Biosensors

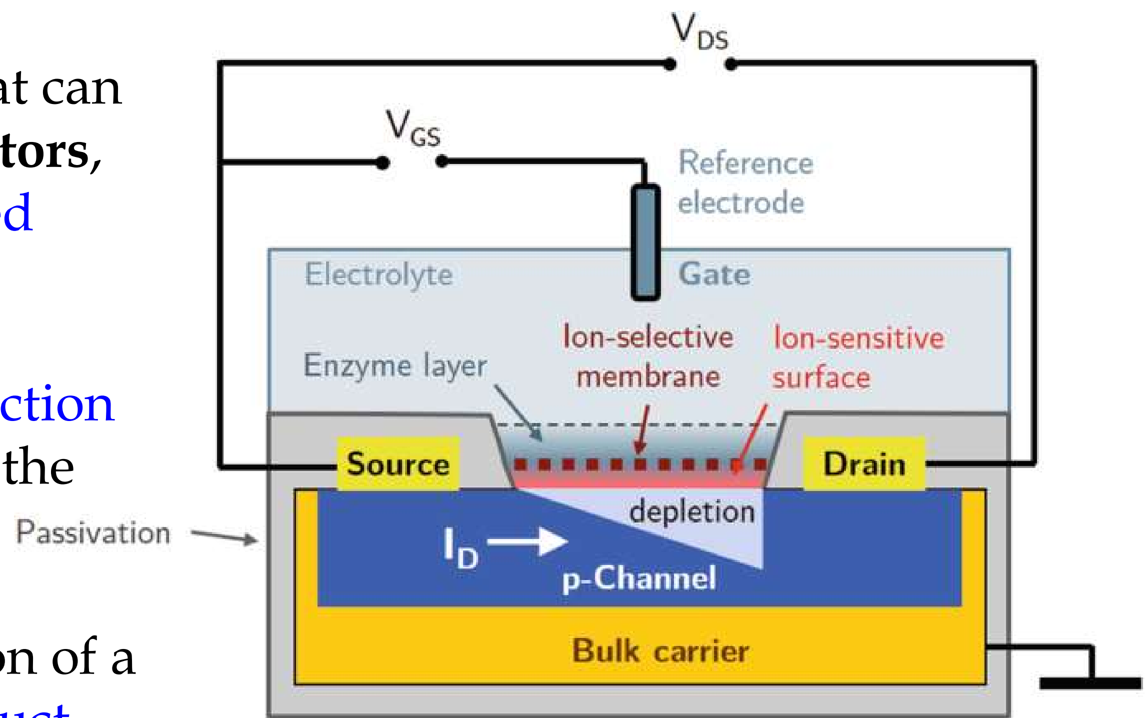
B. Tech.
Course No.: EEL 3050
L-T-P [C]: 3–0–2 [4]

Prof. AJAY AGARWAL
ELECTRICAL ENGINEERING
IIT JODHPUR

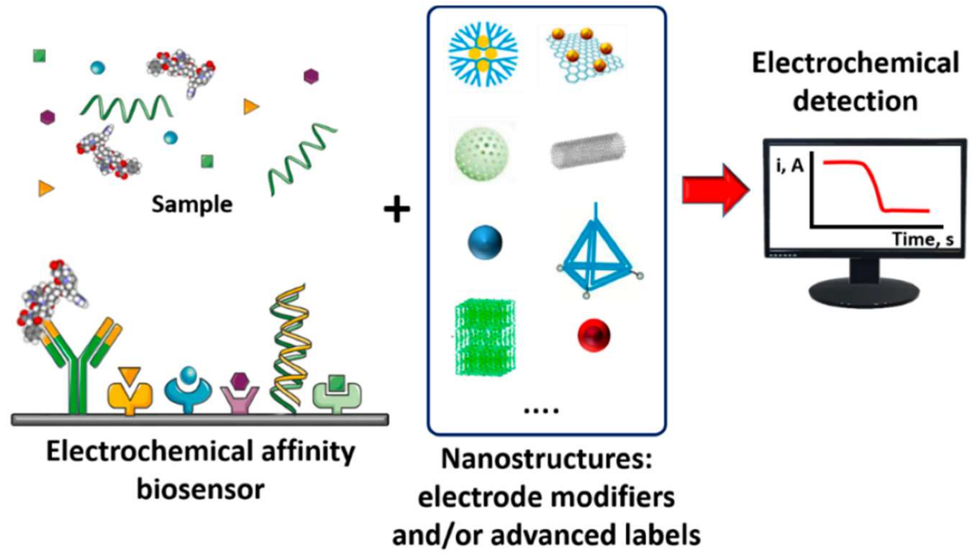
Lecture 08 dated 21st Aug 2024

Signal Transducers used in sensors:

- **Catalytic biosensor:**
  - These are analytical devices that can be considered as **chemical reactors**, with a sensing layer is separated from an external solution by a permeable barrier.
  - The **substrate** can **enter** the reaction volume through the **barrier**, & the **product** can **leave**.
  - The interactions in a catalytic biosensor result in the formation of a new biochemical reaction product.
  -



- **Affinity biosensor:**
  - The affinity biosensor technology are based on specific molecular interaction e.g.:
    - antigen-antibody,
    - DNA -DNA,
    - enzymes-substrates,
    - receptors-specific molecules, etc.
  - These interaction allows **detection** & **quantification** of analytes



Use Cases of Sensors

1. Gas Sensors

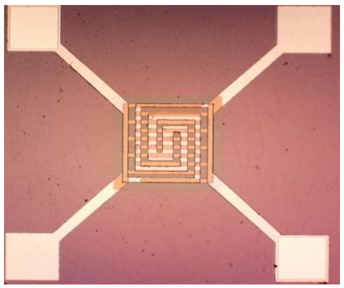
- **MOS based Gas sensors & interface electronics**
- **Applications:**

✓ **Environmental Monitoring:** Pollutant gases - NH_3, NO, CO, VOCs, etc.

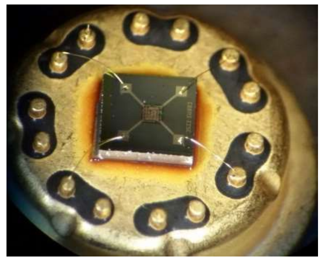
✓ **Health Monitoring:** Breath analysis

Disease	Markers
Asthama	NO, CO, H_2O_2
Lung Cancer	NO
Diabetes	Acetone
Respiratory monitoring	CO_2 / O_2
Kidney function	NH_3

