Handouts of bt405 Nanobiotechnology

What is Nanotechnology

Definitions and Concepts

The most common working definition of nanoscience is: 'Nanoscience is the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale' (1). Bulk materials (the 'big' pieces of materials we see around us) possess continuous (macroscopic) physical properties. The same applies to micron-sized materials (e.g. a grain of sand). But when particles assume nanoscale dimensions, the principles of classic physics are no longer capable of describing their behaviour (movement, energy, etc.) at these dimensions, the principles of quantum mechanics principles. The same material (e.g. gold) at the nanoscale can have properties (e.g. optical, mechanical and electrical) which are very different from (and even opposite to!) the properties the material has at the macroscale (bulk). Nanotechnologies are defined thus: 'Nanotechnologies are the design, characterisation, production and application of structures, devices and systems by controlling shape and size at the nanometre scale.'

Towards a concept system for Nanotechnology

Simplest _ technology at the nonscale

Nanotechnology literally means any technology on a nanoscale that has applications in the real world.

Succinct definition of nanotechnology is engineering with atomic precision or atomically precise technology _ APT

US National nanotechnology _ the essence of nanotechnology is the ability to work at the molecular level, atom-by-atom, to create large structure with fundamentally new molecular organization.

Nanotechnology is group of emerging technology in which the structure of matter is controlled at the nanometer scale to produce novel materials and device that have useful and unique properties.

Nanotechnology encompasses the production and application of physical, chemical, and biological systems at scales ranging from individual atoms or molecules to submicron dimensions, as well as the integration of the resulting nanostructures into larger systems.

Define nanoscale:

Nanoscale is considered to cover the range from 1-100 nm. Nanotechnology is the art and science of manipulating matter at the nanoscale (down to 1/100,000 the width of a human hair) to create new and unique materials and products with enormous potential to change society.1 nanometer (nm) = 1 billionth of a meter. The design, synthesis, characterization, and application of materials, devices, and systems that have a functional organization in at least one dimension on the nanometer scale.

Nanotechnology is likely to have a profound impact on our economy and society in the early 21st century, Comparable to that of semiconductor technology, Information technology, or cellular and molecular biology. Science and technology research in nanotechnology promises breakthroughs in areas such as materials and

manufacturing, nanoelectronics, medicine and healthcare, energy, biotechnology, information technology, and national security.

What is a nanomaterial?

A nanomaterial is an object that has at least one dimension in the nanometre scale (approximately 1 to 100 nm).

Nanomaterials are categorised according to their dimensions as shown in Table 1. Table 1:

Nanomaterials are categorised according to their dimensions

	Nanomaterial dimension	Example
	All three dimensions < 100 nm	Nanoparticles, quantum dots, nanoshells, nanor-ings, microcapsules
	Two dimensions < 100 nm	Nanotubes, fibres, nanowires
	One dimension < 100 nm	Thin films, layers and coatings

Non-intentionally-made nanomaterials', which refers to nano-sized particles or materials that belong naturally to the environment (e.g. proteins, viruses, nanoparticles produced during volcanic eruptions, etc.) or that are produced by human activity without intention (e.g. nanoparticles produced from diesel combustion);

 Intentionally-made nanomaterials, which refers to nanomaterials produced deliberately through a defined fabrication process.

Towards a Concept System for Nanotechnology

Objects are perceived or conceived. The properties of an object are abstracted into characteristics.

The essential characteristics typically falling into different categories e.g. shape and color is combined as a set to form a concept. A set of essential characteristics that come together as a unit to form a concept is called intension. A set of objects abstracted into a concept is called the extension. Concepts are organized into a concept system

A concept system is often called an ontology (study of categories)

A concept system (Ontology) for Nanotechnology

Most of the term would normally prefixed by nano e.g. nanodevice, nanometerology
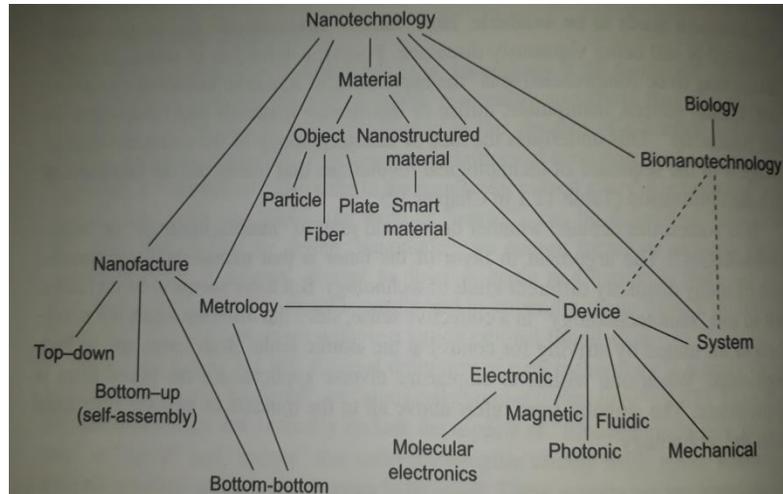
Nanotechnology spans many Areas
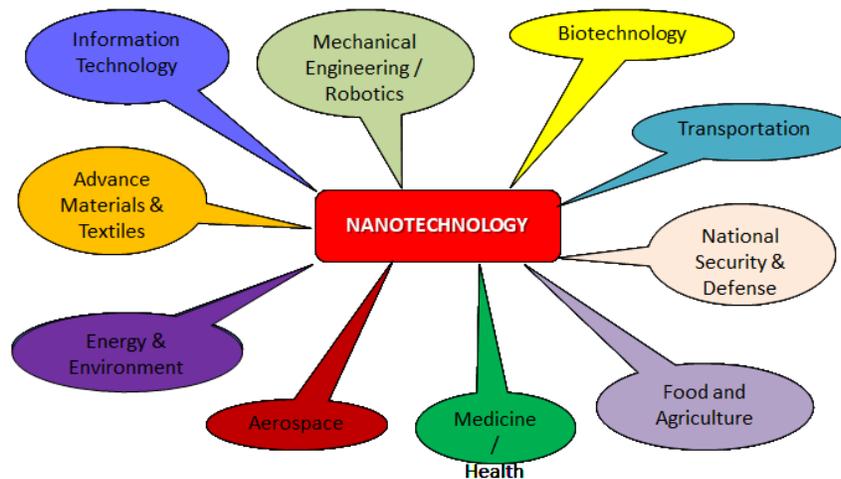
Nanotechnology Language

