

Manipulation of liquid droplets using amphiphilic, magnetic one-dimensional photonic crystal chaperones

JASON R. DORVEE¹, AUSTIN M. DERFUS², SANGEETA N. BHATIA² AND MICHAEL J. SAILOR^{1*}

¹Department of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, Department 0358, La Jolla, California 92093-0358, USA

²Department of Bioengineering, University of California, San Diego, 9500 Gilman Drive, Department 0412, La Jolla, California 92093-0412, USA

*e-mail: msailor@ucsd.edu

Published online: 7 November 2004; doi:10.1038/nmat1253

The controlled manipulation of small volumes of liquids is a challenging problem in microfluidics^{1–4}, and it is a key requirement for many high-throughput analyses and microassays^{5,6}. One-dimensional photonic crystals made from porous silicon have been constructed with amphiphilic properties⁷. When prepared in the form of micrometre-sized particles and placed in a two-phase liquid such as dichloromethane/water, these materials will accumulate and spontaneously align at the interface. Here we show that superparamagnetic nanoparticles of Fe₃O₄ can be

incorporated into the porous nanostructure, allowing the materials to chaperone microlitre-scale liquid droplets when an external magnetic field is applied. The optical reflectivity spectrum of the photonic crystal displays a peak that serves to identify the droplet. Two simple microfluidics applications are demonstrated: filling and draining a chaperoned droplet, and combining two different droplets to perform a chemical reaction. The method provides a general means for manipulating and monitoring small volumes of liquids without the use of pumps, valves or a microfluidic container.

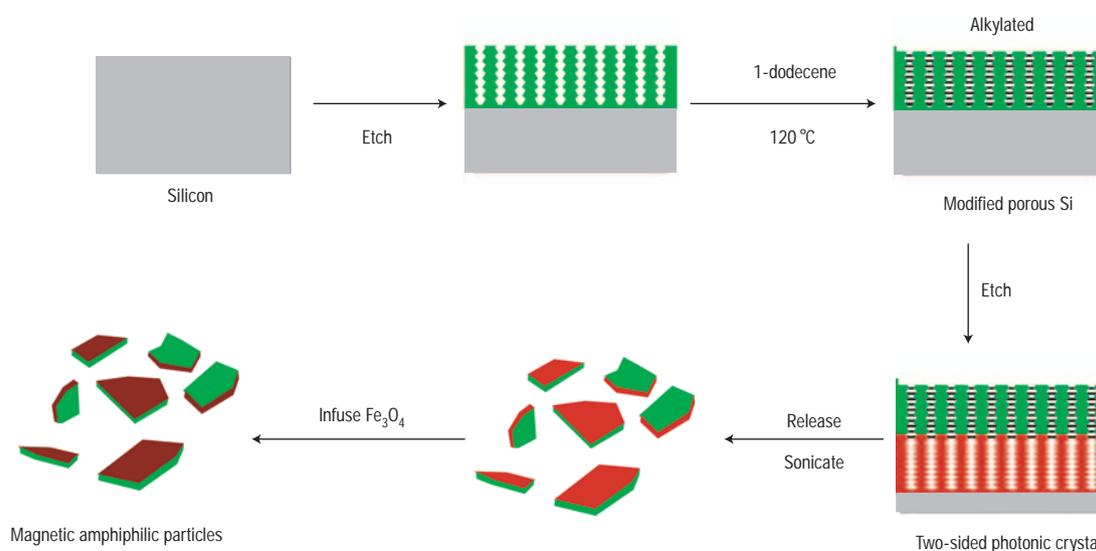


Figure 1 Schematic diagram of the synthesis of bifunctional magnetic particles. A multilayered porous-silicon dielectric mirror (rugate filter) is first etched into the single-crystal Si substrate. The film is then hydrosilylated to generate a chemically stable hydrophobic mirror. A second rugate filter with a different periodicity is etched into the substrate, immediately beneath the first. The entire structure is removed from the Si substrate by application of a current pulse. The bifunctional, freestanding film is placed in water and fractured into micrometre-sized particles by ultrasonication. The particles are then exposed to a solution of superparamagnetic Fe₃O₄ nanoparticles. Oxidation traps the nanoparticles in the porous Si matrix and imparts hydrophilic character to the second layer.

