Lab on a Chip

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HIGHLIGHT

Research Highlights

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Electro-colloidal lithography

Lithographic fabrication methods have emerged as invaluable techniques in the generation of well-defined nanostructures and provide solutions in micro- and optoelectronics, biomedical technology, and chemical sensor applications. Though a variety of lithography-based techniques have already been developed, "colloidal lithography" represents an inexpensive alternative to more conventional approaches in which 2D arrays of sacrificial colloidal particles are utilized as physical masks for subsequent surface functionalization processes.[1] By explicitly defining the arrangement of colloidal particles on the material surface, the user can generate functionalized devices with unique structures and properties.

Recently, Bazin and Faure have demonstrated that electric fields can be exploited in the generation of arranged colloidal surface particles.[2] When particles of uniform ζ-potential are exposed to an AC-generated electric field normal to the plane of an electrode, they will self-organize into bidimensional hexagonal lattices whose size scale can be dictated with the AC-field parameters. While the theory behind this surface arrangement is not yet fully understood, the observed response does provide a means to generate distinct hexagonal patterns of templated colloids through "electro-colloidal lithography."

Furthermore, when the same particles are exposed to a DC-generated electric field, electrophoretic motion carries the particles along the direction of the applied field to the electrode surface. After generating a P1 hexagonal pattern of 2 μm, sulfate-modified polystyrene (PS) beads through an applied AC-field, a DC field was imposed to lock these patterns into place. When the patterned surface was subsequently treated with 200 nm-sized PS beads, the smaller P2 particles were attracted to the electrode and occupied all regions of the surface except those physically excluded by the original hexagonal pattern of larger P1 particles. The sacrificial P1 beads were then removed with rinsing or adhesive tape to generate a reverse hexagonal array of P2 nanoparticles (Fig. 1). By sintering the remaining polymer beads together through a modest thermal treatment, hole-containing polymer films stable upon DC field removal were readily generated.

As this process can be applied to any uniform population of charged particles, it offers a high level of tunability over the produced structure through user-defined parameters. By varying the size of the P1 particles, hole diameter within the resulting polymer film was readily changed. In altering the AC field parameters (*e.g.*, frequency, amplitude), the inter-structure separation was varied while maintaining hole size. Additionally, by controlling the diameter of the deposited P2, the thickness of the sintered polymer film was easily dictated.

Bazin and Faure also demonstrated that the novel electro-colloidal lithography technique could be used to generate hexagonal arrays of copper rings through targeted metal deposition. Here, PS beads were arranged on the device surface with AC-field application as before to generate the P1 patterned template. Subsequently, DC current was applied to the surface in the presence of Cu^{2+}-loaded multilamellar vesicles (MLVs) which attracted the MLVs to and reduced the cupric ions on the electrode surface. Spatially heterogeneous reduction of Cu^{2+} was observed and, upon removal of the PS microbeads, nano-rings were found to have been deposited around and under each PS particle. As this effect was attributed to the deformation of the electric field lines from the PS beads which drag the MLVs toward and under the PS spheres, copper rings of different heights and widths were generated by varying PS bead diameter and MLV solution concentration, respectively.

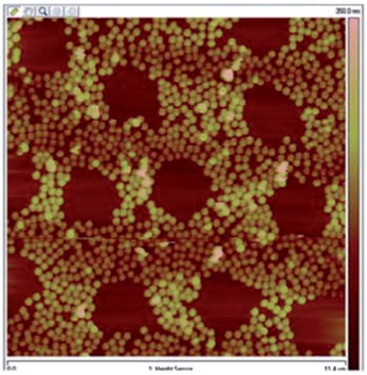

Fig. 1 Reverse micro-arrays of PS beads created by electro-colloidal lithography. Figure reprinted with permission from the Royal Society of Chemistry from Bazin and Faure.[2]

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The proposed electro-colloidal lithographic approach provides a number of advantages over conventional techniques and represents a significant advancement in the generation of polymer patterned surfaces. The technique can be performed rapidly, with no sophisticated materials or equipment, in an environmentally-friendly manner, and offers highly versatile structures for a broad range of applications.

