Introduction to Biosensors

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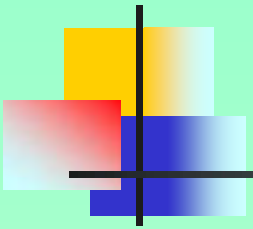
What is a Biosensor?



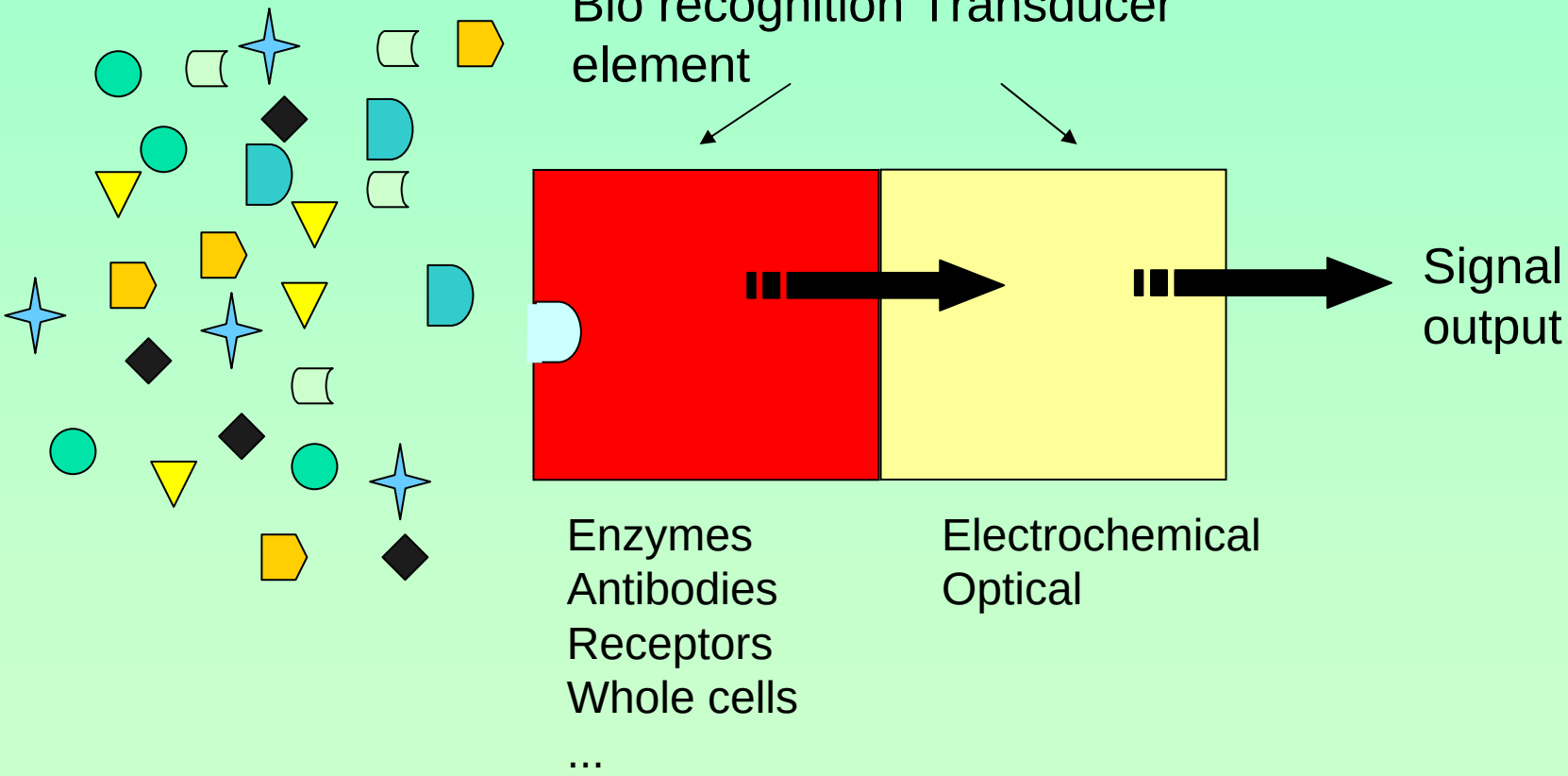
- As many definitions as workers in the field!
- I favour:
  - “a device that utilises biological components e.g. enzymes to indicate the amount of a biomaterial”

Amplification here is useful

- A biosensor need not provide quantitative information to be of value
  - Pregnancy test is an example: pregnancy is quantised, hence a reading 0.75% is not useful!
- The sought material need not be “biological”
  - Trace metal ions & ammonia

