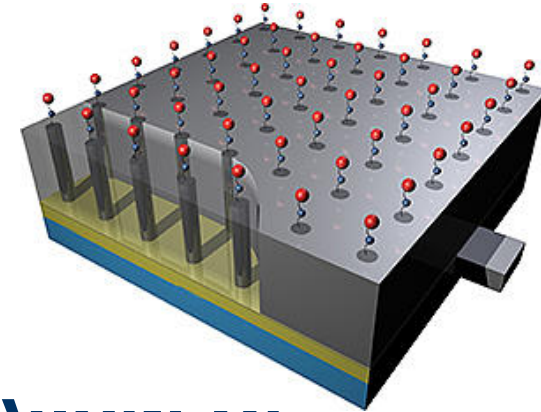


Biosensors and Nano-Bioelectronics

Lecture I

Introduction and Overview of Biosensors and Electrochemistry.



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Outlines

- Introduction of the lecture
- Terms and definition
- Rational of a biosensor
- Types of biosensor
- Applications of biosensors
- Electrochemistry and biosensors
- Nanotechnology in biosensor

“An important player in 21st century engineering will be the ‘biotraditional engineer,’ the recipient of a traditional engineer’s training and a modicum of exposure to life science.” M.H. Friedman, J. Biomechanical Eng, V123, December 2001

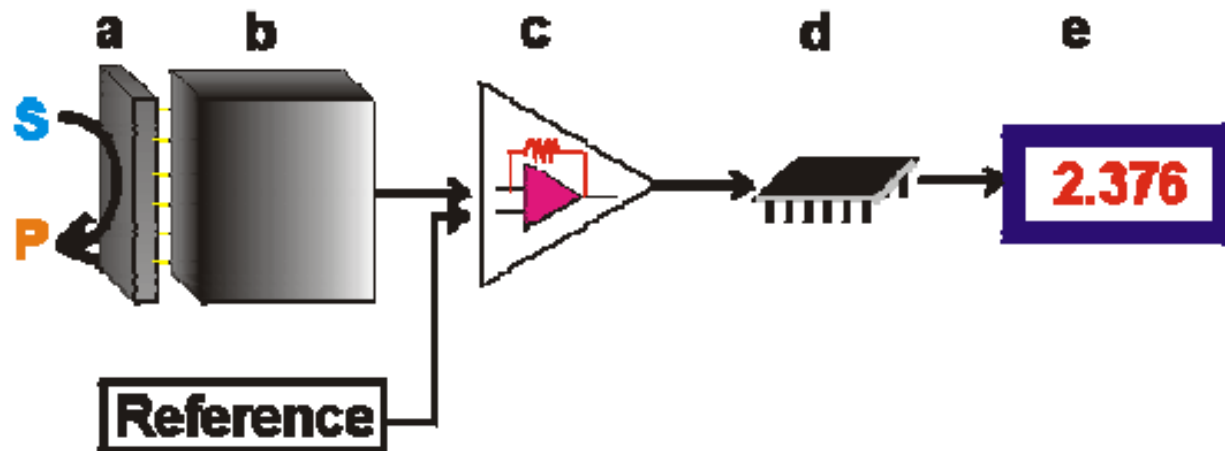
What is biosensor?

Chemical Sensors:

“A chemical sensor is a device that transforms chemical information, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal” – IUPAC

Biosensors: are analytical tools for the analysis of bio-material samples to gain an understanding of their bio-composition, structure and function by converting a biological response into an electrical signal. The analytical devices composed of a biological recognition element directly interfaced to a signal transducer which together relate the concentration of an analyte (or group of related analytes) to a measurable response.

Biosensor Components



Schematic diagram showing the main components of a biosensor. The bio-reaction (a) converts the substrate to product. This reaction is determined by the **transducer** (b) which converts it to an electrical signal. The output from the transducer is amplified (c), processed (d) and displayed (e).

(<http://www.lsbu.ac.uk/biology/enztech/biosensors.html>)

Selective Elements and Transducers

Selective elements

synthetic ionophores
 synthetic carriers
 supramolecular structures, clusters
 solid layers: metals
 – metal oxides, crystals
 – polymers, conducting polymers
 organisms
 micro-organisms
 plant and animal tissues
 cells
 organelles
 membranes, bilayers and monolayers
 enzymes
 receptors
 antibodies
 nucleic acids
 natural organic and inorganic molecules
 micelles, reversed micelles

Transducers

electrochemical: **(Current, potential, Resistance, impedance)**
 – potentiometric
 – amperometric
 – conductimetric
 – voltammetric, polarographic
 – impedimetric, capacitive
 – piezoelectric **(florescence, light scattering, etc.),**
 optical:
 – transmission / absorbance / reflection
 – dispersion, interferometric
 – polarimetric
 – circular dichroism, ellipsometry
 – scattering
 – emission intensity, photon counting
 (luminescence) decay time
 calorimetric **(Thermal, temperature)**
 acoustic / gravimetric: **(Mass Sensitive)**
 – surface photo-acoustic wave
 – quartz microbalance

Ref: Spichiger-Keller U.E., "Chemical Sensors and Biosensors for Medical and Biological Applications, Wiley-VCH, 1998

Defining events in the history of biosensor development

#

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 (Clark)
1962	First description of a biosensor: an amperometric enzyme electrode for glucose (Clark)
1969	First potentiometric biosensor: urease immobilised on an ammonia electrode to detect urea
1970	Invention of the Ion-Selective Field-Effect Transistor (ISFET) (Bergveld)
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 pO ₂ / pCO ₂ optode
1976	First bedside artificial pancreas (Miles)

Biosensor History (cont.)