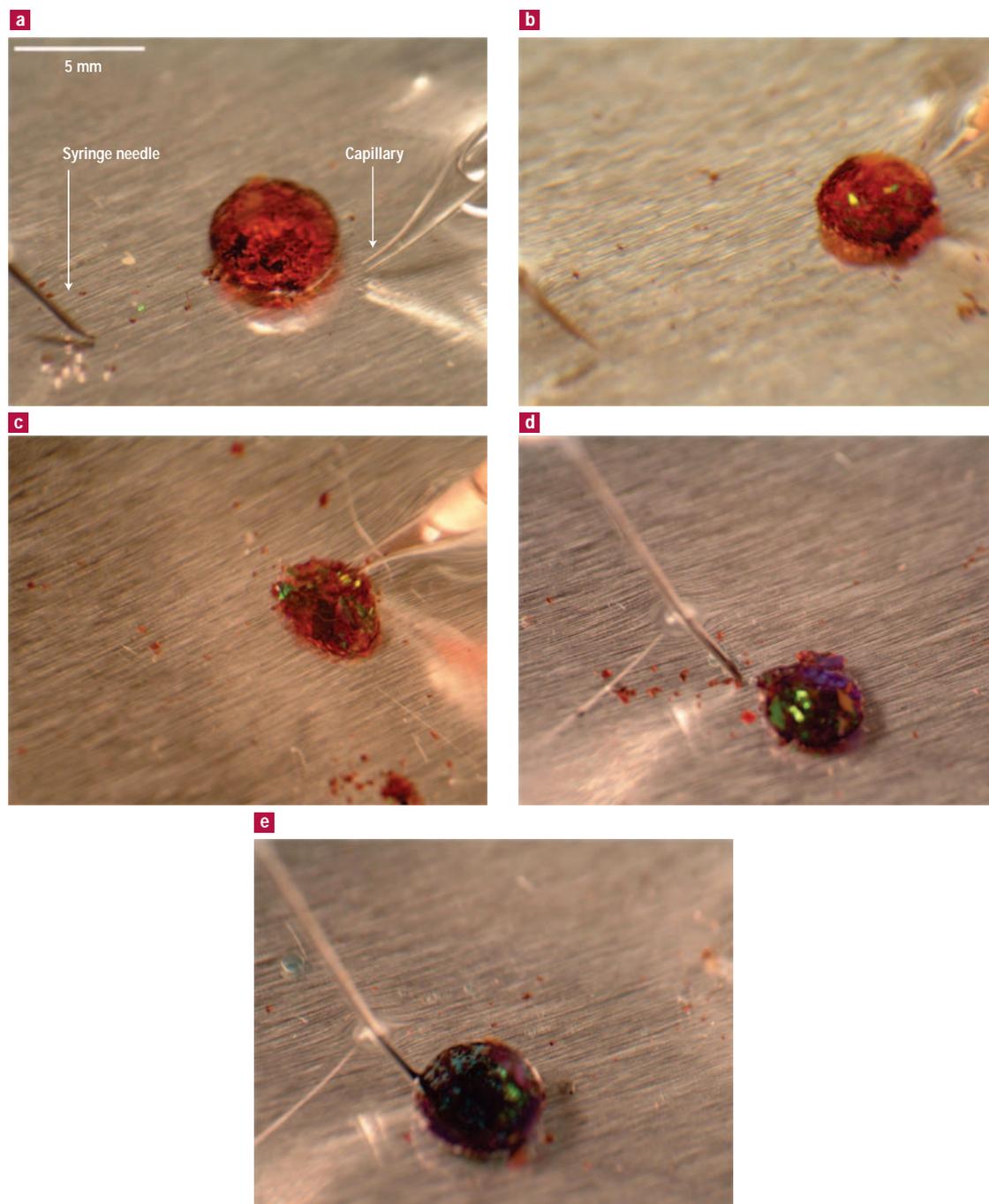


Figure 2 Optical microscope images of bifunctional magnetic porous Si particles. The images show transport and delivery of an aqueous payload to a capillary and then refilling of the assembly. **a**, Water drop surrounded by particles, immersed in 1:3 dichloromethane/hexane. The source needle is shown to the left, the drain capillary to the right. The drop has a volume of about 30 μL , and contains a red dye to aid visualization. **b**, The assembly is moved to the drain capillary under the influence of a magnet (not shown), positioned beneath the container, and begins to deliver the dye-containing water. **c**, Elimination of water from the assembly is completed. **d**, The dry assembly is moved to the source needle by a magnet. **e**, Assembly is refilled with water containing a blue dye.

The synthetic scheme followed to produce the amphiphilic, magnetic one-dimensional (1D) photonic crystals of porous Si is outlined in Fig. 1. A multilayered porous Si dielectric mirror is first electrochemically etched into the (100) face of a single-crystal, p-type Si wafer using a sinusoidal current waveform^{8,9}. The sinusoidal variation in refractive index that results, referred to as a rugate filter¹⁰, produces a sharp resonance feature in the optical reflectivity spectrum of the

film, whose wavelength is determined by the periodicity and current limits used in the etch¹¹. The film is then thermally hydrosilylated with 1-dodecene, following published procedures^{12,13}, to generate a chemically stable hydrophobic mirror. A second rugate filter is etched into the substrate, immediately beneath the first. The entire structure is then removed from the Si substrate by application of a current pulse. The freestanding film is fractured by ultrasonication in ethanol¹⁷ and

