The Future of Biosensors

Analyte Presentation to the Sensor

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Sample Presentation to Biosensor

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

Direct Immersion /Sample Drop

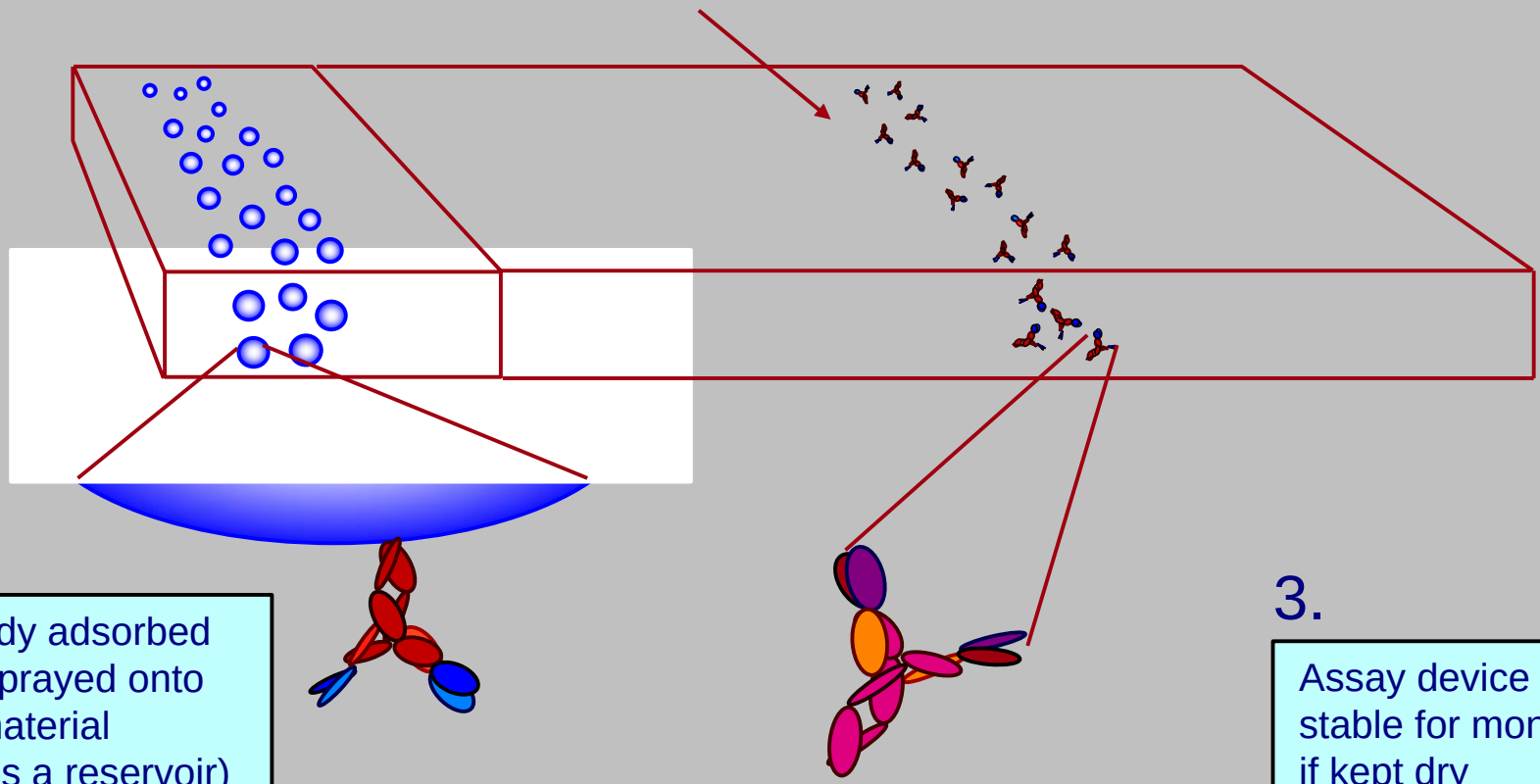
- Not much to say
- Requires robust, encapsulated sensor
- “Low tech” approach – likely to work

