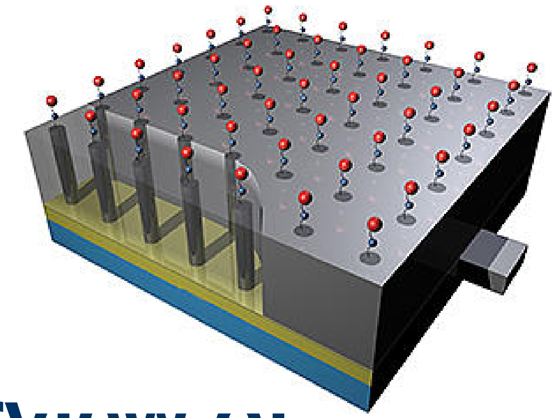
Biosensors and Nano-Bioelectronics

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

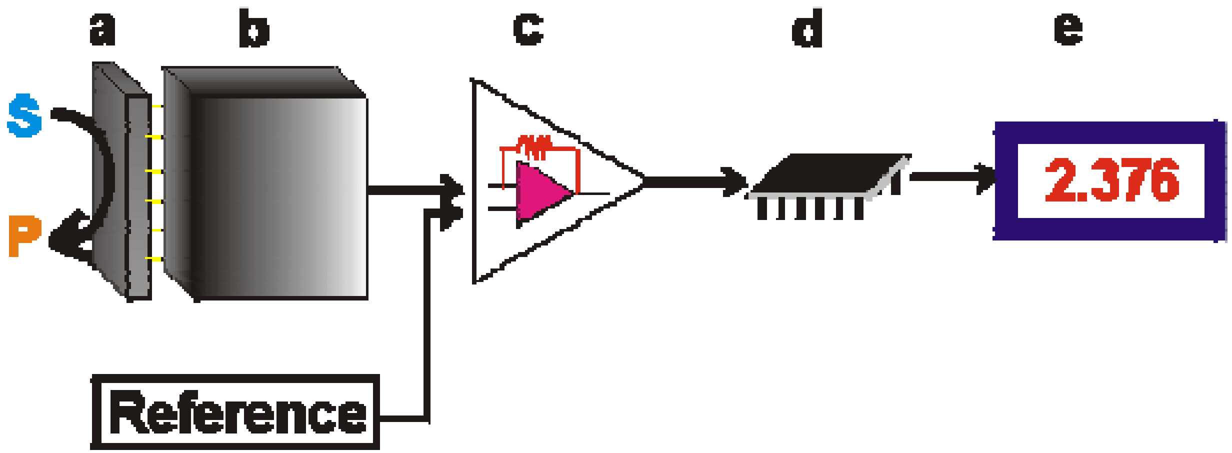
“An important player in 21st century engineering will be the ‘biotraditional engineer,’ the recipient of a traditional engineer’s training and a modicum of exposure to life science.” M.H. Friedman, J. Biomechanical Eng, V123, December 2001

What is biosensor?

Chemical Sensors:
“A chemical sensor is a device that transforms chemcial 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 <u>bio-composition</u>, <u>structure</u> and <u>function</u> 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	Transducers
synthetic ionophores	electrochemical: (Current, potential, Resistance, impedance)
synthetic carriers	– potentiometric
supramolecular structures, clusters	– amperometric
solid layers: metals	– conductimetric
– metal oxides, crystals	– voltammetric, polarographic
– polymers, conducting polymers	– impedimetric, capacitive
organisms	– piezoelectric
microorganisms	optical: (florescence, light scattering, etc.),
plant and animal tissues	– transmission / absorbance / reflection
cells	– dispersion, interferometric
organelles	– polarimetric
membranes, bilayers and monolayers	– circular dichroism, ellipsometry
enzymes	– scattering
receptors	– emission intensity, photon counting
antibodies	(luminescence) decay time
nucleic acids	calorimetric (Thermal, temperature)
natural organic and inorganic molecules	acoustic / gravimetric: (Mass Sensitive)
micelles, reversed micelles	– 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 *in vivo* 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

Type of Biosensors (by analytes)

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

Types of Biosensor (by detection mode)