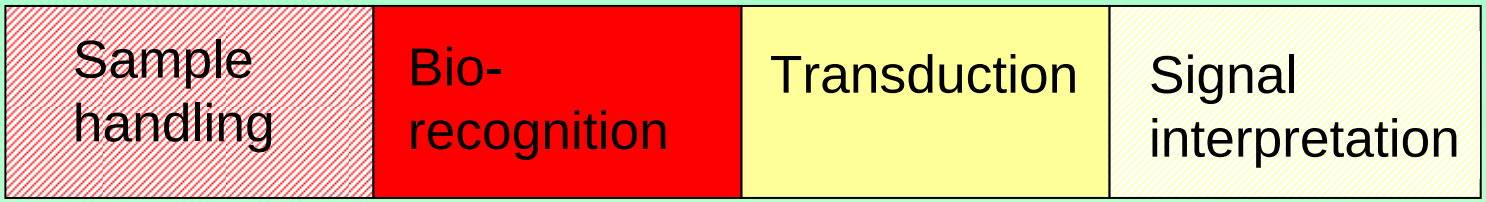
What is a Biosensor?

The “classical” definition



What is a Biosensor?

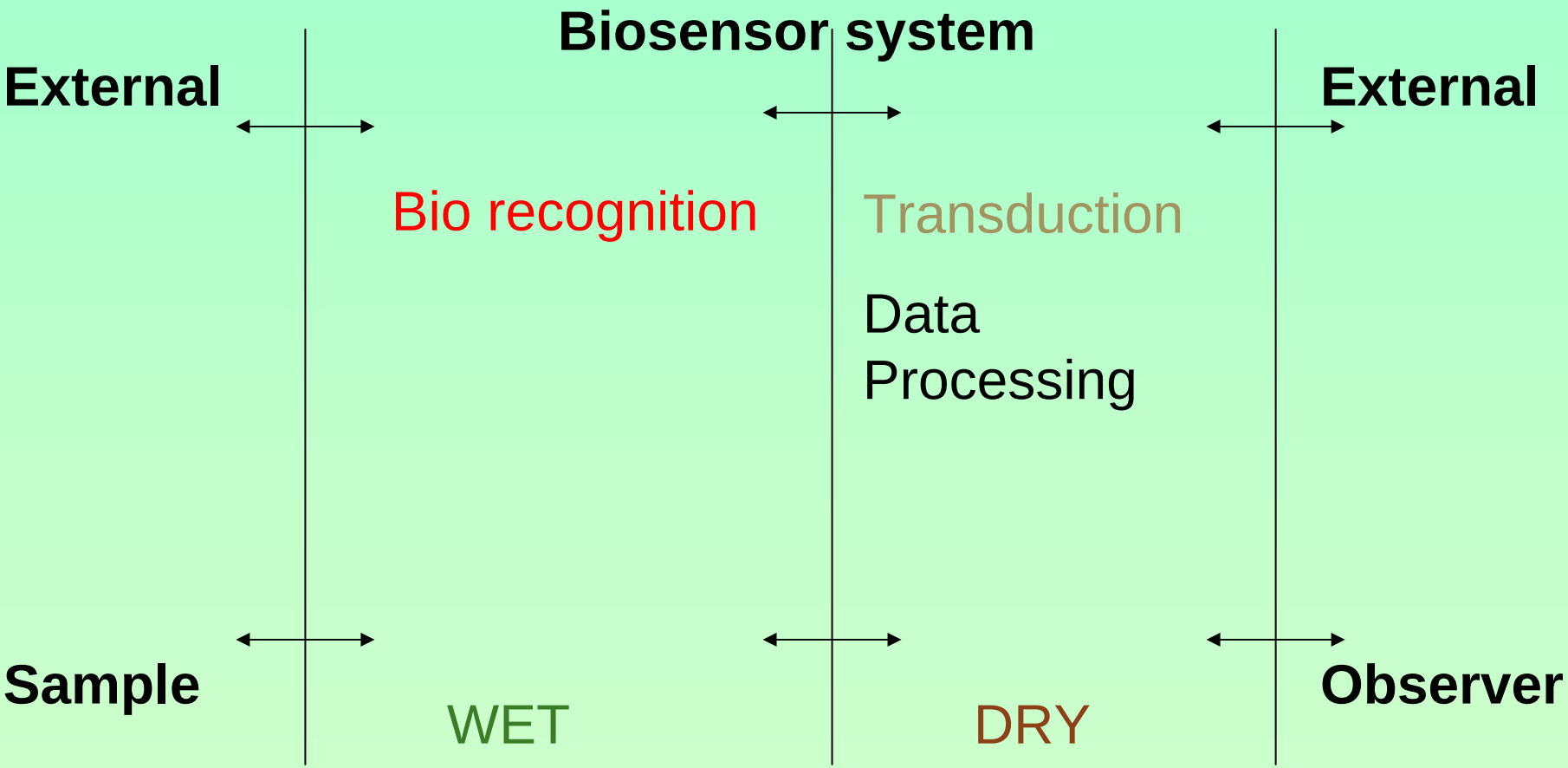
The whole picture



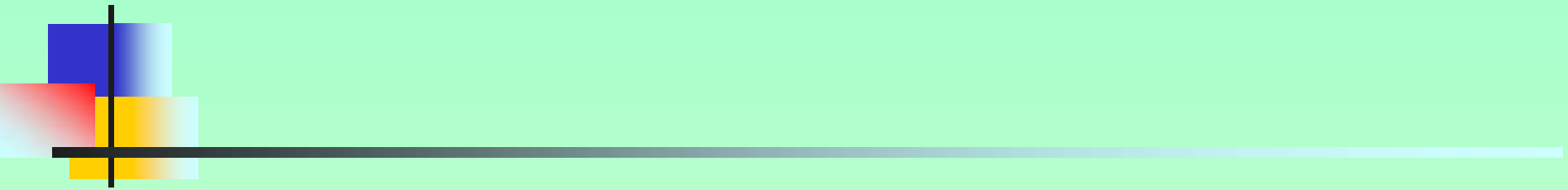
Interference usually means a need for sample pre-treatment

Requires simple read out and data interpretation

Biosensor Measurement World



Biosensors



Basic Electrochemistry

Same Principles/Techniques as "In Beaker"

- Potentiometry – Potential Difference at Zero Current
- Voltammetry – Current with Voltage Change
- Amperometry – Current at Constant Voltage
- Conductimetry – 1/Solution Resistance

Potentiometry

- “Passive” Potential Difference between Two Electrodes
  - Indicator - Biosensor
  - Reference - Invariant Potential with Sample Composition Change

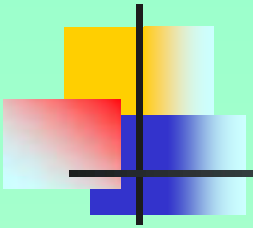
Potentiometry uses Nernst Equation

$$\Delta E = \Delta E^0 + RT/nF \ln\{activity\}$$

Can be used e.g. if a biosensor gives a change in pH with analyte change

Not often used

Conductimetry



- Simple measurement
- Cannot discriminate between different ions
- Very restricted use in biosensors
- Can measure urea with electrode coated with urease
  - NH_4^+ and HCO_3^- produced