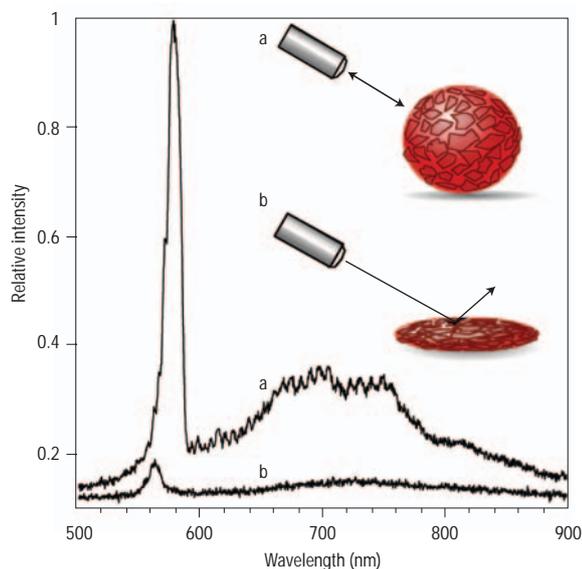


Figure 3 Reflectivity spectra of the bifunctional porous Si particle assembly before and after delivery of payload. **a**, Reflectance spectrum obtained from particles assembled on a water drop immersed in hexane. **b**, Spectrum obtained from the assembly after delivery of the aqueous payload to a capillary. Spectra were acquired using an Ocean Optics SD2000 CCD (charge-coupled device) spectrometer fitted with focusing optics and using a tungsten light source coaxial with the detection optics. The detection optics were positioned as indicated in the inset.

the resulting porous Si microparticles are infused with magnetite nanoparticles from an aqueous suspension.

The high pH of the magnetite suspension spontaneously induces oxidation of the second porous Si layer, presumably trapping the magnetite nanoparticles in an oxide matrix. After isolation from the solution with the aid of an applied magnetic field, the microparticle composites are thermally oxidized to trap the magnetite more completely. Oxidation of the porous Si films is confirmed by Fourier transform infrared (FTIR) spectroscopy (see Supplementary Information, Fig. S1), and the presence and disposition of magnetite in the porous Si film is determined by FTIR and elemental mapping of iron in a cross-sectional electron microscope image using energy dispersive X-ray spectroscopy (Supplementary Information, Figs S1 and S2). Thermal oxidation preferentially produces oxide on the more reactive, hydrogen-terminated porous Si layer. The oxide imparts hydrophilic character to the second mirror whereas the hydrosilylated side retains its hydrophobic nature, allowing the particles to align at an aqueous–organic liquid interface.⁷