Mixing inside paper microfluidic devices

Paper-based microfluidic devices have been of interest to researchers, mainly due to the fast and easy fabrication and low cost. Most paper microfluidic (PMF) chips have been developed for point-of-care diagnostics, *e.g.* the home pregnancy test, because they are also simple to use.[3] These devices usually contain few reagents and are intended to detect one specific chemical. For example, a liquid sample is drawn into the paper microfluidic channel *via* capillary force, which can be aided by evaporation of the sample. The sample is then analyzed in regions of the chip where specific antibodies are stored. Finally, the sample is collected in an absorbent pad at the channel exit. However, it would be helpful to integrate fluid actuators in PMF chips in order to enable more complex fluidic operations.

Yeo and colleagues have recently proposed a fluid actuation mechanism that utilizes surface acoustic waves (SAWs) inside PMF devices. Rezk *et al.*[4] coated cellulose-polyester paper with photoresist and patterned it using photolithography to generate a Y-shaped fluidic channel. The two upper channels of the "Y"-shape served as inputs for two miscible aqueous solutions, and the bottom channel served as the mixing region. Different channel shapes (straight, zig-zag, and serpentine) were generated, all ~ 2 mm wide. The channel exit coincided with the edge of the paper. Here, a piezoelectric material with two interleaving electrodes was placed (Fig. 2). A sinusoidal signal was applied to the electrodes to produce SAWs at a resonant frequency on the order of MHz.

The channel was pre-wetted to obtain a fast fluid actuation. Upon generation of the SAWs, the liquid at the edge of the paper was atomized. As a consequence, a negative pressure gradient was formed which helped draw more liquid through the fluidic channel. The wetting speed inside the channel was similar both for SAW-actuated and capillary flows, but only for channel lengths of up to 2 cm. Beyond this length, the SAW-driven flow was much faster than the Washburn prediction for capillary flow. It was even faster for capillary flows, in which some of the sample was lost due to evaporation.

The increase in speed of SAW-driven flows was utilized for the mixing of two dyes in the Y-shaped channel. Here, the channel shape had a large effect on the mixing behavior. The serpentine channel offered the most efficient mixing. This meant that a large degree of mixing of the two solutions was observed after a short distance inside the channel. The zig-zag channel offered less efficient mixing, and the straight channel performed even worse. A potential explanation of the effect of SAWs on improved mixing was based on this observation. For example, the fiber orientation in the paper helped guide capillary, laminar flow in one specific direction, but provided a hindrance in all other directions. However, SAW-driven flow was not fully laminar and was therefore not bounded by the fiber orientation. Thus, although the mixing was still diffusive, the SAW-driven flow was able to better circumvent obstructions (fibers) in the paper structure.

The actuation of flows inside PMF devices *via* SAWs suggests new opportunities for flow control, multiplexing and other functionalities. As shown in the example on mixing, SAW-driven flows could lead to the development of multiple assays on a single chip by mixing several antibodies. The integration of a small, battery-driven electrode unit into a PMF chip is affordable and simple enough that it could potentially become a standard chip element in the future.

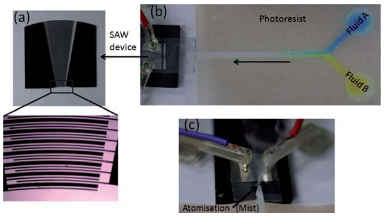

Fig. 2 a) Photograph of the electrodes which generate the SAWs. b) The electrodes are placed at the SAW focus at the exit of the fluidic channel, where they act to draw the sample through the chip. c) The solution is atomized when it reaches the paper edge. This effect is used to draw the sample through the chip. Figure reprinted with permission from the Royal Society of Chemistry from Rezk *et al.*[4]

Field-induced nanolithography

The localized patterning of surfaces with functional molecules such as biomolecules or polymers is helpful for a variety of biomedical devices. These include experiments on cell attachment and proliferation as well as development of microscale diagnostic and biosensing chips. It has been previously shown that self-assembled monolayers and inorganic surfaces can be patterned using a variety of approaches, including lithographic or electrochemical methods.[5] However, such substrates are not always suitable for biological applications, as they are prone to fouling.