- *Nanobio*
- *Nanodots*
- *Nanowires*
- *Nanoelectronics*
- *Nanobots*
- *Nanomaterials*
- *Nanochondria*

Nanotechnology impacts our lives on a daily basis

The study of the controlling of matter on an atomic and molecular scale. Generally nanotechnology deals with structures sized between 1 to 100 nanometer in at least one dimension, and involves developing or modifying materials or devices within that size is already making **today's** products:

- Lighter
- Stronger
- Faster
- Smaller
- More Durable

Nanotechnology is associated with at least three distinct advantages. It offers the possibility of creating materials with novel combinations of properties. Devices in the nanoscale need less materials to make them, use less energy and other consumables, their function may be enhanced by reducing the characteristics dimensions, and they may have an extended range of accessibility. It offers a universal fabrication technology, the apotheosis of which is the personal nanofactory.

10 ways nanotechnology impacts our lives on a daily basis.

Faster, smaller, and more powerful computers that consume far less power, with longer-lasting batteries

Faster, more functional, and more accurate medical diagnostic equipment. Lab-on-a-chip technology enables point-of-care testing in real time, which speeds up delivery of medical care. Nanomaterial surfaces on implants improve wear and resist infection.

Nanoparticles in pharmaceutical products improve their absorption within the body and make them easier to deliver, often through combination medical devices. Nanoparticles can also be used to deliver chemotherapy drugs to specific cells, such as cancer cells.

Improved vehicle fuel efficiency and corrosion resistance by building vehicle parts from nanocomposite materials that are lighter, stronger, and more chemically resistant than metal. Nanofilters remove nearly all airborne particles from the air before it reaches the combustion chamber, further improving gas mileage.

Nanoparticles or nanofibers in fabrics can enhance stain resistance, water resistance, and flame resistance, without a significant increase in weight, thickness, or stiffness of the fabric. For example, "nano-whiskers" on pants make them resistant to water and stains.

Water filters that are only 15-20 nanometers wide can remove nano-sized particles, including virtually all viruses and bacteria. These cost-efficient, portable water treatment systems are ideal for improving the quality of drinking water in emerging countries.

Carbon nanotubes have a variety of commercial uses, including making sports equipment stronger and lighter weight. For example, a tennis racket made with carbon nanotubes bends less during impact, and increases the force and accuracy of the delivery. Nanoparticle-treated tennis balls can keep bouncing twice as long as standard tennis balls.

Most sunscreens today are made from nanoparticles that effectively absorb light, including the more dangerous ultraviolet range. They also spread more easily over the skin. These same nanoparticles are also used in food packaging to reduce UV exposure and prolong shelf life.

Many drink bottles are made from plastics containing nanoclays, which increase resistance to permeation by oxygen, carbon dioxide, and moisture. This helps retain carbonation and pressure and increases shelf life by several months.

Thanks to nanotechnology, a huge variety of chemical sensors can be programmed to detect a particular chemical at amazingly low levels, for example, a single molecule out of billions. This capability is ideal for surveillance and security systems at labs, industrial sites, and airports. On the medical front, nanosensors can also be used to accurately identify particular cells or substances in the body.

A cutting-edge science and technology

Nanoscience and nanotechnologies offer teachers a new instrument to bring exciting science and technology into the classroom. Nanotechnologies are now used in numerous devices with which young students are very familiar, such as computers, mobile phones and iPods. Nanoscience offers the possibility to improve numerous material properties and create new ones; in the future, we will have more and more products that incorporate some form of 'nano' — either a nanomaterial, or a nano-enabled technology. Bringing 'nano' into the classroom means bringing in the latest cutting-edge science and technology and talking about very exciting future scientific developments.

Short *history* of Nanotechnology

The concept of nanotechnology is attributed to Nobel Prize winner Richard Feynman who gave a very famous, visionary speech in 1959 (published in 1960) during one of his lectures, saying: "The principles of physics, as far as I can see, do not speak against the possibility of manoeuvring things atom by atom". At the time, Feynman's words were received as pure science fiction. Today, we have instruments (see the following section) that allow precisely what Feynman had predicted: creating structures by moving atoms individually

Birth of Nanotechnology

Professor Taniguchi of Tokyo Science University used the word "nanotechnology" to describe the science and technology of processing or building parts with nanometric tolerances.

A nanometer is a unit of length in the metric system, equal to one billionth of a meter.

1 nanometer =
1×10^{-9} meter
1×10^{-3} μm
3.281×10^{-9} feet
39.37×10^{-9} inches

Dr. Richard P. Feynman In 1959 at Caltech

Entitled: "**There is a plenty of room at the botom**"

Dr. Richard Feynman, one of America's most notable physicists, 1918-1988.

It expounds his vision of machines making the components of smaller machines, and simply continuing the sequence until the atomic realm is reached.

Dr. Feynman, Continued

The problems of chemistry and biology can be greatly helped if our ability to see what we are doing, and to do things on an atomic level, is ultimately developed – a development which I think cannot be avoided.

Atomic Scale : A computer image of the nano ice double helix. In the nano ice image, oxygen atoms are blue in the inner helix, purple in the outer helix. Hydrogen atoms are white Eric Drexler coined the term "Grey Goo"...the potential problem of self-replicating and autonomous artificial intelligence machines.

Eric Drexler, **Cell Repair Machines:**

 "By working along molecule by molecule and structure by structure, repair machines will be able to repair whole cells. By working along cell by cell and tissue by tissue, they...will be able to repair whole organs...they will restore health." - Drexler, 1986

Buckyballs:

 Three gentlemen—Harold Kroto from the University of Sussex, Robert Curl and Richard Smalley from Rice University—were awarded the Nobel Prize in Chemistry in 1996 for their discovery of a new composition of carbon, Carbon 60.