Lateral Flow

- Best Example is Clear Blue

ClearBlue - Before a Test

1. Antibody plotted on nitrocellulose



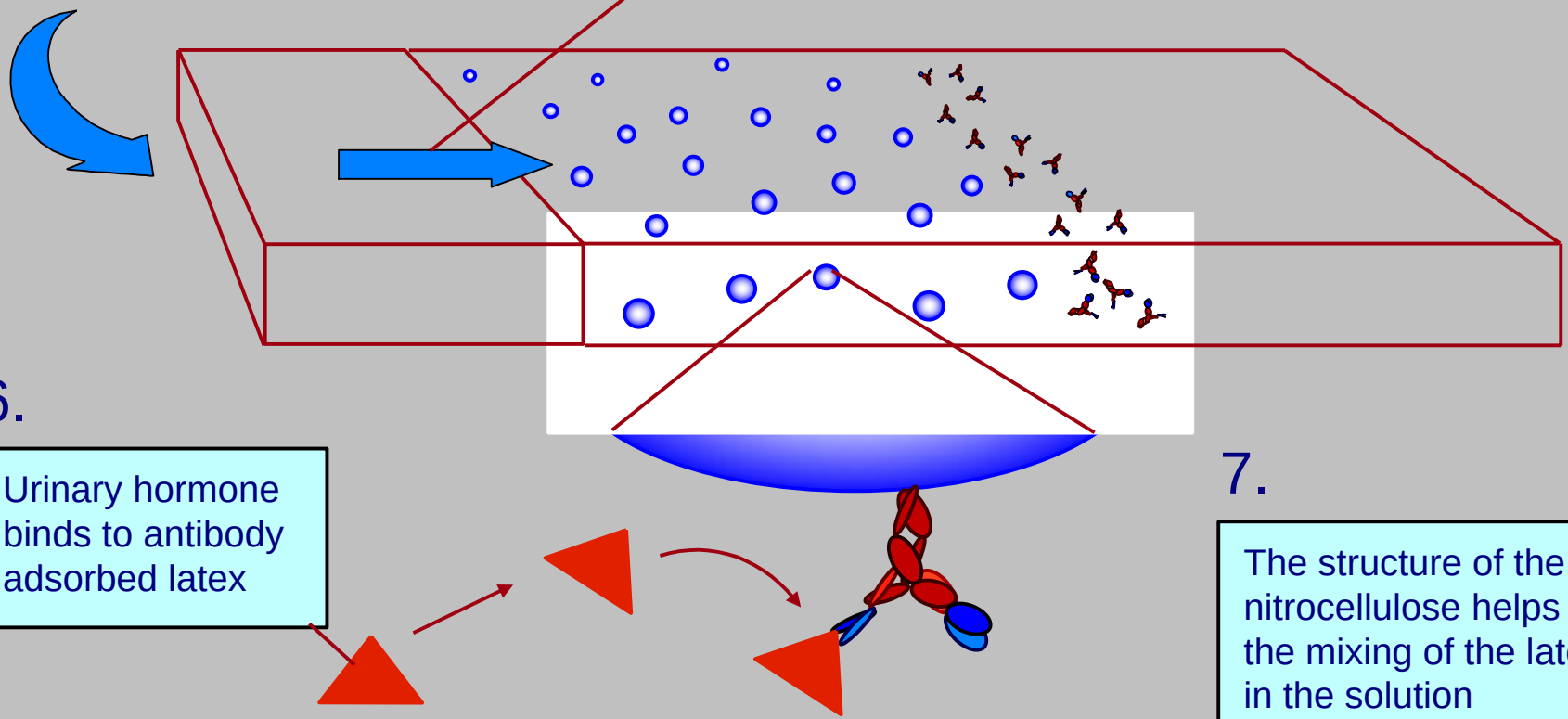
2. Antibody adsorbed latex sprayed onto wick material (acts as a reservoir)