1980	First fibre optic pH sensor for <i>in vivo</i> blood gases (Peterson)
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
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

1999-current	BioNMES, Quantum dots, Nanoparticles, Nanocantilever, Nanowire and Nanotube
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Type of Biosensors (by analytes)

<u>Types of Biological Recognition Elements</u>	<u>Name of the BIOSENSOR</u>
Enzymes	Enzyme electrode
Proteins	
Antibodies	Immunosensor
DNA	DNA sensor
Organelles	
Microbial cells	Microbial sensor
Plant and animal tissues	

Types of Biosensor (by detection mode)

<u>Types of Transducers</u>	<u>Measured Property</u>
Electrochemical	Potentiometric Amperometric Voltametric
Electrical	Surface conductivity Electrolyte conductivity
Optical	Fluorescence Adsorption Reflection
Mass sensitive	Rezonans frequency of piezocrytals
Thermal	Heat of reaction Heat of adsorpsion

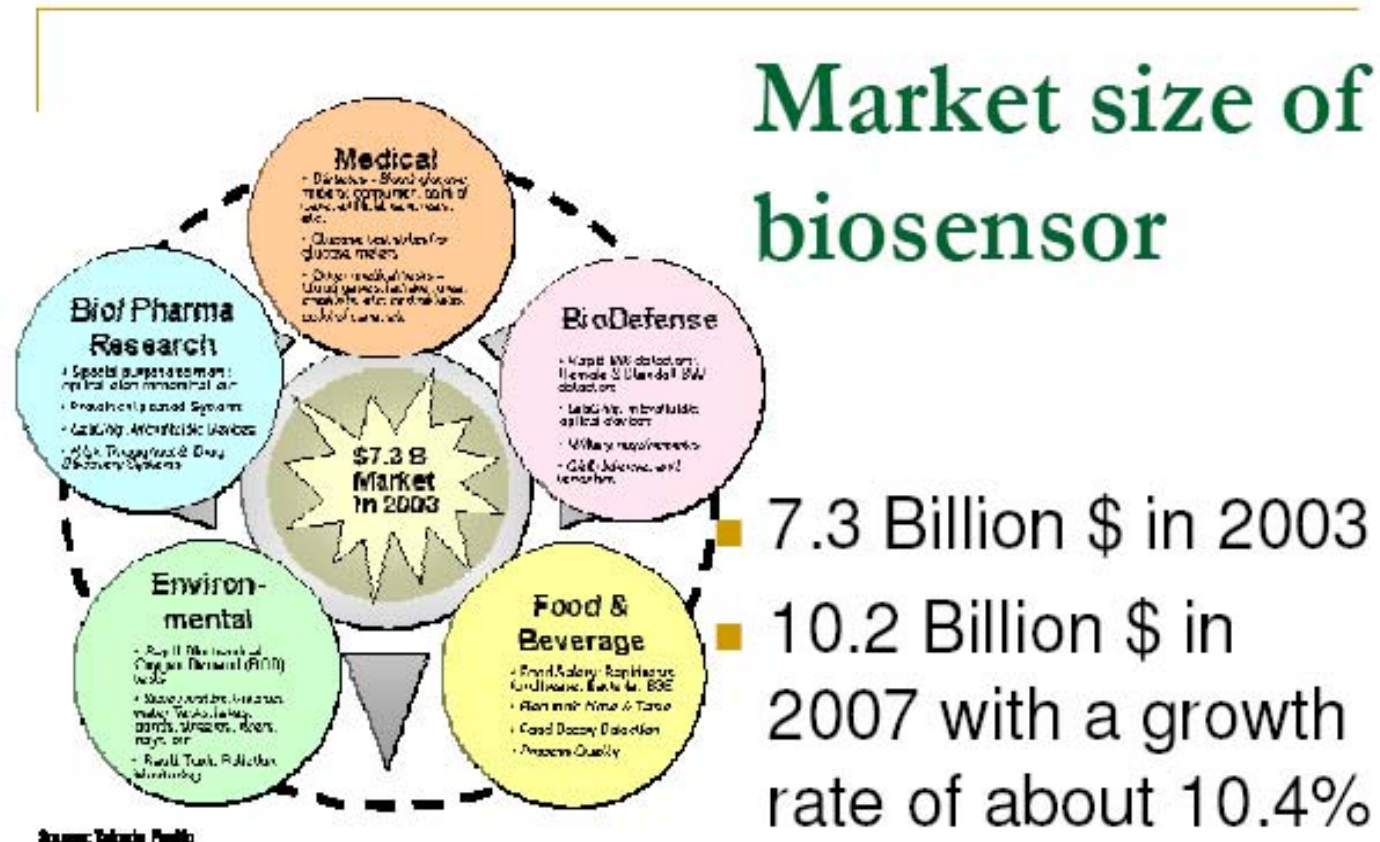
Typical Sensing Techniques for Biosensors

- **Fluorescence**
- **DNA Microarray**
- **SPR Surface plasmon resonance**
- **Impedance spectroscopy**
- **SPM (Scanning probe microscopy, AFM, STM)**
- **QCM (Quartz crystal microbalance)**
- **SERS (Surface Enhanced Raman Spectroscopy)**
- **Electrochemical**

Application of Biosensor

- Applications
 - • Study of biomolecules and how they interact with one another
 - - E.g. Biospecific interaction analysis (BIA)
- • Drug Development
- • In- home medical diagnosis
- • Environmental field monitoring
- • Scientific crime detection
- • Quality control in small food factory
- • Food Analysis

Biosensor Market



Biomedical Diagnostics

- **Doctors increasingly rely on testing**
- **Needs: rapid, cheap, and “low tech”**
- **Done by technicians or patients**
- **Some needs for *in-vivo* operation, with feedback**