In a basic demonstration of a microfluidic application, the bifunctional magnetic microparticles are used to chaperone droplets of water immersed in an organic phase between a source and a drain (Fig. 2). The microparticles spontaneously orient at the interface of the 30- μ L water droplet, with the hydrophilic side facing the aqueous phase (Fig. 2a). The interfacial adhesive forces are strong enough to allow the particles to move the droplet when a magnetic field is applied. When the droplet assembly is brought into contact with a glass capillary (Fig. 2b), water is removed from the assembly by capillary action (Fig. 2c). The magnetic porous Si chaperones can then be moved to a stainless steel syringe needle (Fig. 2d) and refilled with liquid (Fig. 2e), completing the transport cycle.

The reflectivity spectrum from the bifunctional mirrors provides a signal that can be used to identify the payload. The position of the spectral peaks in porous Si dielectric mirrors is a strong function of

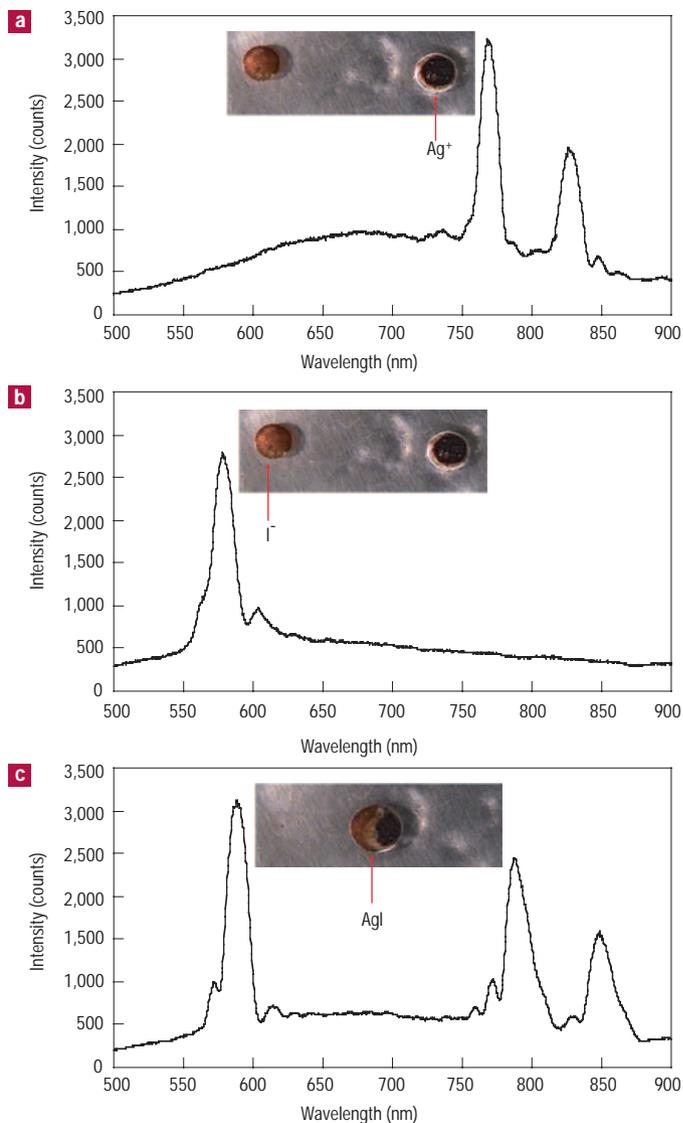


Figure 4 Reflectivity spectra of two sets of porous Si chaperones involved in mixing two chemicals to perform a reaction. The inset of each spectrum shows a photograph of the experiment representing that stage of the reaction. **a**, Reflectance spectrum obtained from particles assembled on a water droplet (4 mm diameter) containing $\text{Ag}^+_{(\text{aq})}$. The particles on this droplet contained a spectral code consisting of two peaks. **b**, Reflectance spectrum obtained from water droplet containing $\text{I}^-_{(\text{aq})}$ and a separate spectral code consisting of a single peak. **c**, Reflectance spectrum obtained from water droplet after the two drops were combined under the force of a magnet, showing the superposition of the two spectral codes. The $\text{AgI}_{(\text{s})}$ product of the reaction is apparent in the image as a white cloud inside the drop. Water droplets were immersed in octadecene throughout the experiment. The detection optics were positioned as indicated in Fig. 3.