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

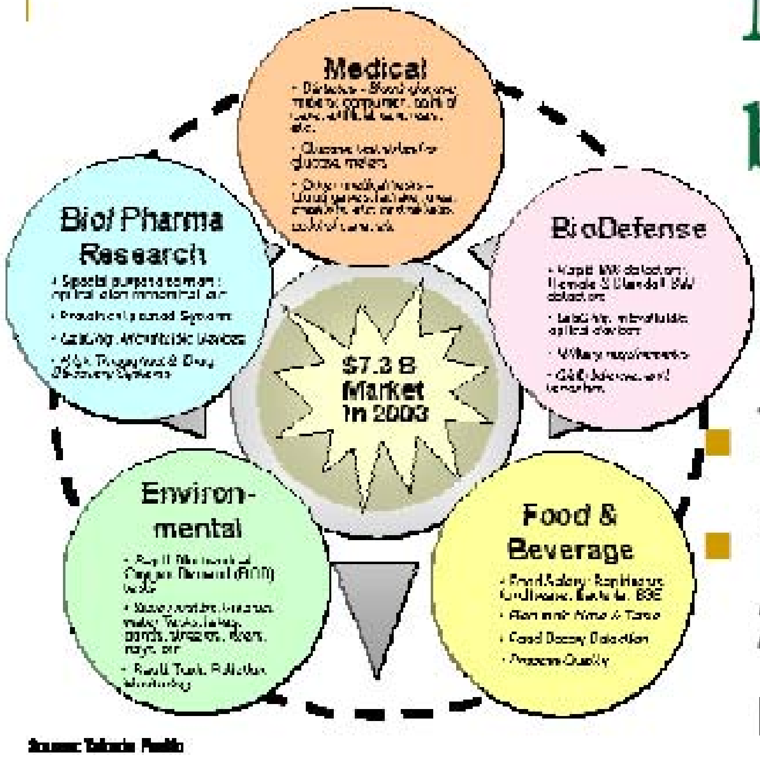
Typical Sensing Techniques for Biosensors

- 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



Market size of biosensor

- 7.3 Billion $ in 2003
- 10.2 Billion $ in 2007 with a growth rate of about 10.4%

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

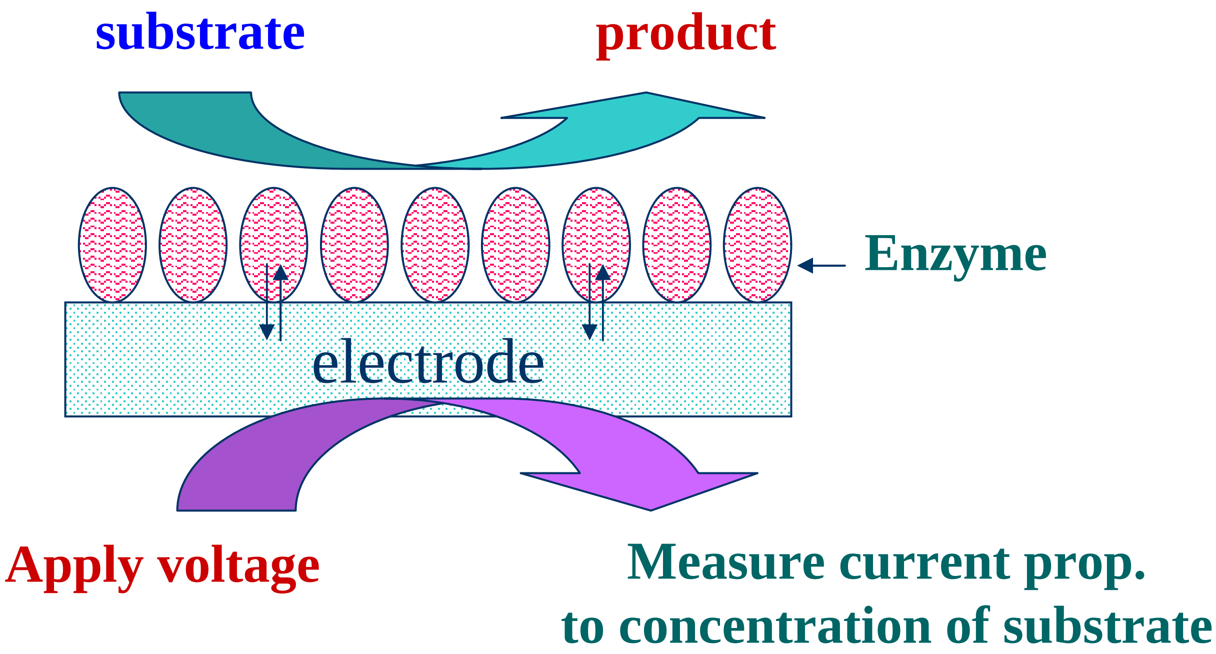
Commercial Glucose Sensors

- 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

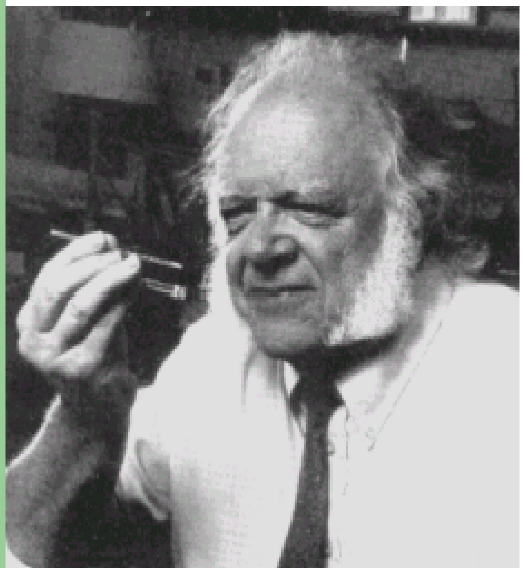
Basic Characteristics of a Biosensor

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.

