CHAPTER 1
BIOSENSORS – AN INTRODUCTION

Learning Objectives:

At the end of this chapter you should be able to:

1. Define the term biosensor

2. State and describe the fundamental components required to make a viable biosensor.

What are Sensors?

- Nose! Tongue! Ears! Eyes! Fingers!
- Sensors can give qualitative or quantitative analysis.

Table 1.1 Test for acids and alkalis

SENSOR	SENSING ELEMENT	QUALITATIVE	QUANTITATIVE
Litmus paper	Dye in litmus paper	Colour change	-
pH indicator solutions	Complex mixture of chemical dyes	Colour change	Semi-quantitative?
pH meter	Glass membrane electrode (pH meter)	-	Digital display (pH value)

Sensors can be divided into three types:

a. physical sensors – distance, mass, temperature etc.

b. chemical sensors – measure an ***analyte*** by chemical or physical responss (eg. litmus paper vs pH meter)

c. biosensors – measure an analyte using ***biological sensing elements / bioelement***

** All these devises have to be connected to a ***transducer***, so that a visibly observable response occurs.

What is a Biosensor?

• Biosensors are analytical devices which are capable of providing either qualitative or quantitative results.

• Biosensors function by coupling a biological sensing element with a detector system using a transducer.

• IUPAC* definition

'A device that uses specific biochemical reactions mediated by isolated enzymes, immunosystems, tissues, organelles or whole cells to detect chemical compounds usually by electrical, thermal or optical signals'.

* International Union of Pure and Applied Chemistry

What is a Biosensor?

- The ***biological sensing element*** has to be connected to a ***transducer*** so that a visually observable response occurs. In the case of the pH meter, the electrical response (a voltage change) has to be converted i.e. transduced = led through, into an observable response (movement of a meter needle or digital display).

- Biosensors are generally concerned with sensing and measuring particular chemicals (***analyte***) which **need not always be biological components themselves.**

- IUPAC definition

'A device that uses specific biochemical reactions mediated by isolated enzymes, immunosystems, tissues, organelles or whole cells to detect chemical compounds usually by electrical, thermal or optical signals'. * International Union of Pure and Applied Chemistry

HISTORY OF BIOSENSOR

1916	First report on the immobilisation of proteins: adsorption of invertase on activated charcoal
1922	First glass pH electrode
1956	Invention of the oxygen electrode
1962	First description of a biosensor: an amperometric enzyme electrode for glucose
1969	First potentiometric biosensor: urease immobilised on an ammonia electrode to detect urea
1970	Invention of the Ion-Selective Field-Effect Transistor (ISFET)
1972/5	First commercial biosensor: Yellow Springs Instruments glucose biosensor
1975	First microbe-based biosensor First immunosensor: ovalbumin on a platinum wire Invention of the pO2 / pCO2 optode
1976	First bedside artificial pancreas (Miles)
1980	First fibre optic pH sensor for *in vivo* blood gases
1982	First fibre optic-based biosensor for glucose
1983	First surface plasmon resonance (SPR) immunosensor
1984	First mediated amperometric biosensor: ferrocene used with glucose oxidase for the detection of glucose

HISTORY OF BIOSENSOR

1987	Launch of the MediSense ExacTech™ blood glucose biosensor
1990	Launch of the Pharmacia BIACore SPR-based biosensor system
1992	i-STAT launches hand-held blood analyser
1996	Glucocard launched
1996	Abbott acquires MediSense for $867 million
1998	Launch of LifeScan FastTake blood glucose biosensor
1998	Merger of Roche and Boehringer Mannheim to form Roche Diagnostics
2001	LifeScan purchases Inverness Medical's glucose testing business for $1.3billion
2003	i-STAT acquired by Abbott for $392 million
2004	Abbott acquired Therasense for $1.2 billion
2007	GlucoTel a bluetooth enabled glucose meter launched

Biosensors

1. The Analyte or Substrate

Any substance consumed / produced in a biochemical process can in principle be analysed by a biosensor (if one can be constructed)

Eg: sugars, urea, cholesterol, lactic acid, paracetamol, ethanol, uric acid, phenol

2. The Biological Component

- Interaction of biological component with substrate highly specific to that substrate alone - avoids interferences from other substances.

