Complex laboratory diagnostics can be incorporated on disposable 'credit cards'

Dr Thomas Stange reports on the use of the lab-on-a-chip concept as a diagnostic tool. Here, microtechnology has enabled standard laboratory process to be incorporated on a piece of equipment the size of a credit card.

Reportage du Dr Thomas Stange sur l'utilisation du concept de laboratoire sur puce en tant qu'outil de diagnostic. Ici, la microtechnologie a permis à des processus standards de laboratoire d'être incorporés sur un dispositif de la taille d'une carte de crédit.

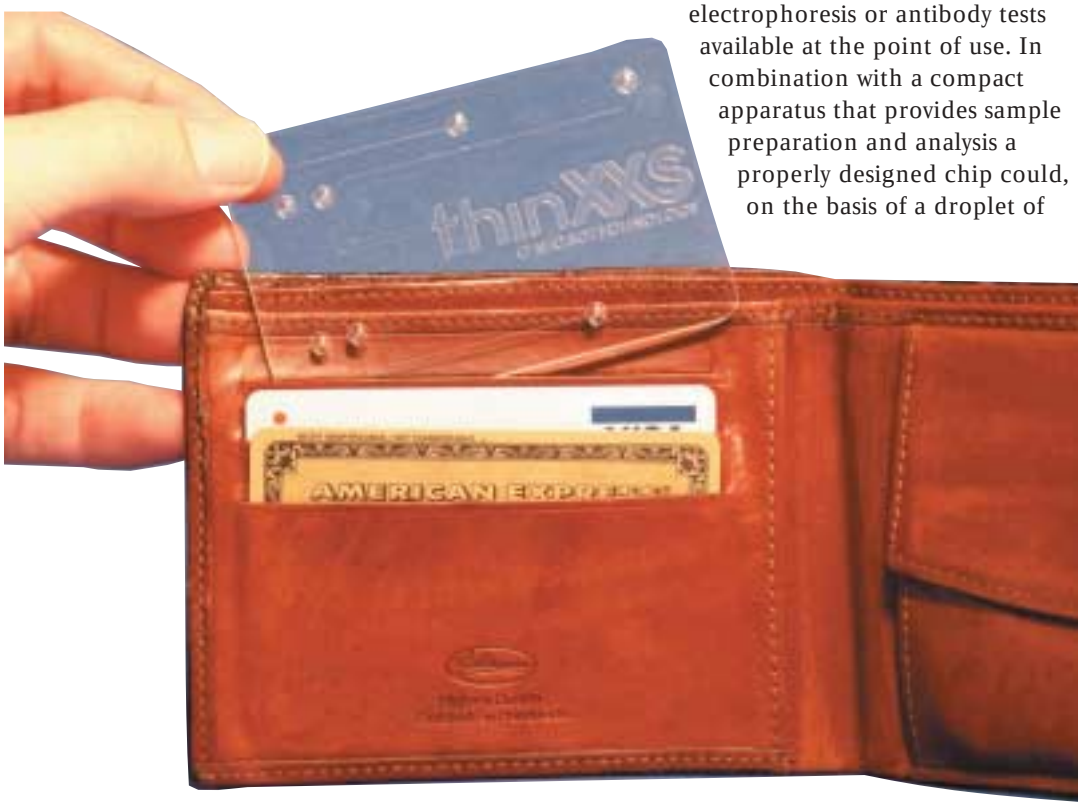
Dr. Thomas Stange berichtet über den Einsatz das Konzept des „Labors auf einem Chip" als Diagniosehilfsmittel. Hierbei hat die Mikrotechnologie die Möglichkeit eröffnet, standardmäßige Laborverfahren in eine Ausstattung zu integrieren, die lediglich die Größe einer Kreditkarte aufweist.

Test strips are rather crude chemical indicators that can tell a woman with a certain probability if she is pregnant or warn somebody suffering from diabetes when it is time to apply a new ampoule of insulin. Their undeniable strength is that they are easy to use: no help of a specialist is required, the test can be carried through in situ and the looked for piece of information is available within seconds or minutes.