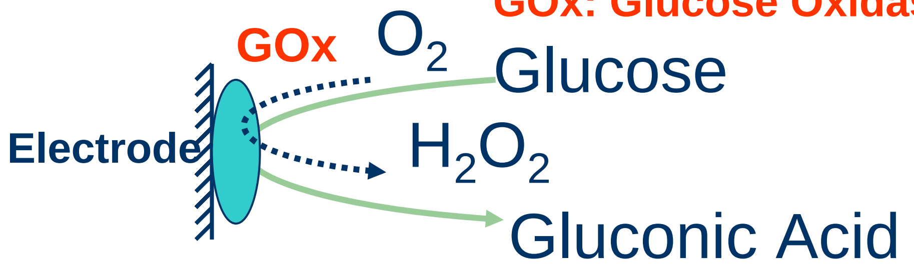
Principle of Electrochemical Biosensors



Electrochemical Glucose Biosensor



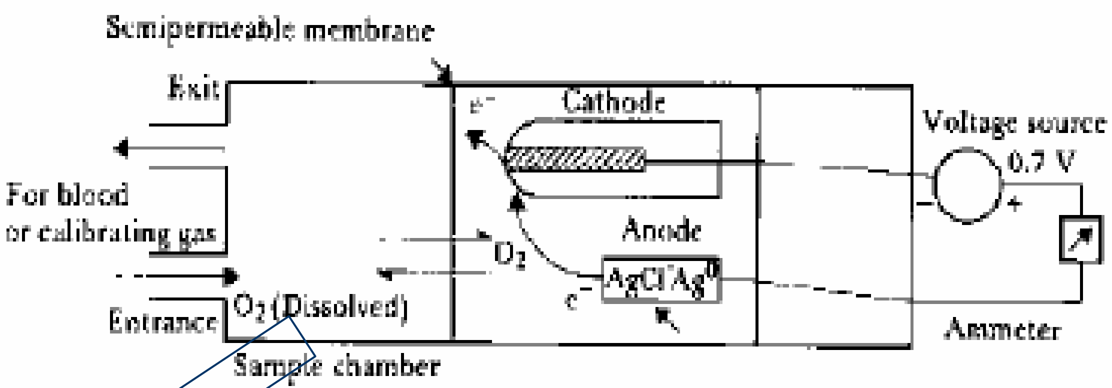
GOx: Glucose Oxidase

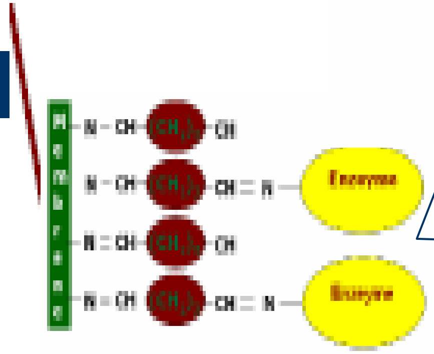


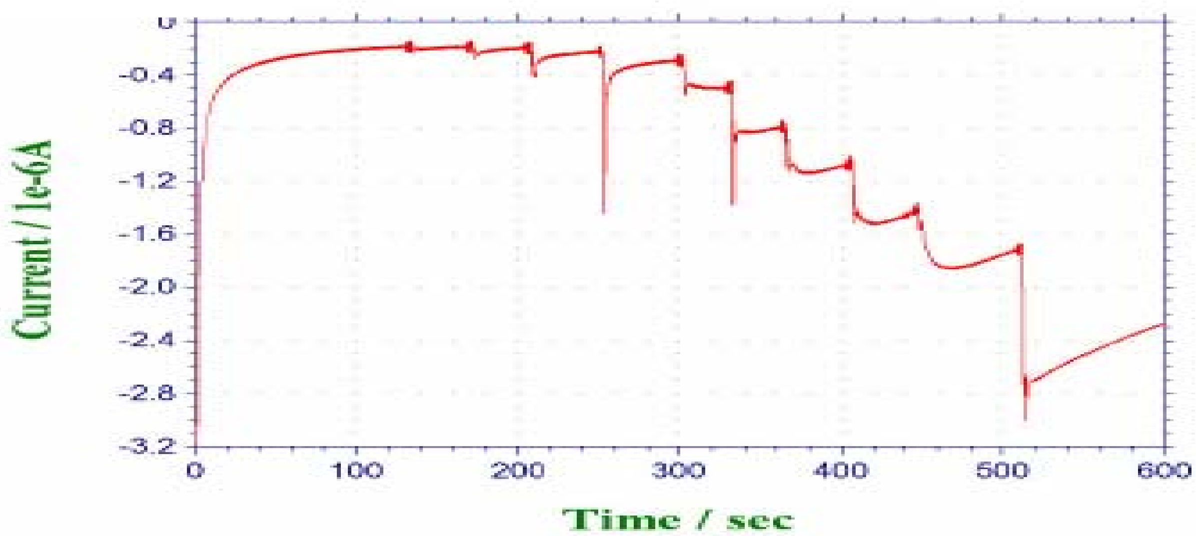
$$\text{Glucose} + O_2 \xrightarrow{\text{GOx}} \text{Gluconic Acid} + H_2O_2$$

$$H_2O_2 \xrightarrow[\text{0.6 V vs. SHE}]{\text{Pt}} 2H^+ + O_2 + 2\,e^-$$

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


Semipermeable membrane
Exit
For blood
or calibrating gas
Entrance
O_2 (Dissolved)
Sample chamber
Cathode
Anode
O_2
AgCl/Ag
Voltage source
0.7 V
Ammeter

