Research Highlights

Petra S. Dittrich*

DOI: 10.1039/c000521p

Biomolecular patterns displayed on, and hidden in hydrogels

In recent times, significant progress has been achieved in the development of responsive and adaptive materials and used to induce the change of the physicochemical properties with temporal and spatial resolution. In a novel approach, Ryan C. Hayward and co-workers from the University of Massachusetts (Amherst, MA, USA) developed revealed in the swollen state of the hydrogel at low temperatures of about 23 °C, that sequesters functionalized regions within tight folds so that these regions are hidden from the surface. Topographic features on the underlying

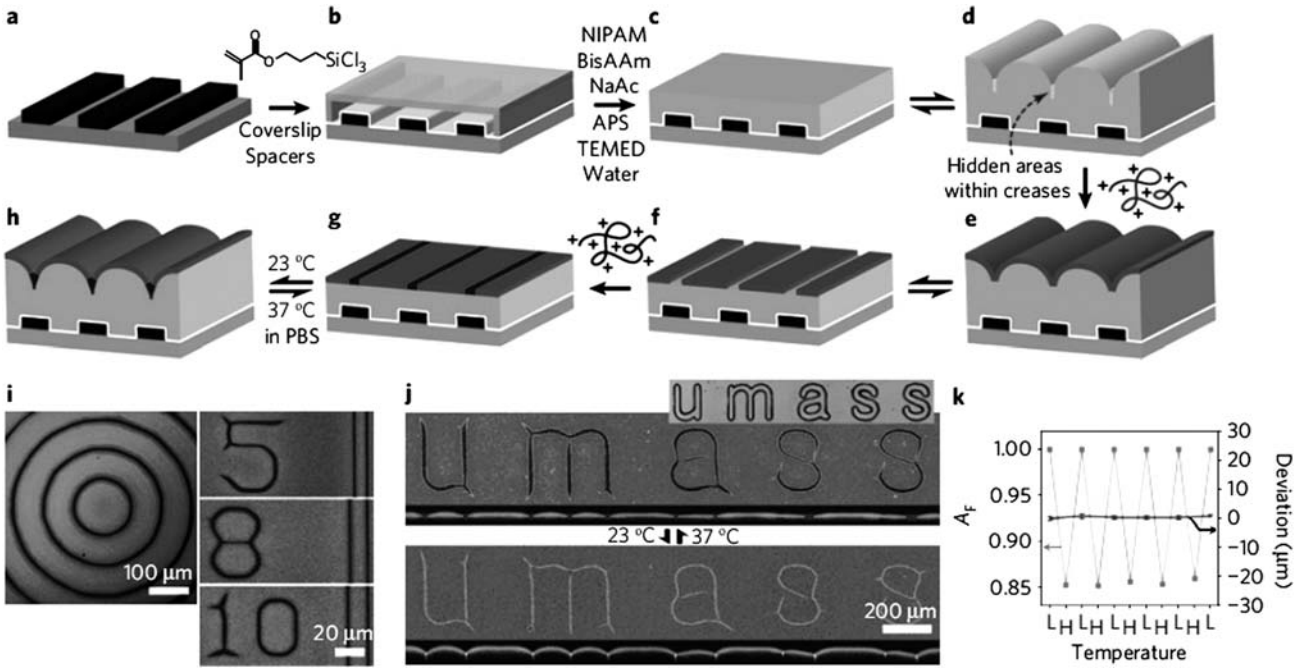

Fig. 1 Dynamic display of surface patterns based on a temperature-responsive hydrogel. The sketches (a–h) show the fabrication processes and functioning of the device. First, a topographically patterned substrate (made of photo-curing adhesive on a coverslip) is prepared and chemically modified. A hydrogel is loaded and polymerised, while spacers at the side and a coverslip on top of it define the final thickness of the hydrogel layer. After detachment of the coverslip, the hydrogel is swelled, thereby forming areas with creases. The displayed surface of the hydrogel is then coated, while the hidden areas remain uncoated. Deswelling of the hydrogel at higher temperature enables the modification of the previously hidden areas. (i) Examples of patterns produced by backfilling the creases with a ligand that is tagged with a fluorescent dye. (j) Reversible actutation of the hydrogel. The letters "umass" appear or disappear, depending on the temperature. (k) The graph demonstrates the reproducibility of switching (A_F is the fraction of the exposed surface coated by a fluorescein derivate). (Reprinted by permission from Macmillan Publishers Ltd: Nature Materials, ref. 1, copyright 2009.)

