

# Research Highlights

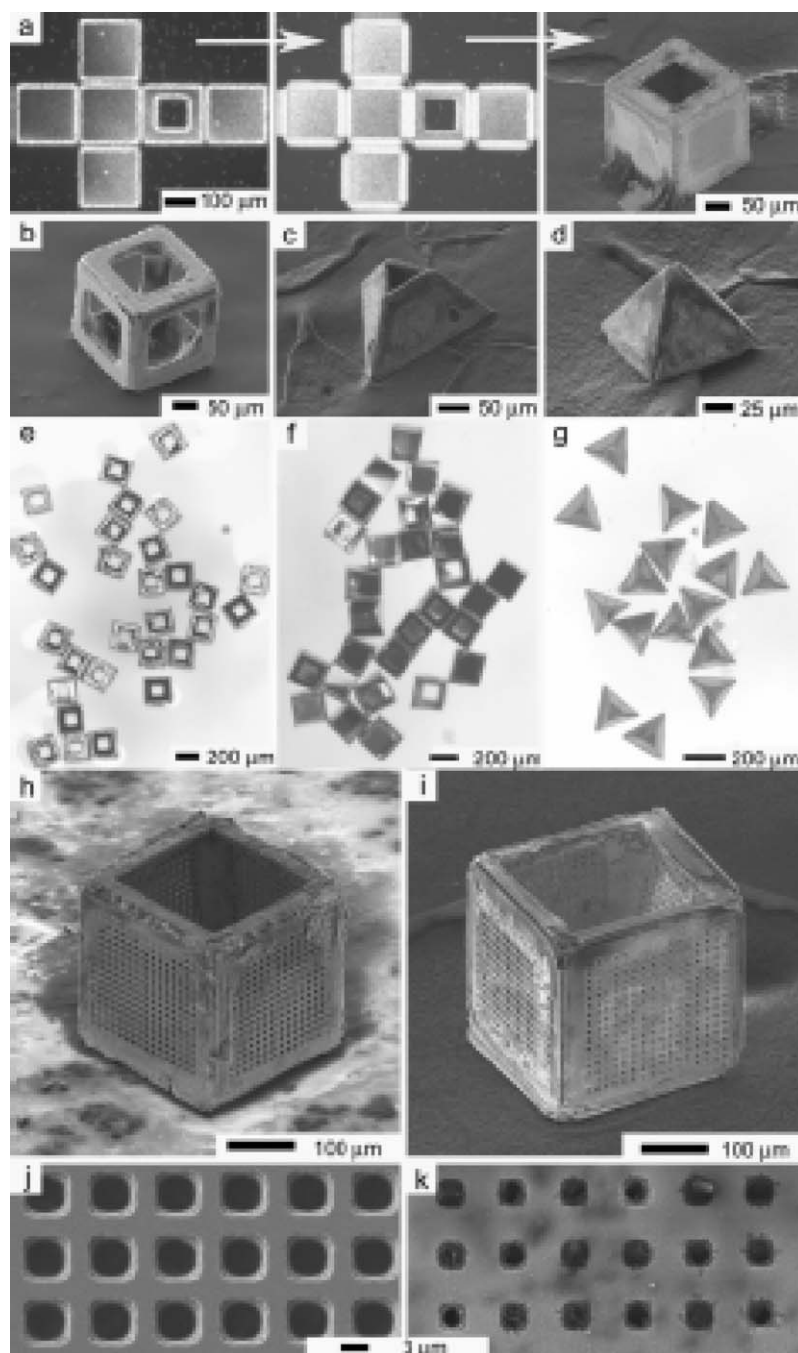
DOI: 10.1039/b613648f

## Metallic microcontainers

In a chemical lab, chemical compounds are stored in macroscopic vessels, and—when required for chemical reactions—the desired amount is simply taken out of the vessels using appropriate macroscopic tools such as spatulas or pipettes. In the microscopic scale, these processes are obviously more difficult to accomplish. On a microfluidic chip, chemicals are typically supplied using tubing systems, which are connected to syringes and pumps on the one side, and to the microchip on the other side. The spatial control of the release of the chemical is limited, since it is predicted by the design of the microfluidic channel.