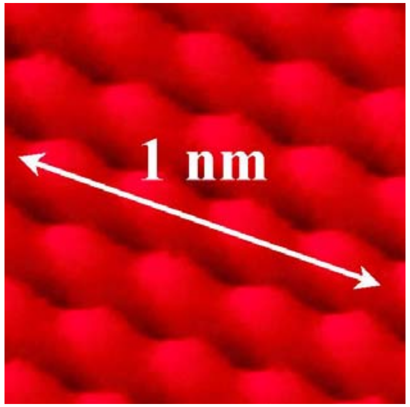

Enzyme
Enzyme


Current / 1e-6A
Time / sec
0
-0.4
-0.8
-1.2
-1.6
-2.0
-2.4
-2.8
-3.2
0
100
200
300
400
500
600

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).

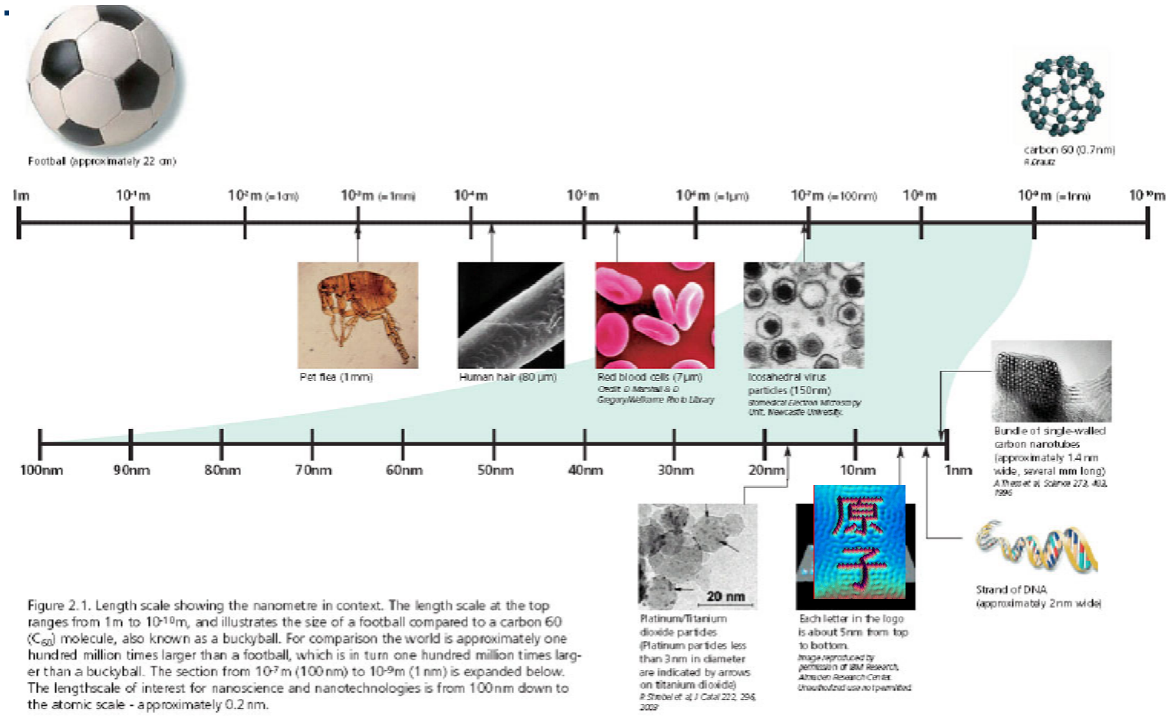


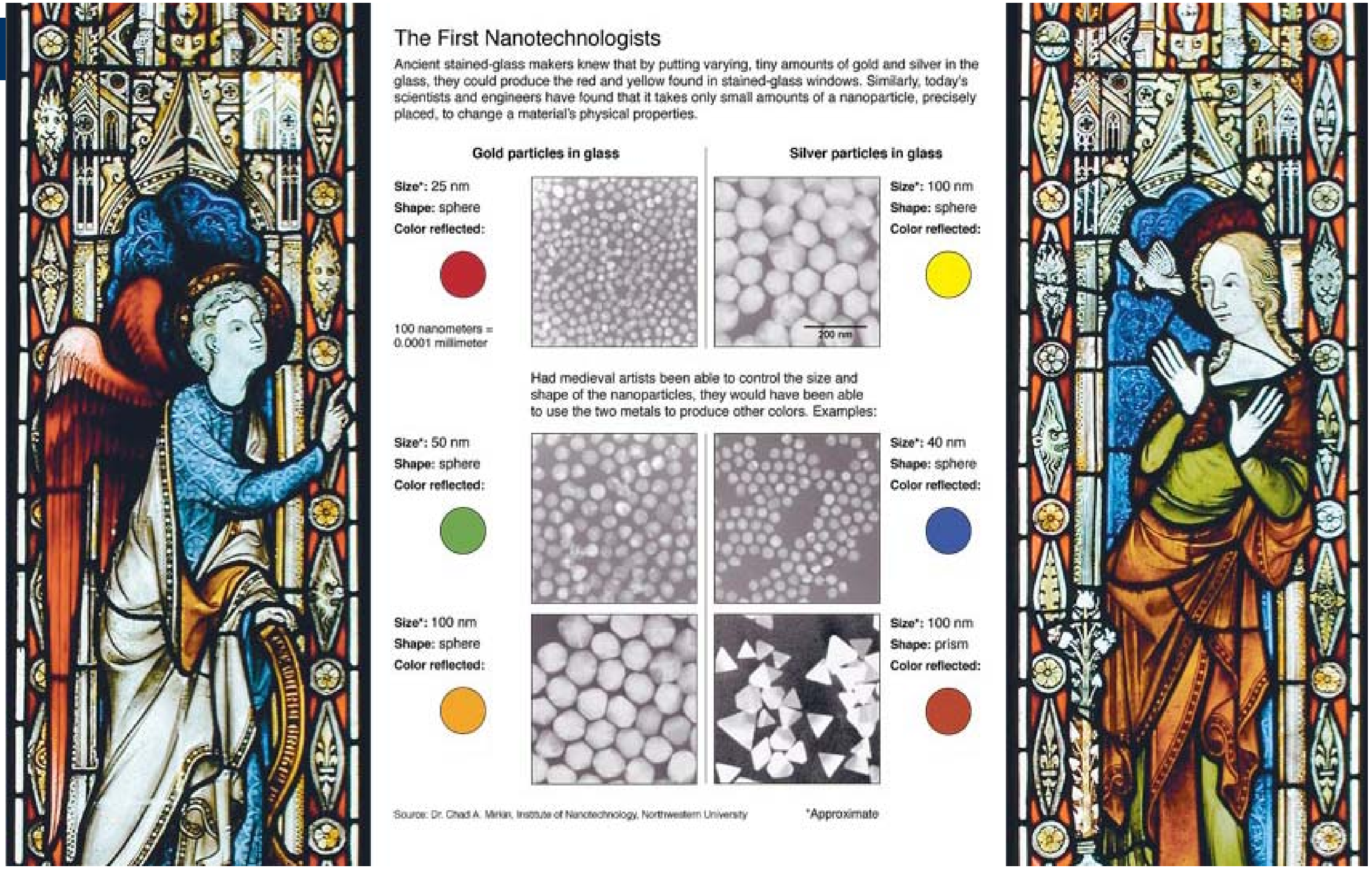
Figure 2.1. Length scale showing the nanometre in context. The length scale at the top ranges from 1m to 10^{-10}m, and illustrates the size of a football compared to a carbon 60 (C_{60}) molecule, also known as a buckyball. For comparison the world is approximately one hundred million times larger than a football, which is in turn one hundred million times larger than a buckyball. The section from 10^{-7}m (100nm) to 10^{-9}m (1nm) is expanded below. The lengthscale of interest for nanoscience and nanotechnologies is from 100nm down to the atomic scale - approximately 0.2nm.

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

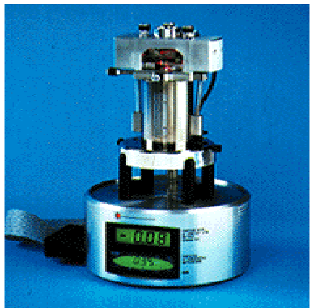
The First Nanotechnology



Application of Nanotech

Nanotech in Daily Life

- **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)

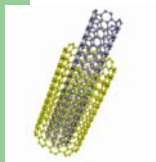


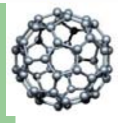
An AFM scanning head from Digital Instruments.