Voltammetry

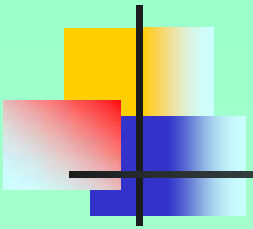
- “Active” Technique – different species have different oxidation or reduction potentials
- Usually operates with a potential ramp
- Species concentration proportional to step or peak
- Amperometry is a sub technique – current at a fixed potential – gives a steady value with time
- Chronoamperometry – current with time

Voltammetry

- 3 electrodes used
  - Working ---- biosensor
  - Counter ---- completes circuit
  - Reference ---- controls potential at biosensor

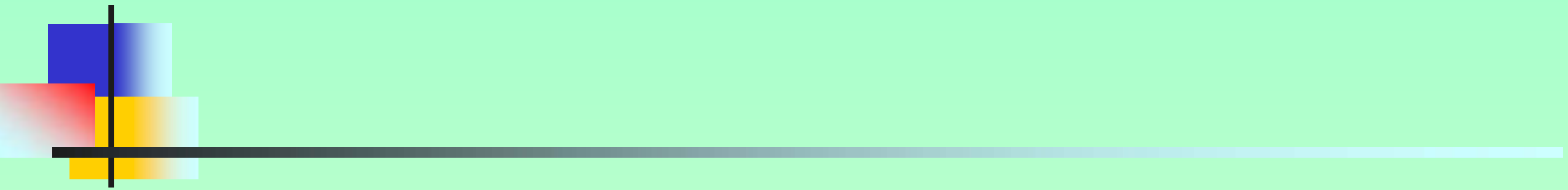
- Many operation modes
  - DC ---- not sensitive
  - Pulsed ---- often in conjunction with:
  - Pre accumulation ---- stripping voltammetry

A Biosensor Should Be



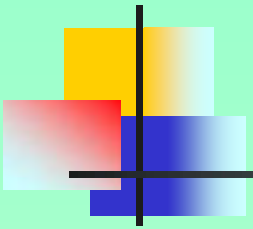
- Small, of a size appropriate for use. Not nano size to show how clever you are!
- Manufacturable in large numbers and at low cost
- Rapid. Result within the timescale of the process/diagnostic test
- Economical. Low cost of ownership
- Always considered as a sensor system with the instrument
- Self calibrating. Minimal action by user. Probably single use

And Most Importantly



Satisfy a Strong, Large Market Need!!