David Gracias and co-workers from the John-Hopkins University in Baltimore addressed this issue.<sup>1</sup> They fabricated metallic microcontainers with volumes ranging from a few hundred picolitres to a few nanolitres. In contrary to organic material used in former studies to form microcontainers, the metallic microcontainers provide a great variety in shape, size and porosity. The 3D microcontainers were fabricated in two steps. First, a 2D template with solder hinges was processed by standard photolithography (Fig. 1(a)). Afterwards, upon increasing the temperature above the melting point of the solder hinges, the 3D container was formed by self-assembly. Hollow polyhedrons such as cubes or pyramids can be created in a parallel manner depending on the initial design of the 2D template, while the side surfaces of the polyhedrons are entirely closed, open, or contain monodispersed micrometre-sized pores (Fig. 1(b)–(k)). Variations in the relative porosity of the different faces facilitate anisotropic diffusion of the compounds out of the microreactor. When magnetic metallic microcontainers are used (here: nickel), the microcontainer can be remotely positioned on a surface, as well as guided along any trajectory by means of a magnetic field. Chemical compounds are encapsulated inside the microcontainers by microinjection in a carrier medium (gel or polymer). The release of

the compounds is achieved by immersing the containers in a solution that softens or dissolves the carrier medium, or by altering the temperature. The authors visualise the spatial controlled release of a chemical compound from cubic



**Fig. 1** (a) Optical and SEM images of the different fabrication steps to form a cubic microreactor from a metallic 2D template with solder hinges. (b–d) Microcontainers with different shapes. The fabrication can be performed in a parallel manner, which is demonstrated in the optical images in (e–g). (h–k) Cubic microcontainers with side surfaces of varying porosity. (Reprinted with permission from Leong *et al.*<sup>1</sup> Copyright 2006 American Chemical Society.)

containers using the pH indicator phenolphthalein. A red trace of phenolphthalein (in the form of the letter G) is created, when the nickel microcontainer is guided by a permanent magnet. When two microcontainers, loaded with different reactants, are positioned opposite to each other, intermolecular chemical reactions occur at the central line between the two diffusing reactants. This is demonstrated for the reactions between potassium hydroxide and copper sulfate to form copper hydroxide, as well as for the reaction between potassium hydroxide and phenolphthalein, which results in the colour change of phenolphthalein from colourless to red.

The microcontainers could be used and moved on the surface of any substrate as described, but also supplied into microfluidic channel networks to carry chemicals to the desired position.

### Determination of heparin in clinical settings

The glycosaminoglycan heparin prevents coagulation of blood, and is used *e.g.* during and after surgery. However, careful and continuous control of the heparin level in blood is required to ensure that the level is sufficiently high to prevent thrombosis yet low enough to avoid bleeding risks. Thus, a sensor capable of on-line analysis of heparin would be valuable to optimise the dose of heparin

supply and hence, to minimise the patient's risks.

Researchers from the MIT in Cambridge developed a sensor on a microfluidic chip to monitor heparin and its low-molecular-weight analogs by the silicon field effect.<sup>2</sup> The electronic field-effect sensor is based on an electrolyte insulator silicon structure to directly monitor the binding of heparin by detecting its intrinsic negative charge (Fig. 2). Selective binding of heparin to the sensor surface is achieved by functionalising the surface with an antidote of heparin, *i.e.* the cationic protein protamine. In a control sensor channel, the surface is passivated by bovine serum albumin (BSA) to prevent heparin binding. The difference in surface potential between two sensors in adjacent channels is measured, and the performance of the sensor is shown by a dose–response curve for varying heparin concentrations in phosphate buffered saline (PBS) buffer. The sensitive region ranges from 0.01 to 1 units ml<sup>-1</sup>, which is even below typical doses of heparin given to patients during surgery (2–8 units ml<sup>-1</sup>). Furthermore, the low-molecular-weight heparin enoxaparin and the synthetic heparin fondaparinux, could be determined, which is not possible with currently existing near-patient clinical methods. The protamine sensor is compared to a standard method for clinical assessment of heparin, namely the Anti-Xa assay. The microchip sensor exhibits higher