Glucose-based on glucose oxidase

Cholesterol - based on cholesterol oxidase

Antigen-antibody sensors - toxic substances, pathogenic bacteria

Small molecules and ions in living things: H^+ , K^+ , Na^+ , NO , CO_2 , H_2O_2

DNA hybridization, sequencing, mutants and damage

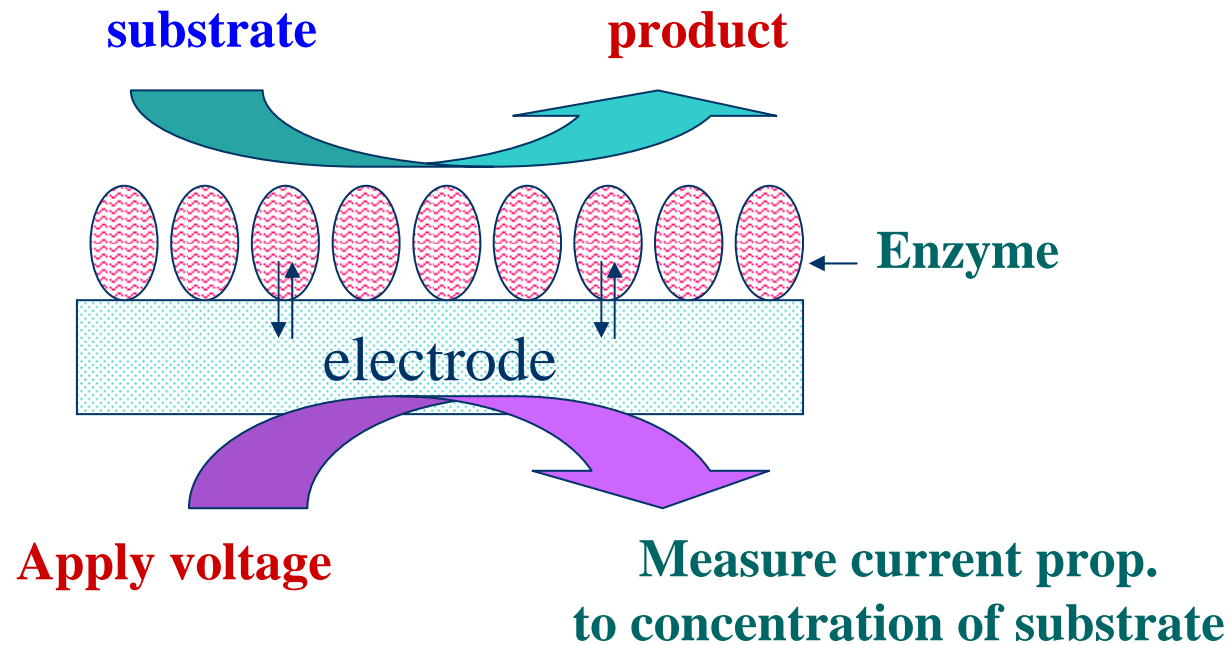
Commercial Glucose Sensors

- **Biggest biosensor success story!**
- **Diabetic patients monitor blood glucose at home**
- **First made by Clark in 1962, now 5 or more commercial test systems**
- **Rapid analysis from single drop of blood**
- **Enzyme-electrochemical device on a slide**

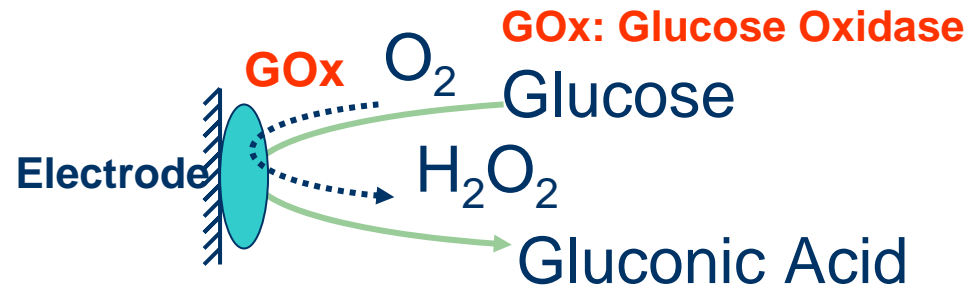
Basic Characteristics of a Biosensor

1. **LINEARITY:** Maximum linear value of the sensor calibration curve. Linearity of the sensor must be high for the detection of high substrate concentration.
2. **SENSITIVITY:** The value of the electrode response per substrate concentration.
3. **SELECTIVITY:** Interference of chemicals must be minimised for obtaining the correct result.
4. **RESPONSE TIME:** The necessary time for having 95% of the response.