1980’s ---- Biosensors Would Solve the World's Analytical Needs



- Industry -- process monitoring and control, particularly food and drink
- Medicine -- diagnostics, metabolites, hormones
- Military -- battlefield monitoring of poison gases, nerve agents & people
- Domestic -- home monitoring of non acute conditions

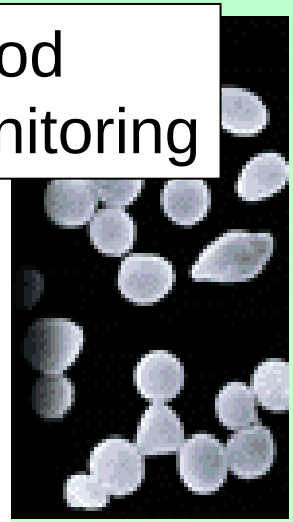
Whatever the application

Water quality

Food quality

In vivo monitoring

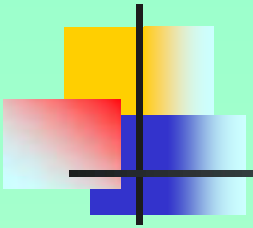
Blood monitoring



Benefits of Biosensors to:

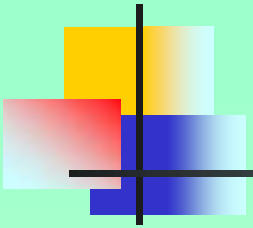
- Academia -- many new and expanded departments and positions
- Scientists --10’s of 1000’s
  - Grants
  - Publications
  - Conferences
- Users ?

Biosensors Commercialised



- ClearBlue – Pregnancy Yes/No
- Blood Glucose – Diabetes Quantitative
  - Colorimetric Test Strip
  - Electrochemical Test Strip

Barriers to Commercialisation

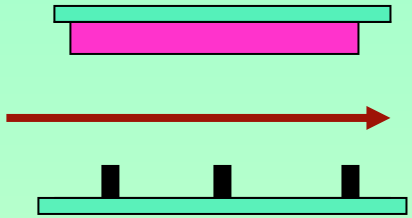


- Economic

  Blood Glucose and Pregnancy are large markets where users will pay economic prices

- Technical
  - Biomaterials are fragile
  - Many different materials needed
  - Issues of e.g. bonding, connection, reader