Integrated Gas Sensor platform

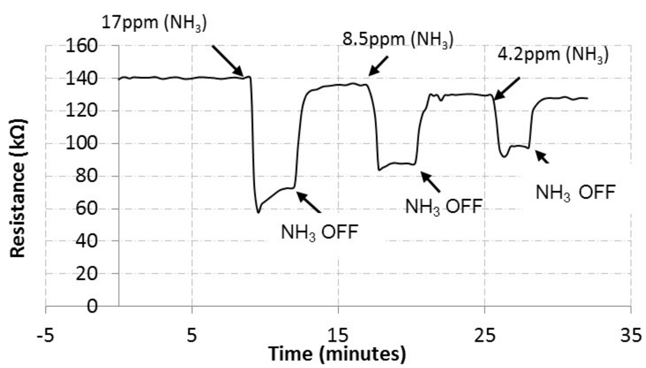


Gas Sensing chip

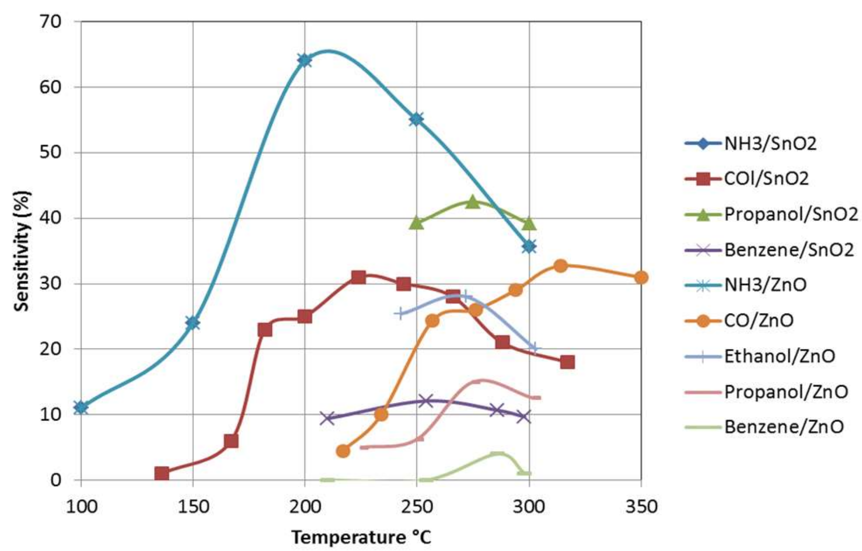


Gas Sensing Packaging

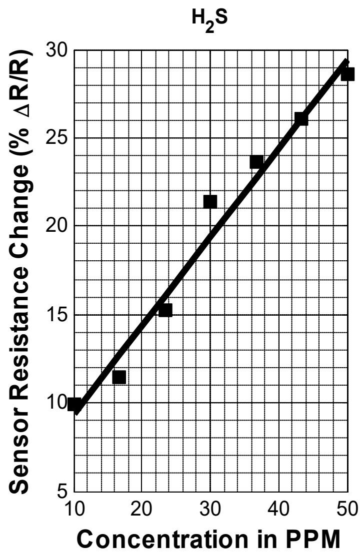
Control Electronics

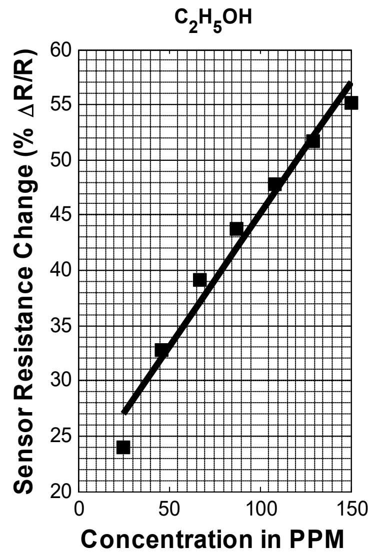


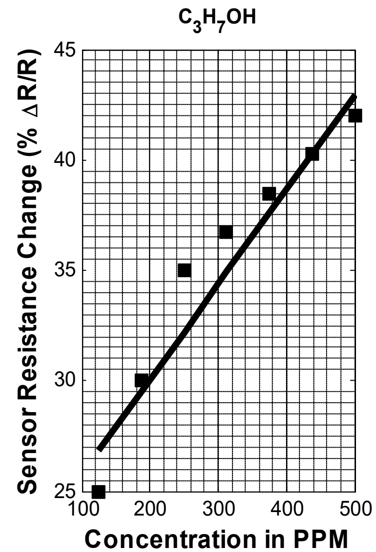
Ammonia Sensing

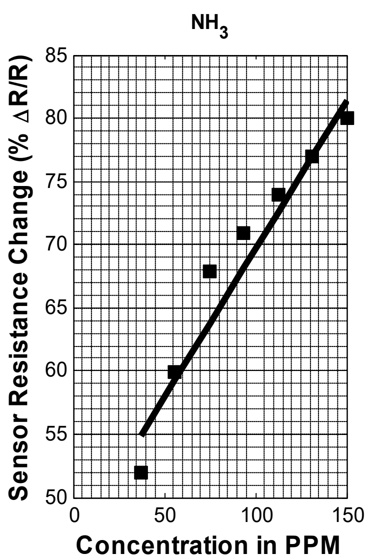


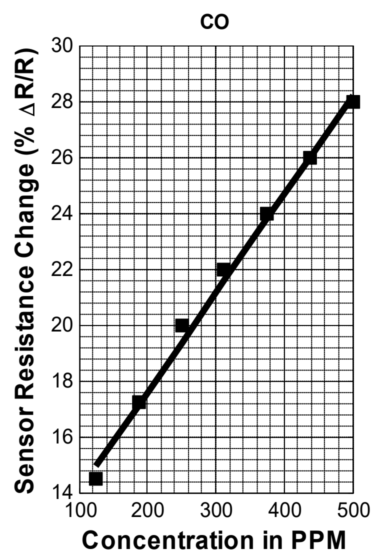
Sensitivity vs. temp. for various gases & films









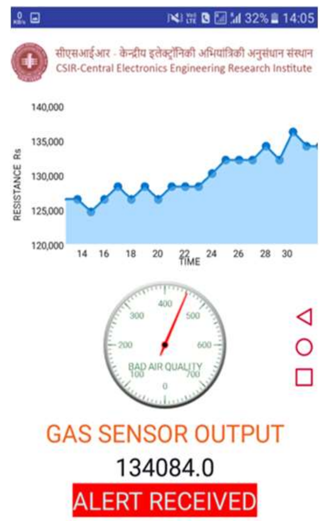


Gas concentration vs. sensitivity plots for H_2S, C_2H_5OH, C_3H_7OH & NH_3, CO

Gas Detection Systems

Gas sensor system with 4-20mA transmitter

Gas Sensor System with mobile APP



NH_3, CO & H_2S

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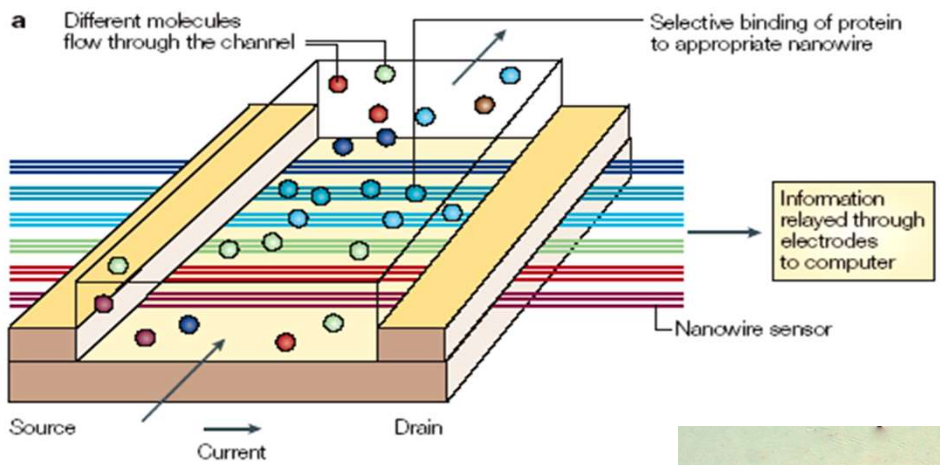
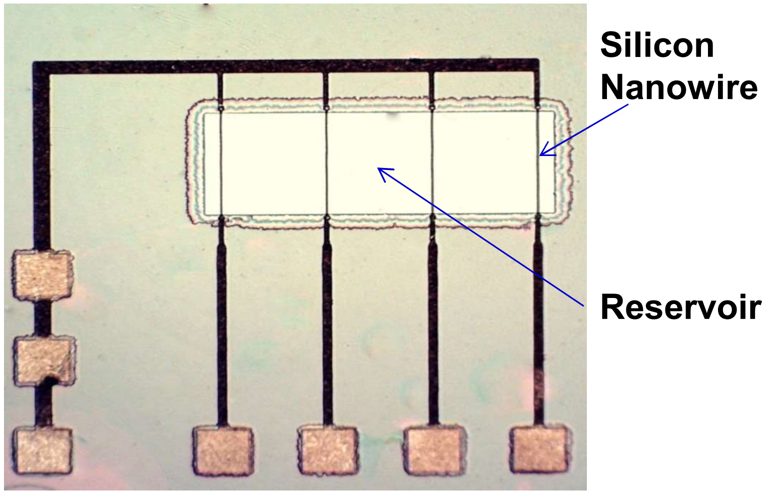
Lecture 09 dated 22nd Aug 2024

2. *Silicon Nanowire* array

For Bio- chemical sensing at very concentrations



Nature Reviews Cancer, 5 (2005) 161



ELSEVIER

Sensors and Actuators A: Physical

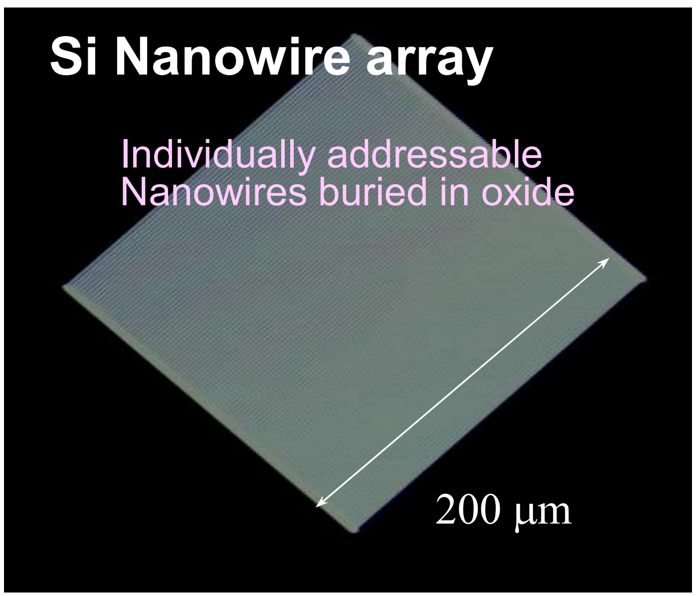
Volumes 145–146, July–August 2008, Pages 207-213

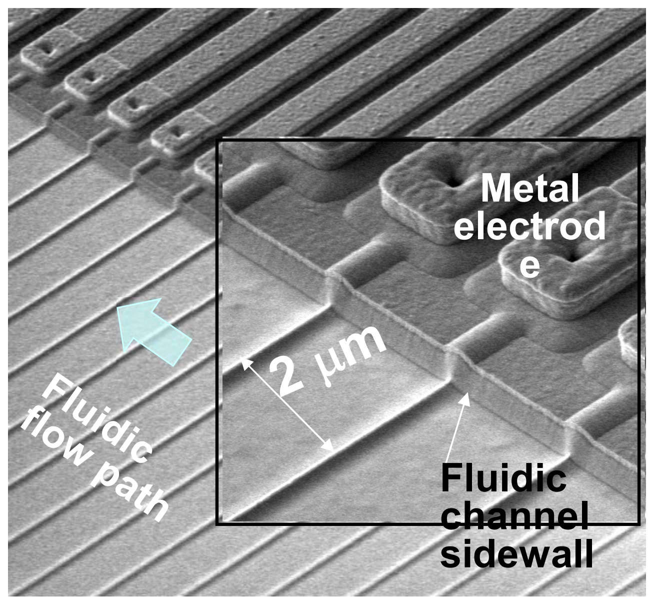
Silicon nanowire sensor array using top–down CMOS technology

Ajay Agarwal, K. Buddharaju, I.K. Lao, N. Singh, N. Balasubramanian, D.L. Kwong

Si nanowires in arrays

- Si Nanowire array made by standard Silicon IC fabrication technology
- Robust, reproducible & allow easy integration with fluidics & electronics