Engines of Creation

*The Coming Era of Nanotechnology*
By K. Eric Drexler
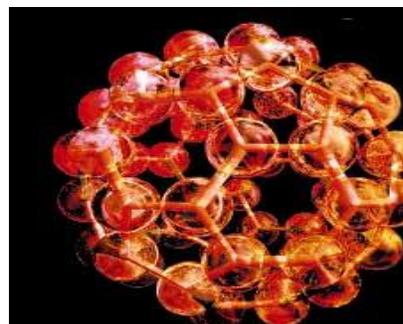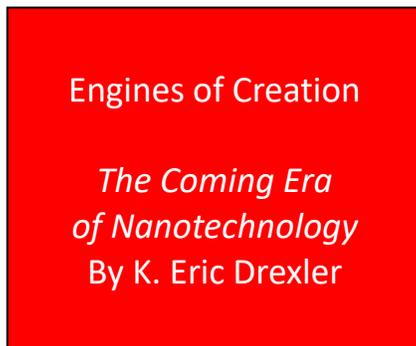
Fullerenes

 Carbon 60 was named after Richard Buckminster Fuller, who went by the nickname "Bucky."

Top-Down Approach

Two approaches used in producing nanotechnology systems. Top-down method is used by computer chip manufacturers.

Bottom-Up Approach

Bottom-up approach to manufacturing is analogous to the way biological systems are made
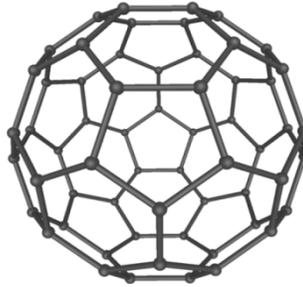
Metal colloids (metal nanoparticles dispersed in a medium) are the best example of nanotechnology throughout ancient, medieval and modern times. In Chapter 4, it was seen how metal nanoparticles possess optical properties (i.e. different colours) that are related to surface plasmons. The size and shape of the metal nanoparticles influence their visible colours! There are numerous artefacts that have notable colour effects precisely because they are made with metal colloids.

Types of Biotechnology

Biological Challenges of the 21st
Century

The Biotechnology Workforce

Biotechnology – using living organisms, or the products of living organisms, for human benefit to make a product or solve a problem. Biotechnology has been defined as the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services.

Biotechnology is a **multidisciplinary in nature**, involving input from Engineering, Computer Science, Cell and Molecular Biology, Microbiology, Genetics, Physiology, Biochemistry, Immunology, Virology.

Recombinant DNA Technology à Genetic manipulation of bacteria, viruses, fungi, plants and animals, often for the development of specific products

Ancient Biotechnology

Early history as related to food and shelter, including domestication

Classical Biotechnology

Built on ancient biotechnology fermentation promoted food production medicine

Modern Biotechnology

Manipulates genetic information in organism genetic engineering

Biotechnology _ Applications

Biotechnology is all around us and a big part of our lives, providing breakthrough products to cure disease, protect against bio-terrorism, feed the hungry, and clean our environment.

Example of "modern" biotechnology

Recombinant DNA technology started modern biotech as an industry

Examples of applications

- development of disease-resistant plants

- food crops that produce greater yields

- golden rice _ engineered to be more nutritious

- genetically engineered bacteria that can degrade environmental pollutants

APPLICATIONS

Pharmaceuticals/Health Care
Biopharma
Gene therapy
Gene "knockout" testing
Fermentation technology

Detection
Forensics
DNA fingerprinting
Disease DNA detection
Species member ID

Regulatory Approval/Oversight
Food and Drug Administration (FDA)
Environmental Protection Agency (EPA)
U.S. Department of Agriculture (USDA)
Occupational Safety and Health
Administration (OSHA)

Agricultural Biotechnology
Transgenic crops
DNA tracking of seeds
Transgenic animals

Drug Development
Bioinformatics
High throughput screening
Cell culture and human testing

Environmental and Aquatic
Aquaculture
Bioremediation
Transgenic modifications
Bioextractions

**Genetic Engineering Through
Molecular Biology and
Analysis Through
Bioinformatics**

Human, animal/plant physiology

Computer Science

Chemical engineering

Mathematics

Physics

Molecular and cell biology

Genetics

Immunology

Biochemistry

Statistics

Microbiology

Most drugs are developed to combat diseases affecting humans – Why?

Which disease has the most drug candidates? Why does that disease have more drug candidates than hepatitis C?

This reflects the current needs of humans- we have too many diseases and currently too few drugs to target them.
By far, cancer has the most drug candidates than any other disease. This disease has many more drug candidates than hepatitis C because hepatitis C affects less people worldwide than different kinds of cancer. Cancer, of course, can affect many different organs. On the other hand, hepatitis C only affects the liver.

Disease	Number of biotech drug candidates
Cancer	465
AIDS	237
Infectious diseases	123
Drug Delivery	117
Gene Therapy	75
Melanoma	74
Vaccines	73
Prostate cancer	71
Breast cancer	63
Diagnostic	58
Diabetes	55
Hepatitis C	48
Influenza	47
Immune system	45
Cardiovascular	41
Lung cancer	39
Hepatitis B	38
Leukemia	38
Colon cancer	36
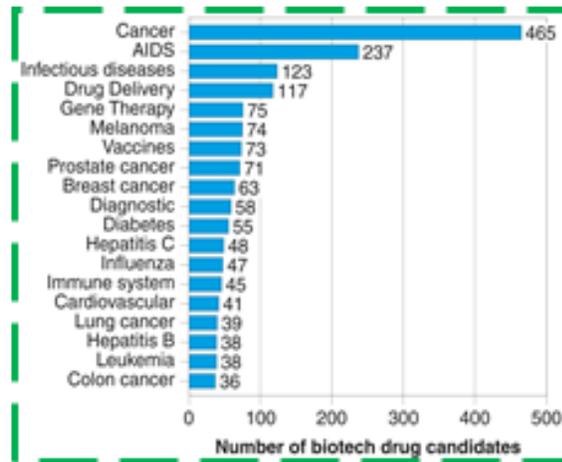
Types of Biotechnology

