Patterning Functional Hydrogels

Introduction

Hydrogels are three-dimensional cross-linked polymer networks that have physical characteristics very similar to those of natural tissue. Due to their low cytotoxicity, immunogenic effect, and high biocompatibility, hydrogels have become one of the most extensively studied materials for biomedical applications. Hydrogels can be formed on the basis of either physical interactions or chemical linking reactions between functional groups. The functional groups can be cross linked with other polymers to fine-tune the mechanical properties of hydrogels. In addition, by adjusting the ratio of functional crosslinkers, hydrogels with unreacted functional groups can be created for conjugating to other molecular species.

Hydrogels fabricated at the sub-cellular scale that contain conjugated functional biomolecules have utility in proteomic analyses, direct drug screening, biological sensor development, and cell culture applications. Here we demonstrate the consistent and reproducible patterning of a thiol-functional hydrogel pattern on a glass substrate using tip based fabrication techniques.

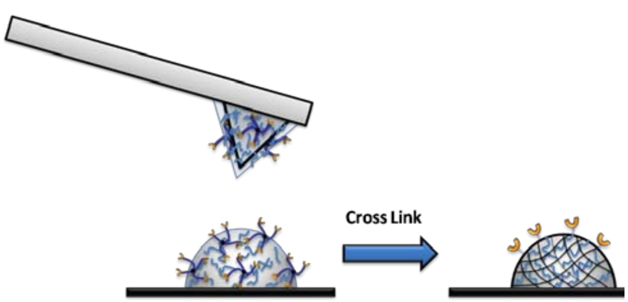

Figure 1. Formation of functional hydrogels using a mixture of PEG-DMA and 4-arm PEG thiol.

Functional Hydrogel Principles

One of the most noteworthy hydrogel fabrication techniques is the Michael addition reaction between thiols and acrylates. In this report, we utilized a combination of the Michael addition reaction and the methacrylate chain reaction to form functionalized hydrogels from PEG-dimethacrylate and 4-arm PEG thiol precursors. We used NanoInk's Nano Lithography Platform (NLP 2000 System) to pattern the precursors. The desired precursor composition was obtained by mixing PEG-DMA and 4-arm PEG thiol. The prepared precursors were then loaded into the reservoirs on the "Inkwells". The reservoirs feed microfluidic channels specifically engineered to transport liquids. The microfluidic channels are designed to match the M-type cantilever pen geometry so that each cantilever can be filled with precursors. The filled pens were then used to print the desired hydrogel pattern.

A brightfield image of a representative hydrogel pattern created by the NLP 2000 System is shown in Figure 2a. The hydrogel precursors were polymerized by exposing them to UV radiation and functionalized hydrogels were subsequently imaged by AFM (Figure 2b). AFM data was used to characterize the size and homogeneity of the hydrogel pattern. Resultant structures were determined to be about 4 micron in diameter with a coefficient of variation of 10%.

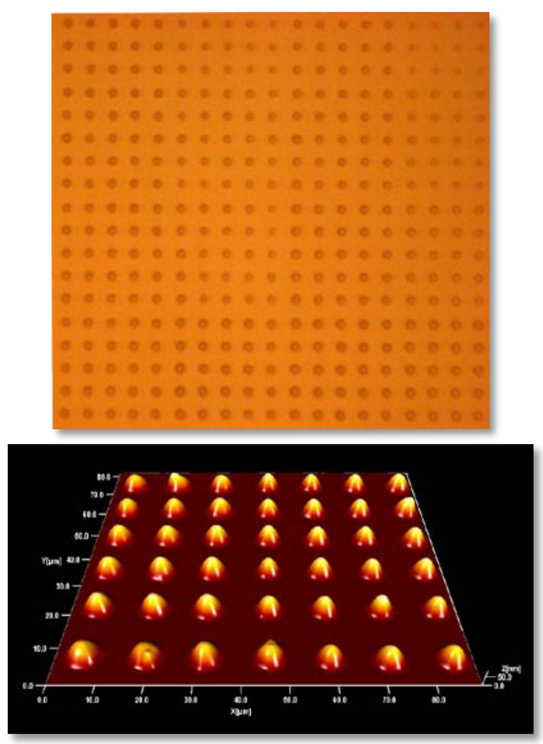

Figure 2. (Top: 2a) Brightfield and (Bottom: 2b) AFM images of functional hydrogels.

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To confirm the presence and functionality of free thiol groups on the hydrogels after printing, hydrogel patterns were incubated with rhodamine red C2 maleimide. After rinsing to remove the excess unreacted fluorophores, the patterned surface was interrogated using fluorescence microscopy. A bright red fluorescence signal from rhodamine bound to hydrogels was observed with a Zeiss Axio Imager Z1m fluorescence microscope (Figure 3).

Functional hydrogel arrays can be generated with biochemical moieties other than PEG-DMA and 4-arm PEG thiol.

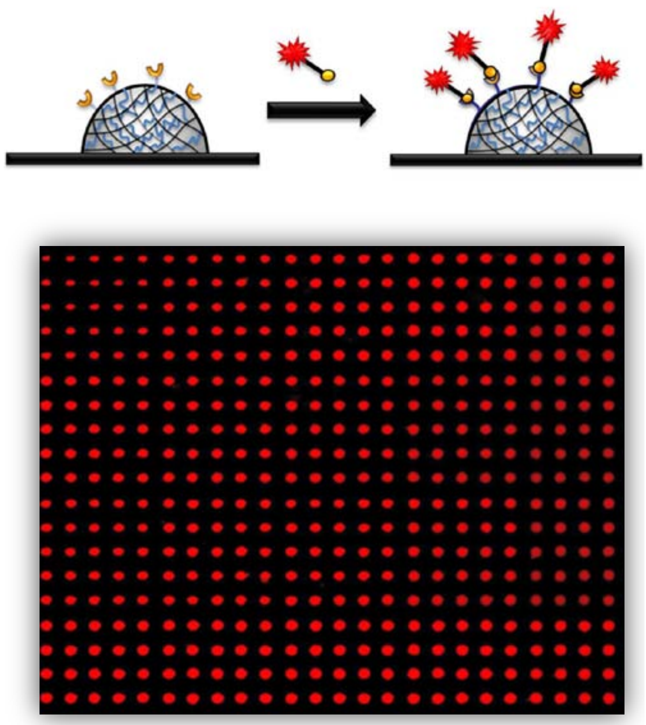

Figure 3. Fluorescence image of rhodamine tagged functional hydrogel pattern.

Conclusion

We have demonstrated successful printing of functional PEG hydrogels at sub-cellular scales using NanoInk's DPN® systems and tools. These results demonstrate the feasibility of generating uniform hydrogel patterns containing specific functional groups for biomolecule conjugations. More importantly, NanoInk's methodology is not confined to printing of a single type of functional hydrogel. Given that conjugation reactions occur after hydrogel printing, the fabrication method can be used as a general prototype for surface modification of glass substrates.

Reference

1. *Modifying network chemistry in thiol-acrylate photopolymers through postpolymerization functionalization to control cell-material interactions.* Rydholm, Amber E., et al. 1, July 2007, Journal of Biomedical Materials Research Part A, Vol. 86, pp. 23-30.

NanoInk Products Used

NLP 2000 System
DPN® Pen Arrays: Type M
DPN® Inkwell Arrays: Type M-12MW

Learn more about NanoInk products and services at www.nanoink.net. Or call us at 847-679-NANO (6266).