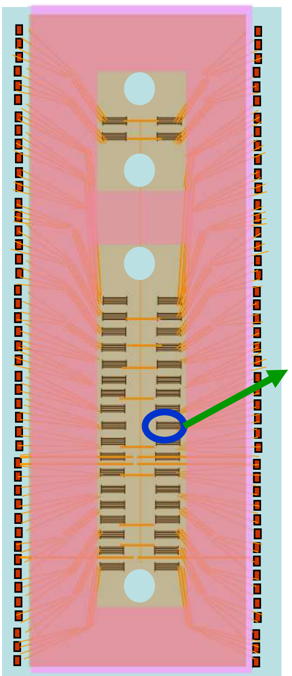


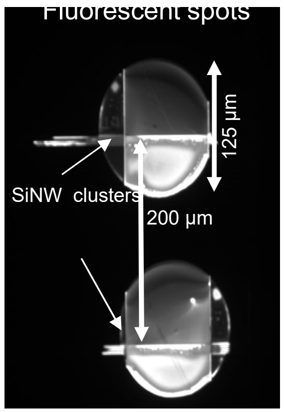


Nanowire cross-section range: 20 – 50 nm

Integrated Detection Module

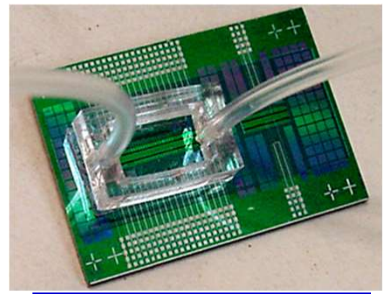
NW Array Chip



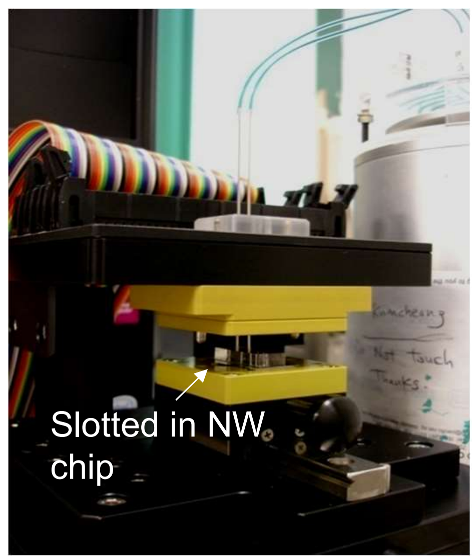


Spotting of capture probes *using an array spotter*

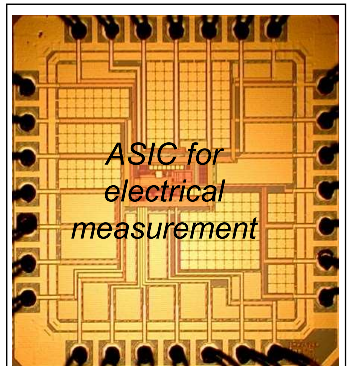
36 clusters of NW



SiNW chip with fluid exchange



Mini-electrical measurement station

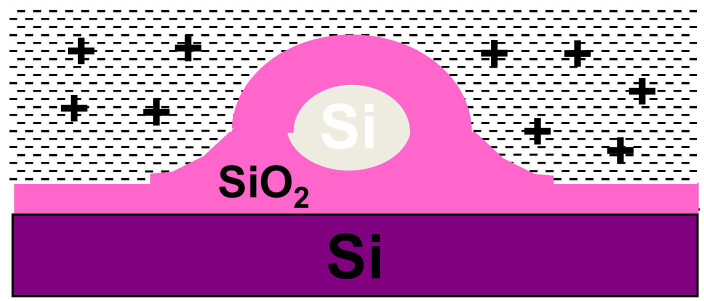


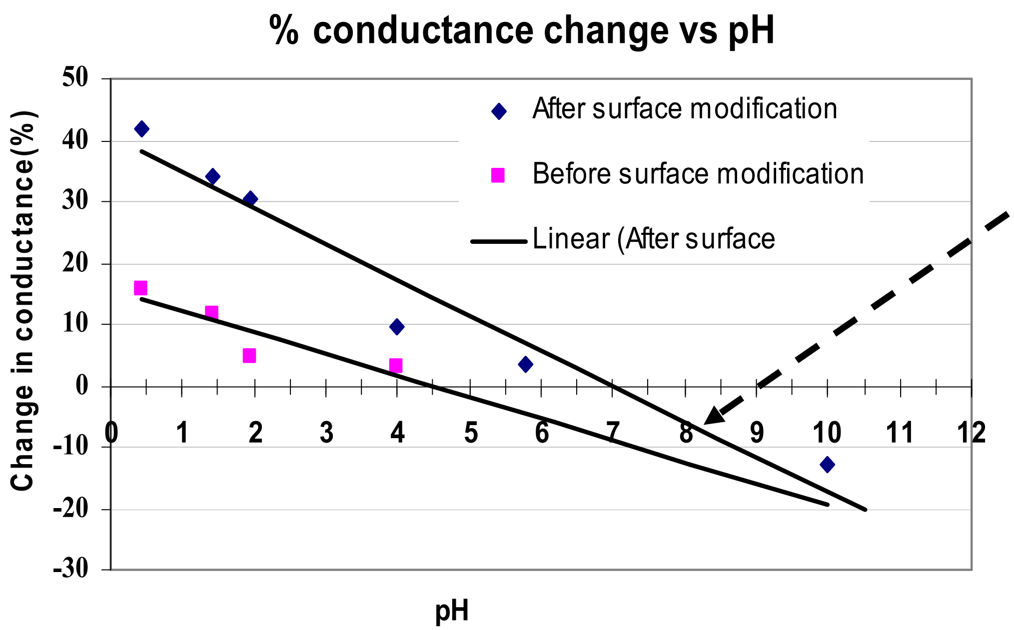
Peripheral electronics

Display / Storage of data

pH sensing by SiNW

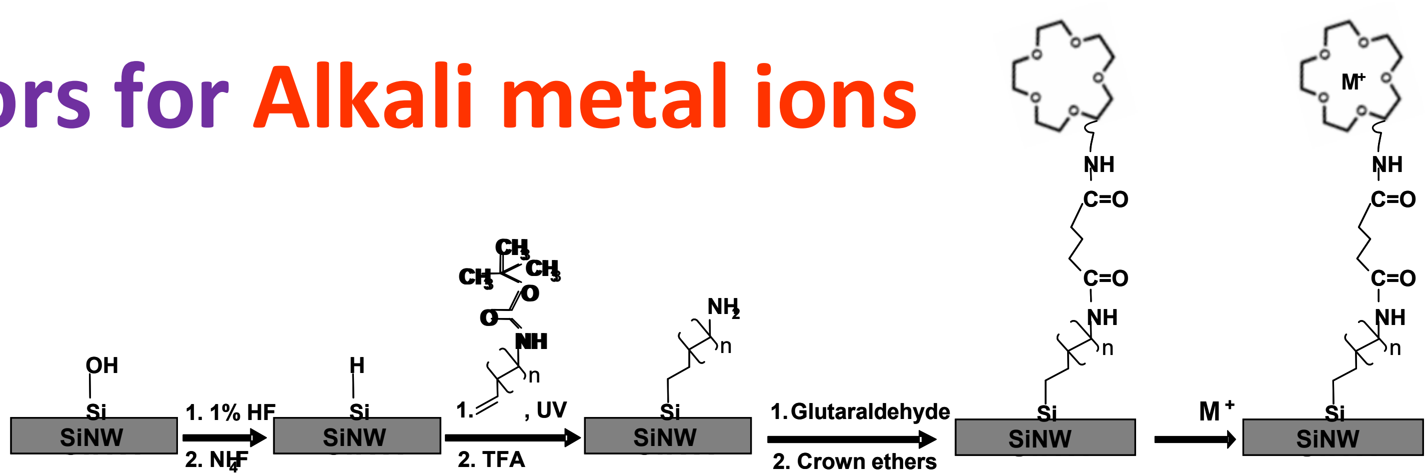
n-Si Nanowire
buried in SiO_2

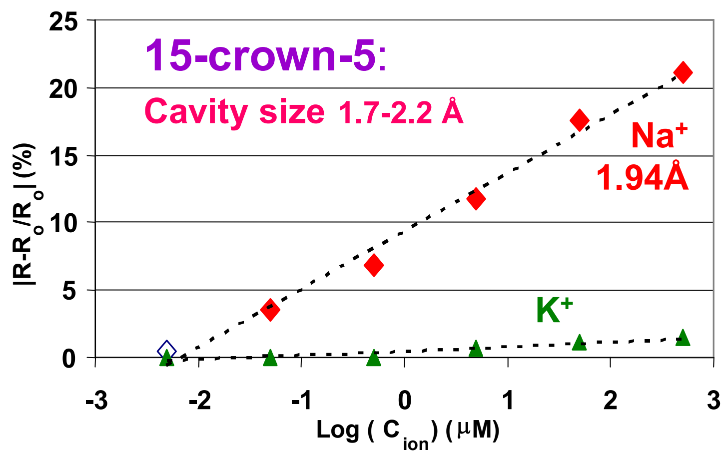


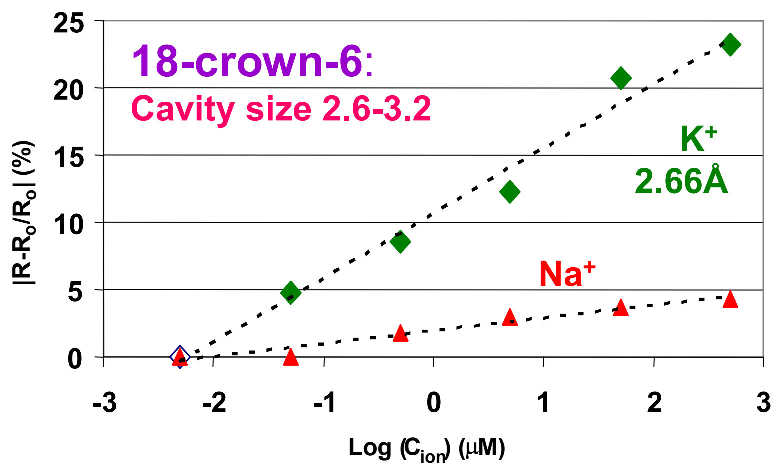


Silanation: Enhances attachment of H^+ (enhanced +ve gate voltage causing accumulation in n-type Si NW and enhanced conductivity)

Sensors for Alkali metal ions



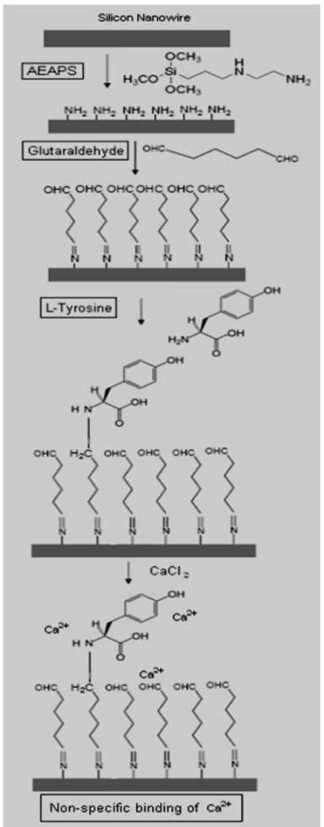


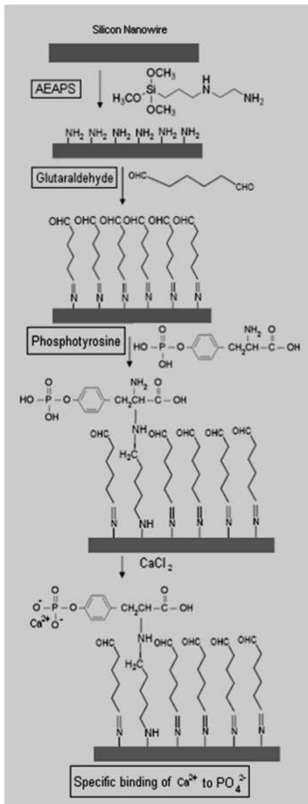


Detection limit of 50 nM; lower by 3 orders than conventional crown ether–based ion-selective electrodes.