3. Assay device stable for months if kept dry

ClearBlue - During a Positive Test

4. Urine sample added containing hormone

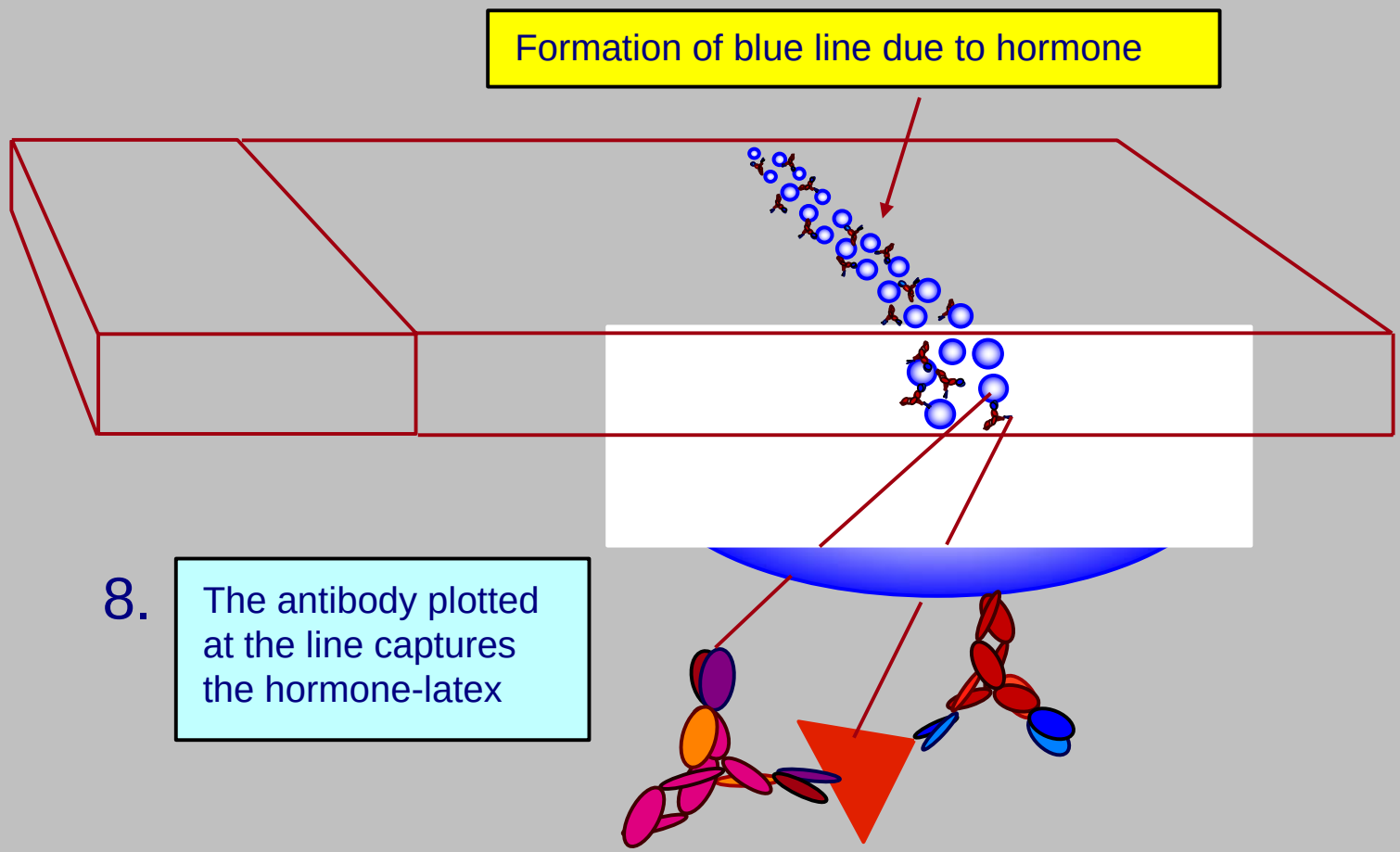
5. Latex resuspended from wick and carried in solution into and through the nitrocellulose



