

Lab-on-a-Chip

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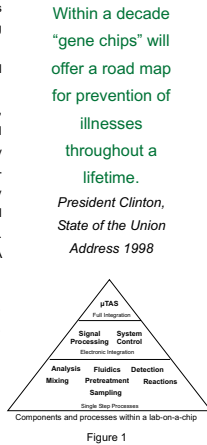
Introduction to the Lab-on-a-Chip Concept.

What is a lab-on-a-chip? A way of making environmental and process measurements for the chemical and biochemical industries lower cost, more reliable, and producing less waste.

How? By applying miniaturisation techniques from the electronics industry to chemical analysis.

Who is interested in lab-on-a-chip? Major companies such as Glaxo-Wellcome, Unilever and Kodak are interested in applications including: DNA, pharmaceutical and environmental analyses. These and other firms are partners in the DTI's recently announced Foresight Link Award for the development and exploitation of lab-on-a-chip technology within the UK. The UK lab-on-a-chip consortium is a multidisciplinary research forum, comprising seven of the UK's leading universities, and ten industrial partners. The US, Japan and Germany are also funding major research programmes. Many biotech companies are investing heavily in development of devices for DNA analysis.

Research into lab-on-a-chip, also known as micro total analysis systems (μ TAS) has been carried out within DIAS, UMIST. Figure 1 shows the components and processes required in a lab-on-a-chip. Presented here are examples of the work undertaken in DIAS relating to the development of both electrochemical (conductivity) and optical (ARROW) detection systems for use in miniaturised analysis systems.



Optical Detection for Lab-on-a-Chip

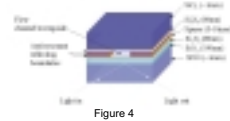
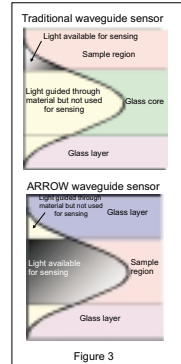
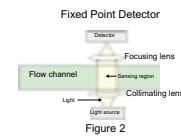
Our work focuses on devices which are called optical waveguides, light is contained and guided within the device, and the interaction of the light with a sample molecule allows the molecule to be seen by a detector mechanism usually a CCD (Charge Coupled Device) camera.

1) The "flow distance" available for detection i.e. the area through which a molecule must pass to allow detection. These systems are known as fixed point detectors. They are not very efficient, since the time a sample molecule spends in the detection region is small, especially when compared to the distances the molecules must travel to reach the detector. (Figure 2)

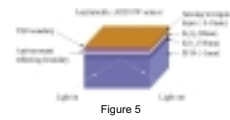
2) The availability of light which can be used in the detection process. Light is often confined in such a way that only a small amount of light (the grey shaded area) is available for the detection process. These systems are traditional optical waveguides. The diagram shows the light intensity profile for this type of system however, these systems allow the entire length of the device to be used to detect the sample molecules, since at any given point along the device, the light intensity is represented by the profile shown. (Figure 3)

A new type of optical detector has been developed at DIAS, UMIST, which offers an alternative to the traditional detector system, and is not limited by the factors shown above. The system is known as the ARROW sensor. ARROW is the abbreviated term for the "AntiResonant Reflecting Optical Waveguide".

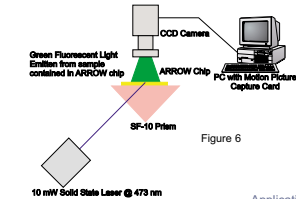
The ARROW Sensor confines and guides light in the sample region instead of the glass region, and as such a greater proportion of light (approximately 10 times more) is available for the sensing process.



We are currently using two different forms of the ARROW sensor system. The first, known as the Symmetric ARROW sensor (Figure 4), is used in conjunction with flow channels to monitor materials as they pass through the central (sample) region. This system has application where ever a constant flow of sample is required, and the detection setup is shown below. (Figure 6)



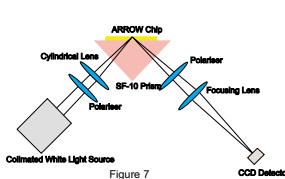
The second variation is the asymmetric ARROW sensor (Figure 5). Here there is no upper cover, and light is guided through a gel layer located on the top of the ARROW structure, below a water or air layer. The sample molecules move from the water or air into the gel, where they are detected. This variation of the ARROW sensor can be used in static analysis procedures, and also where the sample is in a vapour form, again the setup is shown below. (Figure 7)



Applications of ARROW Sensors

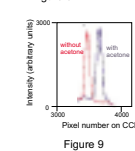
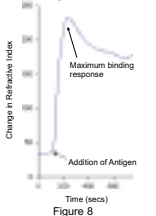
ARROW sensors have many applications, due to the versatility of the system. These include (but are not limited to) :

- Clinical Diagnostics
- Pharmaceutical Analysis and Evaluation
- Analysis for Explosives and Narcotics
- Rapid DNA Sequencing
- Toxicity Monitoring



Results of Optical Detection.

