The Future of Biosensors

Analyte Presentation to the Sensor

Professor Brian Birch
LIRANS University of Luton UK
Sample Presentation to Biosensor

- Direct immersion
- Sample drop onto sensor
- Wicking (lateral flow)
- Capillary fill
- Microfluidics
- Lab on a chip
Direct Immersion /Sample Drop

- Not much to say
- Requires robust, encapsulated sensor
- “Low tech” approach – likely to work
Lateral Flow

- Best Example is Clear Blue
ClearBlue - Before a Test

1. Antibody plotted on nitrocellulose

2. Antibody adsorbed latex sprayed onto wick material (acts as a reservoir)

3. Assay device stable for months if kept dry
ClearBlue - During a Positive Test

4. Urine sample added containing hormone

5. Latex resuspended from wick and carried in solution into and through the nitrocellulose

6. Urinary hormone binds to antibody adsorbed latex

7. The structure of the nitrocellulose helps the mixing of the latex in the solution
ClearBlue - A Positive Test

8. The antibody plotted at the line captures the hormone-latex

Formation of blue line due to hormone
ClearBlue - During a Negative Test

4. Urine sample added (no hormone present)

5. Latex resuspended from wick and carried in solution into and through the nitrocellulose

6. No hormone present so latex remains unaltered
ClearBlue - A Negative Test

A blue line does not appear

7. Latex passes past the plotted antibody line as there is no hormone present to form a 'bridge'
ClearBlue Pregnancy Biosensor
Capillary Fill

- Best Example is Blood Glucose Strip
Blood Glucose Biosensor
Electrochemical – Confined Volume

- Two parallel plates
- Small Gap
- Electrodes
- Reagents (GOD, ferricyanide)

- Blood enters by capillary action
- Reagents + glucose $\rightarrow$ ferrocyanide
- Ferrocyanide $\rightarrow$ ferricyanide $\rightarrow$ glucose
Capillary Fill Glucose Biosensor

Correct - End Fill

Incorrect - Top Fill

Complete vs Partial
Capillary Fill visible through window
Blood Glucose Monitors
Microfluidics in Sample Handling

Micro-structured substrates provide CONTROL

The flow of fluid through a microstructured substrate can be controlled via:

- geometry
- surface chemistry
Micro/ Nano fluidic structures
Passive Manipulation of Fluids

Centrifugal forces can be used to control flow

Very convenient for the customer
Device supplied with fluids already inside
Cantilevers

Microcantilevers are coated with antibody.

Antigen binding causes a mechanical deflection.

Amplitude of deflection is compared to that of a control cantilever.
Material Science

Some major drivers of electronic components

Philips, HP, Sony, Compaq, Panasonic, Motorola, Du Pont

Need for cheaper and easier to manufacture materials for computers, displays and mobile phones.
New materials enable whole circuits to be screen printed, inkjet printed or injection moulded quickly on a single surface.
Trends over the past 4 decades

Biosensor
- Simple
- Specific
- Robust
- Cheap
- Portable
- Easy to use

Integration
- Sensor systems
- Integration of several steps
- Multiple analytes
- Expensive
- Lab environment
- Trained users

Miniaturisation
- Making integrated systems smaller
- Mass production
- Cheaper components
Lab on a Chip Systems

- The principle is to produce an automated, microscale (or nano-scale) laboratory to enable sample preparation, fluid handling, analysis and detection steps to be carried out within the confines of a single microchip.

- Need for science to be smaller, cleaner, cheaper, more reproducible and faster

- LOCs enable precision, flexibility, and ease-of-use
Lab on a Chip Applications

- High throughput drug screening
- POC testing
- DNA analysis
- Ensuring safety of air, food and water
- Combating terrorism and biowarfare
Agilent introduced the first commercial lab-on-a-chip system in 1999.

Agilent first to introduce fully automated lab on a chip system for life sciences research in 2004.

Based on the principles of microfluidics.

Pressure or electrokinetic forces push samples through selected pathways in a controlled manner. The process separates the sample components for subsequent detection.
Micronit Microfluidics B.V., Netherlands: Various LOC products on glass chips
  ● Capillary electrophoresis,
  ● Microreactors
  ● Micromixers
Conclusions – Sample Presentation
Is the Future Smaller Size?

Positives
• Small sample volumes -- convenience
• Faster diffusion of reactants
• Reduction of background noise
• Easier to fill and manipulate
• Cheap and portable

Negatives
• Small sample volumes -- representative?
• Devices easily fouled
• Difficult to package
• Not easier to fill and manipulate
The Future of Biosensors-Lab on a Chip

The ultimate aim is:

to miniaturise biochemical analysis systems
to de-skill biochemical analysis