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

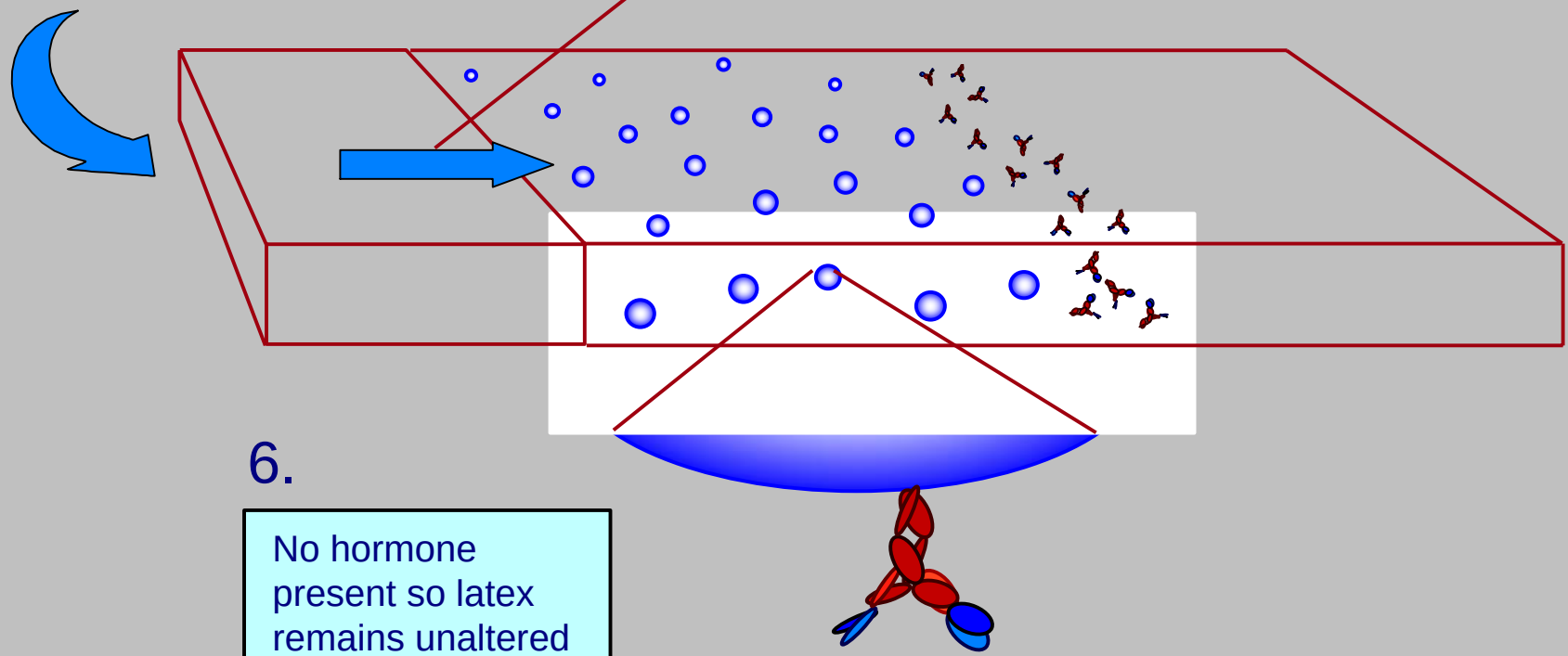


8. The antibody plotted at the line captures the hormone-latex

ClearBlue - During a Negative Test

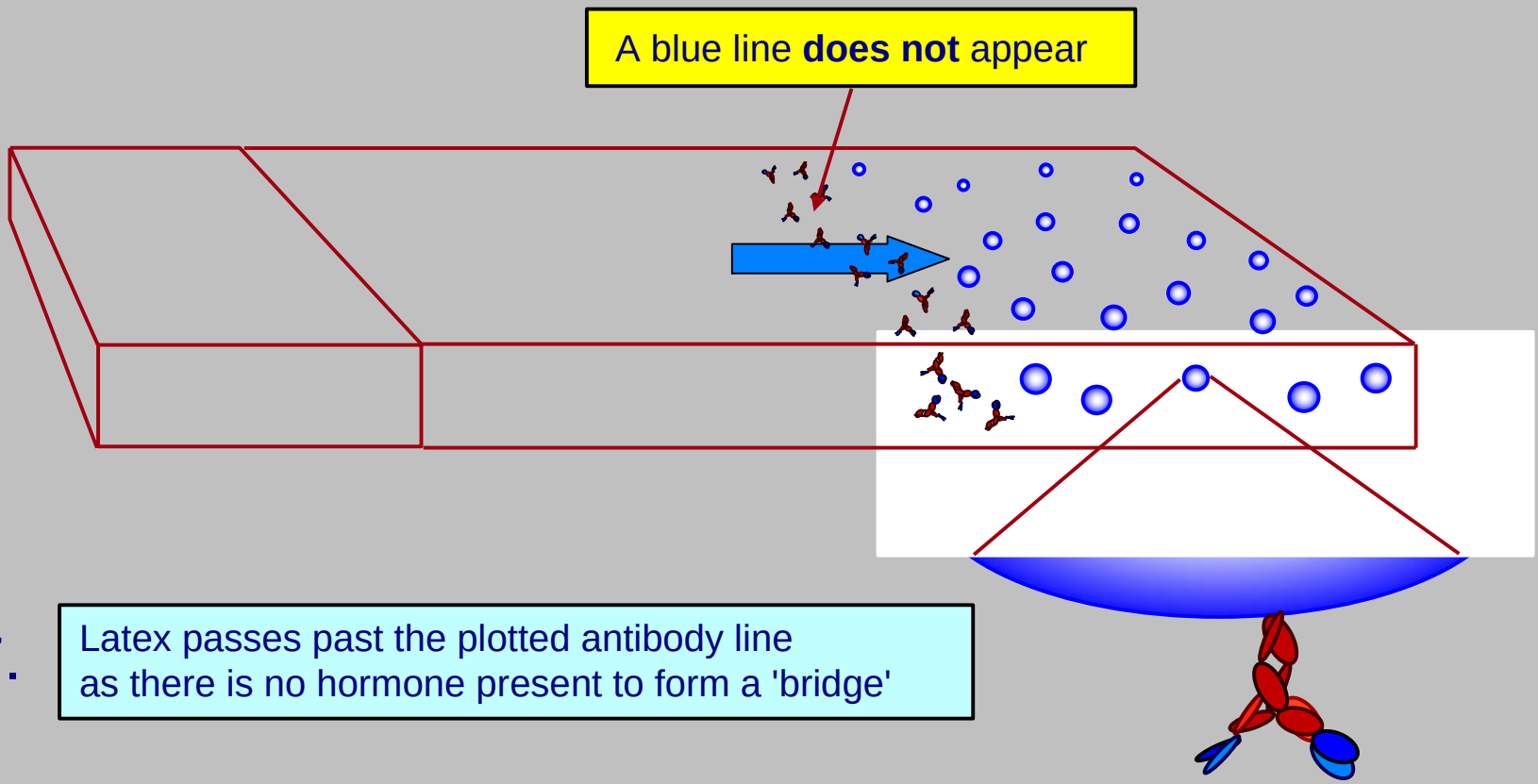
4. Urine sample added (no hormone present)

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