G. Zhang, **Ajay Agarwal**, et al., **Appl. Phy. Lett.** 90, 2007, pp. 233903

Selective Sensor for Ca^{2+}

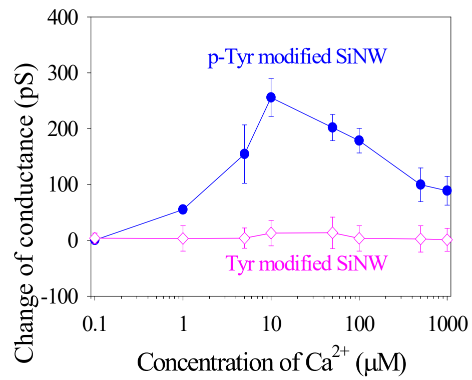


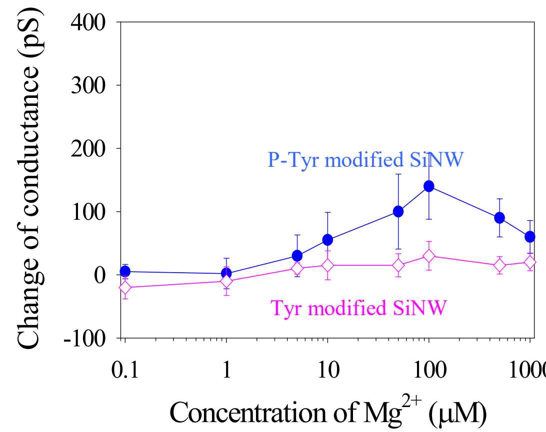


$[Ca^{2+}]$
(in living cell)

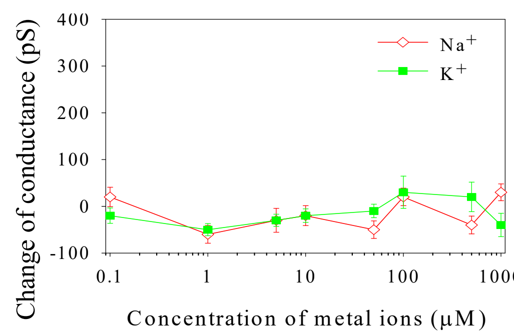
- Cell proliferation
- Cell apoptosis
- Gene expression

Medical diagnosis



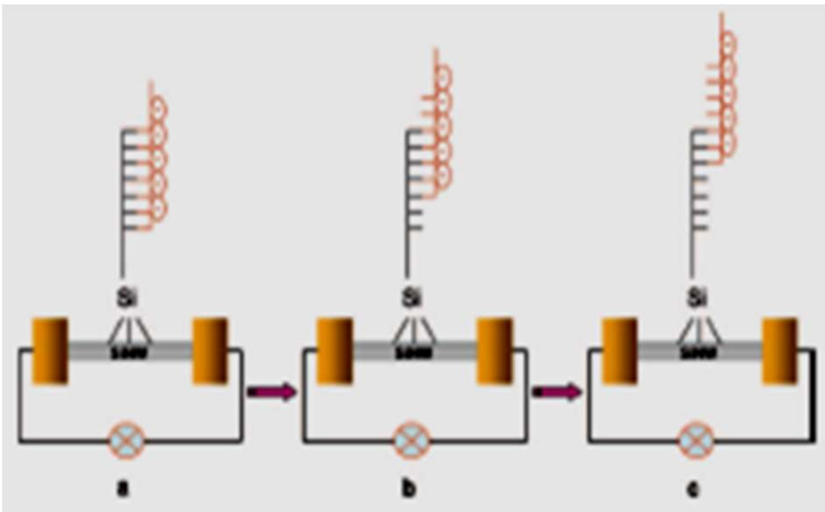


SiNW surface modification by tyrosine/ phosphotyrosine followed by Ca^{2+}

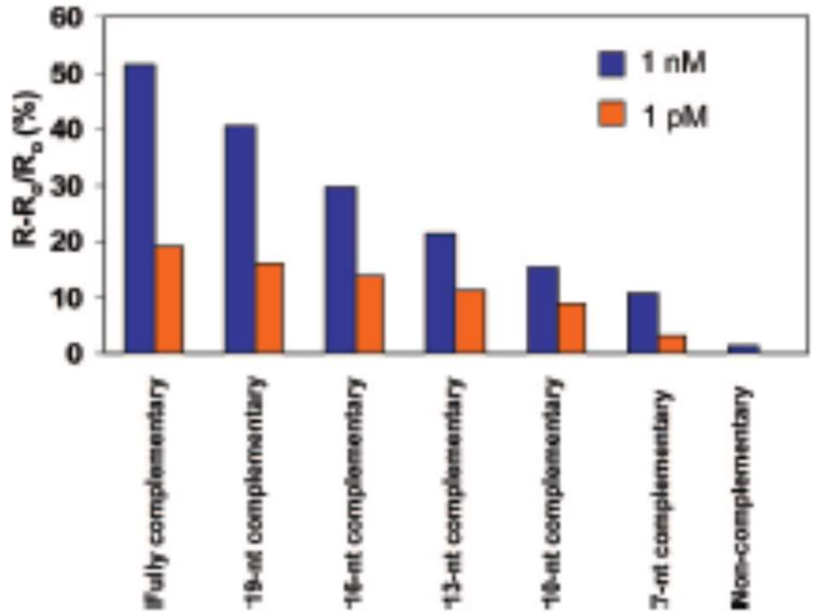


X. Bi, **Ajay Agarwal**, et al., **Biosensors Bioelectronics**, 23 (2008) 1442

DNA Sensing by SiNW:
Charge Layer Distance Dependence



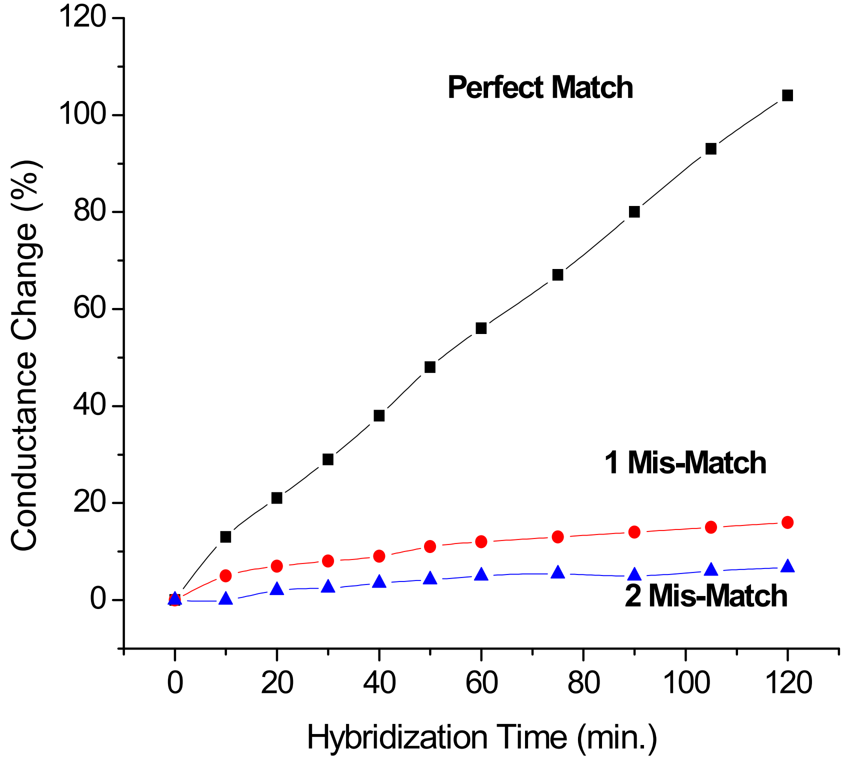
Variation of field effect of the SiNW Sensor caused by varying hybridization sites of Target DNA to PNA



Distinguishable resistance change of the SiNW caused by varying hybridization sites at two different concentrations of the target DNAs.

