip Pen Nanolithography[®] (DPN[®]), a tip-based patterning technique. The primary strengths of this technology are:

- Directed placement of materials at defined locations with nanoscale precision
- Flexible “on-the-fly” pattern generation
- Multi-component patterning at micron and sub-micron scales

The primary bio applications that can be addressed using NanoInk’s instruments include:

Directed Placement of Biomolecules onto Prefabricated Structures

The ability to place multiple biomolecules simultaneously onto prefabricated microstructures with nanoscale precision under biologically friendly environmental conditions is another of the strengths of the NanoInk Instrumentation. This enables the user to functionalize MEMS based sensing elements, which have been a limiting step in the development of miniaturized biosensors and chemical sensors. It also enables the users to functionalize other microstructures that have been developed for a wide range of

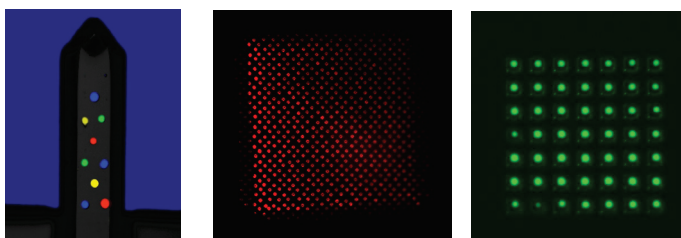


Figure 1: Fluorescence images of protein printed on microfabricated structures. Left: AFM cantilever with four different proteins. Middle and Right: Polymer pillars with fluorescent proteins printed on them. Middle: Pillars are 1.5 microns in diameter. Right: Pillars are 10 microns square.

applications including lab-on-a-chip and cellular mechano-transduction studies. Figure 1 presents fluorescence images of several MEMS structures that have been functionalized using NanoInk instruments.

Single Cell Arrays

Conventional patterning methods are limited to either patterning multi-component patterns with rather large domains or single component patterns at sub cellular scales. NanoInk technology is capable of constructing multi-component patterns at sub cellular scales. This enables its users to address and study the underlying biology at a single

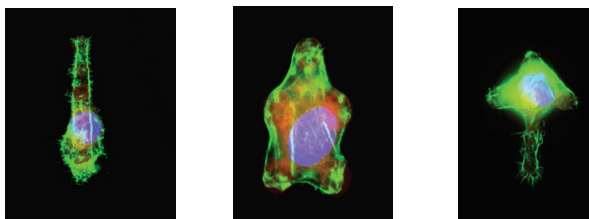


Figure 2: Fluorescence images of cells binding to micropatterned fibronectin domains. The actin filaments (green), nucleus (blue) and the fibronectin (red) are labeled.

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(continued)

cell level. Applications of this technology include studies of cellular migration, focal adhesion, cellular polarization and proliferation studies neuronal development, and stem cell differentiation. Figure 2 presents fluorescence images of cells on micropatterned subcellular sized domains of fibronectin arrayed using NanoInk instruments.

Deposition of Biocompatible Polymers

The ability to place biocompatible polymers with diverse physical properties on to a surface with subcellular scale dimensions and nanoscale precision allows users to tailor make biomimetic scaffolds integrated with multiple components for specific applications. NanoInk's technology is capable of printing a wide range of such materials and also enables the users to modify the chemistry and pattern in subsequent steps. Figure 3 presents

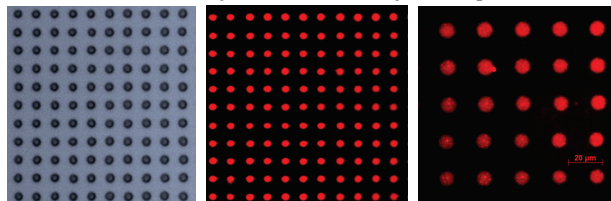


Figure 3: Functional hydrogel arrays: The middle image is the fluorescence image of thiol hydrogel patterns (left), with conjugated rhodamine and the right image is the patterns of epoxy hydrogels conjugated with fibronectin.

images of functionalized PEG hydrogels. Printed hydrogels can be used as a biomolecule encapsulation and delivery vehicle. Free functional groups can be incorporated into the hydrogels for surface modifications such as specific protein conjugation.

Functionalization of Oxide Surfaces

Silane chemistry is typically used for surface functionalization and biomolecule immobilization in biosensor development and cell biology applications. Functionalization of

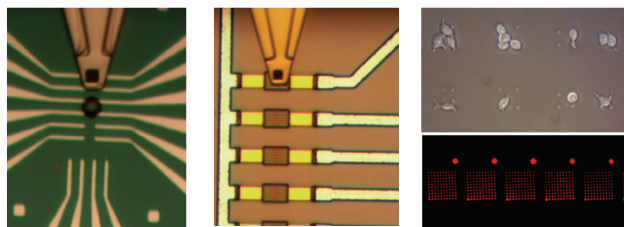


Figure 4: Optical microscope images of surface functionalization examples by means of silane DPN printing: Left) a silicon oxide substrate based Au electrode device functionalization. Middle) Semiconductor nanowire device functionalization. Right) Biomaterials (such as protein and cell) patterning using DPN silane functionalized glass substrates.

only a specific area of interest is advantageous since it limits the non-specific binding to the other areas of the chip surface. NanoInk instruments are able to deliver silanes to specific locales with nanoscale precision. Figure 4 presents the examples of functionalization of nanowire sensors using silane chemistry on a semiconductor device and glass substrate for protein binding.