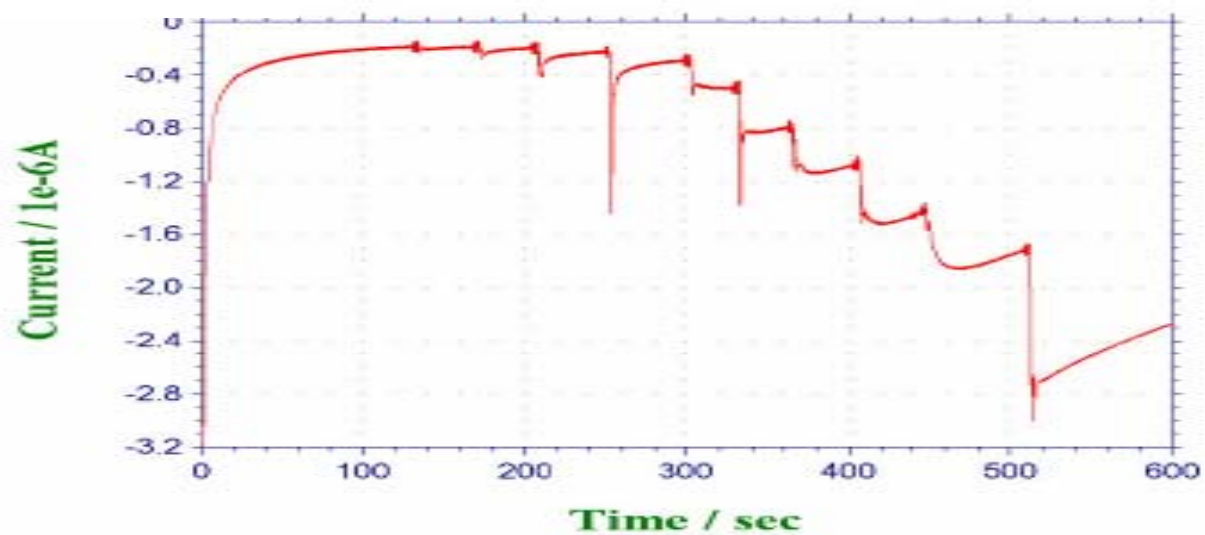
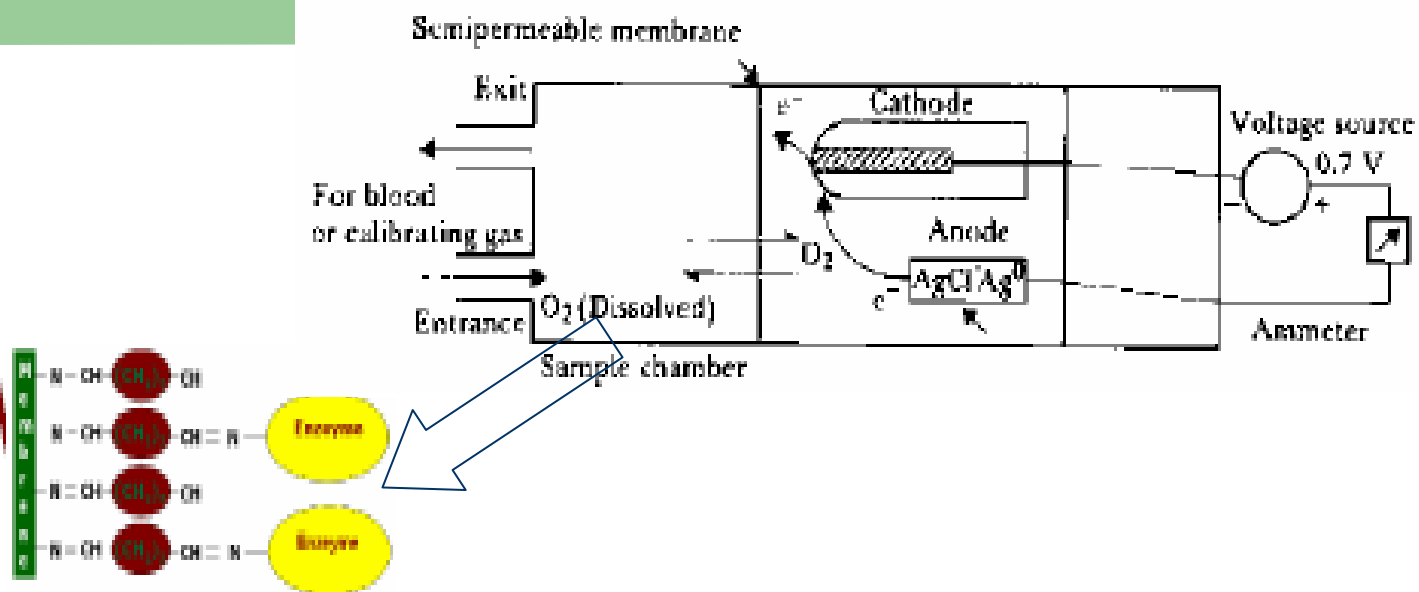
Principle of Electrochemical Biosensors



Electrochemical Glucose Biosensor



The first and the most widely used commercial biosensor:
the blood glucose biosensor – developed by *Leland C. Clark* in 1962

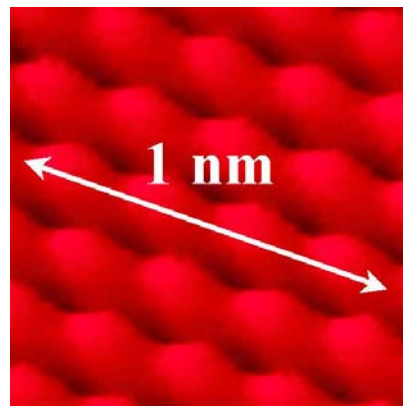


Richard Feynman's (1918-1988)
1959 Talk
"There's Plenty of Room at the bottom"

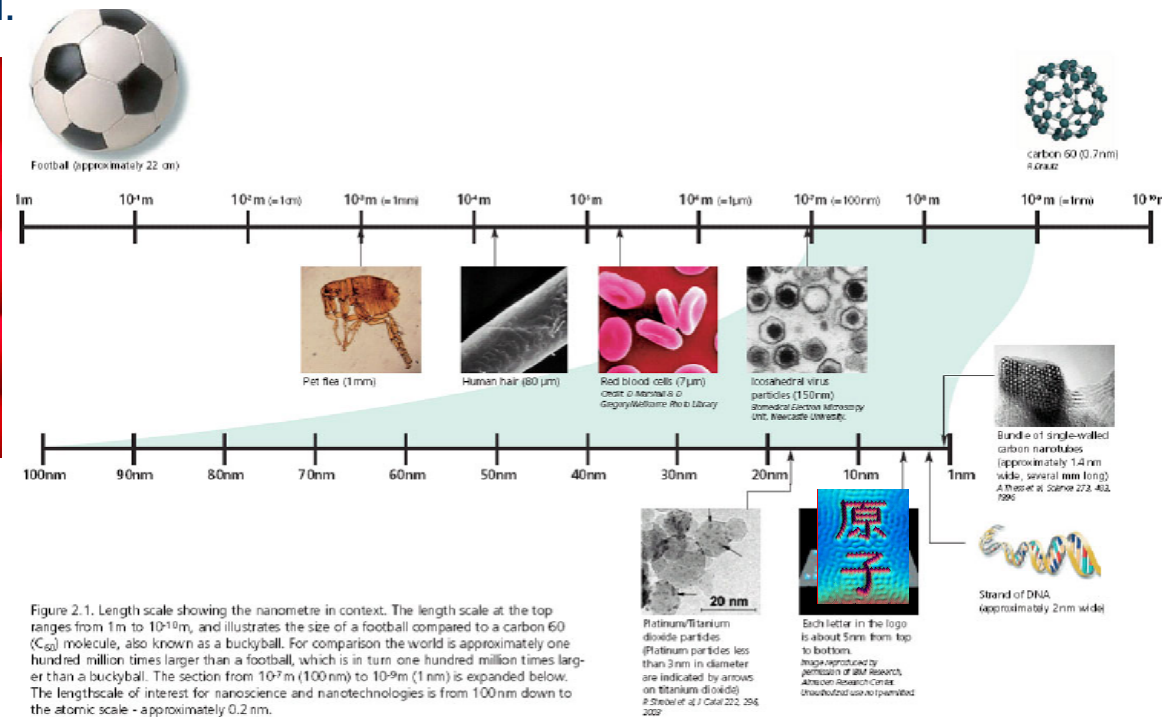


What is Nano?

