

Towards Lab-on-a-Chip Devices for Personalised Medication and Diagnostics

A modular microfluidic kit has been designed that may speed up the development of integrated lab-on-a-chip devices.

Great expectations

There is unanimous agreement that lab-on-a-chip (LOC) devices have great potential. But major drawbacks lie in the high development and production costs involved in bringing them to market.¹ The best way to resolve this stalemate is to make development faster and less risky and at the same time make production less expensive. A possible solution is a microfluidic construction kit based on modern plastic production technology.

Applications of the future

Drug metabolism not only differs between men and women, but between one individual and another. Currently, the only way to determine the application of a drug for a patient is by rule of proportion, or worse, rule of thumb. In the future, drug application will be determined on an

individual basis where everyone will obtain the precise combination of drugs optimised to his or her biological uniqueness. These drug “cocktails” will be mixed by LOC devices that make the process available at the point of care.

This type of drug-mixing unit is rarely discussed because it is far from realisation. A design that is closer to being reality is the LOC device that will provide the information necessary to compose the drug mixtures. This device will be a powerful diagnostic tool that will enable medical staff to screen a patient in situ for a large variety of medical parameters. On a molecular basis the LOC devices will be able to look for

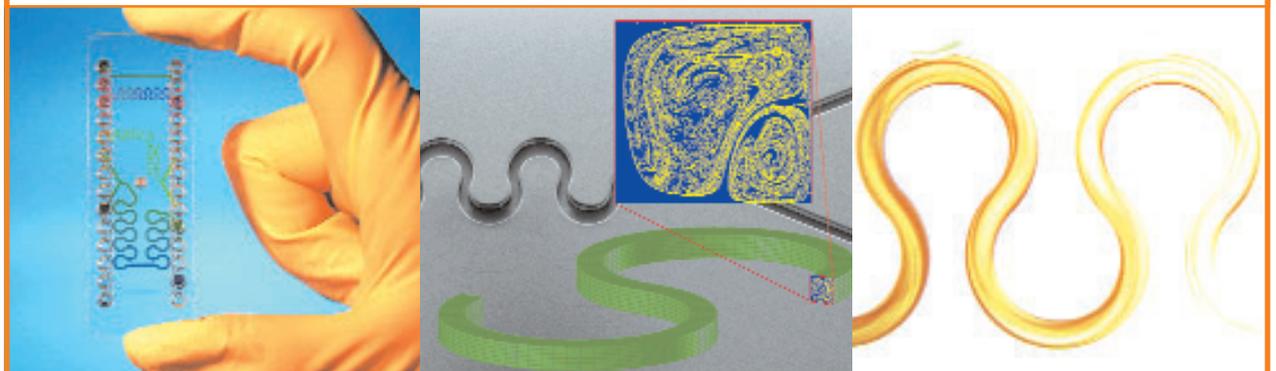
- signs of pathogens such as AIDS or SARS viruses
- individual genetic dispositions for diseases such as Alzheimer’s or diabetes
- metabolic peculiarities.

Process integration

LOC devices integrate a series of laboratory processes such as sample preparation, fluid handling, reaction, analysis and detection. Long-awaited first products have hit the market, but sales do not seem to reflect the fascinating potential of LOC devices. The caution of market players is mainly the result of the high cost of development and production. Demand is waiting for lower prices, yet hardly anyone can afford to offer lower prices because of the investment needed to develop the products.¹ What can be done about it?

In a LOC, tiny channels connect functional elements such as reactors, mixers, valves and pumps to form a complex fluid network. As a rule, the properties of single microfluidic elements are well known and can be simulated reasonably accurately (Figure 1). But when these elements are

Figure 1: Simulation of single components such as this passive flow-through micromixer render satisfactory results. However, numeric calculations are usually inadequate when the behaviour of a system of several microfluidic units needs to be predicted. From left to right: a micromixer slide as part of the construction kit, a scanning electron microscope picture of the mixer with simulation graphics and a photograph of the synthesis of a red substance by mixing two colourless liquids. Source of middle and right images: Institute of Microtechnology Mainz.



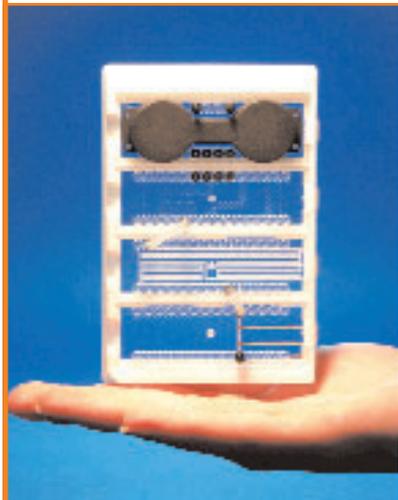
combined they interact with each other. Despite all that is known about the constituents, there has been no way to reliably predict the system's behaviour by simulation.

A way forward

Prototyping LOC devices, therefore, is rather risky. It is often too risky for many companies that could make use of LOCs to bring novel biomolecular techniques to the market. The modular concept of the microfluidic construction kit (Figure 2) offers the possibility to optimise single components independently. Interconnection of the components is easily achieved by standardised microfluidic interfaces. The ensuing system can be tested extensively and consecutively improved by replacing a given element with a better one. As a consequence, development will become faster and cheaper.

The fluidic interfaces are important in this concept. They should have low dead volume, must be leakproof for fluids and gases and the laboratory assistant should be able to connect and disconnect the components without any tools. Because none of the solutions currently on the market satisfy all of these requirements, the German Ministry of Education and Research (www.bmbf.de) funded a project to develop devices with these features. One variant was designed to connect two adjacent components and another variant was designed to be used to connect the device with peripheral equipment.

Figure 2: The microfluidic construction kit can prove the viability of a LOC design before going into integration.



Several components for pumping, mixing, retention, separation and detection were manufactured in standard slide format (25.5 × 75.5 mm). Inside a frame with the outer dimensions of a microplate, four slides can be assembled for testing. This allows, for example, a microfluidic system for the purification of ribonucleic acid. In the months to come, more microfluidic functions will become available on a slide. The intention is to build up a library of modules that cover a range of standard fluid operations. Depending on the application, these standard slides will need to be supplemented by customised ones.

Cost-efficient production

Once the LOC principle has been proven, the modular system can be turned into an integrated system. The modules of the construction kit are made of cyclic olefin copolymer, but are not limited to the use of this material. Up to this point the construction kit has helped to lower the hurdles of the development process. The fact that all microfluidic modules are made of plastic also plays a decisive role: the LOC devices can be produced by microinjection moulding. Because microinjection moulding is generally accepted as the most cost-efficient production technology, this approach not only promises to resolve the stalemate of risky development, but also of high production costs.

References

1. Technical Insight, Frost & Sullivan, www.frost.com/prod/servlet/press-release.pag?docid=24548027 **mdt**

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