Research Highlights

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Microchip calorimeter: measuring heat

Calorimeters are used to characterise the thermodynamics of chemical reactions. Usually, the volume of the reaction systems is quite large for calorimetric measurements, typically a few hundred microlitres. A significant decrease of the volume would raise the prospect of high-throughput biochemical measurements with minimal sample consumption. Current microchip calorimeters are designed for fluid volumes down to tens of picolitres, but the low sensitivity and the lack of sample handling have reduced their utility. In a recent publication, Michel L. Roukes and co-workers from California Institute of Technology (Pasadena) developed a novel closed-chamber calorimeter on a microchip with greatly enhanced sensitivity.[1] The microchip consists of three components for (i) fluid handling, (ii) temperature measurements and (iii) thermal isolation from the environment. The microfluidic chip has a measurement chamber, and microfluidic channels with integrated pneumatic pumps and valves for handling volumes of a few nanolitres. Temperature determination is performed by means of Au/Ni thermopiles (Fig. 1). The particular improvement of the new calorimeter compared to former devices is the thermal isolation. By fabrication of a "vacuum space" on chip, heat losses are minimised and hence, the sensitivity is increased (to a resolution of 4.2 nW). This configuration is possible by a smart combination of different materials. In particular, the polymeric coating material, parylene, is used to form the measurement and the vacuum chamber, providing excellent conditions for thermal isolation. It is interfaced with polydimethylsiloxane, a flexible material that facilitates the formation of the pneumatic valves. The excellent performance of the device is demonstrated by monitoring the generation of heat during the hydrolysis of urea and the mixture of water with methanol.

Temporal regulation of neuron growth

Our nervous system is a network of axons that are connected by functional synapses. One key step in the formation of the nervous system is the axonal elongation, and it is of particular interest to understand the mechanism of axonal growth and its regulation. It is known that factors such as netrin-1 and nerve growth factor (NGF) increase the rate of axonal elongation; the precise pathways, however, are unclear. In a recent work, U. Hengst *et al.* explored the role of intra-axonal protein translation of netrin-1 and NGF-stimulated axon growth.[2] The study was possible by means of a microfluidic device consisting of two microchambers, separated by microgrooves that allows local treatment of the neurons. While the neurons are plated into one side compartment of a microfluidic chamber, axons grow through 450 μm long microgrooves into the other compartment of the chamber, where they can be treated selectively. The researchers could investigate the role of local protein translation and the role of a polarity complex protein, known to be present in growth cones of axons. They found that both local protein translation and the complex protein are required for stimulated nerve growth. Factors such as netrin-1 or NGF increase the synthesis and the levels of the complex protein in the axons thereby triggering a switch to a rapid axonal growth mode. The findings may help to understand the mechanism for the regulation of the complex protein in various cell types.

Droplet analysis: MS

Microfluidic platforms are nowadays extensively used to create aqueous microdroplets within a hydrophobic carrier stream. The fast and reproducible production of microdroplets opened the door to novel methods in various fields including protein and single cell analysis. In order to fully exploit the unique properties of droplet-based microfluidics, the analysis of individual droplets by comprehensive detection

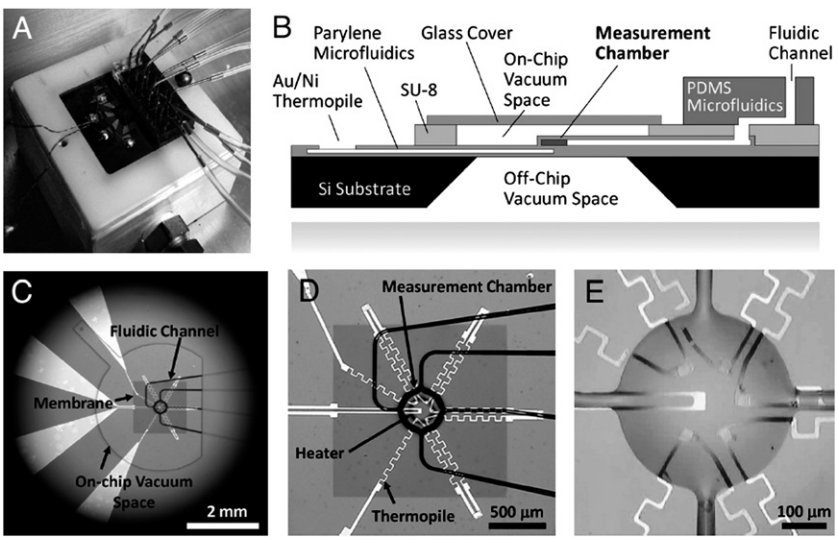

Fig. 1 Design of the microchip calorimeter. (a) Photograph of the device, mounted on a vacuum chuck. (B) The measuring chamber is enclosed by a thin layer of parylene while fluid transport is conducted through a polydimethylsiloxane (PDMS) microchip with integrated valves. Thermal isolation is achieved by an on-chip vacuum chamber. (c)–(e) These images show the design of the microchamber and the thermopiles. (Reprinted with permission from ref. 1. Copyright 2009, National Academy of Sciences, USA.)

methods is most important, but most challenging as well. As reported in an earlier Research Highlights (issue 19),[3] the connection to mass spectrometry would be the most valuable method to identify the content of individual droplets. In a recent work by Ryan T. Kelly and colleagues from Pacific Northwest National Laboratory, a microchip is presented and tested that is capable of droplet generation and analysis by electrospray-ionisation mass spectrometry (ESI-MS).[4] One of the key challenges of such devices is the separation of the aqueous droplets from the hydrophobic carrier before MS analysis. In the new device, this problem is solved by a clever microchannel design: the microchannel carrying the droplets is contacted with another microchannel filled with an aqueous solution. The interface between these two channels is comprised of 6 cylindrical columns that create 3 μm apertures in between. This design enabled the direct and continuous transfer of the aqueous droplet content into the aqueous stream within *ca.* 200 μm, while the hydrophobic solvent would not pass the apertures. In this way the analytes are directly transported to the nano-ESI emitter that is integrated into the microchip. The device facilitates fast, high-sensitivity nano-ESI MS-detection of individual droplets, which is shown for the analysis of the two pentapeptides, leu-enkephalin and met-enkephalin. In future, the presented approach may be particularly useful in the fields of proteomics and single cell analysis.

Petra S. Dittrich
ETH Zürich, Switzerland
dittrich@org.chem.ethz.ch

References

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