the average refractive index of the layers, and shifts in the wavelength of the spectral features have been shown to provide a very sensitive transduction modality for sensing condensable liquids, proteins, DNA and other molecules^{14–18}. In the samples represented in Fig. 2, the hydrosilylated layer displays a spectral wavelength maximum of 540 nm that shifts to 579 nm when it is immersed in hexane (Fig. 3). The opposite side of the particle displays a band at 660 nm in air that shifts to 760 nm when in contact with water. The porous Si photonic

crystals contain enough repeat layers (100) that cross-talk between opposite sides is not readily observed in the spectra. The approximate spherical shape of the water droplet/chaperone assembly leads to a strong reflection from the hydrophobic side over a large range of incident angles (Fig. 3, trace a). On delivery of the aqueous payload, the sphere is deflated and reflection from the assembly is greatly reduced in intensity (Fig. 3, trace b). A slight blueshift is observed in the spectrum on deflation of the droplet, as expected from the angular dependence (Bragg's law) observed with photonic crystals¹⁹. These spectral characteristics can thus indicate the identity of the chaperones and the status of the chaperoned droplet.

A common microfluidic application is the mixing of two reagents to perform a chemical transformation. In an experiment demonstrating this concept, we mixed a water droplet containing KI_(aq) with one containing AgNO_{3(aq)} (Fig. 4, and Supplementary Information, movie S1). The chaperones for these two droplets each contain a different spectral 'barcode', prepared by etching the Si wafer using a superposition of sine waves as previously described^{10,20}. The droplets are forced to coalesce under the influence of a small magnet, and the AgI_(s) reaction product is observed as a white precipitate in the resulting droplet. The spectral code measured on the coalesced droplet contains three peaks, resulting from a combination of the two spectral signatures of the parent Ag⁺ (two peaks) and I⁻ (one peak) droplets.

As is apparent in movies of the experiment (Supplementary Information, movie S1), the presence of chaperones at their surface exerts a stabilizing influence on the water droplets, somewhat impeding coalescence. The presence of hydrophobic particles on the surface of a water droplet suppresses wetting, restricting the ability of two drops to merge¹. Here it is found that coalescence is aided by increasing the rate at which the two drops collide. The droplets deform on impact, creating a large contact surface that overcomes the effect of surface tension.

The method presented here provides a simple means for manipulating small volumes of liquids without a microfluidic container. Because the magnetic porous Si particles adhere to the surface of the water drop, they do not require a specific payload composition such as a high ionic strength to effect liquid motion. The electrochemical synthesis of porous Si photonic crystals allows the incorporation of spectral 'barcodes'^{11,20}, allowing the possibility of distinguishing between multiple distinct liquid drops in combinatorial assays. Because either water or an organic liquid can be encapsulated by the amphiphilic particles, a wide range of inorganic or organic molecules can be manipulated for the purpose of carrying out microreactions. Mammalian or bacterial cells can also be incorporated in this system for cell-based assays^{21,22}.

METHODS

PREPARATION OF POROUS SI FILMS

Multilayered porous Si dielectric mirrors were prepared by electrochemical etch of a single-crystal, (100)-oriented p-type Si wafer with a resistivity between 0.08 and 0.2 mΩ cm, by application of a sinusoidal current waveform oscillating between 13.3 and 39.8 mA cm⁻². The periodicity of the waveform was 8 s, repeated for 100 cycles in a 3:1 (vol/vol) aqueous 49% solution of HF/ethanol. Thermal hydrosilylation was accomplished by placing the porous Si sample in liquid 1-dodecene (95%, Sigma-Aldrich) in a Schlenk flask, degassing the liquid with three successive freeze-pump-thaw cycles, and then heating at 120 °C under nitrogen for two hours. A second rugate filter with a periodicity of 10 s was then etched into the substrate, immediately beneath the first layer for the same number of repeats. The porous Si structure was then removed from the crystalline Si substrate by application of a current pulse of about 15 mA cm⁻² in a 1:13.5 (vol/vol) aqueous 49% HF:ethanol solution for about 1 min, and the freestanding film was rinsed with ethanol.

