Biosensors

B. Tech.

Course No.: EEL 3050

L-T-P [C]: 3–0–2 [4]

AAgarwal

Prof. AJAY AGARWAL

ELECTRICAL ENGINEERING

IIT JODHPUR

Lecture 01 dated 31st July 2024

Course Title	*Biosensors*	Course No.	EEL3050			
Department	Electrical Engineering	Structure (LTPC)	3	0	2	4
Offered for	B.Tech.	Status	Elective/ Compulsory-BB			
Prerequisite: Fundamentals of Electrical Engineering and Bioengineering						

Class: Slot C (10 AM TO 10.50AM)

MON WED THU

Co-instructors: DR SWATI RAJPUT

PROF MEENU CHHABRA

Objective

1. Make the students understand the fundamentals of working principles of biosensors
2. Describe the bio-specific interaction used for various applications
3. Evaluate & compare techniques used in today’s time like electric, optics and mechanical
4. Show & explain the examples of practical & real-world biosensors

Contents

1. Introduction to basics of biosensors and biospecific interactions: Different components of biosensors, functionalization layers and their importance, Biomolecules for biosensors, catalytic biosensors, affinity biosensors, biomolecular interaction. (8 lectures)
2. Electrical and optical techniques for biosensing: Electrical (CV, ISFET), optical (fluorescence, ELISA,SERS, SPR) (8 lectures)
3. Electrochemical, mechanical and advanced techniques for biosensing: Electrochemical (sub classifications like impedemetric, voltammetric, amperometric), mechanical (Bio-MEMS), color based, microfluidics (including packaging), AI based biosensors (11 lectures)
4. Sensor key parameters and examples of commercially available biosensors: Sensitivity, selectivity, response- and recovery time, LOD etc., Explain and describe few industry standards and commercially available bio-sensors and their functioning. The need and relevance of biosensors in our Indian context (7 lectures)
5. Readout Electronics: Basic circuitry to make readout electronics, Potentiostats, amperometric circuits, charge to voltage converter, variable gain amplifier, low noise amplifier, high resolution and low noise data converters, mismatch insensitive data converters (8 lectures)

Contents

Lab work:

Biosensor material selection and characterization;

Biochemical reagents and assays;

Surface functionalization (Covalent/non-covalent) for Biosensing;

Biosensor fabrication;

Biosensor operation and signal generation;

Biosensor sensitivity assay;

Biosensor reproducibility;

Biosensor Selectivity;

Determination of limit of detection;

Use of appropriate controls; Biosensor application on real samples.

Course Evaluation

1. Continuous evaluation: 40%
    i. Lab 20%
    ii. Quizzes
    iii. Assignments
    iv. Minor projects

2. Minor examination: 20%
3. Major/ final examination: 40 %

Textbooks

1. Yoon J.-Y., (2016), Introduction to Biosensors, Springer
2. Banica F.-G., (2012), Chemical Sensors and Biosensors: Fundamentals and Applications , Wiley
3. Rasooly A., Herold K. E., (2008), Biosensors and Biodetection, Humana Press, Science

Self Learning Material:

1. Materials for Biomedical Applications, MIT Open Courseware,
https://ocw.mit.edu/courses/materials-science-and-engineering/3-051j-materials-for-biomedicalapplications-spring-2006/lecture-notes/

Introduction to Sensors

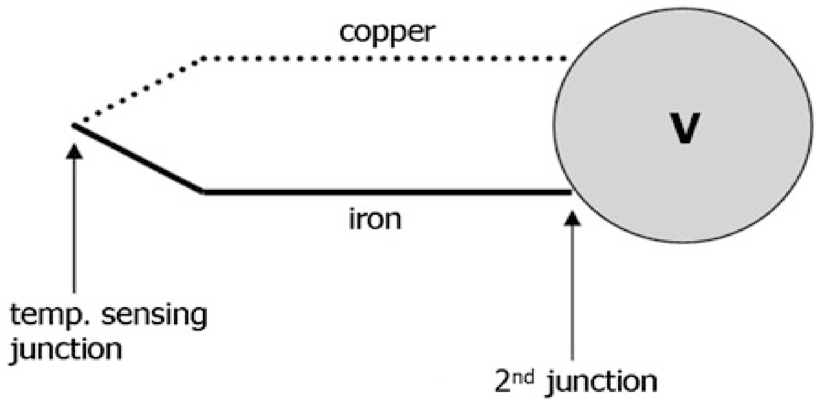
What is a **Sensor**?