Monitoring of Biological Action



Shown here are examples of results obtained using the ARROW sensor system.

As can be seen, the applications include:

- The monitoring of biological reactions (Figure 8), where antibody binding is occurring.
- Gas sensing, since acetone is being detected in the vapour form (Figure 9), and the peak position is moving as a result of its presence.
- Focusing of a dye by a method known as Isoelectric Focusing (Figure 10), a technique often used in biological laboratories. The focusing occurs due to the application of an electric current on the components of the channel.
- The monitoring of beads moving through a flow channel (Figure 11). The beads are intended to represent cells, and as such are the equivalent size. The flows pressure driven.

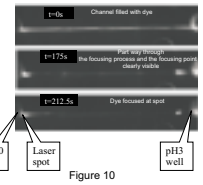


Figure 10

Cell and Bead Flow Monitoring

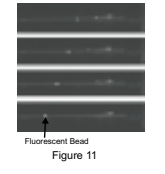


Figure 11

Conductivity Detection for Lab-on-a-Chip.

Plastic devices were fabricated for performing conductivity detection. Chemical analyses were performed by using an electrophoretic separation method which separates out sample components on the basis of their differing mobilities (i.e. their size and charge) in an applied electric field.

Channel containing polymer substrates can be bonded to a printed circuit board (PCB) to enable on-chip conductivity detection. Figure 12 depicts the layout of the miniaturised device. The PCB has been designed so as to allow for various combinations of electrodes to be used. As can be seen from figure 12, there are three sets of detection electrodes and four pads for the supply of high voltage to enable electrophoretic separations. The electrophoretic separation technique used in this case, was isotachopheresis (ITP).

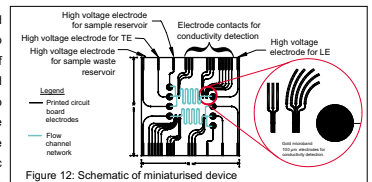


Figure 12: Schematic of miniaturised device

Theory of Isotachopheresis (ITP).

Isotachopheresis (ITP) is an electrophoretic separation technique which utilises the differences in effective ion mobilities to achieve a separation. The main feature of ITP is that it is performed in a discontinuous buffer system, unlike capillary zone electrophoresis (CZE) which is performed in a uniform carrier buffer. Sample components migrate between a leading and terminating electrolyte, producing a steady-state migrating configuration composed of consecutive sample zones. See figures 13 and 14.

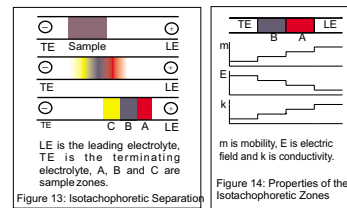


Figure 13: Isotachopheretic Separation

Figure 14: Properties of the Isotachopheretic Zones

Results of Isotachopheresis with Conductivity Detection.

Utilising the miniaturised devices with on-chip conductivity detection, ITP separations of various ions have been performed. Separations of three anionic dyes were performed: amaranth (red), bromophenol blue, and fluorescein (yellow). Figure 15 shows the progression of the anionic dye ITP separation around a meander bend on the chip. Figure 16 shows a conductivity isotachopherogram of an anionic dye separation. Separation of other anions have also been performed. For example the separation of sulfate and fluoride ions has also been achieved on-chip. Figure 17 shows a conductivity trace of a fluoride and sulfate separation.

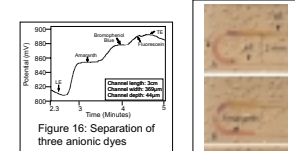


Figure 15: Anionic dye separation

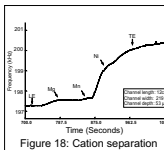


Figure 16: Separation of three anionic dyes

Separations of metal cations have also been achieved. Figure 18 shows a separation of Magnesium, Manganese and Nickel.

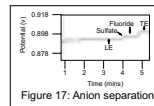


Figure 17: Anion separation.

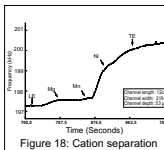


Figure 18: Cation separation

Conclusion.

Illustrated here are optical and electrochemical detection methods for use in lab-on-a-chip devices. Further work will be aimed at increasing the application range of these detectors.

In the near future Lab-on-a-chip technology could provide:

- universal pollutant detectors, self diagnosis of diseases, rapid pharmaceutical screening and much more.

References

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