G. Zhang, **Ajay Agarwal**, et al., **Nano Letter**, 8, (2008) 1066.

Single Nucleotide Polymorphisms (SNP) detection using PNA modified SiNW sensors



PNA target:
3'-ACT CCA TCA TCC AAC ACA CCA A

Probes:
Matched
5'-TGA GGT AGT AGG TTG TGT GGT T

1-base mismatched
5'-TGA GGT AGT AGG TTG TAT GGT T

2-base mismatched
5'-TGA GGG AGT AGG TTG TAT GGT T

Z. Gao, **Ajay Agarwal**, et al, **Anal. Chem.**, 79 (9), 2007, pp. 3291 - 3297

Biosensors

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ELECTRICAL ENGINEERING

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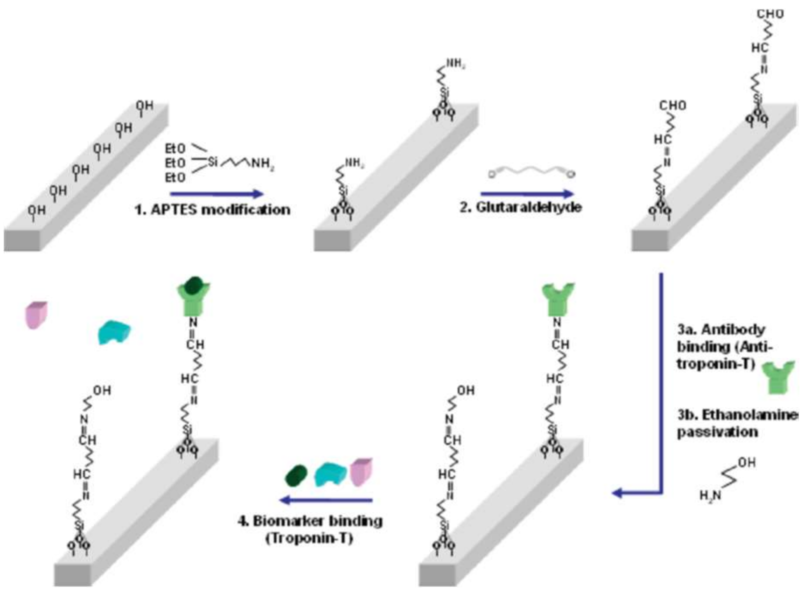
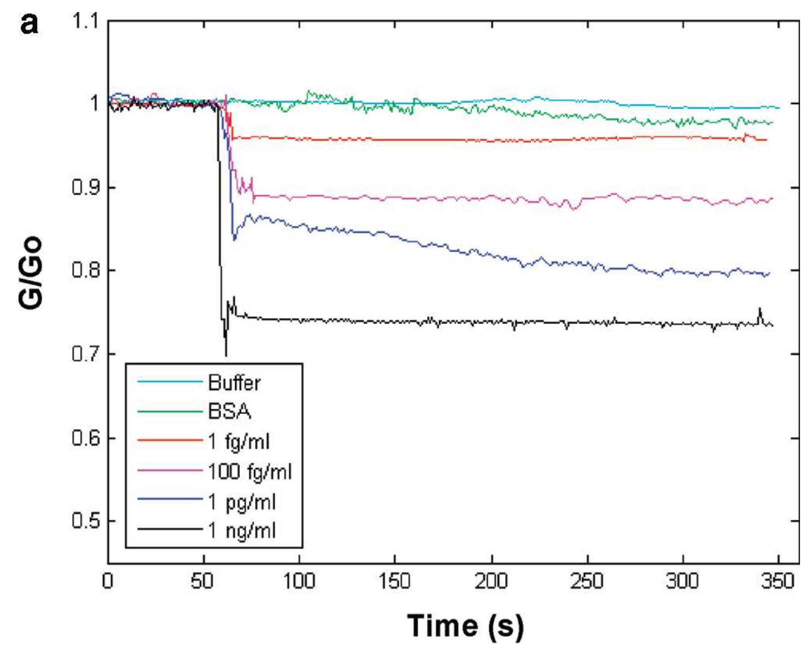
Lecture 10 dated 28th Aug 2024

Label-Free Electrical Detection of Cardiac Biomarker - Troponin-T (cTnT)



Schematic of the chemical process for surface functionalization of SiNW devices

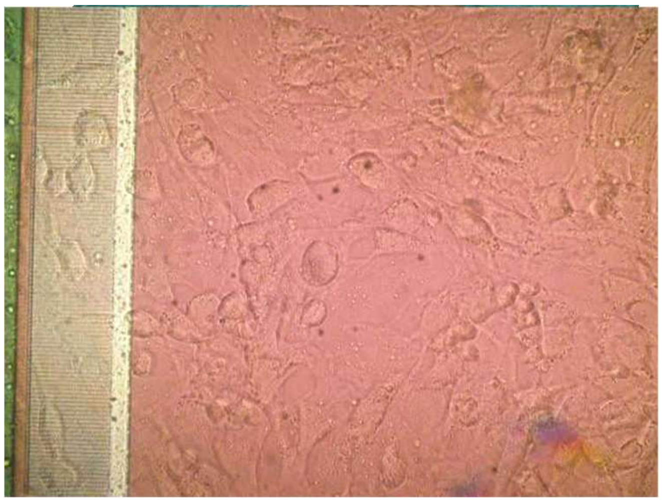


Conductance of SiNWs functionalized with anti-cTnT showing the detection response with decreasing cTnT concentration.

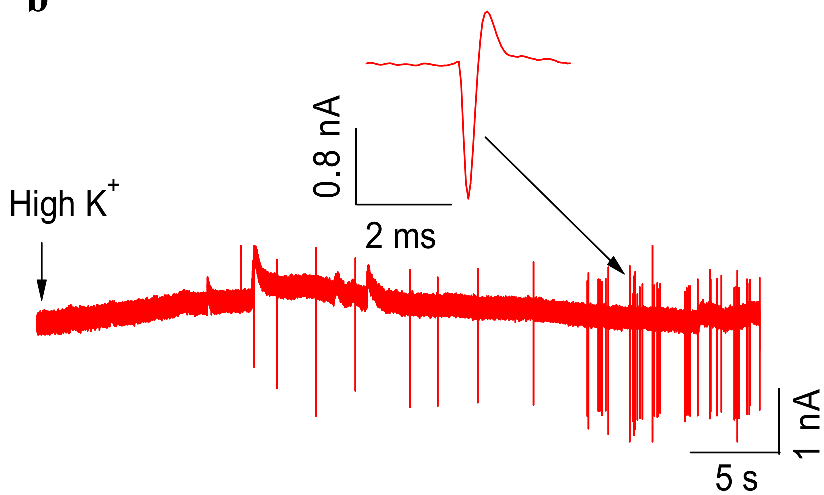
J H Chua, **A. Agarwal**, et al, Anal. Chem. 2009, 81, 6266–6271

Detection of Cellular Bioelectricity

a

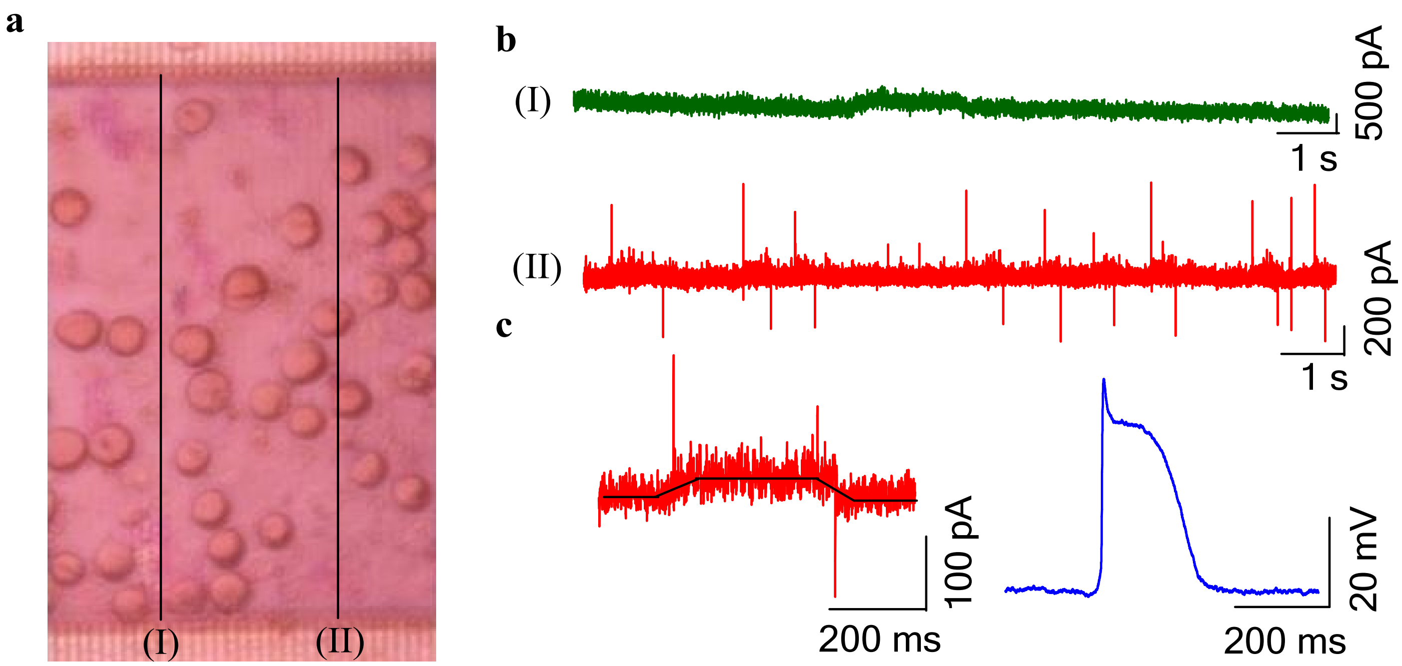


b



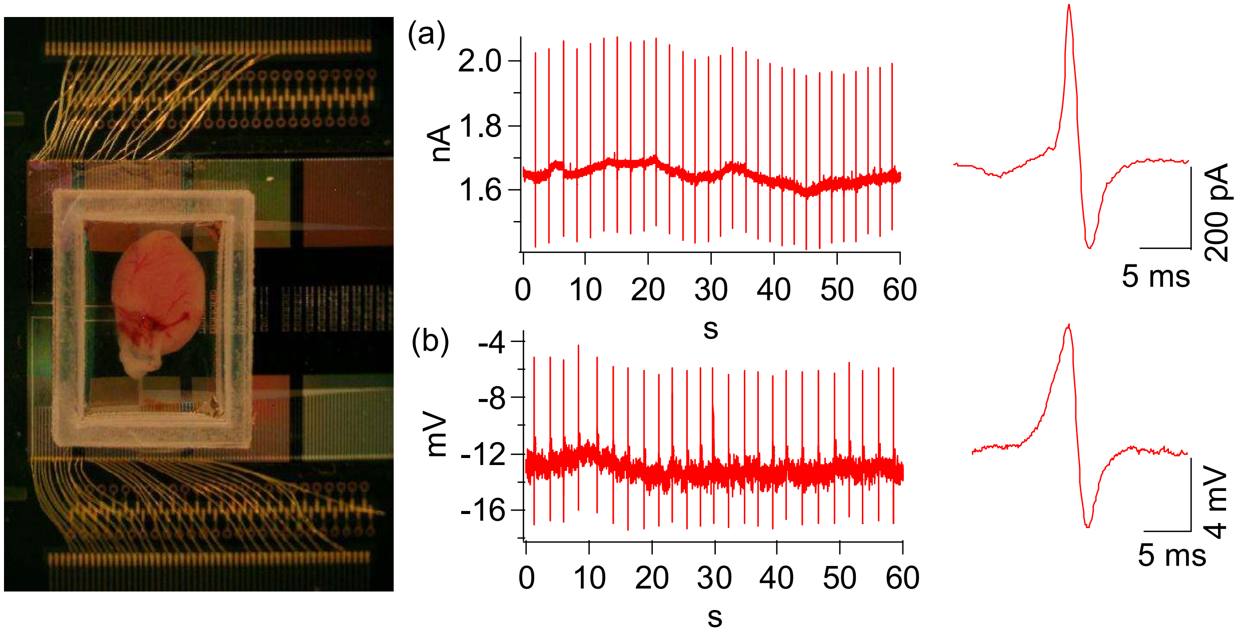
*Nanowire recordings on **aortic smooth muscle cells**.*
Transient nanowire current signals were induced by membrane depolarizing high K^+ solution.