- Sensor
    - a **device** which **detects or measures** a **physical** property and records, indicates, or otherwise responds to it.
    - Example: temperature, strain, humidity, pressure, mass, light, and voltage
- Transducer
    - A device that converts one form of energy into another, such as converting mechanical energy into electrical signals.

Difference between a **Sensor & Transducer**

- All transducers are **Not** sensors, but most sensors are transducers.
- For example, a **thermistor** is a type of sensor; it will respond to the **change in temperature** but **does not convert the energy** into a different format to what it was originally sensed in.

- **Thermocouple**, the oldest and the simplest temperature transducer



Thermocouple

What is a **Biosensors**?

- a **device** or sensor which **detects or measures** a **biologically** relevant analyte…

Example:

- a simple biochemical compound (e.g., glucose),
- a sequence of nucleic acid (DNA or RNA),
- a specific protein,
- a virus particle,
- a bacterium, and so on …

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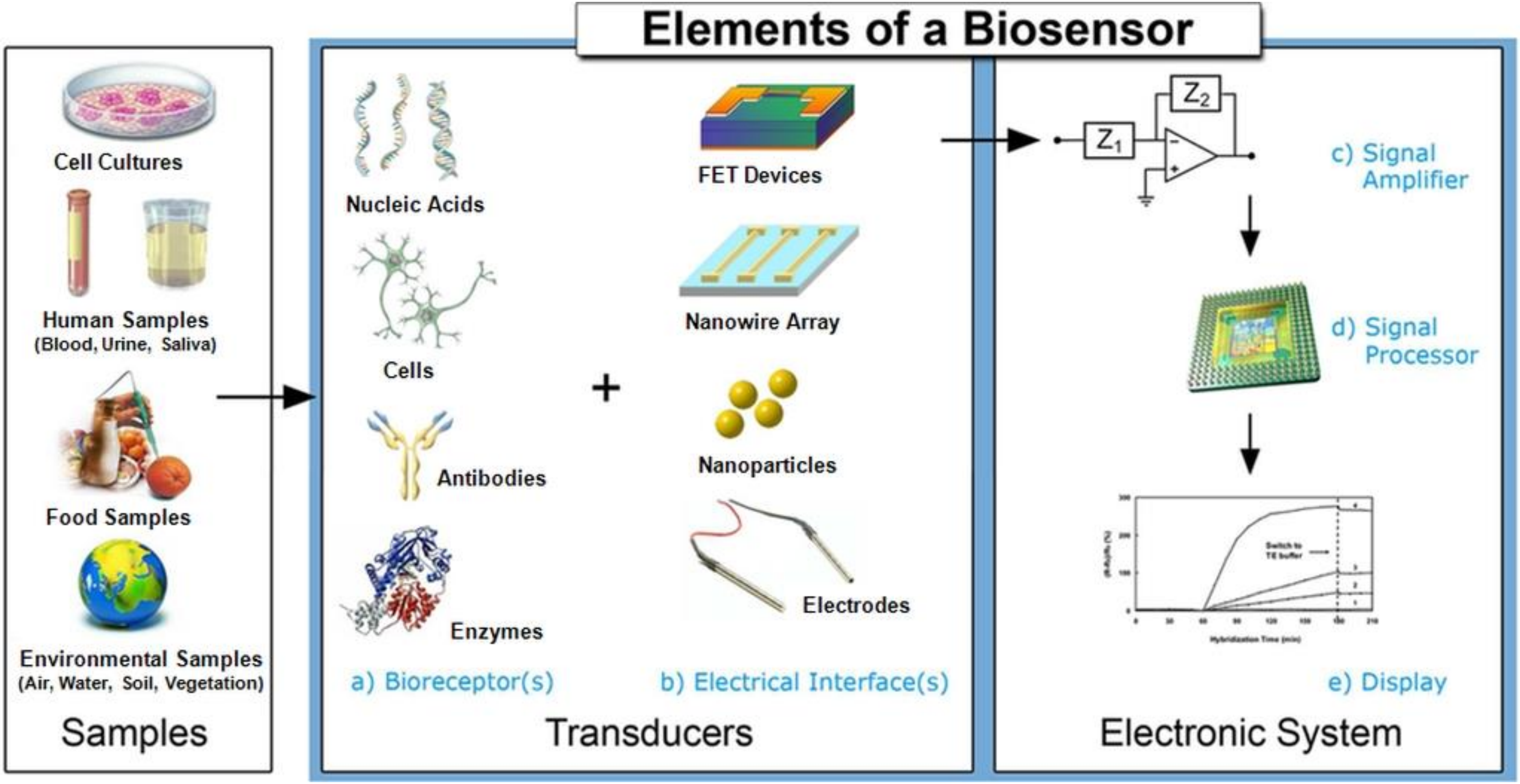
Lecture 02 dated 1st August 2024