Blood Glucose Biosensor
Electrochemical – Confined Volume



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

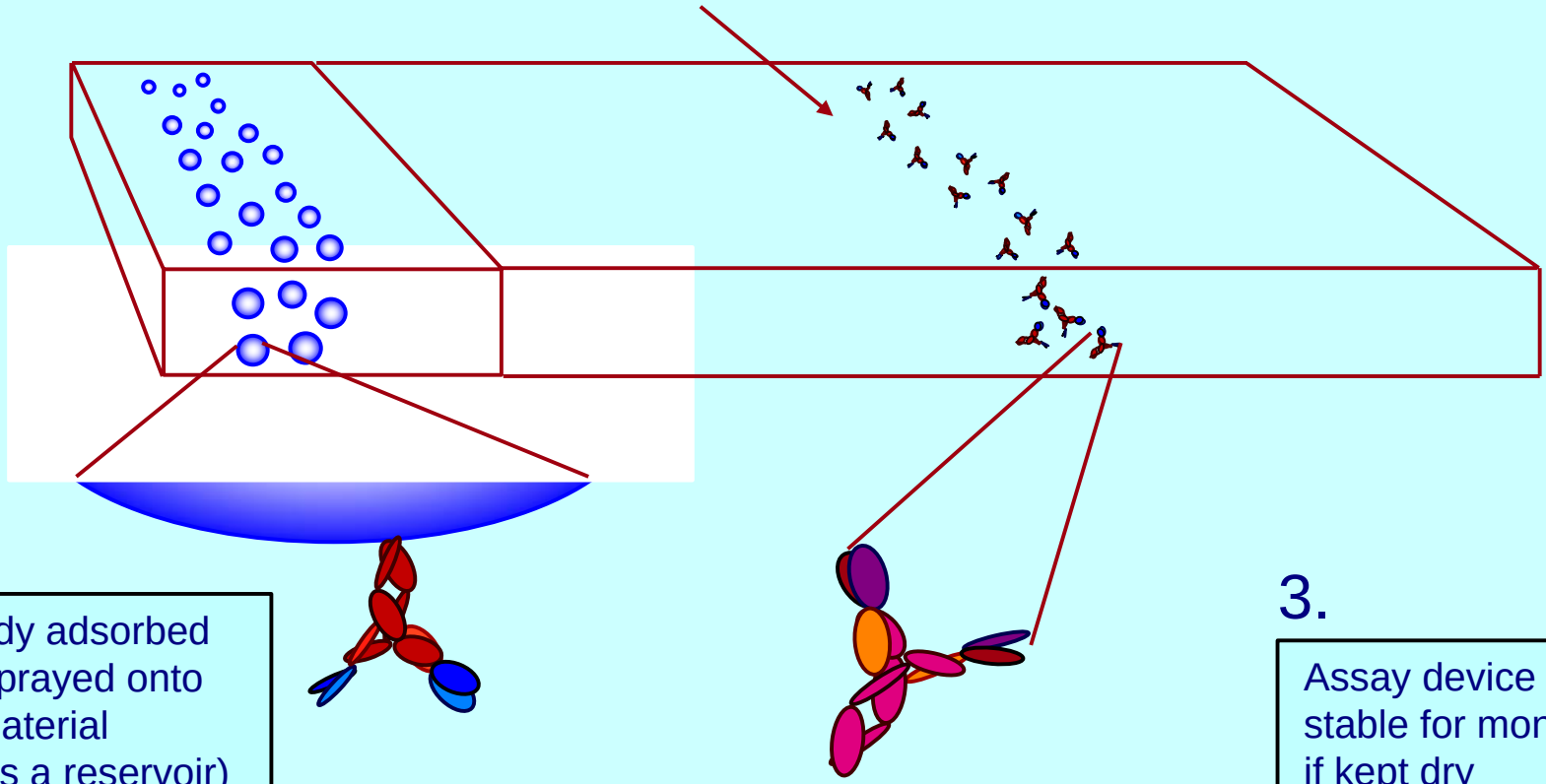
- Blood enters by capillary action
- Reagents + glucose $\rightarrow$ ferrocyanide
- Ferrocyanide $\rightarrow$ ferricyanide $\rightarrow$ glucose

Blood Glucose Monitors

ClearBlue Pregnancy Biosensor

ClearBlue - Before a Test

1. Antibody plotted on nitrocellulose



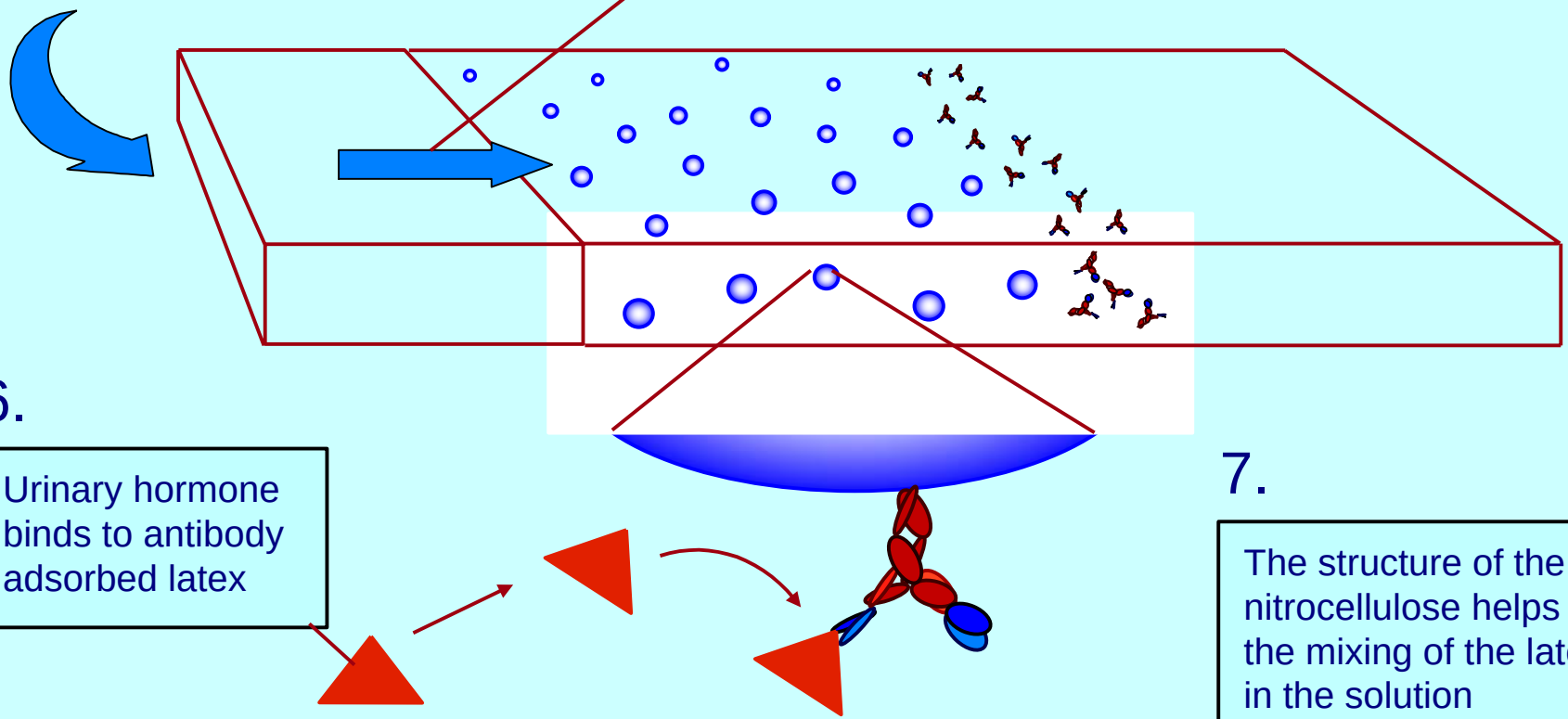
2. Antibody adsorbed latex sprayed onto wick material (acts as a reservoir)