Detection of Cellular Bioelectricity



*SiNW recordings on **individual cardiac myocytes**. A typical episode response from nanowire II, involving one upstroke current followed by a downward one (c. left). Duration for a pair of events similar to action potential recorded using nano-pipettte (c. right).*

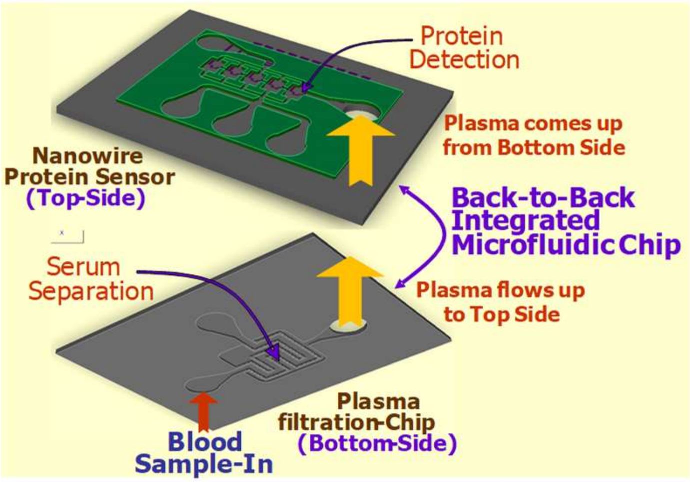
Detection of Cellular Bioelectricity



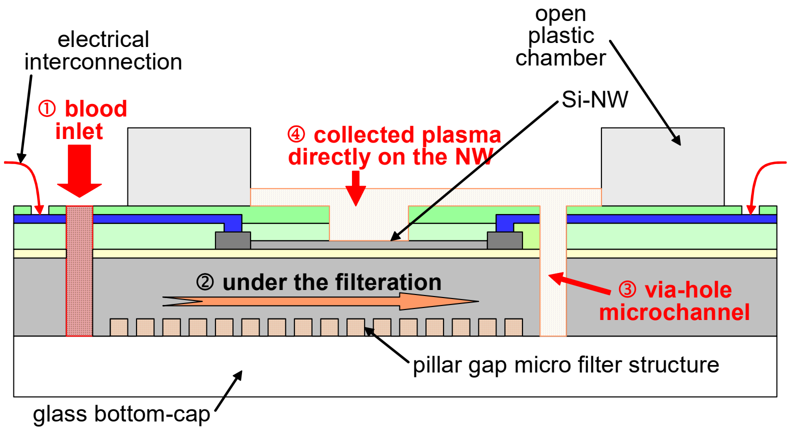
ECG recording from an intact beating heart. A train of current spikes (a) & voltage signal (b) that was in concert with the heart beating recorded from nanowire and nano-pipette electrode respectively. They share the similar waveforms.

Tze-Sian Pui, **Ajay Agarwal**, et al., Small, 5 (2009) 208-212.

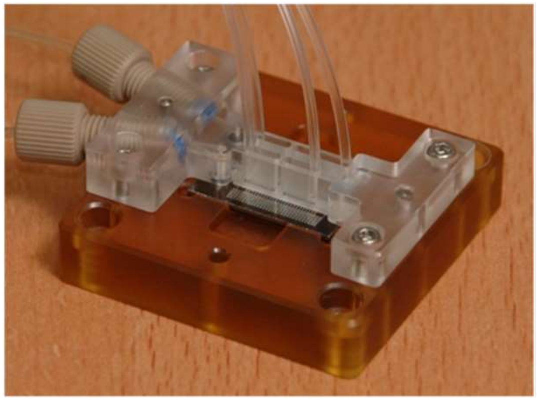
System-on-Chip



Conceptual drawing of back-to-back integration of Si-NW biosensor for protein detection with microfiltration chip for plasma separation



Working principle of sample flow in the back-to-back integrated microfluidic device..



Customized plastic housing for back-to-back integrated microfluidic device

TG Kang, **Ajay Agarwal**, et al., µTAS2007, 3-7 Oct 2010, Groningen, The Netherlands.

Assignment 1

1. Choose any journal article on Nanowire Biosensor and write a review on it in 100 words (app.) mentioning
    i. Its working principal
    ii. Analytes
    iii. Linkers/ capture probes used
    iv. Its sensitivity &
    v. It's citation

Biosensors

B. Tech.

Course No.: EEL 3050

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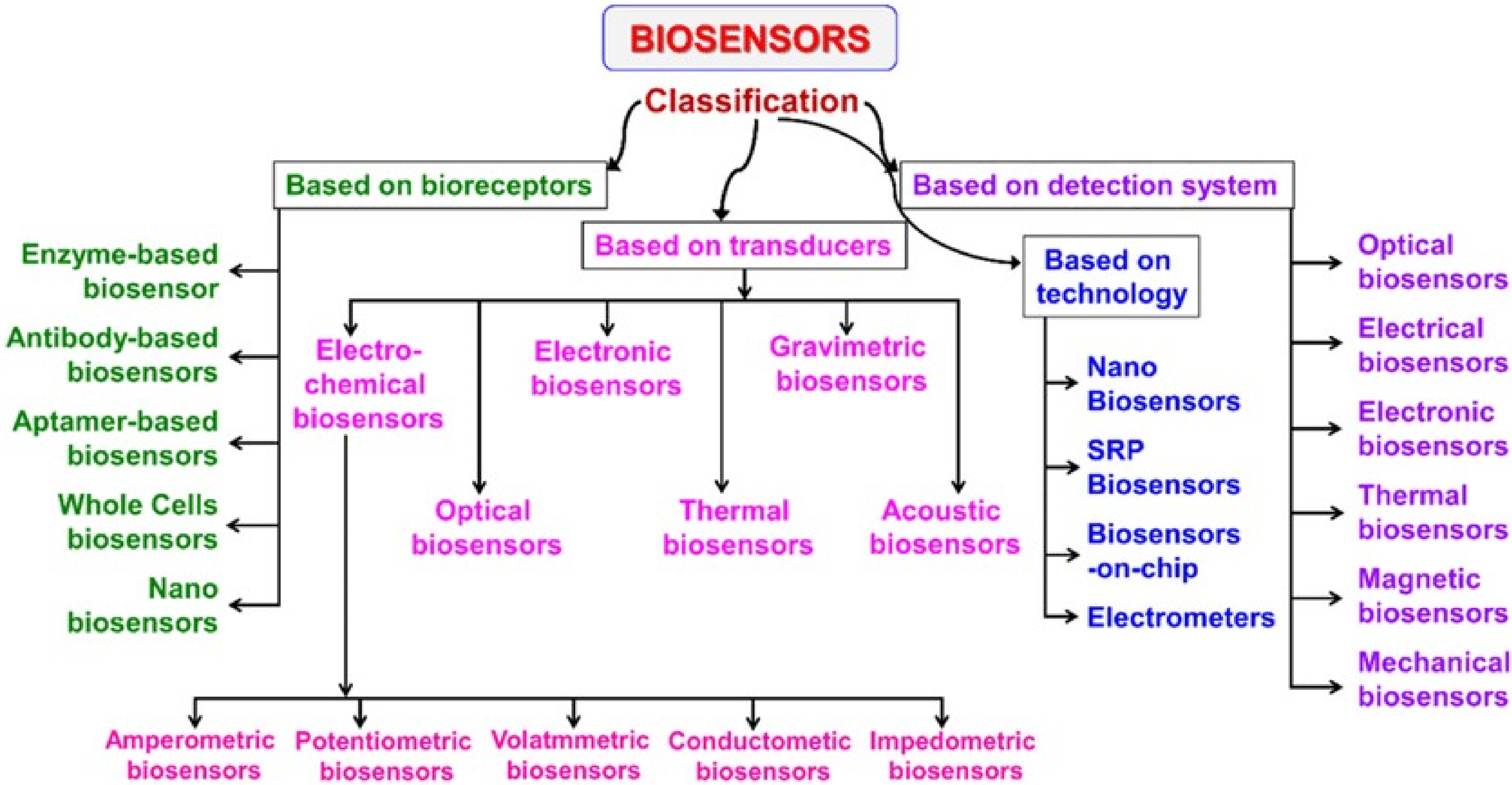
Prof. AJAY AGARWAL