- A nanometre is 1/1,000,000,000 (1 billionth) of a metre, which is around 1/50,000 of the diameter of a human hair or the space occupied by 3-4 atoms placed end-to-end.



A few carbon atoms on the surface of highly oriented pyrolytic graphite (HOPG). Image obtained by Scanning Tunneling Microscope (STM).



What Is Nanotechnology?

(Definition from the NNI)

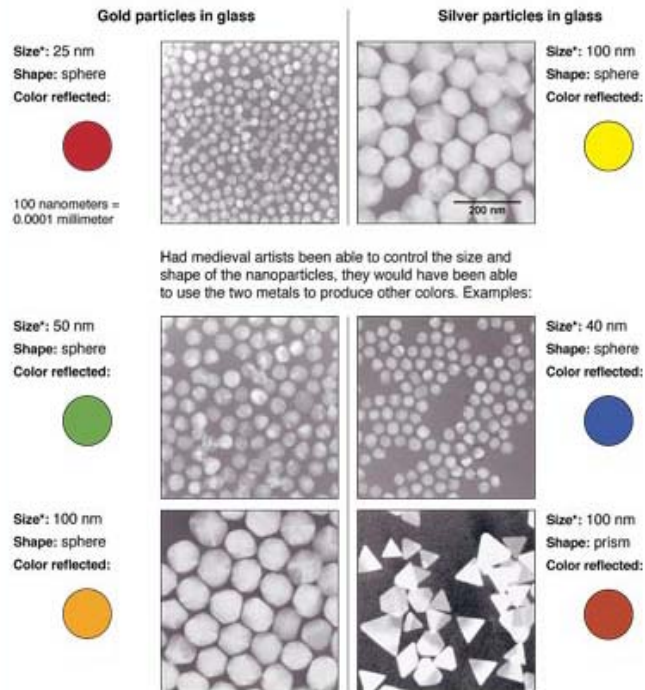
- ❖ Research and technology development aimed to understand and control matter at dimensions of approximately 1 - 100 nanometer – the nanoscale
- ❖ Ability to understand, create, and use structures, devices and systems that have fundamentally new properties and functions because of their nanoscale structure
- ❖ Ability to image, measure, model, and manipulate matter on the nanoscale to exploit those properties and functions
- ❖ Ability to integrate those properties and functions into systems spanning from nano- to macro-scopic scales

The First Nanotechnology



The First Nanotechnologists

Ancient stained-glass makers knew that by putting varying, tiny amounts of gold and silver in the glass, they could produce the red and yellow found in stained-glass windows. Similarly, today's scientists and engineers have found that it takes only small amounts of a nanoparticle, precisely placed, to change a material's physical properties.