3. Assay device stable for months if kept dry

ClearBlue - During a Positive Test

4. Urine sample added containing hormone

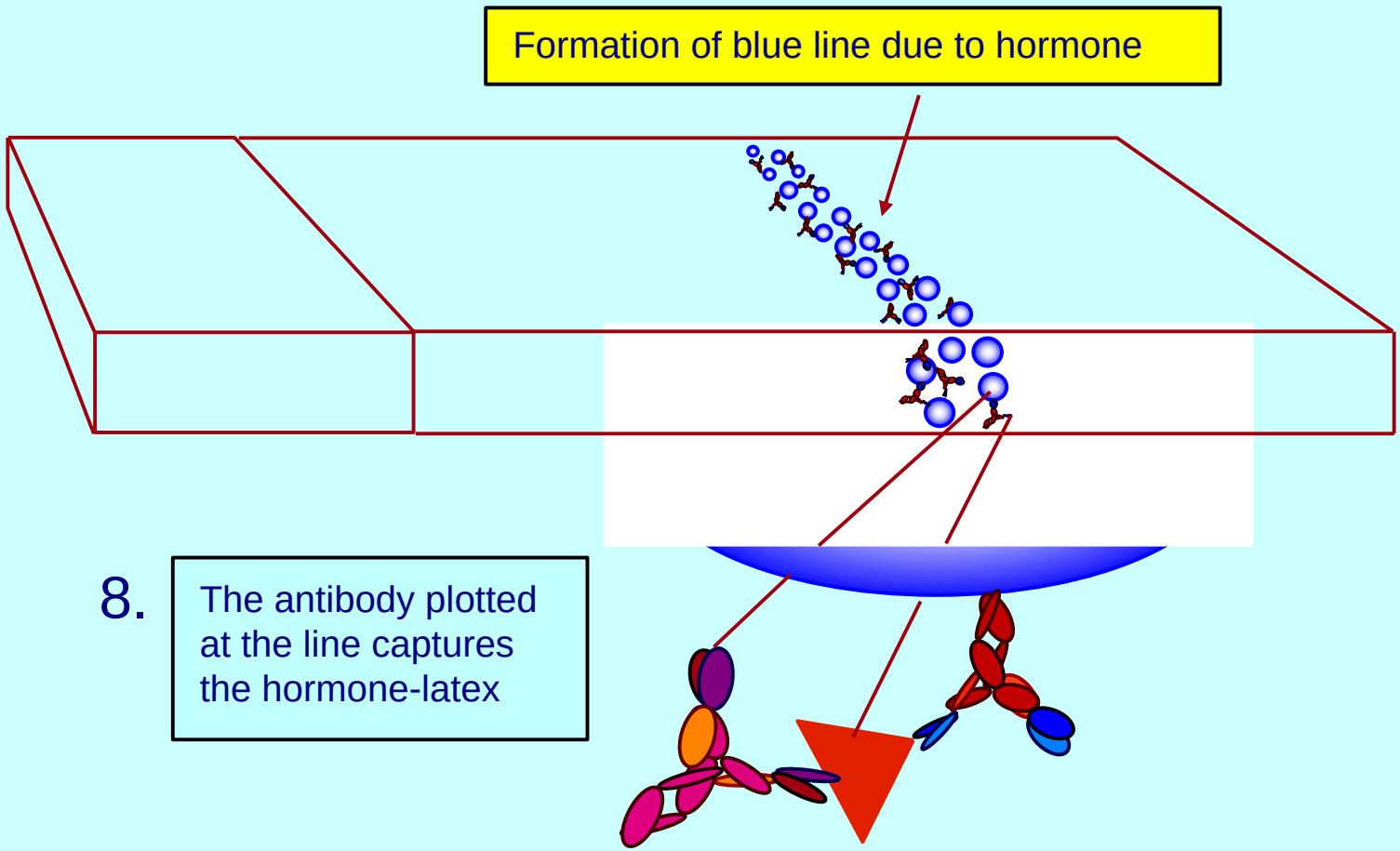
5. Latex resuspended from wick and carried in solution into and through the nitrocellulose