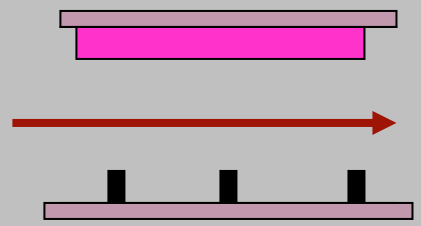
7. Latex passes past the plotted antibody line as there is no hormone present to form a 'bridge'

ClearBlue Pregnancy Biosensor

Capillary Fill

- Best Example is Blood Glucose Strip

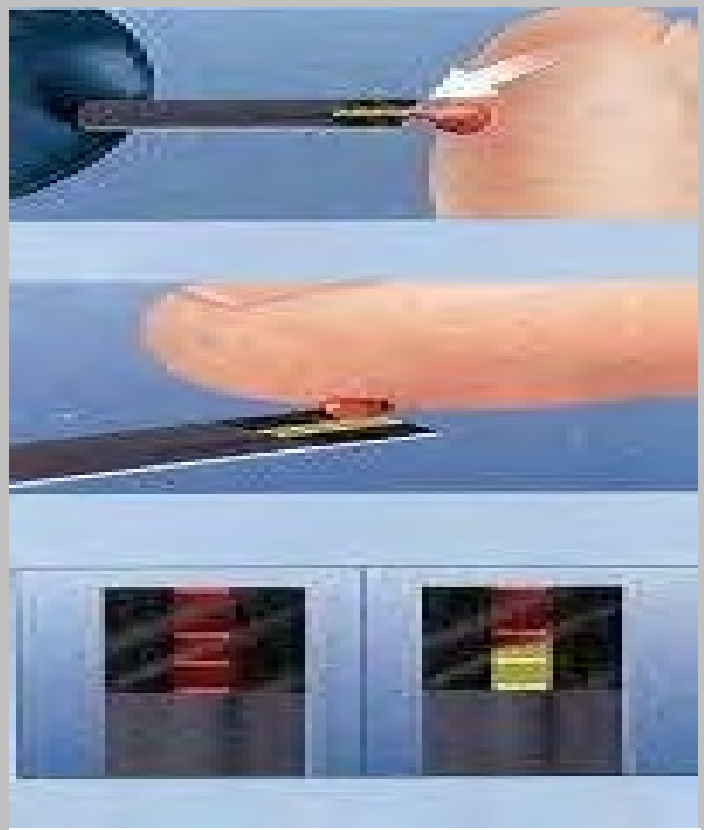
Blood Glucose Biosensor
Electrochemical – Confined Volume