Elements of Biosensors …



Elements of a Biosensor
Cell Cultures
Human Samples
(Blood, Urine, Saliva)
Food Samples
Environmental Samples
(Air, Water, Soil, Vegetation)
Samples
Nucleic Acids
Cells
Antibodies
Enzymes
FET Devices
Nanowire Array
Nanoparticles
Electrodes
+
a) Bioreceptor(s)
b) Electrical Interface(s)
Transducers
Z_1
Z_2
c) Signal Amplifier
d) Signal Processor
e) Display
Electronic System

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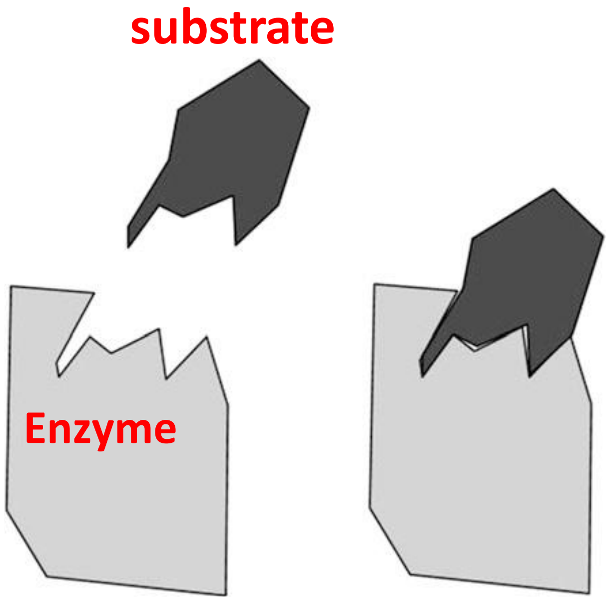
Lecture 03 dated 5th August 2024

Bioreceptors:

A molecule that specifically recognizes the analyte is known as a bioreceptor. Ex. Enzymes, cells, aptamers, deoxyribonucleic acid (DNA) and antibodies, etc.