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

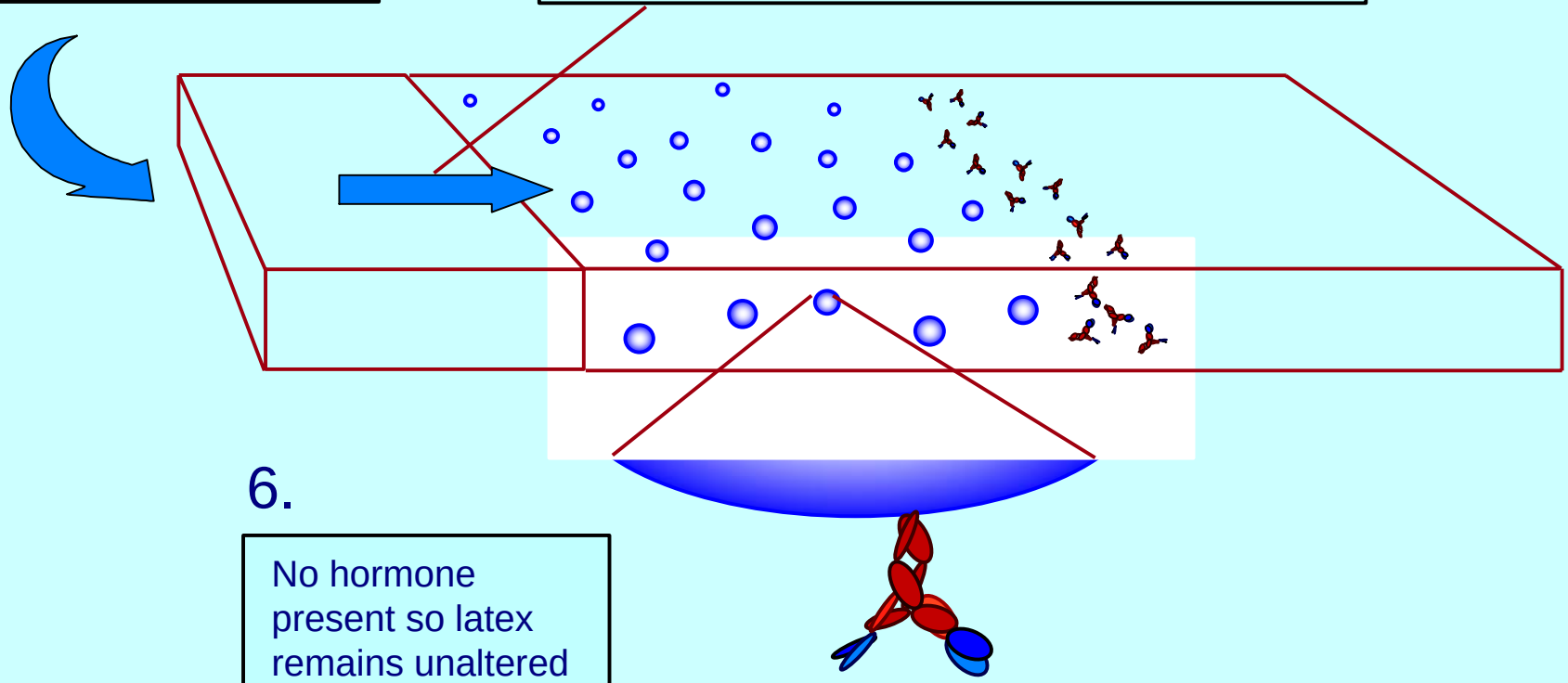


8. The antibody plotted at the line captures the hormone-latex

ClearBlue - During a Negative Test

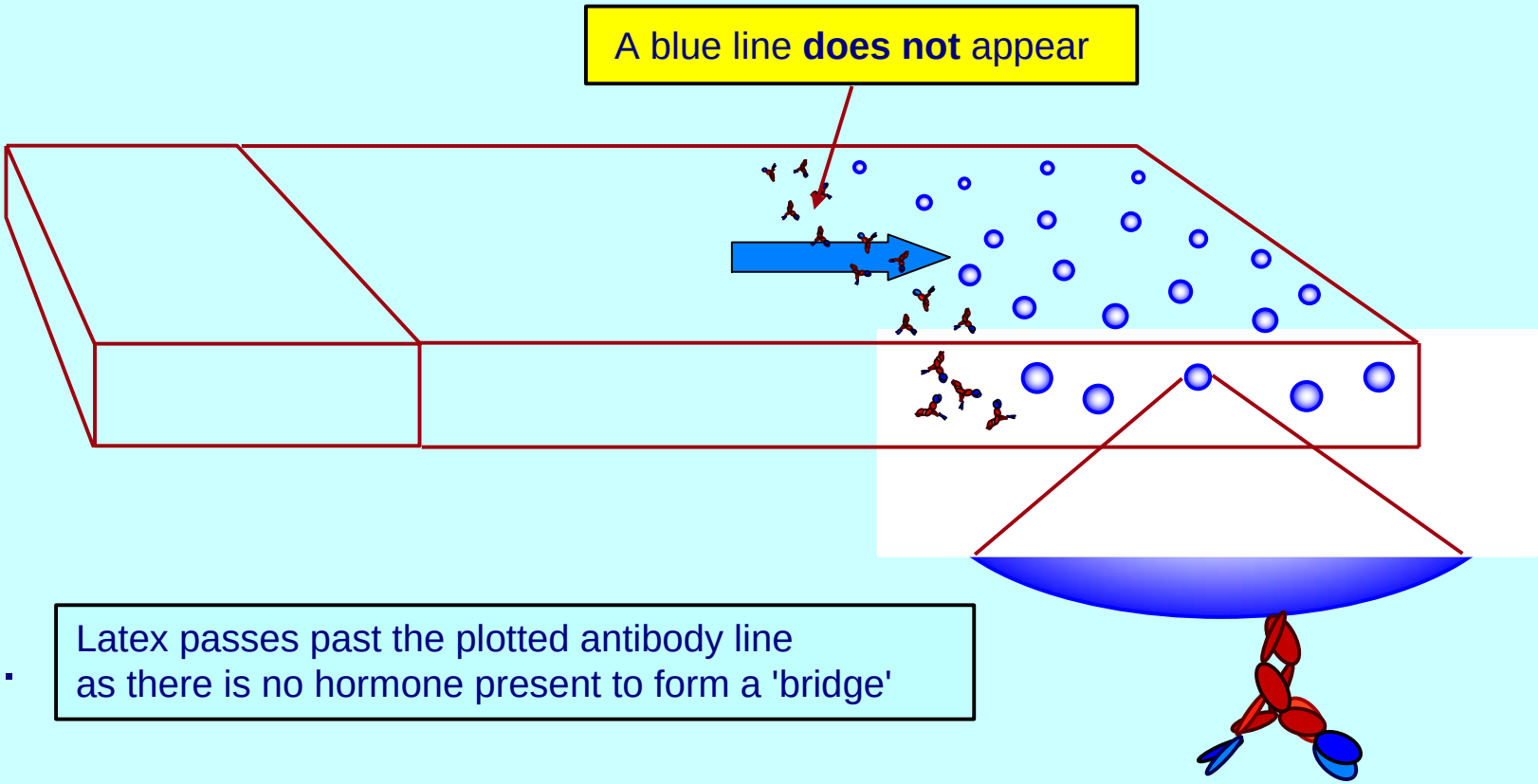
4. Urine sample added (no hormone present)

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'

Yellow Springs Instruments

- Glucose and lactate analyzer
- Electrochemical detection
- Result in ≤ 1 minute
- High precision
- Small sample volume (25 μl)
- Low cost per test but instrument investment needed

- Centralised hospital lab / Research

Biacore

- Direct monitoring of bio molecular interactions
- No need to use labelled reagents
- Detection based on Surface Plasmon Resonance
- Flow system
- Expensive

- Research / Drug discovery / Food analysis

Cholesterol monitoring

1) Low incentive to use (effects are long term)
2) Cost high
3) What do you do with the information?
4) Learnt nothing from the Glucose industries development.

Trends over the past 4 decades

Biosensor

- Specific
- Robust
- Cheap
- Portable
- Simple
- 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

Conclusions

- Inputs are required from: Biology, Chemistry, Material Science, Electronics & Physics

- This multidisciplinary process has accelerated during the past 5 years

- Biomaterial stability has become a reality

- The large scale manufacture of repeatable sensors for a range of analytes is now almost feasible

- More must still be done to realise the potential of biosensors (will be market led)