- 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

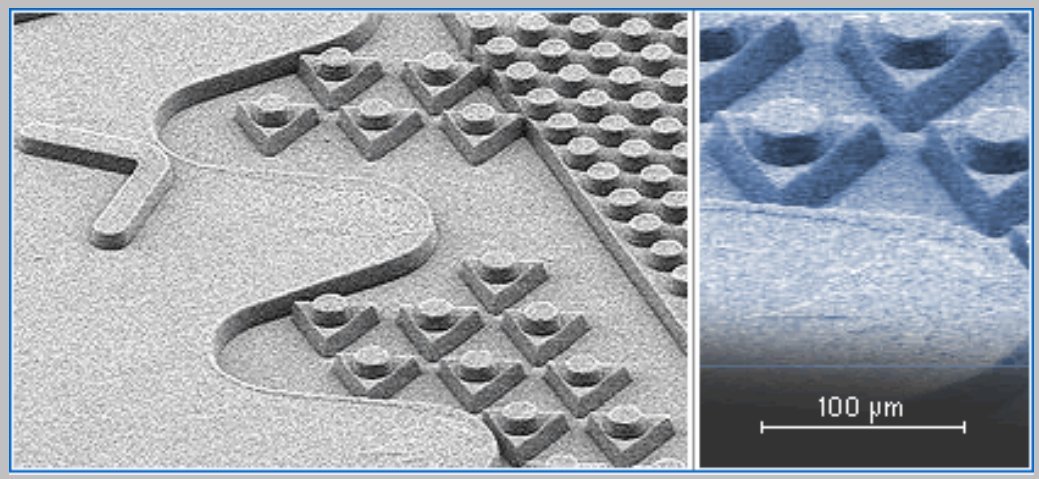
Microfluidics in Sample Handling

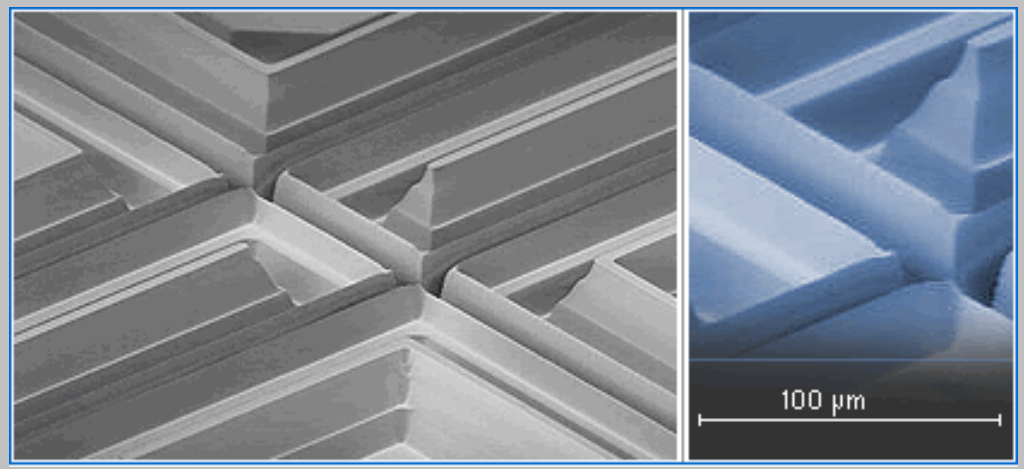
Micro-structured substrates provide CONTROL