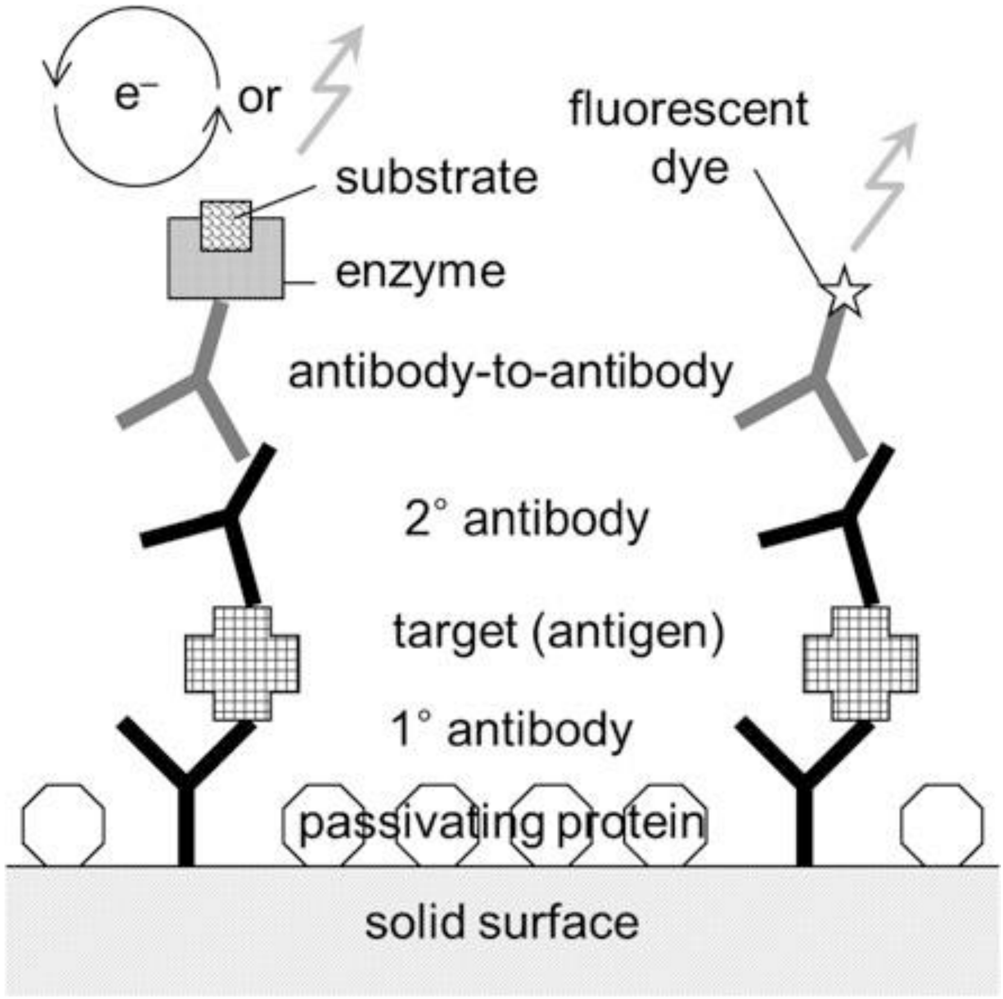
- **Enzyme:**
  - An **enzyme** is a **protein** molecule that acts as a biological **catalyst**, and it always **binds** to a **specific substrate** molecule, which is usually a chemical compound smaller than a protein molecule.
  - Upon binding, the enzyme chemically converts the substrate into a different molecule.
  - This enzyme–substrate binding is highly specific to shape, similar to a lock-and-key mechanism



- **Enzyme:**
  - In a **glucose sensor**, an **enzyme** called **glucose oxidase (GOx)** is used to **capture** & **detect** the **glucose** molecule (names of enzymes usually end with - **ase**.).
  - **GOx binds only** to **glucose**, & **oxidizes** it into another chemical called gluconolactone, & eventually to gluconic acid.

  - A series of further reactions creates an **oxidation**/reduction cycle that **generates**/consumes electrons and can be represented as an electric current.
  - This **current** is **directly proportional** to the **concentration** of glucose.
  - The current can be converted easily into voltage using a resistor.
  - This transducer is specifically called an electrochemical transducer.

- **Antibody–antigen binding:**
  - **Antibody–antigen binding** can also be quantified with both **electrochemical** & **optical** transducers
  - First, the **antibody** is immobilized on a solid surface.
  - Empty spaces on a surface are filled with a passivating protein, typically bovine serum albumin (BSA), to **prevent nonspecific reaction**.
  - A specimen containing the **target molecule** (protein, virus, bacterium, etc.) is added.
  - Upon rinsing, only a target molecule specific to an antibody remains on the surface.
  - The same antibody is added again (secondary antibody), followed by the addition of "antibody-to-antibody" (or anti-IgG) that is **tagged** with an **enzyme** or a **fluorescent** dye.