Microbial Biotechnology, agricultural Biotechnology, Animal Biotechnology, Forensic Biotechnology, Bioremediation, Aquatic Biotechnology, Medical Biotechnology, Regulatory Biotechnology

BIOTECHNOLOGY
- Medicine Pharmacy
- Agriculture Plants
- Sea Resources
- Industry
- Waste Industry
- Environment

AREAS OF BIOTECHNOLOGY
- GOLD: Bioinformatics, Nanobiotechnology
- RED: Health, Medical, Diagnostics
- GREEN: Agricultural, Environmental Biotechnology
- WHITE: Industrial Biotechnology
- BLUE: Aquaculture, Coastal and Marine Biotech
- PURPLE: Patents, Publications, Inventions
- YELLOW: Food Biotechnology, Nutrition Science
- DARK: Bioterrorism, Biowarfare
- BROWN: Desert Biotechnology

Microbial Biotechnology

Manipulation of microorganisms such as yeast and bacteria

Create better enzymes

More efficient decontamination processes for industrial waste product removal

Microbes used to clone and produce batch amounts of important proteins

Agricultural Biotechnology

United Nations Food and Agricultural Org. predicts by 2050, we will need to feed a world population of 9.1 billion! This requires raising food production by approximately 70%!

Work in groups to brainstorm a few solutions to better feed the world by 2050.

Genetically Engineered Plants - Resistance to diseases and insects

Foods with higher protein or vitamin content

Drugs developed and grown as plant products

Animal Biotechnology

Animals as a source of medically valuable proteins, Antibodies, Transgenic animal. Animals as important models in basic research.

Gene "knockout" experiments

Design and testing of drugs and genetic therapies

Animal cloning

Source of transplant organs

Transgenic animal: way to achieve large scale production of therapeutic proteins from animals for use in humans. Female transgenic animals express therapeutic proteins in milk (contains genes from another source) Example: human genes coding for clotting proteins can be introduced into female goats for production of these proteins in their milk

Forensic Biotechnology

DNA fingerprinting

Inclusion or exclusion of a person from suspicion, Paternity cases, Identification of human remains, Endangered species, Tracking and confirmation of the spread of disease

Bioremediation

The use of biotechnology to process and degrade a variety of natural and manmade substances

Particularly those that contribute to environmental pollution

 Example – stimulated growth of bacteria that degrade components in crude oil

1989 Exxon Valdez oil spill in Alaska

2010 Deep Water Horizon spill promoted research into natural oil-degrading organisms and enzymes

Aquatic Biotechnology

Aquaculture – raising finfish or shellfish in controlled conditions for use as food sources

50% of all fish consumed by humans worldwide

Genetic engineering

Disease-resistant strains of oysters

Vaccines against viruses that infect salmon and
other finfish

Transgenic salmon that overproduce growth hormone

Bioprospecting: rich and valuable sources of new genes, proteins and metabolic processes with important applications for human benefits

Marine plankton and snails found to be rich sources of antitumor and anticancer molecules

Medical Biotechnology

Involved with the whole spectrum of human medicine, preventive medicine, diagnosis of health and illness, treatment of human diseases, new information from Human Genome Project such as gene therapy

Stem cell technologies

Stem cells – grown in lab and then treated with different chemicals to allow them to develop into specific kinds of tissues needed for transplant

Current use: stem cells are used for diabetes; spinal cord injuries

Genes are headline news items

New test uses mother's blood
to test for fetal genetic defects

**Genetic switch
puts hair on chest**
■Researchers have isolated
biological changes in the
embryo that separate
boys from girls.

*Genes induce
human obesity*

Science Notebook
*Team nabs second
breast cancer gene*

DNA study:

Cavemen not same
as humans

*Gene evidence could give
life-term prisoner new trial*

**Parkinson's disease
gene mutation found**

**Scientists find gene
that causes skin cancer**
*Genetic studies of fruit flies uncover
mutated gene that causes common
basal cell carcinoma.*

• *Gene that causes bed-wetting found* •

*Program to identify
cancer genes*

**Fat gene a
lead in
solving
obesity**

Gene defect for muscle disorder identified

There are a wide variety of products that the biotechnology field has produced.

More than 65% of biotech companies in the U.S. are involved in pharmaceutical production (relating to drugs developed for medical use).

1982 - Genentech developed Humulin (human insulin) to treat diabetes.

It was the first biotech drug to be FDA approved.

There are more than 80 biotech drugs, vaccines, and diagnostics with more than 400 biotech medicines in development targeting over 2oo diseases!

Nearly 1/2 of new drugs target cancer

What is the real risk of nanotechnologies? Presently, nanotechnology is an umbrella term that covers a very large number of materials, applications and instrumentations. There is a need to classify nanotechnology applications and nanomaterials. This also applies to the risk debate: the starting point for this debate is to identify the real safety concerns of nanomaterials. Presently, while there is, at times, hype in describing the benefits of nanotechnology, there is also hype in the associated risk debate. The starting point should be to identify the safety concerns that are peculiar to nanotechnologies and to identify the key safety needs in specific areas of applications. This will allow us to move from a rather uncoordinated and scattered toxicological assessment of nanomaterials to coordinated research and cooperation between different institutions. Precisely for this reason, it is now preferred to use the plural (nanotechnologies) rather than the singular (nanotechnology) in discussing these matters.

Nanotechnology is beginning to allow scientists, engineers, and physicians to work at the cellular and molecular levels to produce major benefits to life sciences and healthcare. In the next century, the emerging field of nanotechnology will lead to new biotechnologybased industries and novel approaches in medicine.

Bionanotechnology and Nanobiotechnology are terms that refer to the intersection of nanotechnology and biology These two terms are often used interchangeably. Bionanotechnology generally refers to the study of how the goals of nanotechnology can be guided by studying how biological "machines" work and adapting these biological motifs into improving existing nanotechnologies or creating new ones.

➢ Nanometer-scale features are mainly built up from their elemental constituents.

➢ Examples include chemical synthesis, spontaneous self-assembly of molecular clusters (molecular self-assembly) from simple reagents in solution, biological molecules (e.g., DNA) used as building blocks for production of three-dimensional nanostructures, and quantum dots (nanocrystals) of arbitrary diameter (about 10–105 atoms).