PREPARATION OF MAGNETITE

In a representative preparation²³, 100 ml of a 1 M aqueous NH₄OH solution was added over a period of ten minutes to 10 ml of a 4:1 solution of 1 M FeCl₃ and 2 M FeCl₂ in water. The resulting black precipitate (magnetite) was filtered and then redispersed in 10 ml of 40 wt% aqueous tetrabutylammonium hydroxide. Dynamic light scattering measurements indicated that the particles were about 30 nm in diameter.

TRAPPING OF MAGNETITE INTO POROUS SI PARTICLES

The freestanding film was fractured by ultrasonication in ethanol and the resulting microparticles allowed to settle. The supernatant was removed, and the aqueous magnetite colloidal suspension

was added. After stirring for 5 min, the magnetic porous Si photonic crystal particles were isolated from solution by removal with a bar magnet. While still being held in the flask with a magnet, the particles were rinsed several times with acetone to remove free magnetite nanoparticles. The isolated magnetic microparticles were then thermally oxidized in air at 100 °C for 1–2 h.

PRECIPITATION OF AgI USING ENCODED CHAPERONES

Two batches of magnetic nanoparticles were prepared as described above, except that the hydrophobic (hydrosilylated with dodecene) layer of each batch was etched to display either one peak at ~580 nm (code 100) or two peaks at ~770 nm and ~830 nm (code 011). The etching conditions to produce the double peak (code 011) consisted of two superimposed sine waves of different frequencies²⁰. The specific conditions for preparation of the particles were: code 100: 20–60 mA cm⁻² current density, 50 repeats, 6.8-s period; code 011: 30–80 mA cm⁻² current density, 50 repeats, two superimposed sine waves with 6.1- and 5.7-s periods. The hydrophilic, magnetite-loaded layer for each set of particles was produced by etching a layer beneath the hydrosilylated film at a constant current density of 60 mA cm⁻² for 8 min. Removal of the film from substrate and preparation of particles followed the procedure described above. The isolated magnetic microparticles were then added to separate solutions of deionized water. One particle-coated water drop from each set was then added to a mixture of 95% octadecene and 5% CH₂Cl₂ in an aluminium dish. The deionized water was removed from each drop using a syringe fitted with a 30-gauge needle, leaving two collapsed masses of particles. Each set of particles was re-inflated with the appropriate solution: code 001 with 0.1 M KI(aq) and code 011 with 0.1 M AgNO_{3(aq)}. The particles were then manipulated with a magnet held underneath the dish, allowing the drops to combine and mix.

Received 2 July 2004; accepted 20 September 2004; published 7 November 2004.