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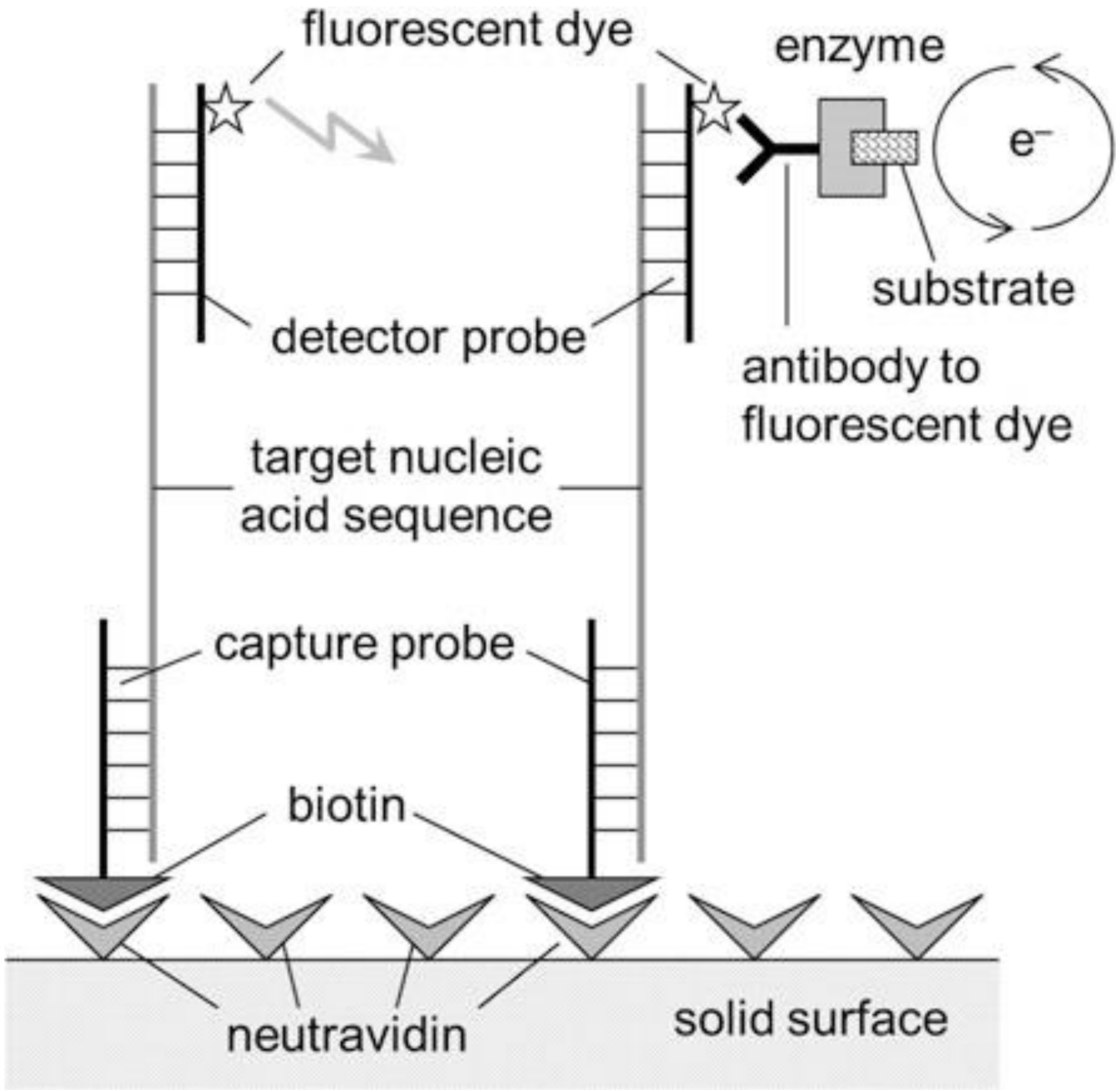
Lecture 04 dated 7th August 2024