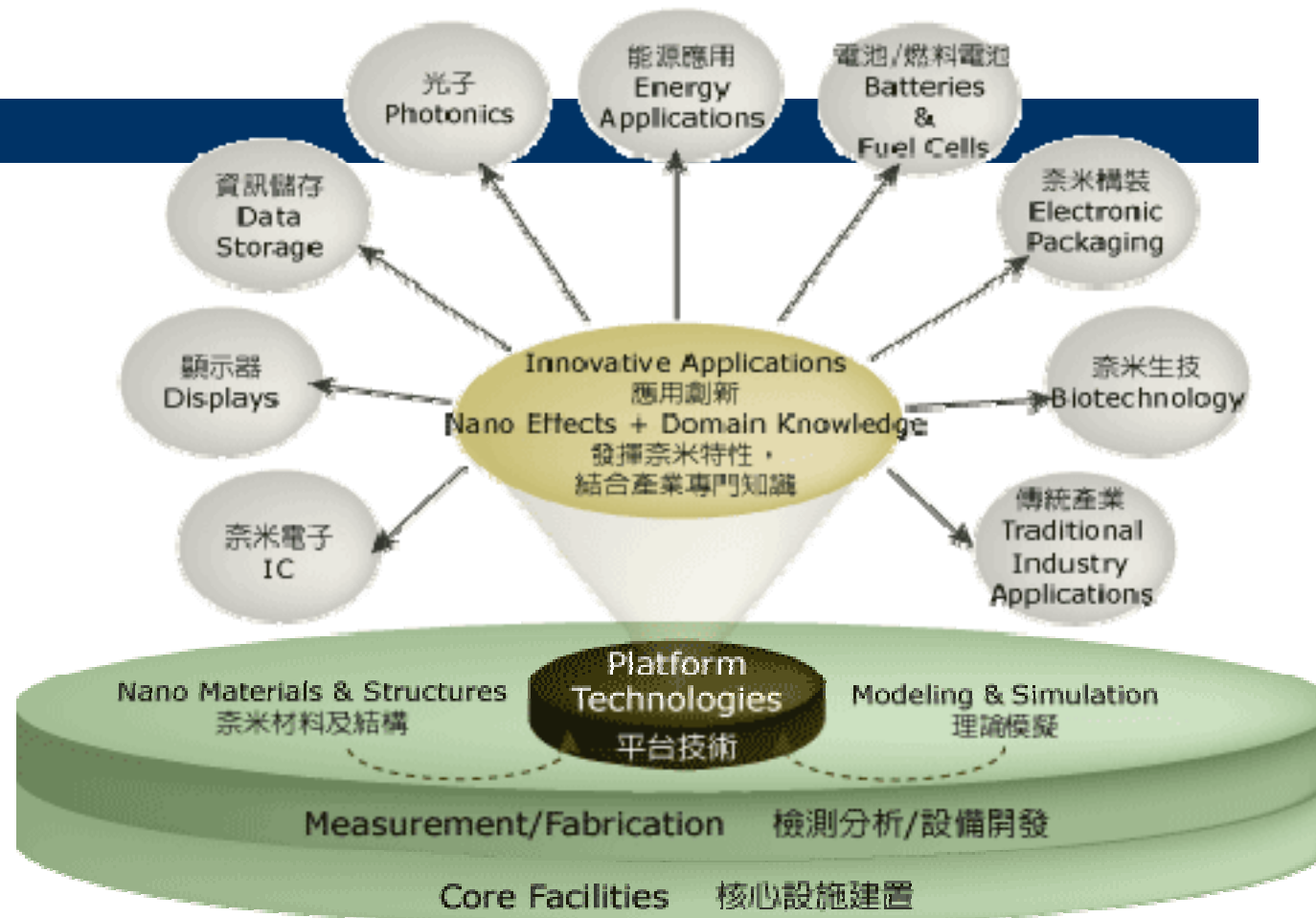


Source: Dr. Chad A. Mirkin, Institute of Nanotechnology, Northwestern University

*Approximate



Application of Nanotech



Nanotech in Daily Life

BASIS FOR OPTIMISM

Current Successes in Nanotechnology

NANOPARTICLES



M
I
C
R
O

NANOCOATINGS



NANOCOMPOSITES



Transparent sunscreen TiO_2 , ZnO

Cosmetics

- **Tools In Nanotechnology**

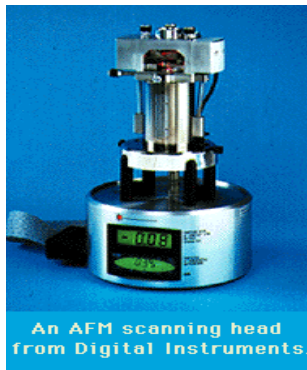
- The main tools used in nanotechnology are four main microscopes

- Transmission Electron Microscope (TEM)

- Atomic Force Microscope (AFM)

- Scanning Tunneling Microscope (STM)

- Scanning Electron Microscope (SEM)



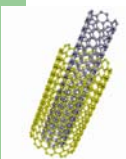
An AFM scanning head
from Digital Instruments.



Nano-Biotechnology

Current, Potential, Impedance, Electrical power

Nanomaterials



Carbon
nanotubes



Fullerene

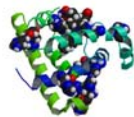


Nano-
particles



Dendrimers

Biomaterials



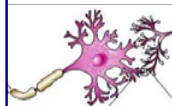
Protein/
enzymes



Peptides



Antigens/
antibodies



Neurons

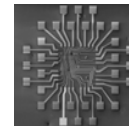


DNA/RNA

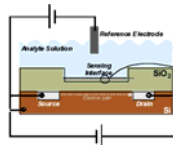


Cells

Electronic elements



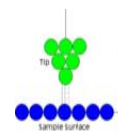
Electrodes



Field-effect
transistors



Piezoelectric
crystals

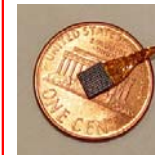


STM Tip

Application



Biosensor



Medical
devices



Solar cell



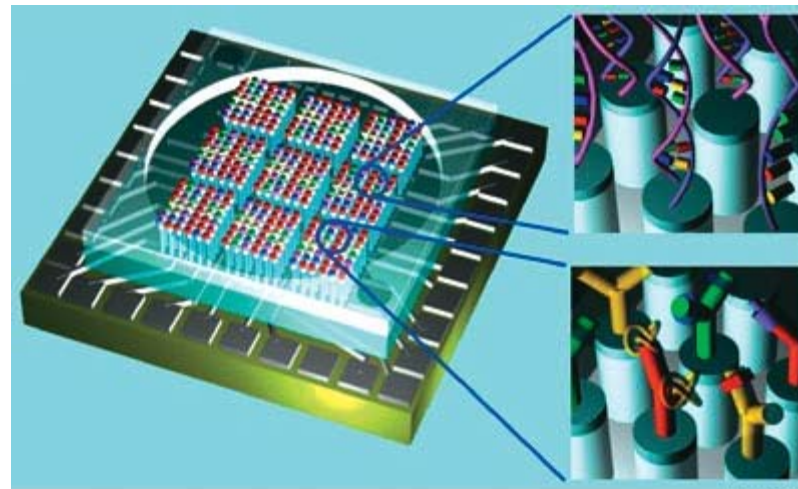
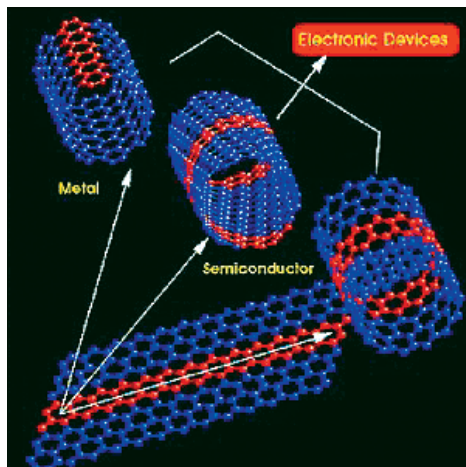
Biofuel cell

Biological Sciences – Pharmacy – Chemistry/Biochemistry – Physics – Biomedical Eng.
– Electrical Eng. – Mechanical Eng. – Material Eng. – Bioinformatics

Nanotechnology will enable us to design sensors that are much smaller, less power hungry, and more sensitive than current micro- or macrosensors.

