Thomas Jefferson is spotted in large numbers

SURFACE PATTERNING

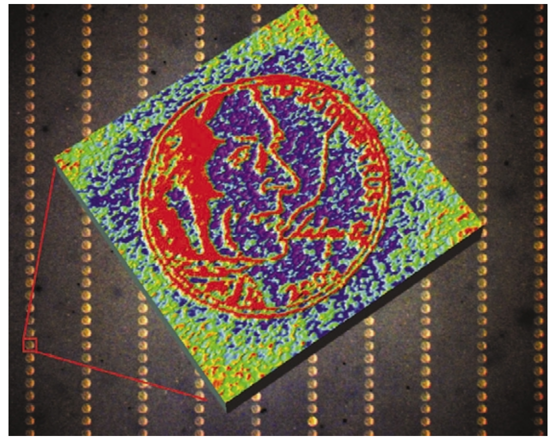
Researchers at Northwestern University, the University of Illinois at Urbana-Champaign, and NanoInk, California have taken dip-pen nanolithography a step further by fabricating a 55 000 pen array that can create patterns on Au or glass substrates using a 1-octadecanethiol (ODT) ink [Salaita *et al.*, *Angew. Chem. Int. Ed.* (2006) doi: 10.1002/anie.200603142].

Arrays consisting of Au-coated Si_3N_4 cantilevers, having sharp tips at one end, are used as pens to fabricate surface patterns in parallel on a massive scale. The arrays are organized over a 1 cm^2 area with cantilever spacings of 90 µm and 20 µm in the *x* and *y* directions, respectively, and are set in place with respect to the atomic force microscope (AFM) scanner head by means of an epoxy resin. Unlike normal AFM imaging, a bent cantilever architecture and a large tip size are adopted to allow for any misalignment in the pattern during scanning. "We have discovered a way to fabricate arrays that consist of over one million cantilevers," says Chad A. Mirkin of Northwestern. "That's the easy part! We have learned how to overcome the alignment problems that have plagued scanning probe lithographies since the inception of atomic force microscopy, and we can now generate molecule-based nanostructures over large areas adapting the techniques used in conventional AFM technology."

The 55 000 pens can fabricate approximately 88 million, 1 molecule high ODT dots with a diameter of 100 ± 20 nm and a spacing of 400 nm. More complex images can be built up from the dots using a software package integrated into the system.

An image of Thomas Jefferson is reproduced 55 000 times in under 30 minutes by holding the probe array in contact with a substrate for 0.08 s and then traveling between specific points at a scan speed of 60 µm/s.

"This is the first example of large-area molecular printing using any scanning probe system," says Mirkin. "This now opens the door to using the technology to prepare soft nanostructures on surfaces over large areas in the context of nanocombinatorial arrays."



55 000 miniature images of a 2005 US nickel reproduced by dip-pen lithography are shown in the background. (Each circle is only twice the diameter of a red blood cell.) Each image (in foreground), showing Thomas Jefferson's profile, is made from a series of 80 nm dots. (© 2006 Wiley-VCH.)

Katerina Busuttil

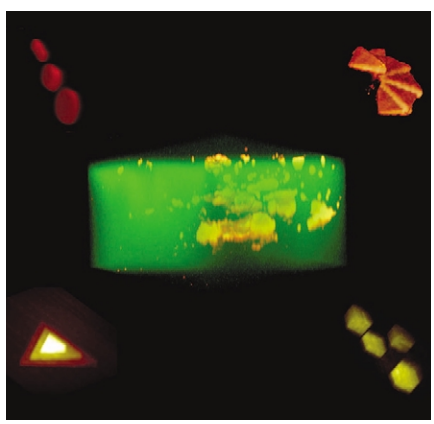
Photolithography paves the way to migration patterns

SURFACE PATTERNING

The ability to tailor transport properties of biocompatible scaffolds is highly relevant to the future of tissue engineering and drug delivery. In an attempt to address this issue, a team at Rice University led by Jennifer L. West, has generated complex three-dimensional bioactive patterns in hydrogels using single- and two-photon absorption (SPA and TPA) photolithography. [Hahn *et al.*, *Adv Mater.* (2006) **18**, 2679]

"In tissue engineering, the key limitation has been the ability to create a microvascular network, preferably a defined network with clear and usable inputs and outputs," says West.

The researchers use poly(ethyleneglycol) (PEG)-diacrylate hydrogels (PEGDA) as scaffolds as they are both biocompatible and resistant to protein adsorption. Fluorescently labeled acryloyl (ACRL)-PEG-peptide or low molecular weight PEGDA solutions containing a photoinitiator diffuse into the hydrogel, and a previously prepared patterned mask is applied to the gel. The acrylate conjugates to specific regions of the gel on illumination of the mask with ultraviolet light, altering the cross-linking density. Although the researchers found that SPA is very effective at patterning gels rapidly, it is limited to producing features with a uniform axial cross-section.



Center: Patterned region (green) with migrated HT-1080 fibrosarcoma cells (orange). Surrounding images: Features formed in PEGDA hydrogels by TPA photolithography. (© 2006 Wiley-VCH.)

To overcome the limits of SPA, the team investigated TPA photolithography using the same hydrogel systems. A virtual pattern is first created on the gel using laser scanning microscope software and the feature is then created by irradiation at 720 nm. Incremental changes in the focal plane can be used to create a pattern of irregular dimensions in the gel.

Varying spatial biomechanical gradients are known to affect cell alignment and locomotion, which are particularly important processes in developing embryos. This is illustrated by the researchers in an experiment using HT-1080 human fibrosarcoma cells. Confocal microscopy data of a four-week-old hydrogel culture show that HT-1080 cells only migrate to patterned regions of the hydrogel, illustrating the effects of varying spatial gradients on cell alignment.

"We have found that we can use two-photon laser scanning lithography to create three-dimensional structures in hydrogels" says West. "Cells then migrated into the gels only in the regions that were patterned."

Katerina Busuttil