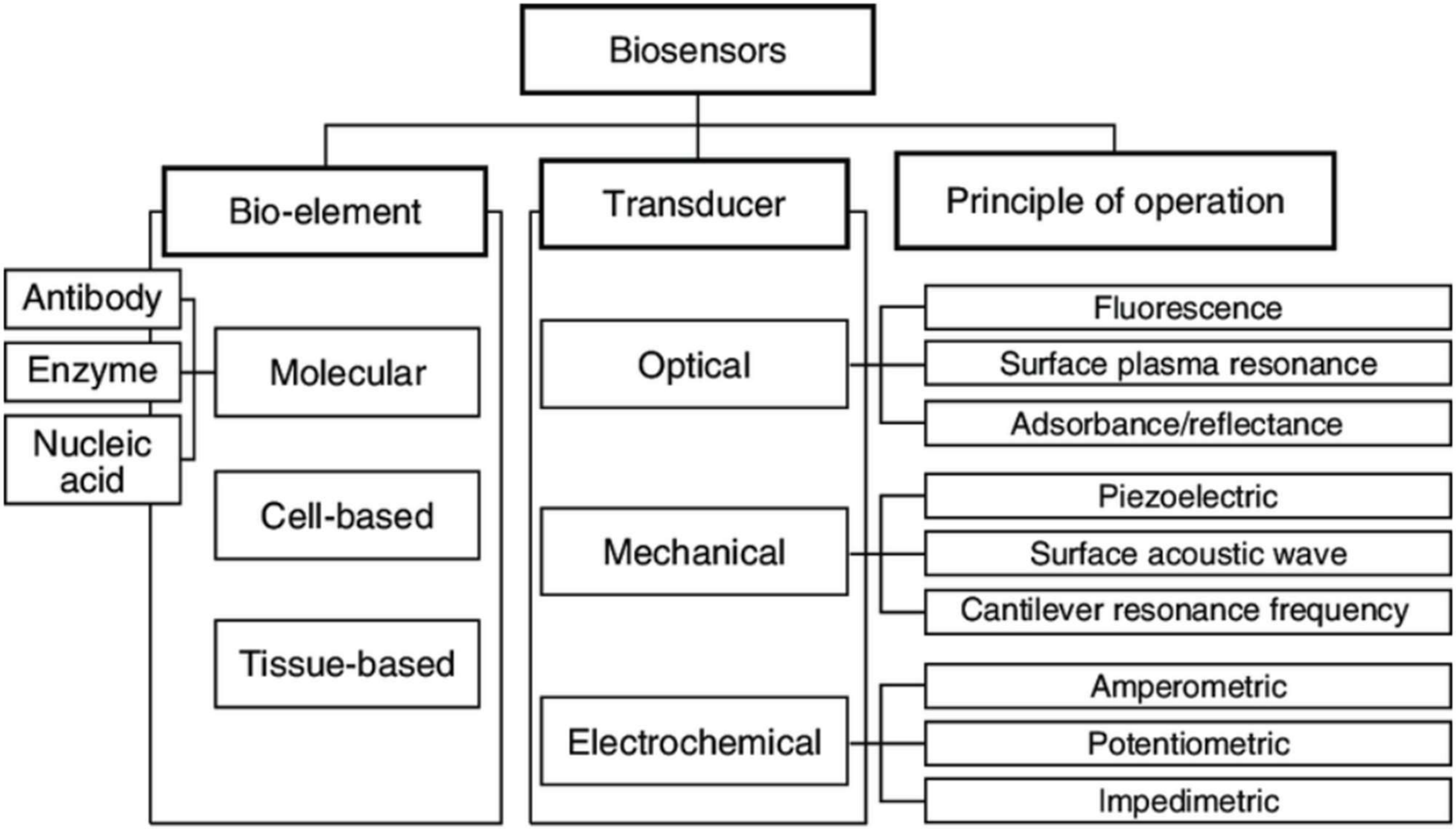
ELECTRICAL ENGINEERING

IIT JODHPUR

Lecture 11 dated 29th Aug 2024

Classification:



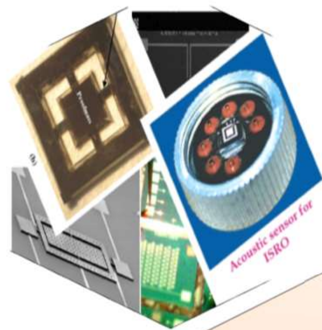


Biosensors
Bio-element
Transducer
Principle of operation
Antibody
Enzyme
Nucleic acid
Molecular
Cell-based
Tissue-based
Optical
Mechanical
Electrochemical
Fluorescence
Surface plasma resonance
Adsorbance/reflectance
Piezoelectric
Surface acoustic wave
Cantilever resonance frequency
Amperometric
Potentiometric
Impedimetric

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 …

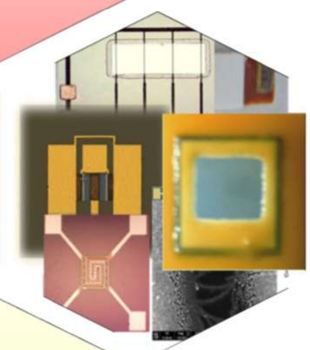


Inertial Sensors

Pressure sensors
Accelerometers
Acoustic Sensor
Magnetometer
Gyroscope
CMUT

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

Bio-Chemical Sensors



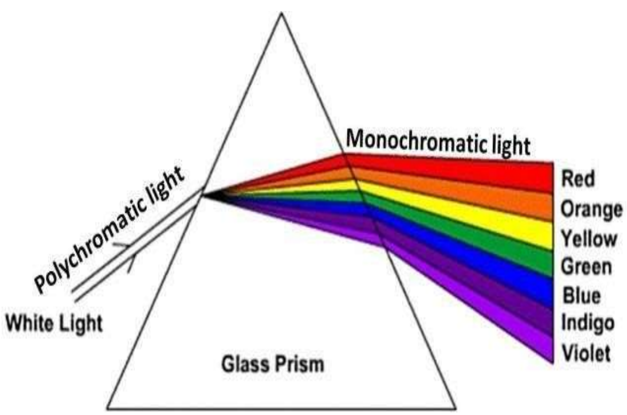
μ-fluidic Platforms

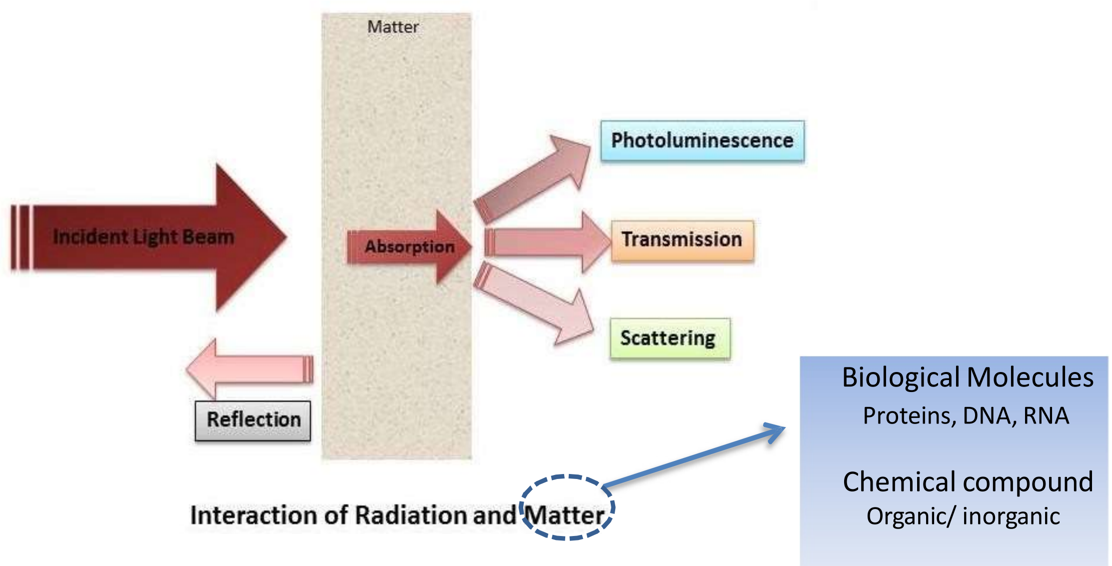
LOC for Particles Separation & Counter
Micro-Viscometer
Fluid FET

Spectroscopy for Sensing

Spectroscopy/ Spectrometry/ Spectrophotometry

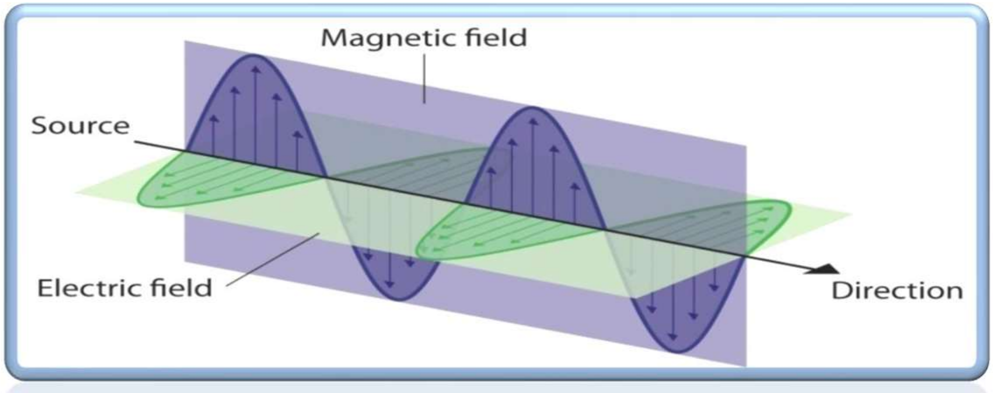
- **Spectroscopy is the branch of science that deals with the study of interaction of electromagnetic radiation with matter [**as a function of wavelength (*λ*)]**.**





Electromagnetic Radiation

- Electromagnetic radiation consist of discrete packages of energy which are called as **photons**.
- A **photon** consists of an oscillating electric field (E) & an oscillating magnetic field (M) which are perpendicular to each other.



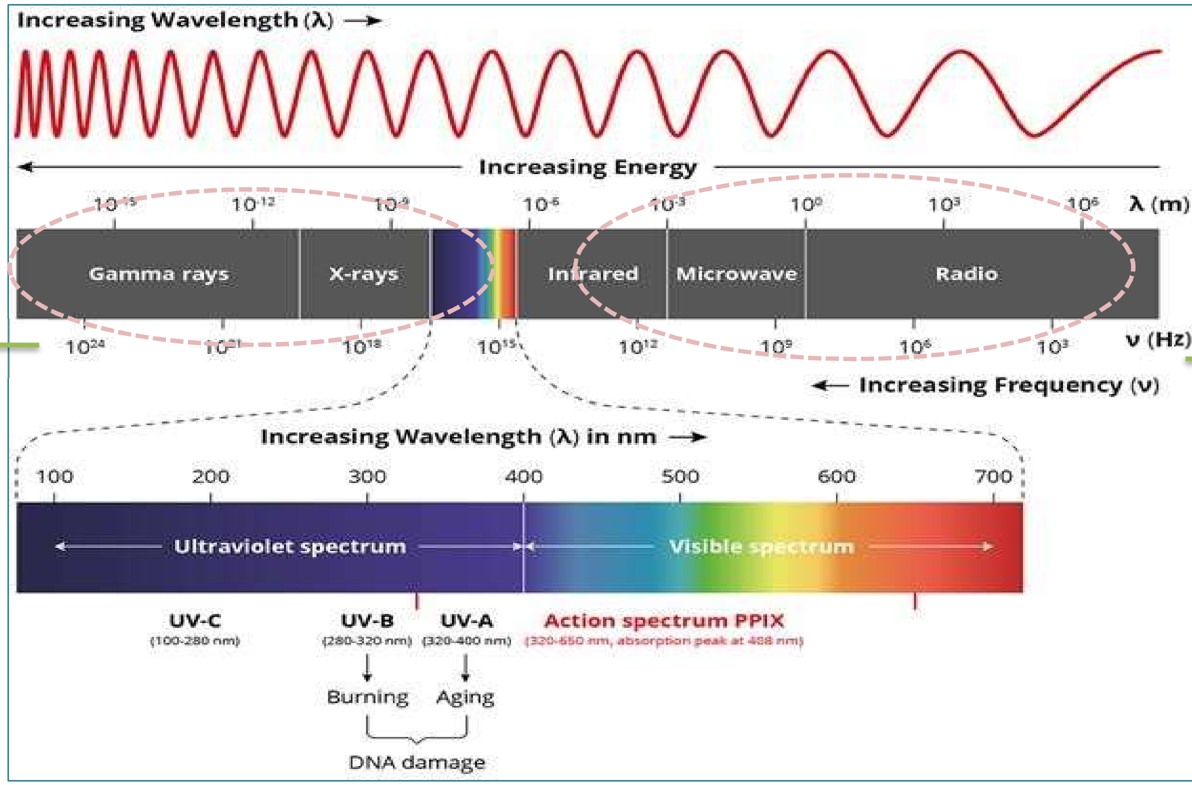
- The relationship between frequency & wavelength can be written as: $\nu = c/\lambda$
- Photon energy, $E = h\nu = hc/\lambda$