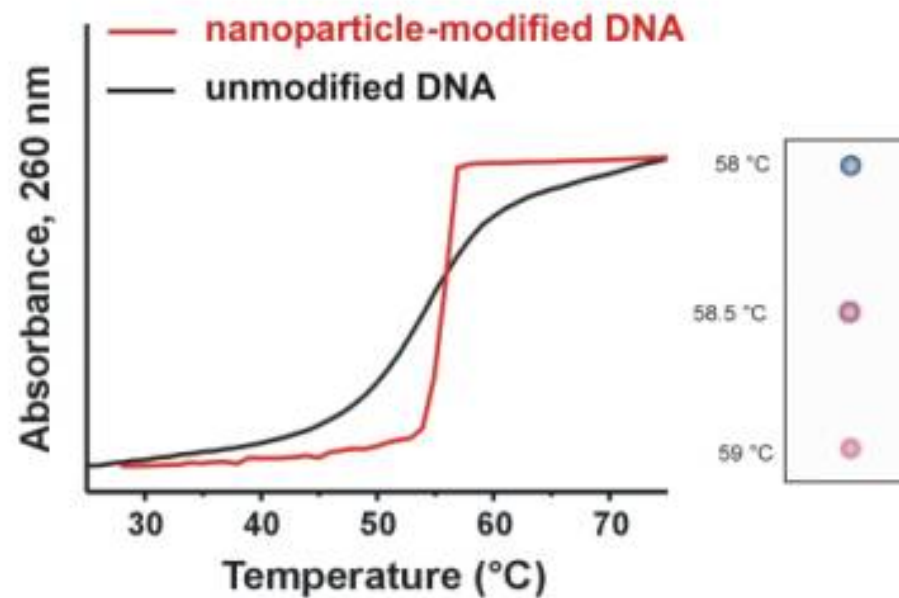
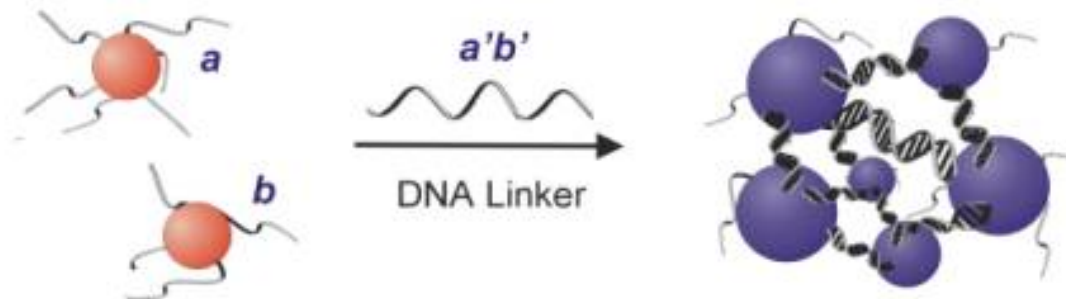


- **Nano Materials:** Carbon Nanotube-Electrodes; Metallic Nanoparticles-sensor probes and electrodes; Nanorod-sensor probes; Magnetic Particles-sensor probes; Nanowires-FET sensing system, quantum dot (AsSe, CdSe, etc.)
- **Bio-Nanomaterial Hybrids:** DNA-Np; DNA-CNTs; Drug-Nps, Peptide-CNTs, etc.



Source: NASA

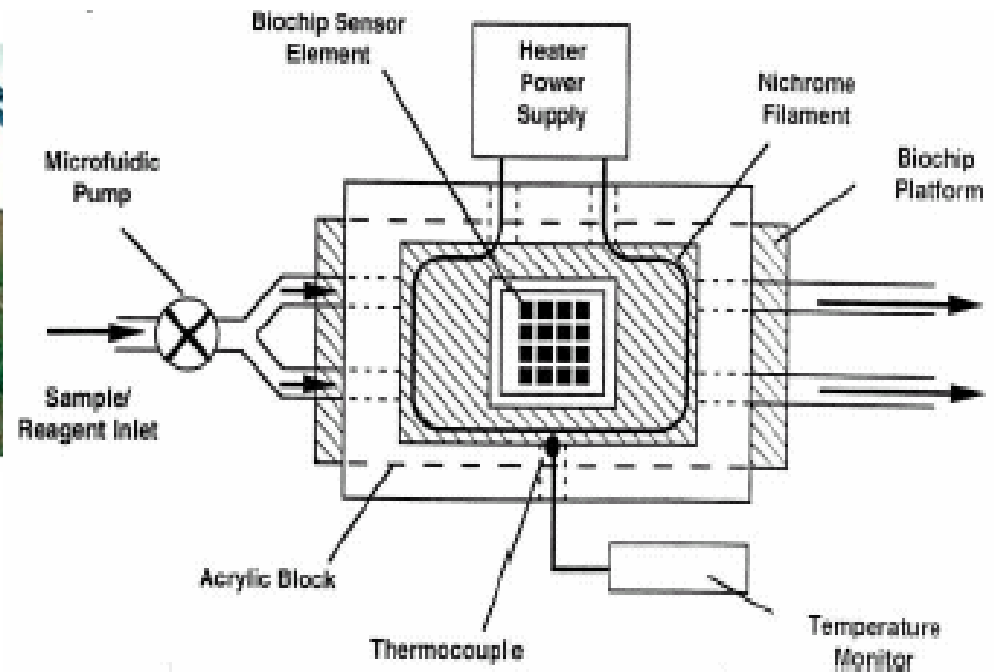
Integration of nano-scale technologies could lead to tiny, low-power, smart sensors that could be manufactured cheaply in large numbers. sensing the interaction of a small number of molecules, processing and transmitting the data with a small number of electrons, and storing the information in nanometer-scale structures



- **Nano/Micro-Electro-Mechanical Systems (N/MEMS) for Sensor Fabrication**
- **BioMEMS/BioNEMS, Lab-on –Chip, Microfluidic System, Sensor Arrays, Implantable Sensor**



SnifferSTAR is a nano-enabled chemical sensor integrated into a micro unmanned aerial vehicle



Nanofabrication (Top-Down; Bottom-Up)