Nano-Biotechnology

Current, Potential, Impedance, Electrical power

Nanomaterials


Carbon nanotubes


Fullerene

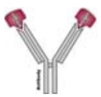

Nano-particles

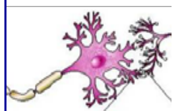

Dendrimers

Biomaterials


Protein/ enzymes


Peptides

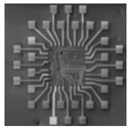

Antigens/ antibodies

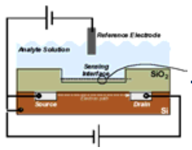

Neurons


DNA/RNA

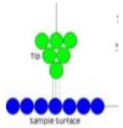

Cells

Electronic elements


Electrodes

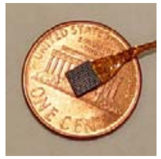

Field-effect transistors


Piezoelectric crystals


STM Tip

Application


Biosensor


Medical devices


Solar cell

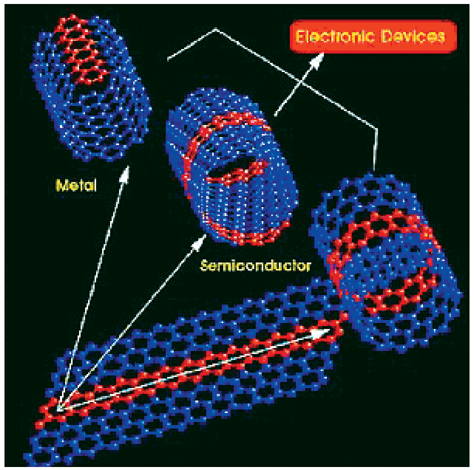

Biofuel cell

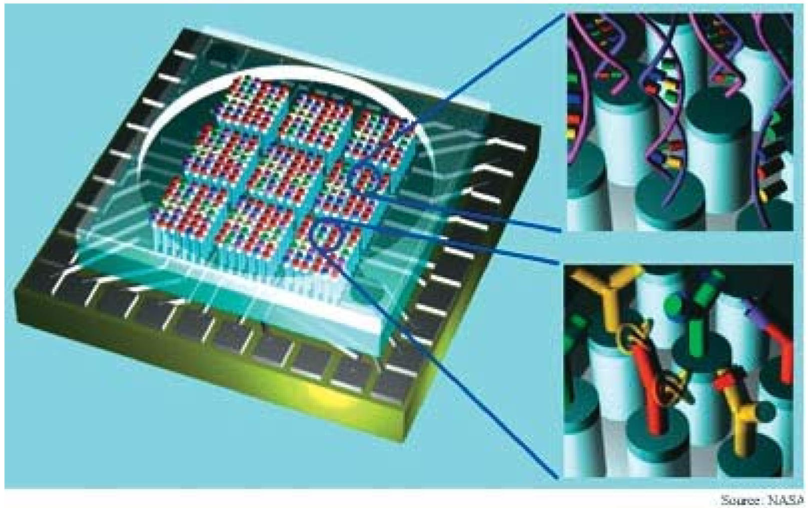
Biological Sciences – Pharmacy – Chemistry/Biochemistry –Physics – Biomedical Eng. – Electrical Eng. – Mechanical Eng. – Material Eng. – Bioinformatics

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, quantam dot (AsSe, CdSe, etc.)**

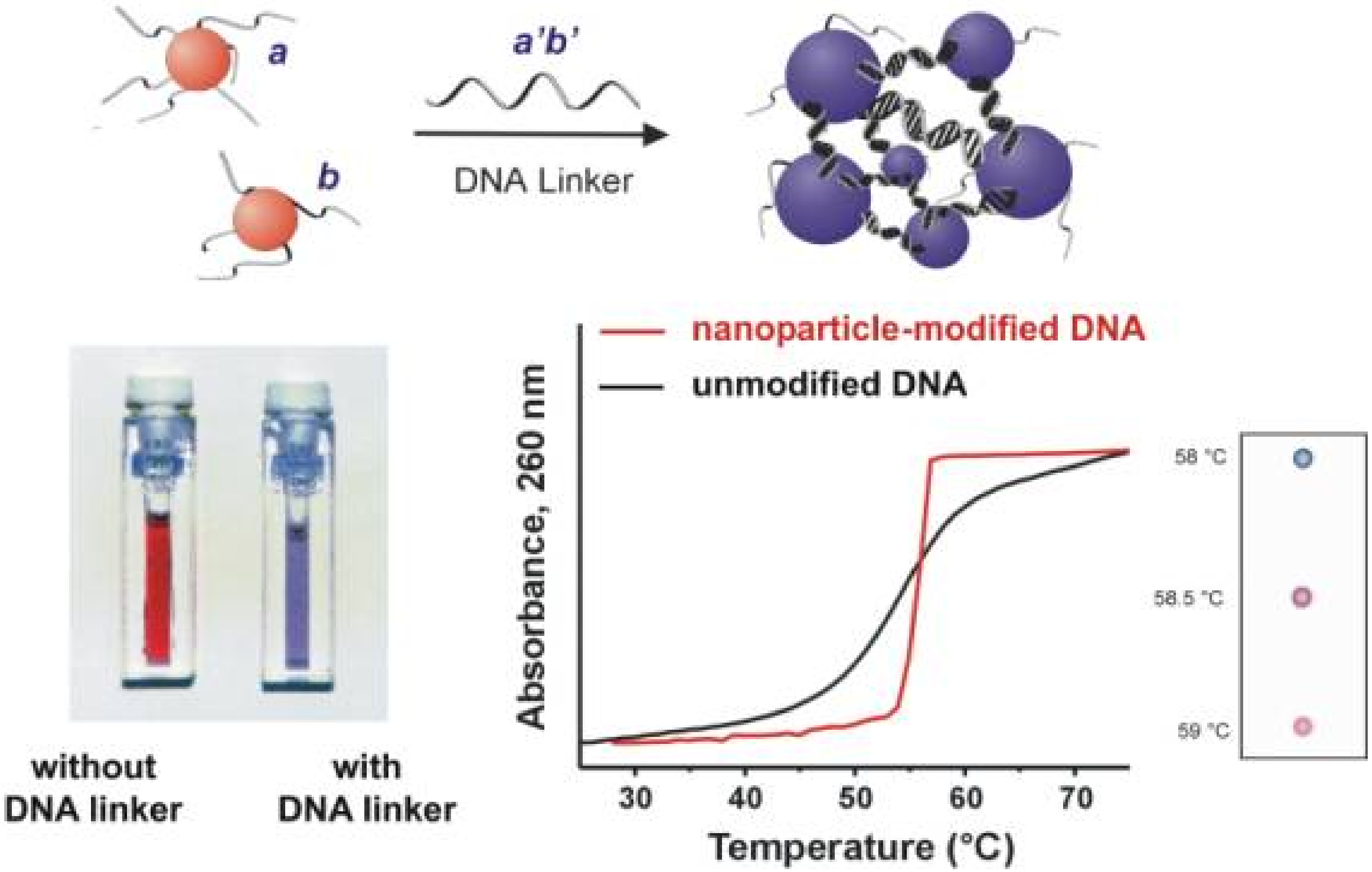
➢**Bio-Nanomaterial Hybrids: DNA-Np; DNA-CNTs; Drug-Nps, Peptide-CNTs, etc.**