Biology as Paradigm:

Bionanotechnology is biological applications of nanotechnology (science and technology of miniaturization at scales of <100nm)

It is hoped that nanotechnology can deliver a valuable set of research tools and clinically helpful devices in the near future.

The Nanotechnology Initiative expects new commercial applications to be developed in the pharmaceutical industry including advanced drug delivery systems, new therapies, and in vivo imaging.

Neuro-electronic interfaces and other nanoelectronics-based sensors are also current goals of research.

In the speculative field of molecular nanotechnology it is thought that cell repair machines could further revolutionize the field of medicine.

Nanotechnology is designed to provide a novel and improved approach to cancer diagnosis and treatment.

Nanoscale devices can interact with large biological molecules on both the surface and inside cells involved in cancer.

Since biological processes, including events that lead to the development of cancer, occur on a nanoscale at the surface of and inside cells, nanotechnology offers many tools.

Benefits for diagnosis:

- In the fight against cancer, winning half the battle is based on early detection.
- Nanotechnology is contributing new molecular agents and methods to enable earlier and more accurate diagnoses and treatment monitoring.

Imagine instead if cancerous or even precancerous cells could somehow be tagged for detection by conventional scanning devices. Two things would be necessary:

- Something that specifically identifies a cancerous cell and
- Something that enables it to be seen

Antibodies that identify specific receptors found to be over-expressed in cancerous cells can be coated on to nanoparticles that then produce a high contrast signal when Magnetic Resonance Images (MRI) or Computed Tomography (CT) scans are used.

Nanotechnology imaging in cancer diagnosis:

Nanoparticles can enhance the efficacy of magnetic resonance imaging (MRI) in detecting the spread of cancer.

In clinical trials, lymphotropic iron oxide nanoparticles acted as effective contrast agents and allowed the detection of small nodal metastases in men with prostate cancer that would otherwise have been overlooked.

Nanoparticulate iron oxide particles were used with MRI to accurately detect metastatic lesions in lymph nodes without surgery.

Nanoparticle contrast agents for ultrasound have also been developed that can enhance the sensitive detection of vascular and cardiac thrombi, as well as solid tumors of the colon, liver and breast, in a noninvasive manner.

Biomarker Screening:

Diagnostic screening for biomarkers in tissues and fluids could also be enhanced and potentially revolutionized by nanotechnology. Individual cancers differ from each other and from normal cells by changes in the

expression and distribution of tens to hundreds of molecules. As therapeutics advance, it may require the simultaneous detection of several biomarkers may be required to identify a cancer for treatment selection.

Nanoscale cantilevers and nanowire sensors can detect biomarkers of cancer from a single cell. Nanoparticles such as quantum dots, which emit light of different colors depending on their size, could enable the simultaneous detection of multiple markers.

Applications of Nanotechnology:

Nanotechnology is the act of manipulating materials at very tiny scales – at the level of atoms and molecules

Two principal parts to defining what is to be considered

    nanotechnology:

    (i) Scale and (ii) Uniqueness/novelty

Nanotechnology is the understanding and control of matte

    (i) at dimensions between approximately 1 nm to 100 nm

    (ii) where unique phenomena enable novel applications

Nanotechnology is one of the leading scientific fields today since it combines knowledge from the fields of Physics, Chemistry, Biology, Medicine, Informatics, and Engineering. It is an emerging technological field with great potential to lead in great breakthroughs that can be applied in real life.

Novel nanoand biomaterials, and nanodevices are fabricated and controlled by nanotechnology tools and techniques, which investigate and tune the properties, responses, and functions of living and non-living matter, at sizes below 100 nm

The application and use of nanomaterials in electronic and mechanical devices, in optical and magnetic components, quantum computing, tissue engineering, and other biotechnologies, with smallest features, widths well below 100 nm, are the economically most important parts of the nanotechnology nowadays and presumably in the near future.

The number of nanoproducts is rapidly growing since more and more nanoengineered materials are reaching the global market .The continuous revolution in nanotechnology will result in the fabrication of nanomaterials with properties and functionalities which are going to have positive changes in the lives of our citizens, be it in health, environment, electronics or any other field.

In the energy generation challenge where the conventional fuel resources cannot remain the dominant energy source, taking into account the increasing consumption demand and the CO_2 emissions alternative renewable energy sources based on new technologies have to be promoted.

Innovative solar cell technologies that utilize nanostructured materials and composite systems such as organic photovoltaics offer great technological potential due to their attractive properties such as the potential of

large-scale and low-cost roll-to-roll manufacturing processes. The advances in nanomaterials necessitate parallel progress of the nanometrology tools and techniques to characterize and manipulate nanostructures.

Revolutionary new approaches in nanometrology will be required in the near future and the existing ones will have to be improved in terms of better resolution and sensitivity for elements and molecular species. For centuries, silver has been used for its ability to destroy bacteria — from ancient Romans treating their water with silver coins to NASA using the metal to purify water aboard the Space Shuttle.

Silver(Ag) nanoparticles are embedded in sticking plasters for their ability to inhibit the transmission of viruses.

Silver Nanoparticles
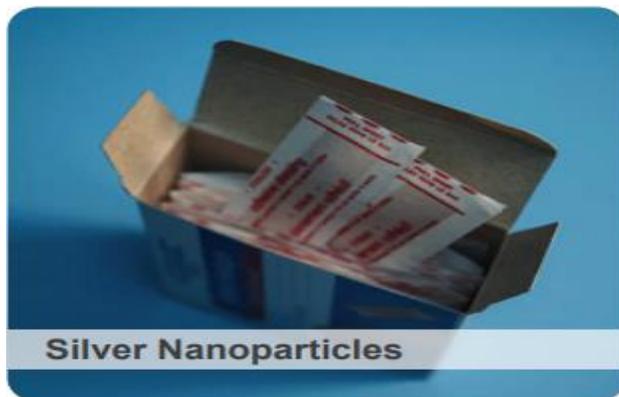
Pancreatic cancer has a devastatingly low survival rate (less than 5 percent after 5 years) because it is usually diagnosed at an advanced stage. Scientists have created tools for the early diagnosis of pancreatic cancer by attaching a molecule that binds specifically to pancreatic cancer cells to iron oxide nanoparticles that are clearly visible under magnetic resonance imaging (MRI).