sensitivity, and better precision and accuracy in determination of unknown heparin concentration, while consuming only nanograms of sample.

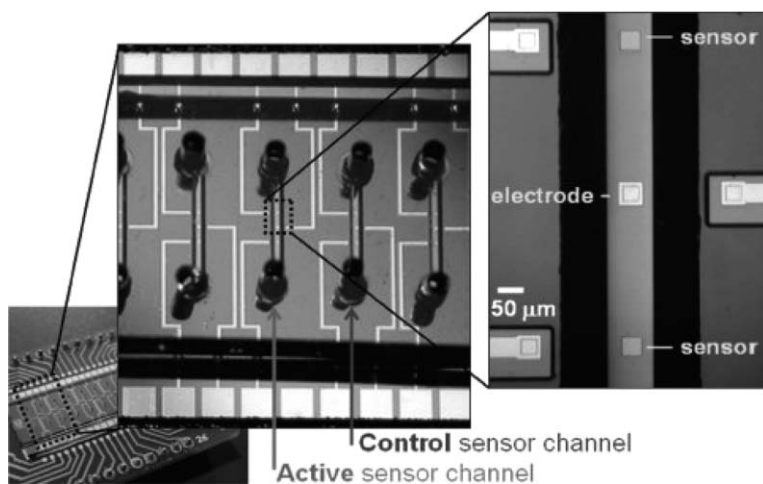
So far, the sensor has only been tested for laboratory use. For use in clinical applications, several requirements have to be addressed, such as shorter calibration time, improved reproducibility of the microchip sensor, and an adaptation to enable heparin to be measured directly in plasma samples rather than in buffer solution. The routine use of the microchip sensor in the clinical setting could increase the efficacy and safety of heparin and heparin-based drugs.

### Steam reforming in ceramic microreactors for on-site hydrogen production in fuel cells

Due to their high efficiency, hydrogen fuel cells are promising electrical power sources. Among the different fuel cell types, polymer electrolyte membrane (PEM) fuel cells are particularly suitable for use in mobile applications, *e.g.* in buses or other vehicles and in portable electronic devices. However, for production of electrical power in a mobile fuel cell hydrogen is required. Since the storage of compressed hydrogen bears a high safety risk, hydrogen supply in mobile applications is rather accomplished by on-site generation *e.g.* by steam reforming of liquid hydrocarbons.

Paul Kenis and co-workers present in the current issue of *Lab on a Chip* the development of a ceramic microreactor for steam reforming of propane.<sup>3</sup> The ceramic microreactor is composed of an alumina housing structure that comprises five SiC monoliths with pore sizes of 7.2 μm. The catalyst ruthenium was deposited on these monoliths. The device is placed inside a furnace. Steam of water is generated and introduced into the microreactor together with helium (which serves as internal standard) and propane.

The conversion of propane as well as the composition of the product gas is investigated for several temperatures between 800–1000 °C, and for varying steam-to-carbon ratios. Moreover, kinetic analysis of propane conversion is performed. The results indicate that a low steam-to-carbon ratio could be used



**Fig. 2** Images of the silicon field-effect device showing the array of parallel microfluidic channels, each containing two field-effect sensors, and a gold signal electrode. For differential measurements, two channels are utilized, one for the active sensor and another one for the control sensor. (Reprinted with permission from Milović *et al.*<sup>2</sup> Copyright 2006 National Academy of Sciences, USA.)