- Include *enzymes* (most common)*, microorganisms* (yeast, bacteria, algae), *tissue material* (liver, banana), *antibodies, & nucleic acids*.

3. Biocomponent Immobilisation (details in Chap 2)

i. *Adsorption* on to surface – simplest, weak bonding

ii. *Microencapsulation* or trapping between membranes – (glucose ; oxygen electrode, urea ; CO_2 , NH_3)

iii. *Entrapment.* Biocomponent trapped in matrix of a gel/paste/polymer (*bananatrode*) - Popular method.

iv. *Covalent Attachment*. Covalent chemical bonds formed between biocomponent & transducer surface.

3. Biocomponent Immobilisation (details in Chap 2).

v. *Cross-linking*. A bifunctional agent (gluteraldehye) used to chemically bind biocomponent to transducer. Method helps stabilise adsorbed enzymes. Also used with method (ii).

vi. Bioaffinity Immobilization – gentle oriented immobilization of proteins. Can be achieved by use of affinity tags (His-tag, Strep-tag etc).

4. Transducers/Detector Device (details Chap 3)

i. Electrochemical transducers:

a. *Potentiometry*, the measurement of a cell potential at zero current.

b. *Voltammetry*, an increasing (decreasing) potential is applied to cell electrode until oxidation (reduction) of substance occurs. (current vs potential)

c. *Amperometry* - If oxidation (reduction) potential known, step potential directly to that value (constant voltage) and measure current. (current vs time)

d. *Conductimetry*, measure of ease of passage of electric current through a solution.

ii. Optical Transducers

- absorption, fluorescence, (bio)luminescence

iii. *Piezoelectric devices*

- Involve generation of electric currents from a vibrating crystal. (QCM-quartz crystal microbalance)
- The frequency of vibration affected by mass of material adsorbed on its surface, which could be related to an active biochemical rxn.

iv. *Thermal methods*

- Devices such as thermistors measure heat produced/adsorbed which can then be related to the amount of reaction.

5. Performance Factors

- *LINEARITY:* Maximum linear value of the sensor calibration curve. Linearity of the sensor must be high for the detection of high substrate concentration.

- *Selectivity* – the ability to discriminate between different substrates; most important characteristic of biosensors; function of biocomponent, but sometimes due to operation of tranducer. Interference of chemicals must be minimised for obtaining the correct result

- *Sensitivity* Range – mM but can go down to femtomolar (10^{-15} M) range. Eg. The value of the electrode response per substrate concentration.

5. Performance Factors (Continued)

- *Accuracy* – around ±5%
- *Nature of solution* – pH, temperature, ionic strength
- *Response times* : The necessary time for having 95% of the response. Typically longer than chemical sensors (30s or longer)
- *Recovery time* : time before biosensor is ready to analyse the next sample; should not be more than a few mins.
- *Working lifetime* : determined by instability of the biological material; vary from a few days to few months; Exactech glucose biosensor is usable for over 1 year.

Where are Biosensors Being Used?

- ✓ Healthcare (glucose, artificial pancreas)
- ✓ Process control:fermentation control and analysis
- ✓ Food and drink production and analysis
- ✓ Industrial Effluent Control
- ✓ Pollution control and monitoring
- ✓ Mining, industrial and toxic gases
- ✓ Military applications
- ✓ Pharmaceutical and drug analysis

Read more about it

- B.D. Malhotra, R. Singhal, A. Chaubey, S.K. Sharma, and A. Kumar, “Recent trends in biosensors,” *Curr. Appl. Physics, vol. 5, no. 2, pp. 92–97,* 2005.
- Rodriguez-Mozaz, S., M. Maria-Pilar. M. J. Lopez de Alda, and D. Barceló, “Biosensors for environmental applications: Future development trends *Pure Appl. Chem., Vol. 76, No. 4, pp. 723–752, 2004.*