- **Nucleic acids:**
  - These include specific sequences of deoxyribonucleic acid (DNA) or ribonucleic acid (RNA).
  - Genetic information is stored within DNA or RNA in quaternary (base-4) system consisting of four different bases:
    - adenine (A), thymine (T), guanine (G) and cytosine (C) for DNA; &
    - adenine (A), uracil (U), guanine (G), and cytosine (C) for RNA.
  - **A** always binds to **T** (**U** for RNA) &
  - **G** always binds to **C**.
  - A specific RNA sequence of bases, e.g., **AGA GGA GAU**, can be used to **detect** their complementary sequence, **UCU CCU CUA**.
  - The specificity of the nucleic acid bioreceptor is enhanced by increasing the length of the DNA/RNA sequence.
  - For practical applications, **several** hundred codes can be used.
  - **Longer** the sequence is, the **better** the **specificity** is, but the **binding** of **complementary** sequences becomes **harder** & **harder**.

• Nucleic acids (cont …)

- The **nucleic acid bioreceptor** is **powerful** in identifying different viruses or bacteria.
- E.g., it is possible to distinguish influenza A virus **subtype** H1N1 (known as **swine flu**) and the **subtype** H5N1 (highly pathogenic **bird flu**), with a well-designed nucleic acid sequence.



An example of a nucleic acid bioreceptor with a fluorescent dye (left) or an enzyme (right)