surfaces. For example, various surface coatings have been developed that are capable of dynamically changing the wettability, adhesion properties or optical characteristics of a surface, and many stimuli such as light, temperature, electrical potential and solvent have been

ETH Zurich, Zurich, Switzerland CH-8093. E-mail: dittrich@org.chem.ethz.ch

a surface coating based on a temperature-responsive hydrogel that facilitates the display or hideout of chemical patterns bound to the surface.[1] In contrast to former approaches, the new method is reversible and at the same time flexible concerning the choice of surface functionalities and pattern geometry. The distinctive feature of the hydrogel surface is an elastic creasing instability (Fig. 1), rigid substrate, fabricated by photolithography and micromoulding, determine the crease positions and enable the creation of nearly any two-dimensional pattern. The surface of the swollen hydrogel can be coated by binding poly-(L-lysine) tagged with fluorophors or other functional groups such as poly-(ethylene glycol) or biotin to the hydrogel. At higher temperature, deswelling of the

hydrogel results in the display of the previously hidden areas. These still uncoated areas can be selectively backfilled with another molecule. Once functionalised, the patterned surface can be reversibly switched on and off within one second simply by changing the temperature. The researchers demonstrate several applications including the adhesion and encapsulation of beads and cells within the creases. Furthermore, by attaching enzymes it is possible to control the catalytic activity of the enzyme: An enzyme (here: lipase) bound to the surface within the creases has a reduced effective catalytic activity as long as the hydrogel is swollen. In future, the dynamically modifiable surface could be valuable components in lab-on-chip devices.

Microchip-in-a-cell

Thanks to the progress in micro- and nanofabrication in past years it is nowadays possible to fabricate micrometer-sized slices of a semiconductor material, incorporating even smaller features with nanometer precision in shape and dimensions. These microchips are potentially even small enough to be incorporated in living cells. With the exciting prospect of creating an intracellular microchip sensor, researchers from Barcelona and Madrid (Spain) evaluated the possibility of internalizing polysilicon devices with dimensions smaller than 3 μm inside living cells.[2] They first optimised the fabrication and collection of the polysilicon microchips (Fig. 2). Polysilicon is deposited on a silicon oxide-coated silicon wafer, and the dimensions and patterns of the polysilicon chips are defined by standard photolithography techniques. More than 150 million polysilicon microchips are produced on a single four-inch silicon wafer in parallel. They are released from the silicon wafer by etching of the silicon oxide sacrificial layer in vapours of hydrofluoric acid. The researchers successfully internalised the polysilicon microchips into two types of cells, the social organism *Dictyostelium discoideum* and human HeLa cells. *D. discoideum* can uptake the devices by phagocytosis, whereas uptake in HeLa cells was achieved by lipofection, *i.e.* the cells were incubated with liposomes that encapsulate the polysilicon microchips. To prove the vitality of the cells, a fluorescent assay is employed that utilises the