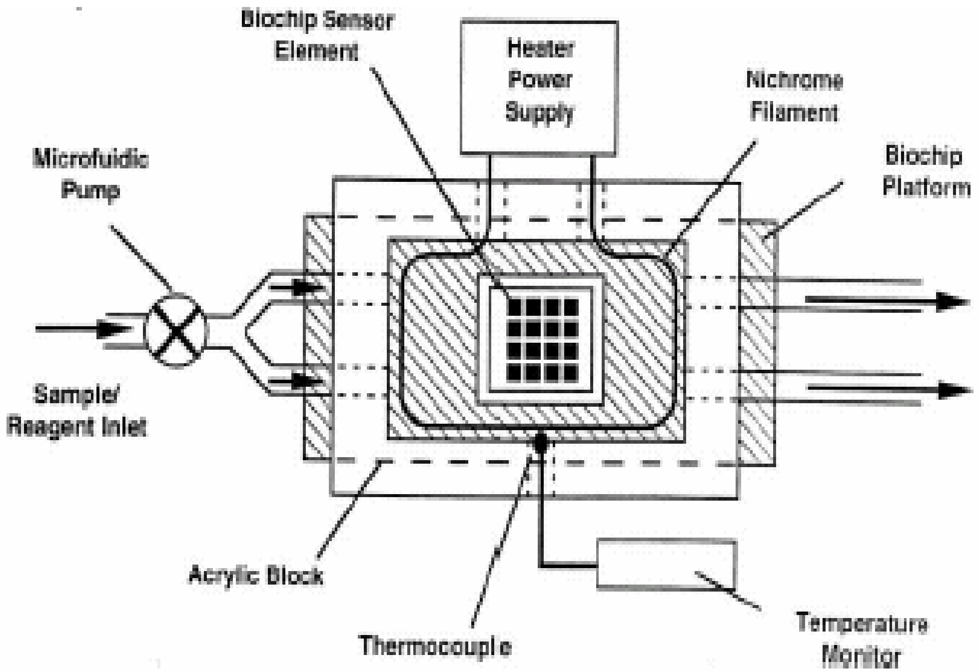


Integration of nano-scale technologies could lead to tiny, low-power, smart sensors that could be manufactured cheaply in large numbers.

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)

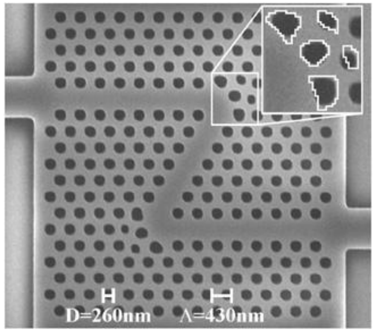
Nanofabrication

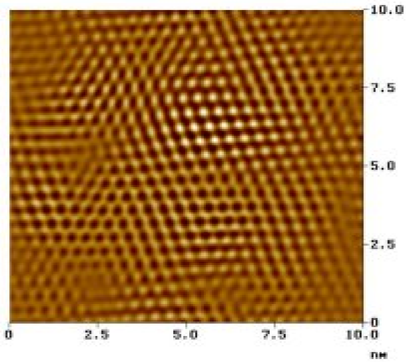
! Nanofabrication methods can be divided into two categories:

• **"Top down" approach**

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

•Electron-beam lithography – 10-100 nm

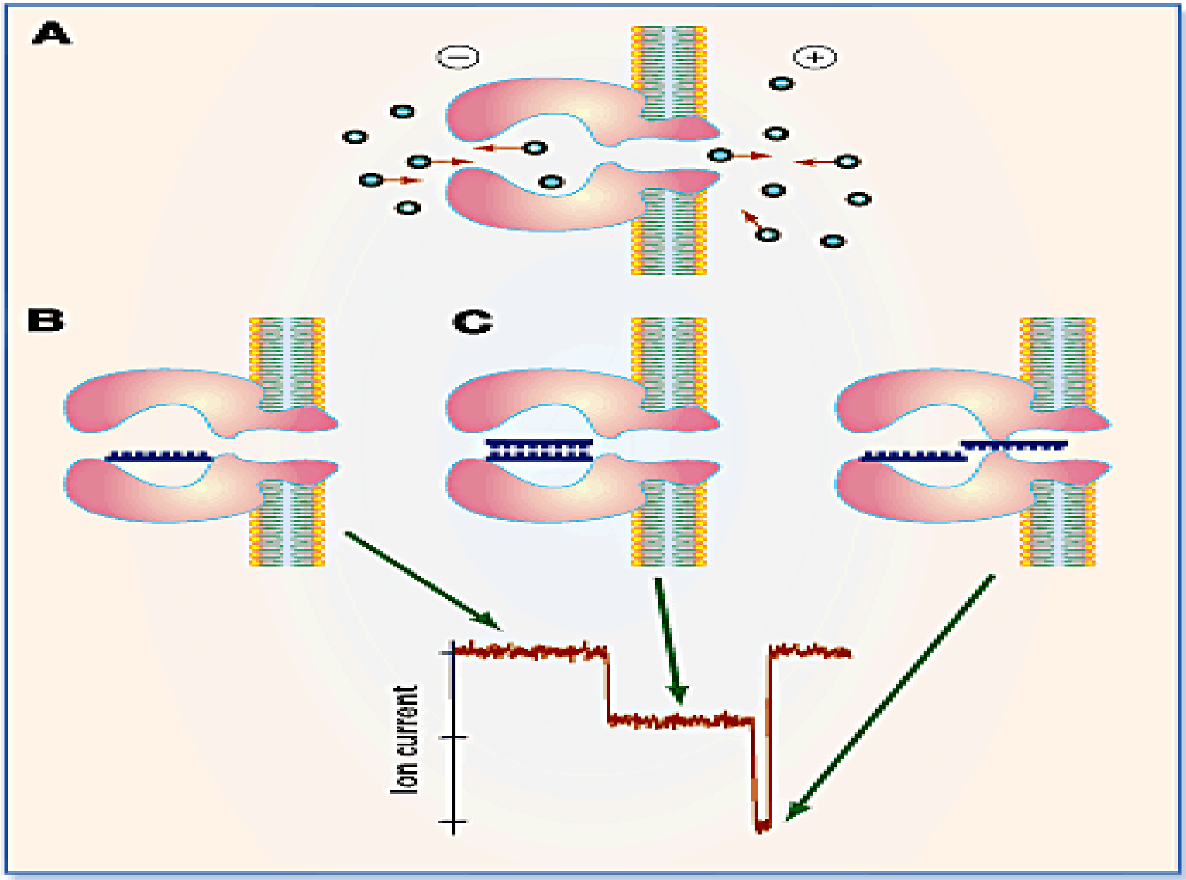




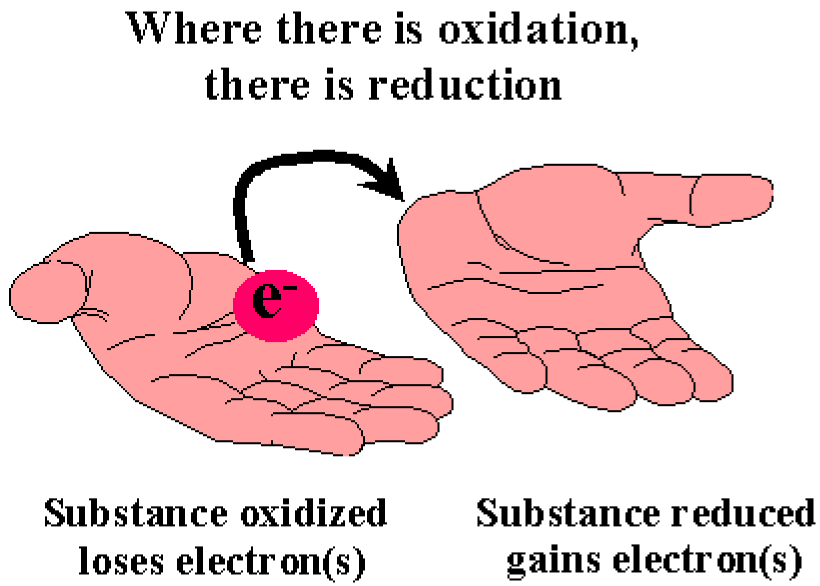
• **"Bottom up" approach**

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

Nanopore Technology



Electrochemistry



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.