Diagnostics

If you hate injections, you'll be glad to hear that oral administration of drugs that are currently delivered by injection may be possible in many cases. The drug is encapsulated in a nanoparticle which helps it pass through the stomach to deliver the drug into the bloodstream.

There are efforts underway to develop oral administration of several different drugs using a variety of nanoparticles. One company has progressed to the clinical testing stage with a drug for treating systemic fungal diseases.

Drug Delivery

Titanium dioxide confers the white appearance of high-protection sunscreens. Titanium oxide nanoparticles have a comparable UV protection property to the bulk material, but lose the cosmetically undesirable whitening since the particle size is decreased.

Sunscreen

Nanotechnology can be used to create fabrics with superior performance without compromising the look, feel or comfort of the fabric. For instance, nanomaterials can be added to the fabric and make them stain resistant.

Fabric

Nanotechnology in Medicine:

Nanotechnology is a new field with many possible uses, medicine being one of them

❖ The manufacturing technology of the 21ˢᵗ century

The study and manufacture of devices of molecular dimensions, in the range of nanometers or one-billionth of a meter. Most of industrial manufacturing processes are based on top-down technologies i.e., they take larger objects and make them smaller yielding products of fairly high precision and complexity

Most products of living organisms are constructed by tiny molecular machines, such as cells and organelles, working from the bottom up. By organizing individual atoms and molecules into particular configurations, these molecular machines are able to create works of astonishing complexity and size, such as the human being

Nature shows that molecules can serve as machines because living things work by means of such machinery. Enzymes are molecular machines that make, break, and rearrange the bonds holding other molecules together

Muscles are driven by molecular machines that haul fibers past one another.

DNA serves as a data-storage system, transmitting digital instructions to molecular machines e.g., the ribosomes, that manufacture protein molecules. Using special bacterium-sized "assembler" devices, nanotechnology would permit on a programmable basis exact control of molecular structures that are not readily manipulated by natural molecular machines and molecular techniques presently available.

With nanotechnology, atoms will be specifically placed and connected, all at very rapid rates, in a fashion similar to processes found in living organisms

Nanomedicine:

Some medicines are made through biotechnological processes, for example those using recombinant DNA (human hepatitis vaccine). Under these processes the DNA of living creatures (usually bacteria) is altered. Nanotechnology represents a similar approach to the manufacture of pharmaceuticals and other goods.

Nanorobots: Medicine of the Future:

What are they?

Nanorobots are nanodevices that will be used for the purpose of maintaining and protecting the human body against pathogens. They will have a diameter of about 0.5 to 3 microns and will be constructed out of parts with dimensions in the range of 1 to 100 nanometers. The powering of the nanorobots can be done by metabolizing local glucose and oxygen for energy

Other sources of energy within the body can also be used to supply the necessary energy for the devices. They will have simple onboard computers capable of performing around 1000 or fewer computations per second.

Nanorobots:

A navigational network may be installed in the body, which may provide high positional accuracy to all passing nanorobots. This will enable the physician to keep track of the various devices in the body. These nanorobots will be able to distinguish between different cell types by checking their surface antigens. When the task of the nanorobots is accomplished, they can be retrieved by allowing them to exfuse themselves via the usual human excretory channels

Mechanical drilling of a small tumor mass by a nanorobot
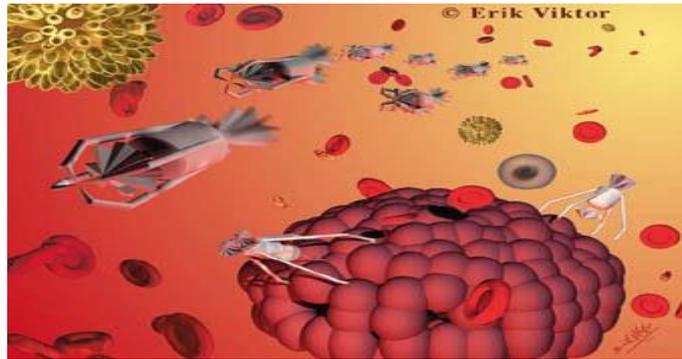
Global Market for Nanotechnology Products:

The total market for nanobiotechnology products was $19.3 billion in 2010 and is growing at a compound annual growth rate (CAGR) of 9% to reach a forecast market size of $29.7 billion by 2015.

Medical applications, including drug delivery and microbicides, dominate today's market, with sales of $19.1 billion in 2010. This market segment is growing at a compound annual growth rate (CAGR) of 8.7%, and is forecast to reach sales of $29 billion by 2015 (BCC).

 More and more consumer products are branded worldwide as nano.

The Most Common Nanoscale Substance Used in Consumer Products:

Yet, very little is known about how companies are using nanotechnology for innovation and product development.

As of March 10, 2011, the nanotechnology consumer products inventory contains 1317 products or product lines, up substantially from 2006 when it originally contained 212 products.

 The most common nanoscale substance used in consumer products is nano-silver (anti-bacterial and anti-fungal properties)

Baby bottle nipples, door handles, food contact products, interiors of refrigerators and washing machines, clothing, bedding, paints, cleaning products, food storage containers, bandages, medical devices, mattresses, and children's teddy bears

Nanotechnology: Current Uses:

Carbon based nanomaterials are the second most common nanoscale materials found in consumer products (light-weight, high strength, electrical and thermal conductivity).

Sports equipment, vehicle parts, storage of power in batteries, moisturizing effectiveness of cosmetics, drug delivery

Nano-sized TiO2 and ZnO – sunscreens

Silver nanoparticles – antibacterial properties (soaps, toothpastes, deodorants, lip products, make-up instruments, hair brushes, curling tongs, foils for electric razors, foot massagers, tooth brushes, rubber gloves, hair dryers, facial ionic steamers).

Nanosomes - improve the solubility of ingredients and add shimmer.

Nano emulsions and nanosomes -preserve active ingredients, such as vitamins and anti-oxidants.

Nano gold - healing and anti-oxident properties.