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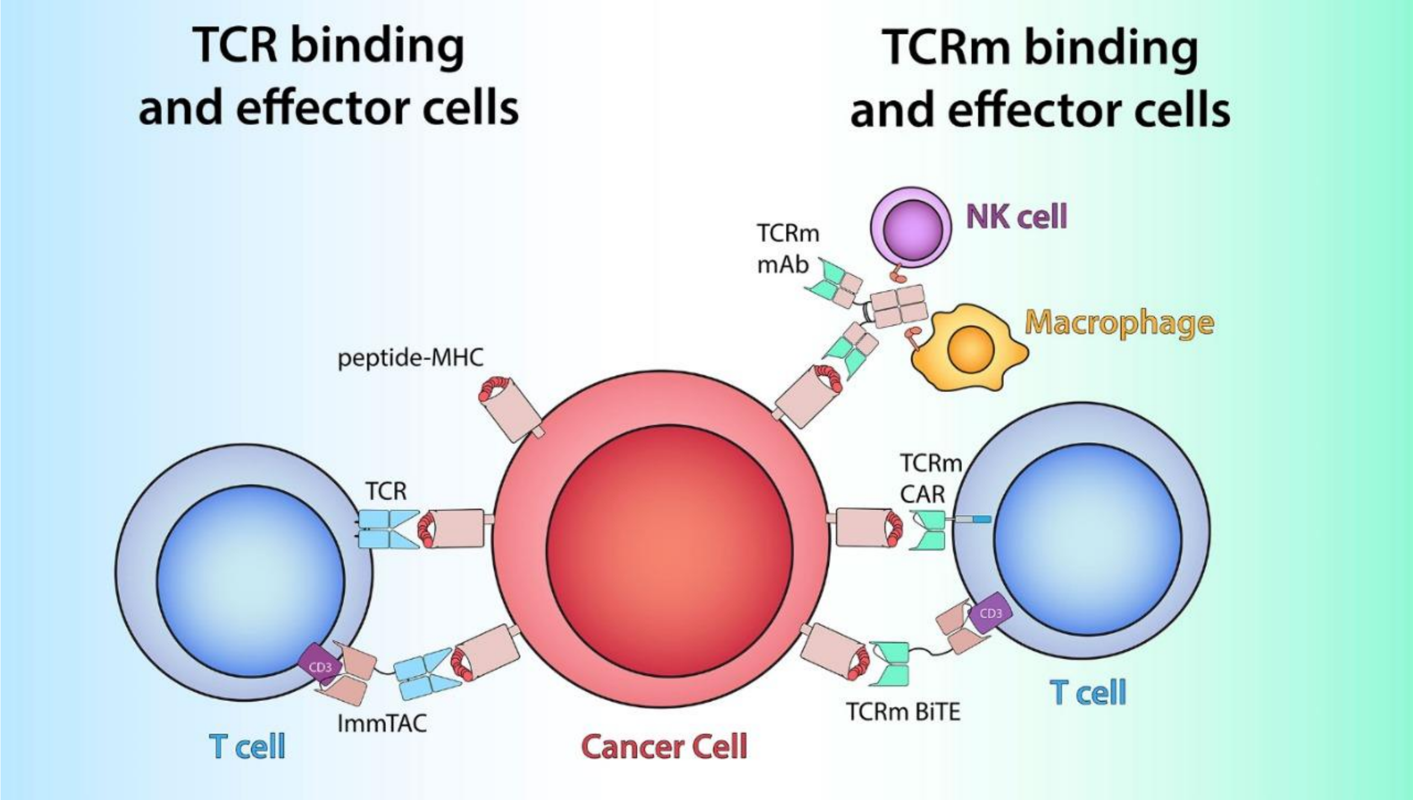
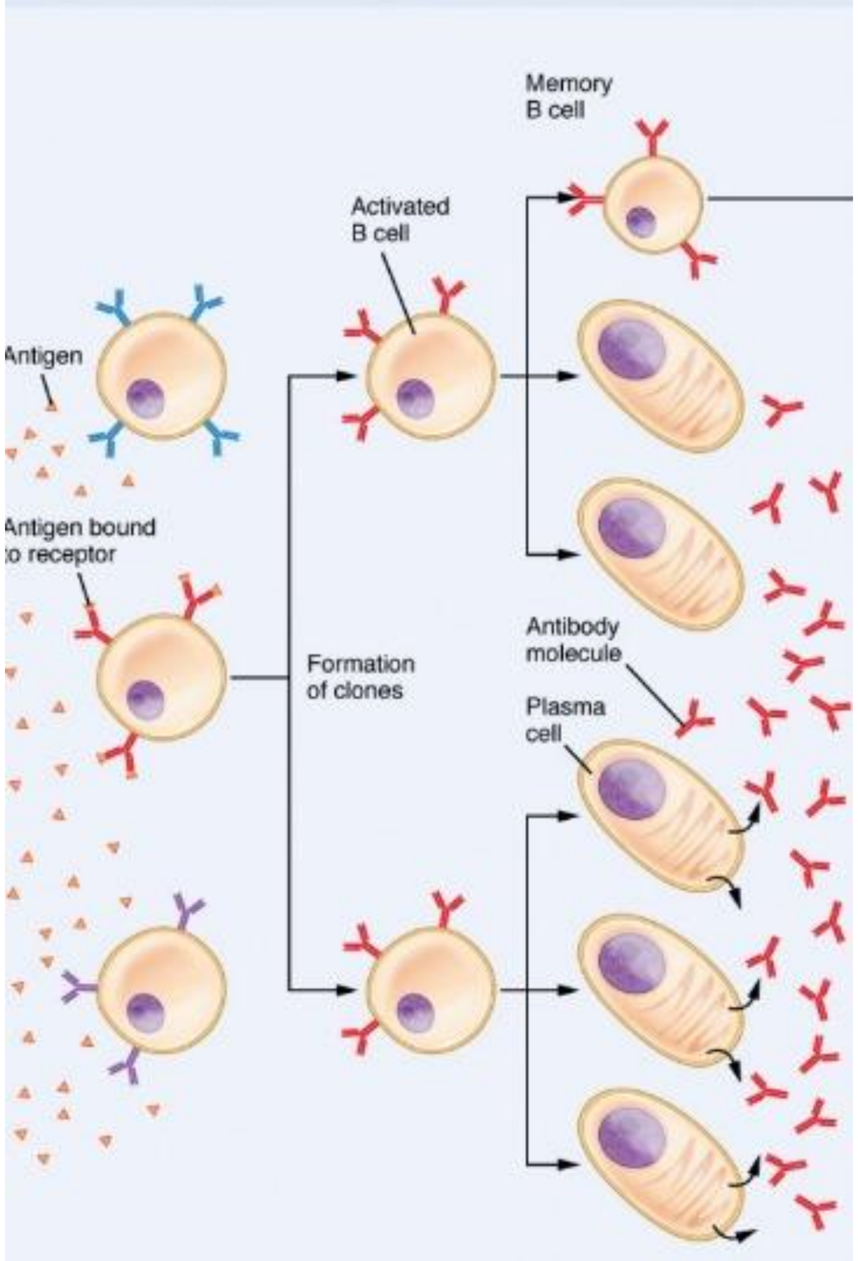
Lecture 05 dated 7th August 2024