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

- geometry
- surface chemistry

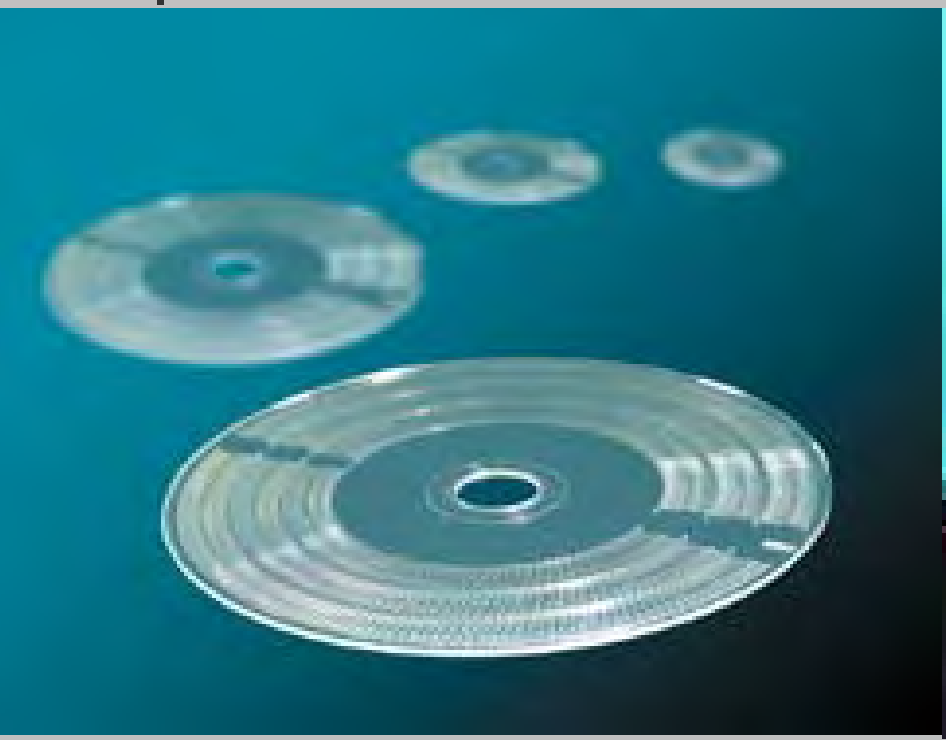
Micro/ Nano fluidic structures





Passive Manipulation of Fluids

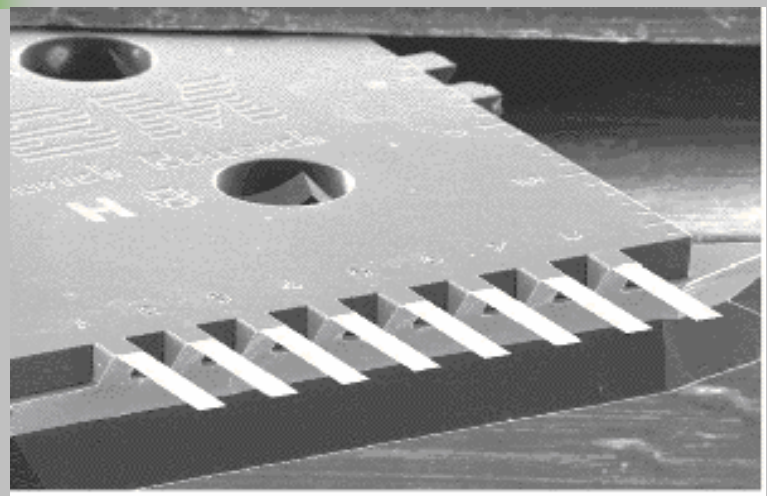
Centrifugal forces can be used to control flow

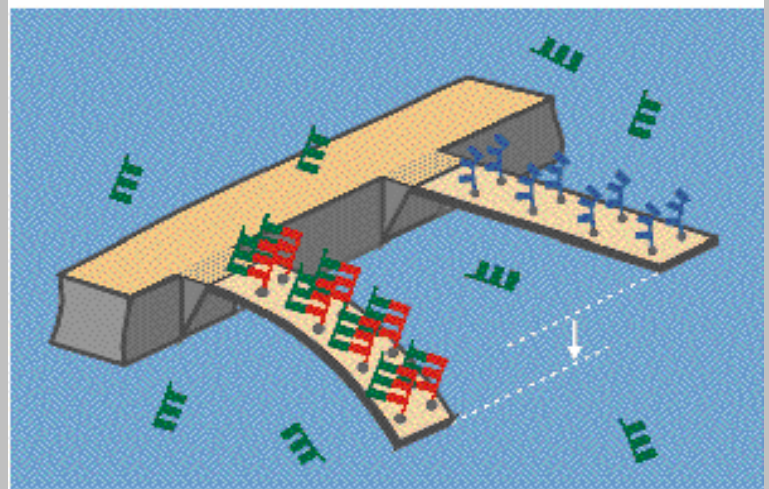


Very convenient for the customer

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.

Printable Electronic Components

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

Lab on a Chip -- Commercial

- 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.

Lab on a Chip -- Commercial

- 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