Fullerenes, bucky balls - anti-oxidant and smoothing properties in moisturisers, increased penetration into the skin , anti-aging properties.

FOOD & PACKAGING: Natural and engineered nanomaterials in the food, additives and packaging.

New flavours and textures, less use of fat, enhanced absorption of nutrients, blockage of ingredients that contribute to elevated blood cholesterol.

Smart packaging identifying contaminated food, nanoscale sensors identifying the presence of bacteria and releasing chemicals as food spoils.

Nanomaterials preventing adhesion of the microbes to the surfaces and equipment.

Nanosilver - food contact utensils and containers.

TEXTILE AND CLOTHING: Stain resistant, waterproof, wrinkle resistant, antibacterial, radiation absorbency properties , waterproof, windproof, ultraviolet protection, breathable, grime resistant fabrics.

SPORTS & LEASURE, HOUSEHOLD: Tennis rackets, skis, snowboards, golf balls, nano-bike, baseball bats, sports clothing.

Nanoceramic- smoothness and heat resistance of household equipment (flat iron)

Nanoparticles - household appliances to kill bacterial and odors (refrigerators), shoe protection nano-sprays, etc.

COMPUTING & ELECTRONICS: Computer technologies, mobile phones, digital cameras and other high technology equipment.

Moore's law decrease in size and increase in density

Faster and smaller non-silicon-based chipsets, memory and processors, new materials for semiconductors that increase processing speeds, advanced microscopy, faster and smaller telecom switches, higher-speed transmission, new class of display using carbon nanotubes as emission device, flat-screen TVs and computer monitors.

TRANSPORT, BUILDING, CONSTRUCTION: Nanotechnologies in transport- lighter and stronger materials, more efficient fuels (cars, aeroplanes, ships)

Paints with improved adhesion and anti-mildew properties, insulation with increased insulating properties, concrete and steel with increased strength and durability, glass that acts as a fire barrier (Nanoforum), self-cleaning sheet glass based on a layer of titanium dioxide nanoscale particles (nano titanium dioxide is fixed in layers onto glass which enables sunlight to break down any dirt making it easy for the rain to wash the dirt away on ships and tankers) (Meandnano).

MEDICAL_Use:

Diagnostic devices, contrast agents, analytical tools, physical therapy applications and drug delivery vehicles.

Cancer diagnosis - "molecular imaging" intended to improve diagnostic accuracy.

Targeting and localized delivery of drugs - delivering drugs specifically to cancer cells using nanoparticles that can be loaded with drugs

The US Food and Drug Administration has already approved first generation nanodrugs such as Abraxane, a nanoformulation of the anti-cancer chemotherapy paclitaxel

An anti-cancer drug approved by Health Canada containing a nanomaterial designed to find cancer cells, which attaches itself to the cells and then releases a chemical that kills them

The drug is only released when attached to the cancer cell, the toxic side effects associated with many drugs used for chemotherapy are thereby reduced

Further advances in nanomedicine may help to reproduce or to repair damaged tissue and replace today's conventional treatments like organ transplants or artificial implants.

ENVIRONMENT:

Safer and more efficient approaches to waste management, air and water purification, reduction in pollution.

Nanofiltration to remove dissolved salts, heavy metal contaminants, soften water and treat wastewater.

Nanofibers filtrate dangerous bacteria in the air, gold nanoparticles clear volatile organic compounds.

Developed by the oil industry, MCM-41 (known also as "self-assembled monolayers on mesoporous supports," SAMMS), with pore sizes in the range of 10–100 nanometers, is used for the removal of ultrafine contaminants.

A nanoparticle-reinforced polymeric material can replace structural metallic components in automobiles and lead to a reduction of 1.5 billion liters of gasoline consumption over the life of one year's production of vehicles, thereby reducing carbon dioxide emissions annually by more than 5 billion kilogram.

Nanotechnology_Healthcare:

Drug Delivery Drug Detection	Targeted Molecular & Thermal Therapy	Blood Brain Barrier Permeability	Gene Therapy Delivery	Oxygen Delivery Thrombolysis
Tissue Engineering Magnetic Bio-separation	Pathogen & Contaminant Detection Sterilization	Bio-Medicine Bio Chips Probes	Diagnostic & Stem Cell Imaging	Surgery Catheters Endoscopes
Displays Nano - electronics	Microfluidics Lab-on-a-Chip	Transducers Detectors	X-Ray Tubes Low Friction Bearings	Body Sensors Wireless

With the use of nanotechnology, scientists hope to prevent illness, more quickly diagnose, control disease and treat disease with fewer side effects, and create better medical aids such as more compatible prosthetics. Nanoparticles and surfaces made of nanostructures are used in many areas of healthcare research. Specific applications for nanotechnology in medicine include these developments:

- Better tools for prevention

- Nanoscopes and nanotweezers

- Novel membranes for cleaning blood

- Miniaturized probes for recognizing disease

  ➢ Nano-dots that trace disease

  ➢ Improved detection through medical imaging

- MRI (Magnetic Resonance Imaging) with better contrast agents

- CAT (Computerized Axial Tomography) scans

  ➢ Innovative medicines and drug delivery for detection and treatment

- Cancer medicines that only target cancer cells

- Antimicrobials (germs)

Implants and orthopedics (having to do with your bones) that are more compatible and that last longer. Small molecules and biological barriers - Small molecules (< 100nm) pass through capillary membranes. Small molecules pass through the Blood Brain Barrier, when lipophilic or transport mechanism is available

  Mean free path $\propto \sqrt{t/r}$:

  $r \propto t$ for fixed diffusion distance

Nanoparticles have easier access into cells with applications in chemotherapy and as antibacterial agents. High aspect ratio nanorods pass cell membranes more easily and penetrate deeper into cells than low aspect ratio particles. Reptated polymers and nanorods can enter angiogenic endothelial cells

Nanoscience can potentially help us detect and treat cancer at the molecular level. Nanotechnologies will most likely allow us to rapidly sequence DNA (nanosequencing). Doctors could know right away if you have a genetic tendency for a disease or a drug interaction.