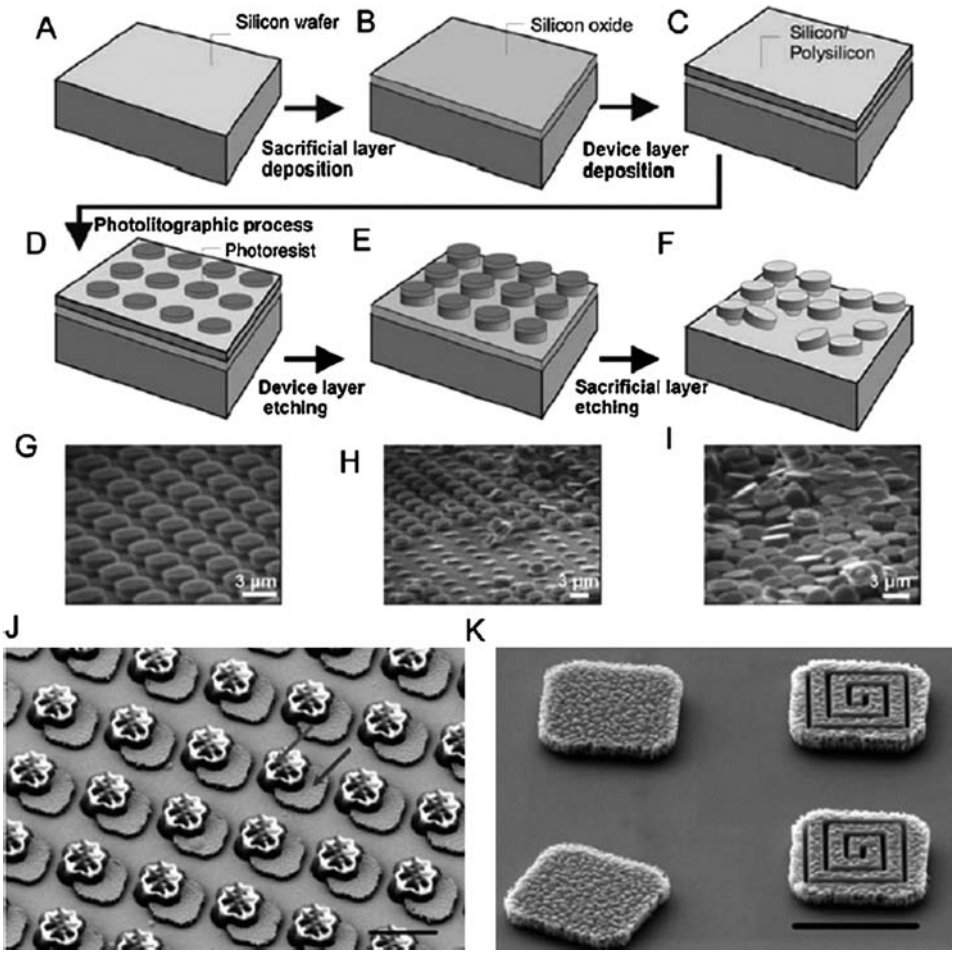

Fig. 2 Fabrication of silicon-based intracellular sensing chips. (A–C) A silicon wafer is coated with silicon oxide and afterwards, a layer of polysilicon is deposited onto the wafer. (D–F) Shape and size of the polysilicon chips are defined by standard photolithography processes, and the individual chips are released afterwards from the silicon wafer by etching the sacrificial layer. (G–K) Scanning electron microscope images of the polysilicon chips (G–I) during the fabrication process, (J) joined to a gold platform and (K) before and after coil nanostructuring on the polysilicon platforms by focussed ion beam nanomachining. (Reprinted with permission from ref. 2. Copyright Wiley-VCH 2009.)

dye fluorescein diacetate (CFDA). In a living cell, intracellular esterases hydrolyse the acetate groups thereby producing fluorescein, which can be observed in a fluorescence microscope. It could be demonstrated that cells are viable over several days, *i.e.* the polysilicon microchips are not toxic. Moreover, by internalising polysilicon microchips that have been derivatised with CFDA, fluorescence can be observed as well, demonstrating that cytosol constituents such as the esterases are interacting with the integrated "foreign object". Based on these results, the authors anticipate that the polysilicon microchips, that can incorporate three-dimensional nanostructures and can be fabricated from various materials, will facilitate sensing of intracellular mechanical properties and cellular events inside a single cell.

References

1 J. Kim, J. Yoon, R. C. Hayward, Dynamic display of biomolecular patterns through an elastic creasing instability of stimuli-responsive hydrogels, *Nature Materials*, DOI: 10.1038/NMAT2606.

2 R. Gómez-Martínez, P. Vázquez, M. Duch, A. Muriano, D. Pinacho, N. Sanvicens, F. Sánchz-Baeza, P. Bojy, E. J. de la Rosa, J. Esteve, T. Suárez and J. A. Plaza, Intracellular Silicon chips in Living Cells, *Small*, 2009, DOI: 10.1002/smll.200901041.