References

- Aussillous, P. & Quere, D. Liquid marbles. *Nature* **411**, 924–927 (2001).
- Velev, O. D., Prevo, B. G. & Bhatt, K. H. On-chip manipulation of free droplets. *Nature* **426**, 515–516 (2003).
- Zheng, B., Tice, J. D., Roach, L. S. & Ismagilov, R. F. A droplet-based, composite PDMS/glass capillary microfluidic system for evaluating protein crystallization conditions by microbatch and vapor-diffusion methods with on-chip X-ray diffraction. *Angew. Chem. Int. Edn* **43**, 2508–2511 (2004).
- Srinivasan, V., Pamula, V. K. & Fair, R. B. Droplet-based microfluidic lab-on-a-chip for glucose detection. *Anal. Chim. Acta* **507**, 145–150 (2004).
- Liu, J., Hansen, C. & Quake, S. R. Solving the "world-to-chip" interface problem with a microfluidic matrix. *Anal. Chem.* **75**, 4718–4723 (2003).
- Hong, J. W. & Quake, S. R. Integrated nanoliter systems. *Nature Biotech.* **21**, 1179–1183 (2003).
- Link, J. R. & Sailor, M. J. Smart Dust: Self-assembling, self-orienting photonic crystals of porous Si. *Proc. Natl Acad. Sci. USA* **100**, 10607–10610 (2003).
- Schmedake, T. A., Cunin, F., Link, J. R. & Sailor, M. J. Standoff detection of chemicals using porous silicon "Smart Dust" particles. *Adv. Mater.* **14**, 1270–1272 (2002).
- Vincent, G. Optical properties of porous silicon superlattices. *Appl. Phys. Lett.* **64**, 2367–2369 (1994).
- Berger, M. G. *et al.* Dielectric filters made of porous silicon: advanced performance by oxidation and new layer structures. *Thin Solid Films* **297**, 237–240 (1997).
- Cunin, F. *et al.* Biomolecular screening with encoded porous silicon photonic crystals. *Nature Mater.* **1**, 39–41 (2002).
- Stewart, M. P. & Buriak, J. M. Photopatterned hydrosilylation on porous silicon. *Angew. Chem. Int. Edn Engl.* **37**, 3257–3260 (1998).
- Boukherroub, R., Wojtyk, J. T. C., Wayner, D. D. M. & Lockwood, D. J. Thermal hydrosilylation of undercyclic acid with porous silicon. *J. Electrochem. Soc.* **149**, 59–63 (2002).
- Chan, S., Horner, S. R., Miller, B. L. & Fauchet, P. M. Identification of gram negative bacteria using nanoscale silicon microcavities. *J. Am. Chem. Soc.* **123**, 11797–11798 (2001).
- Sailor, M. J. in *Properties of Porous Silicon* (ed. Canham, L.) 364–370 (Short Run Press, London, 1997).
- Collins, B. E., Dancil, K.-P., Abbi, G. & Sailor, M. J. Determining protein size using an electrochemically machined pore gradient in silicon. *Adv. Funct. Mater.* **12**, 187–191 (2002).
- Snow, P. A., Squire, E. K., Russell, P. S. J. & Canham, L. T. Vapor sensing using the optical properties of porous silicon Bragg mirrors. *J. Appl. Phys.* **86**, 1781–1784 (1999).
- Arwin, H. *et al.* Protein adsorption in thin porous silicon layers. *Phys. Status Solidi A* **182**, 515–520 (2000).
- Urbas, A., Fink, Y. & Thomas, E. L. One-dimensionally periodic dielectric reflectors from self-assembled block copolymer-homopolymer blends. *Macromolecules* **32**, 4748–4750 (1999).
- Meade, S. O., Yoon, M. S., Ahn, K. H. & Sailor, M. J. Porous silicon photonic crystals as encoded microcarriers. *Adv. Mater.* (in the press).
- Bayliss, S. C., Heald, R., Fletcher, D. I. & Buckberry, L. D. The culture of mammalian cells on nanostructured silicon. *Adv. Mater.* **11**, 318–321 (1999).
- Chin, V., Collins, B. E., Sailor, M. J. & Bhatia, S. N. Compatibility of primary hepatocytes with oxidized nanoporous silicon. *Adv. Mater.* **13**, 1877–1880 (2001).
- Berger, P. *et al.* Preparation and properties of an aqueous ferrofluid. *J. Chem. Educ.* **76**, 943–948 (1999).

Acknowledgements

We thank Erkki Ruoslahti of the Burnham Institute for discussions, and Evelyn York of the Scripps Institute of Oceanography, Analytical Instrument Facility, for assistance with the electron microscopy measurements. This project has been funded in part by the Air Force Office of Scientific Research under grant no. F49620-02-1-0288 and by the National Cancer Institute, National Institutes of Health, under contract no. N01-CO-37117. J.D. thanks the UCSD California Institute of Telecommunications and Information Technology for a fellowship.

Correspondence and requests for materials should be addressed to M.J.S.

Supplementary Information accompanies the paper on www.nature.com/naturematerials.

Competing financial interests

The authors declare that they have no competing financial interests.