- **Cells:**
  - Certain cells that possess a strong affinity for a specific target can also be used as a bioreceptor.
  - **T cell** is a good example.
  - Recall that the antibody is one of the major players in the immune system. There are three important cells in charge of the body’s immune response: the **B cell**, the **T cell**, and the **natural killer cell (NK cell)**.
  - B cell produces antibodies to fight against foreign molecules, whereas the
  - T cell recognizes and fights against the foreign molecules by itself. This indicates that the T cell can also be used as an excellent bioreceptor.
  - In fact, any group of cells that **forms a tissue** can be used as a bioreceptor, provided **they can recognize and bind** to a **target** molecule.


TCR binding
and effector cells
TCRm binding
and effector cells
NK cell
TCRm
mAb
Macrophage
peptide-MHC
TCR
TCRm
CAR
CD3
CD3
T cell
ImmTAC
Cancer Cell
TCRm BiTE
T cell


Memory
B cell
Activated
B cell
Antigen
Antigen bound
to receptor
Formation
of clones
Antibody
molecule
Plasma
cell

Questions?

Signal Transducers used in sensors:

- **Potentiometric Transducers:**
  - Based on charge related to the analyte
- **Amperometric Transducers:**
  - **Rely on enzyme system that converts analytes into products, that is oxidized or reduced at a working electrode.**
  - **Conductance/ capacitance change of the soln. is measured**
- **Optical measurements:**
  - **linear phenomenon -** adsorption, fluorescence, phosphorescence, polarization, interference, etc.
  - **non-linear phenomena -** 2^{nd} harmonic generation
- **Acoustic Transducers:**
  - **Use of piezoelectric crystal as a mass sensor resulting in its oscillating frequency change**

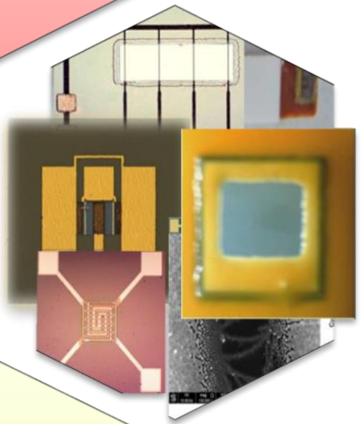
Platform Sensors Devices …

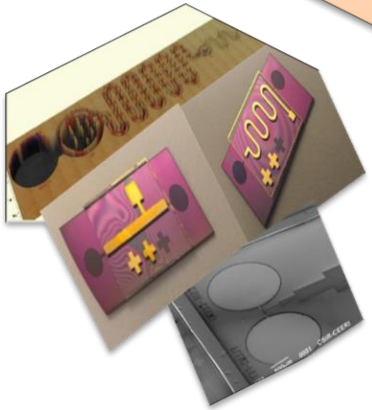
Inertial Sensors

Pressure sensors
Accelerometers
Acoustic Sensor
Magnetometer
Gyroscope
CMUT

Bio-Chemical Sensors

Si-Nanowire Array
ISFET & EGFET
Gas sensors
CNT FET
HEMT





µ-fluidic Platforms

LOC for Particles Separation & Counter
Micro-Viscometer
Fluid FET

End of lecture 5

Questions??