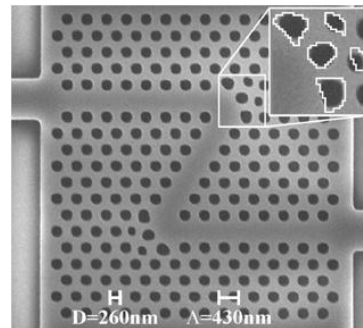
Nanofabrication

! Nanofabrication methods can be divided into two categories:

- **“Top down” approach**

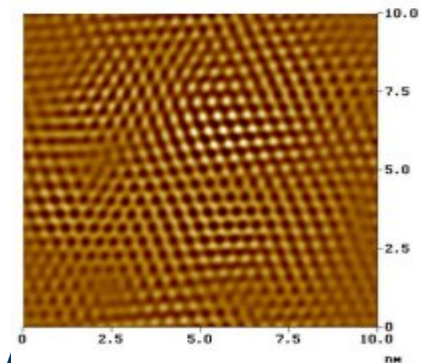
- Micron scale lithography: optical, ultra-violet, Focused Ion Beam

- Electron-beam lithography – 10-100 nm

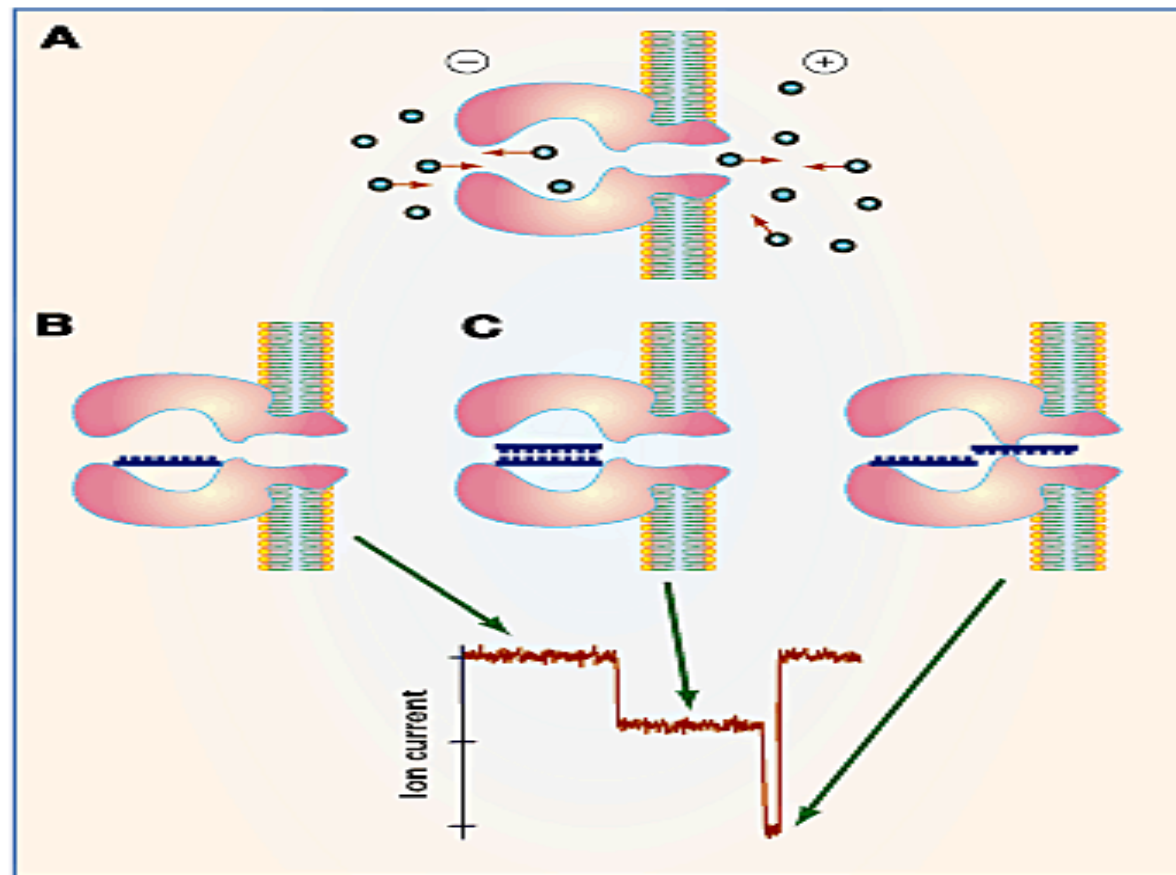


- **“Bottom up” approach**

- Chemical self-assembly: Man-made synthesis (e.g. carbon nanotubes); DNA SAMs, Biological synthesis (DNA, proteins)

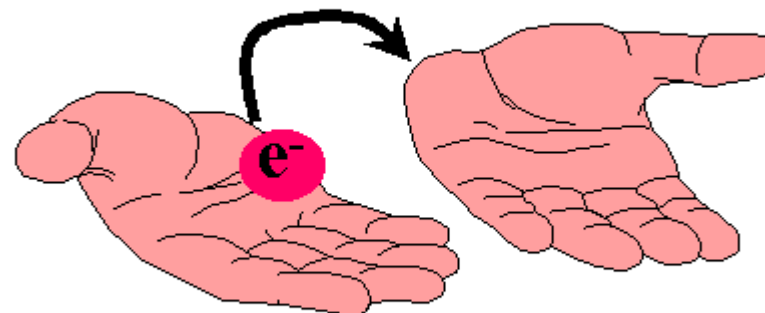


Nanopore Technology



Electrochemistry

Where there is oxidation,
there is reduction



Substance oxidized
loses electron(s)

Substance reduced
gains electron(s)

Introduction

- Electrochemistry can be broadly defined as the study of charge-transfer phenomena. As such, the field of electrochemistry includes a wide range of different chemical and physical phenomena. These areas include (but are not limited to): battery chemistry, photosynthesis, ion-selective electrodes, coulometry, and many biochemical processes. Although wide ranging, electrochemistry has found many practical applications in analytical measurements.