Zauscher and coworkers have addressed the scarcity of non-fouling patterned microscale substrates and recently presented a method of creating surfaces for potential biosensing microdevices. These surfaces consisted of polymer brushes and were patterned using serial field-induced nanolithography (FINL). Ferris *et al.*,[6] instead of a self-assembled monolayer used a polymer brush (up to 200 nm thick) grown on a Si or Au substrate. This conductive substrate was electrically connected to a scanning probe microscopy tip. A bias voltage was applied between the tip and the substrate, where each functioned as an oppositely charged electrode. The applied bias voltage induced electrochemical alteration of the polymer brushes by means of oxidation or reduction reactions. For example, functional aldehyde groups were formed on non-fouling POEGMA (poly(oligo(ethylene glycol) methyl methacrylate) brushes.

The polarity of the bias applied to either electrode depended on the material that the polymer brush was made of. Of the four polymers that were tested, PNIPAAm (poly(*N*-isopropylacrylamide)), and POEGMA had to be charged negatively for patterning. Conversely, PAA (poly(acrylic acid)) and PSMBA (poly(sulfobetaine methacrylate)) had to carry a positive charge to be patterned successfully. The bias voltage (2 to 10 V) and exposure duration (60 s to a few hours) were shown to affect the patterned feature size. Namely, an increase in voltage and exposure time led to an increase in the feature width and depth. An increase in the relative humidity of the ambient environment had the same effect. Interestingly, the polymer brushes could be patterned even at relative humidity levels as low as 5%. It was suggested that this was enabled by the retention of water in the brushes.

The serial FINL method yielded features with an edge roughness on the order of 30 nm. The feature resolution was comparable to electron beam lithography. In addition to serial FINL, the researchers also developed a parallel FINL approach. Here, instead of a tip, a stamp was fabricated from Si or a Si-based material. The parallel processing method enabled several regions of the polymer brush to be patterned simultaneously. In both FINL approaches, the polymer brushes were not removed from the substrate and the patterns created were not affected by rinsing with de-ionized water. Hence, the polymer brush substrates and the formed patterns were shown to be robust. In the case of PO-EGMA, the patterned surface was also non-fouling.

The presented FINL technique can be considered an important addition to the existing substrate patterning methods, especially in the case of polymer brush-based substrates. Thus, although this method does not offer large improvements upon other approaches, it could potentially find a niche application in the development of non-fouling biosensing devices.

References

1 S. M. Yang, *et al.*, Nanomachining by colloidal lithography, *Small*, 2006, **2**(4), 458–475.
2 D. Bazin and C. Faure, Electro-colloidal lithography: a versatile approach combining colloidal particles and electrical fields for the fabrication of patterned polymer and metal films, *Soft Matter*, 2012, **8**, 3053–3057.
3 A. W. Martinez, S. T. Phillips and G. M. Whitesides, Diagnostics for the Developing World: Microfluidic Paper-Based Analytical Devices, *Anal. Chem.*, 2010, **82**, 3–10.
4 A. R. Rezk, *et al.*, Uniform mixing in paper-based microfluidic systems using surface acoustic waves, *Lab Chip*, 2012, **12**, 773–779.
5 R. K. Smith, P. A. Lewis and P. S. Weiss, Patterning self-assembled monolayers, *Prog. Surf. Sci.*, 2004, **75**(1–2), 1–68.
6 R. Ferris, *et al.*, Field-Induced Nanolithography for Patterning of Non-Fouling Polymer Brush Surfaces, *Small*, 2011, **7**(21), 3032–3037.