Unfortunately, the instances in which a simple yes or no does not suffice to determine what appropriate action to take are by far more common. Symptoms like coughing or a running nose may have quite a variety of causes, from a harmless cold to a life threatening infection. To distinguish the one from the other, more sophisticated tests need to be carried through in special laboratories. They provide more detailed information, but usually take up a considerable amount of time. In the case of a pregnant woman a few more days surely will not be of vital importance, but for a sick patient precious time is being lost.

It consequently would be more than desirable if devices existed which would be (almost) as simple to apply as test strips and at once render the sensitive, accurate and complex checks of a full-scale laboratory analysis quickly and on the spot.

In past years the lab-on-a-chip concept has come the closest towards the potential combination of these two demands in a diagnostic tool. The underlying idea stems from the world of microtechnology and usually is associated with a chip of approximately credit card size. Embedded on the chip's surface are microstructures such as channels, mixers or reservoirs in order to facilitate the required manipulation of a biological sample. The goal is to make standard laboratory processes such as polymerase chain reaction, capillary electrophoresis or antibody tests available at the point of use. In combination with a compact apparatus that provides sample preparation and analysis a properly designed chip could, on the basis of a droplet of



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blood, saliva or urine, allow for a most precise diagnosis in a time frame which may range from a number of minutes to a few hours.

Although the concept has been explored for more than a decade by now, such labs-on-a-chip are still in their early stages. One difficulty lies in the biochemical prerequisites for any analysis of a sample of only a few microlitres. Sensitivity, for instance, is a crucial point: a test method which does not reliably indicate the presence or absence of a looked for substance will, rightly enough, never make it to the market. Thanks to recent advances in biochemistry, however, a good number of biotech companies presently work on the realisation of such tests, and many promising results have already been reported.

Besides the biochemistry the manufacturing of such devices remains part of the challenge. In order for the microfluidics (ie the manipulation of minute amounts of liquids or gases) to function, the structures of the chips need to be realised with extremely high precision. In certain cases this can mean an accuracy of nanometric dimensions.

For many years research and development concentrated on glass or silicon substrates, due to the prevailing technical capabilities in microtechnology. Yet, a new diagnostic tool will only be competitive with established procedures if it does not only show a practical, but also a cost advantage. Therefore, a process technology is needed which ensures the reliable replication of structures of down to some 10 microns with the required accuracy and at competitive unit costs.

Most experts agree that this may only be achieved when turning to the microinjection moulding of plastics. Although principally derived from conventional injection moulding, this technique is fairly young. The reason why is that the production of small plastic pieces with miniscule structure details asks for a whole range of new solutions in process control as well as in the production steps prior and after the moulding. Thus, a chip with features of down to a few microns requires a metal mould insert with even higher precision; and one can easily imagine that handling, finishing, assembly or quality control of the chips are quite demanding. As a consequence, only a handful of companies worldwide have got the know-how necessary to realise labs-on-a-chip out of plastic.

A further challenge of labs-on-a-chip yet to be tackled includes the development of practical interfaces between different microstructured components and between these components and the macroscopic control and analysis units.

To overcome these obstacles, a consortium, headed by thinXXS, intends to devise components with micro channels, miniature pumps, integrated valves or electrodes which may be modularly combined with each other. The aim is to lay the foundations of a microfluidics construction kit from which one can assemble a process chain of single, miniaturised laboratory operations.

Obviously, a good number of core competencies have to be brought together in order to arrive at disposable, credit card sized chips. Such systems are, by and large, still a vision of the future, but the technological prerequisites are no longer the time limiting factor. Advances in biochemistry and production technology go at a pace that the wishful thinking of the early days in lab-on-a-chip design is likely to soon turn into a phase in which products are realised, products which would improve medical diagnosis and therapy considerably. ■

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