Where, ν is frequency; c is speed of light; λ is wavelength

E, known as photon energy, *h*, is known as the Planck constant.

Electromagnetic Radiation

Shorter Wavelengths
High Energy Rays



longer Wavelength
low Energy Rays

Importance and Principle of Spectroscopy

Spectrometry is the spectroscopic technique often used in physical & analytical chemistry, materials analysis, and biological laboratories for the identification of molecular structure of chemical compounds

- ✓ **Detection of Functional Groups**
- ✓ **Detection of Impurities**
- ✓ **Measurement of the concentration of molecules (or amount of given species).**
- ✓ **Determination of nature of the chemical bonds/ conjugation in the organic compounds**

- *The principle is based on the **measurement** of intensity spectrum of the radiation when passed through a sample containing atoms / molecules.*
- *Spectrometer is an instrument design to measure the spectrum of a compound.*
- *Spectrum is a graph of intensity of absorbed or emitted radiation by sample verses frequency (v) or wavelength (λ).*

Classification of Spectroscopy

Most spectroscopic methods are differentiated as either atomic or molecular based on whether or not they apply to atoms or molecules.

The study of spectroscopy can be carried out under the following two heads:

Atomic Spectroscopy

- Interaction of electromagnetic radiation with **atoms** is called atomic spectroscopy.
- This results in **transitions within the electronic state** (ground state to higher energy states).
- The spectrum obtained is a line spectrum.

Molecular Spectroscopy

- Interaction of electromagnetic radiation with **molecules** is called Molecular spectroscopy.
- This may result in **transitions between rotational, vibrational and electronic energy levels**.
- The spectrum obtained is a complicated spectrum.

Differences between Atomic and Molecular spectra		
	Atomic spectra	**Molecular spectra**
1	It is produced due to interaction of atoms with Electromagnetic radiation	It is obtained from the interaction of molecules with electromagnetic radiation.
2	Atomic spectra are Line spectra.	Molecular spectra are complicated spectra.
3	It is obtained due to electronic transition in an element	It is produced due to vibrational, rotational and electronic transition in a molecule.

Interaction of EMR with matter

1. Absorption Spectroscopy:

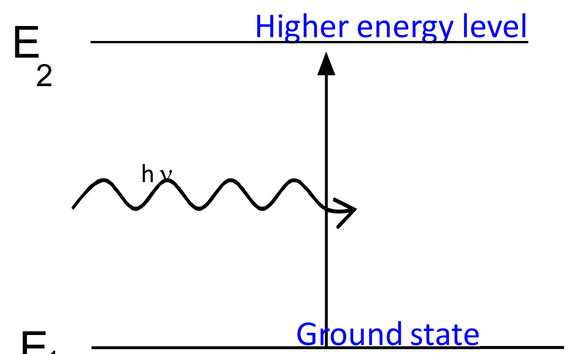
An analytical technique which concerns with the measurement of absorption of electromagnetic radiation.

e.g. UV (190 - 400 nm), Visible (400 - 800 nm) Spectroscopy, IR Spectroscopy (0.76 - 15 µm), Nuclear Magnetic Resonance Spectroscopy (NMR) (Radio frequencies,10 - 1000 cm)

If electromagnetic radiations of certain wavelength range are passed through the substance under analysis, radiations of certain wavelengths are absorbed by the substance.

The wavelength is absorbed by some specific functional group of the compound.

The characterization of the material by study of absorption is called the absorption spectroscopy.



Absorption Spectroscopy

Absorption spectroscopy uses the range of the electromagnetic spectra in which a substance absorbs.

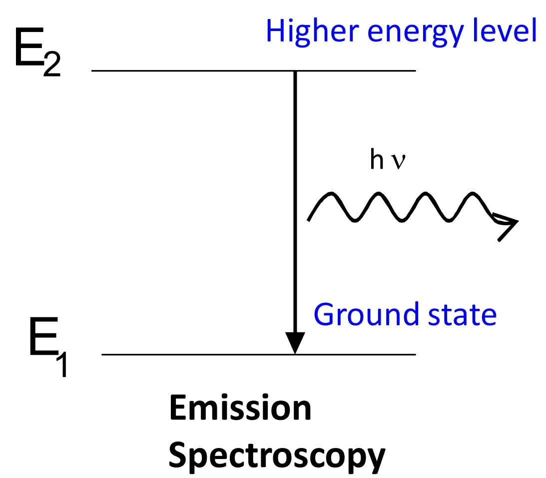
2. Emission Spectroscopy:

An analytical technique in which ***emission*** *(of a particle or radiation) is dispersed according to some property of the emission & the amount of dispersion is measured.*

e.g. Mass Spectroscopy (MS) and Photoluminescence (PL)

Emission spectroscopy

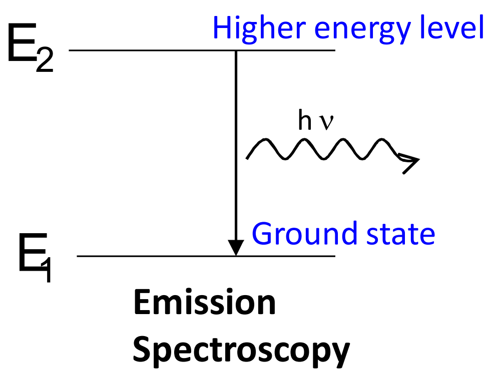
- If electromagnetic radiation is passed through a substance or thermal energy is given to the substance under analysis, the energy is absorbed by the atom.
- The electrons in the ground state get excited to higher energy metastable states.
- These excited electrons are short lived. So, they emit energy to return to the stable state.
- The study of this is called the emission spectroscopy.
- The spectrum obtained is called the emission spectrum.



2. Emission Spectroscopy:

Fluorescence

- The electron in the excited level return to it's ground state either directly or in steps with the emission of certain amount of energy.
- When this **emission of light is instantaneous** the phenomenon is known as **fluorescence**



Phosphorescence

- When the electron in the excited level return to it's ground state with the **emission of light after some time lag**, it is known as **phosphorescence**

Photochemical reaction

- When the absorbed energy is stored by the atom or molecule and used in producing some chemical reaction, the resulting chemical reaction is called **photochemical reaction.**

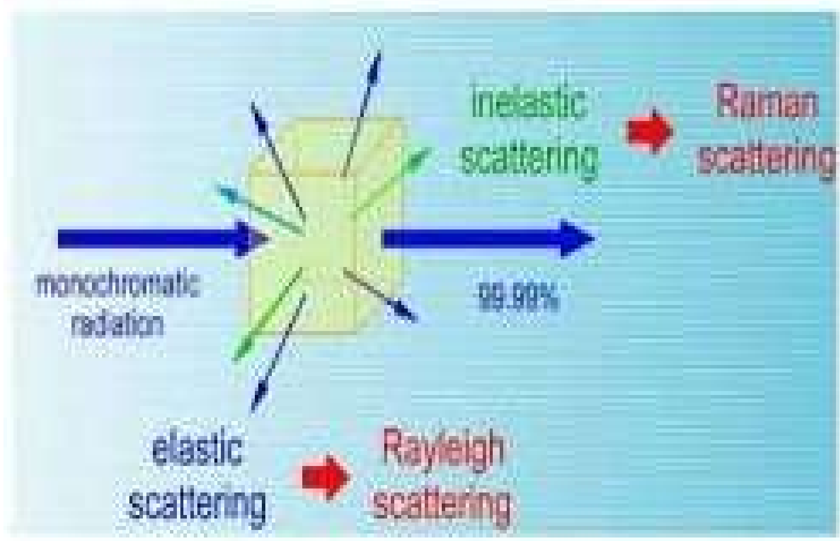
Emission spectroscopy uses the range of electromagnetic spectra in which a substance radiates (emits).
The substance first must **absorb** energy. This energy can be from a **variety of sources**, which determines the name of the **subsequent emission**, like luminescence.

3. Scattering Spectroscopy:

An analytical technique which concerns with the measurement of scattering of electromagnetic radiation.

e.g. Raman Spectroscopy,

- Scattering spectroscopy measures the amount of light that a substance scatters at certain wavelengths, **incident angles**, & polarization angles.
- The scattering process is much faster than the absorption/ emission process.
- One of the ***most useful applications*** of light scattering spectroscopy is → **Raman spectroscopy.**



Classification of Different Spectroscopic Methods

Absorption Spectroscopy

Atomic Spectroscopy

- *Atomic Absorption Spectroscopy*

Molecular Spectroscopy

- *Ultraviolet-visible Spectroscopy*
- *IR Spectroscopy*
- *Nuclear Magnetic Resonance Spectroscopy*

Emission Spectroscopy

- *Fluorescence/ Photoluminescence Spectroscopy (light)*
- *Mass Spectroscopy (particles)*

Scattering Spectroscopy

- *Raman Spectroscopy*

End