- Enhanced Permeability and Retention(EPR) Effect
- Causes accumulation of nanoparticle drugs in tumours due
to the increased permeability of angiogenic blood vessel

  ➢ Drug loaded carbon nanotubes 100nm long and a few nm

wide enter angiogenic blood vessels but not normal blood vessels

Structure and Physical Properties:

Structural properties of nanomaterials lead to advanced physical characteristics increased mechanical strength, low coefficient of friction, high electrical & thermal conductivity etc.

Applications

- Nanowire: superconducting magnets for MRI
- Nanocomposites: X-Ray tube anodes
- Carbon nanotube, Spindt electrodes: field emitters for X-Ray tube cathodes, displays for point of care devices
- Nanolayers: ow friction bearings for X-Ray tube anodes
- Nanomaterials: high density electronics, thermal expansion compensation for miniature medical devices
- Nanoneedles: biosensors
- Block copolymers: tissue engineering.

Nanotechnology in Imaging and Therapy:

➢ Contrast agents for Medical Imaging and Pathogen Detection

- MRI Magnetic Resonance Imaging
- Optical imaging
- Ultrasound
- CT Computerized Tomography with X Rays
- PET Positron Emission Tomography (PET)
- Photo-Acoustic Tomography (PAT)
- Surface Enhanced Raman Spectroscopy (SERS)
- Surface Plasmon Resonance Imaging SPRI

 Microfluidics synthesis of PET molecules

Targeted agents for molecular imaging

Targeted image guided therapy

Magnetic heating of nanoparticles during therapy

Infra-red heating of nanoshells/nanotubes during therapy

Convection enhanced delivery with liposomes:

Applications of nanotechnology are being developed for cancer therapies and diagnostics.

In the diagnostic realm, nanoparticles have been used to enhance the efficiency of Magnetic Resonance Imaging (MRI) to detect the spread of cancer. In one study, lymphotropic iron oxide nanoparticles were demonstrated to act as effective contrast agents and allowed the detection of small nodal metastases in men

with prostate cancer that would otherwise have been overlooked. Such imaging with nanoparticles might also help eliminate invasive biopsy procedures as the only means to monitor a cancer's spread.

Nanoparticle contrast agents for Ultrasound have also been developed, which may enhance the sensitive detection of vascular and cardiac thrombi, as well as solid tumors of the colon, liver and breast, in a noninvasive mannerRecently developed nanowires -- silicon strands containing receptors for tumor markers such as prostate specific antigen (PSA) -- were shown to be sensitive enough to detect markers from as few as ten tumor cells. They can test a drop of blood in a few minutes, providing a simultaneous scan for multiple cancers.

Nanotubes, developed by materials science engineers and used to increase the strength and elasticity of concrete and plastics, have also been shown to be capable of crossing cell membranes and ferrying proteins into cells. Because eliminating specific RNA molecules has been shown to down-regulate cancer growth, attaching RNA-degrading enzymes to nanotubes is one approach under development.

In addition to the enzymes, additional drugs can be inserted inside the tubes as secondary payloads. More than 25 million patients in the U.S. undergo MRIs each year. Doctors use contrast agents in about 30% of MRIs. The contrast agents increase the sensitivity of the scans, making it easier for doctors to deliver a diagnosis. Gadolinium agents are the most effective agents and the most commonly used.

Carbon nanotubes have become an unexpected source of highly effective contrast agents for enhancing MRI scans. The new agents - dubbed gadonanotubes - use the same highly toxic metal, gadolinium, that is given to more than a quarter of MRI patients today, but the metal atoms are encased inside a hollow nanotube of pure carbon. Shrouding the toxic metals inside the benign carbon is expected to significantly reduce or eliminate the metal's toxicity to patients.

Diagnostic Applications of Nanotechnology in Medicine:

Improved imaging of the human (or any) body.

Nanoprobes (miniature machines) can attach themselves to particles in the body (e.g., antibodies) and emit a magnetic field. Probes that aren't attached to anything don't create a detectable magnetic Nano-tracking may be able to detect tumors that are a few cells in size.

A single inhaled nanorobot reaches, deeply inspired into the lungs, enters an alveolar duct and attaches to the tissue surface.

Another way to use nanotech as tracking devices is to use "quantum dots. These tiny semiconductors are able to emit wavelengths of light (colors) that depend on their size. If quantum dot A is twice as big as quantum dot B, it will emit a different color.

Quantum dots are better than conventional dyes:

- They last much longer
- More colors can be made available.

A microscopic machine roaming through the bloodstream, injecting or taking samples for identification and determining the concentrations of different compounds
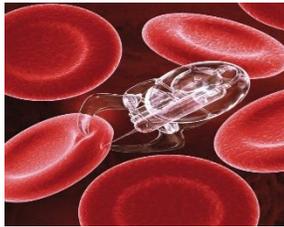
Therapeutic Applications of Nanotechnology in Medicine:

Nanotech is capable of delivering medication to the exact location where they are needed – hence lesser side effects

- Organic dendrimers - a type of artificial molecule roughly the size of a protein- would be ideal for the job of delivering medicine
- Hollow polymer capsules - gold-coated glass beads that are near infrared light sensitive
- Destruction of harmful eukaryotic organisms / cancer cells by interrupting their division process
- Certain proteins are capable of doing this (e.g., Bc12 family of proteins)

Nanoprobe can be made to generate radiation, that could kill bacteria, viruses and cancer cells. Nanoprobe comprising of a single caged actinium-225 atom would detect (using antibodies) and enter a cancerous cell. Location and destruction of cancer cells by acoustic signals
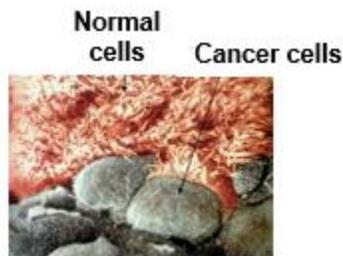
Comparison of normal and cancerous cells in respiratory airway of the lung

Nanotechnology also theoretically allows the mimicking of natural biological processes e.g., repair of damaged tissues

- Using nanotech to build scaffoldings of artificial molecules that bone cells often adhere to and grow bones on

- Broken bones would heal much faster.

Transport of oxygen within the body by creating an artificial red blood cell.

To cure skin diseases, a cream containing nanorobots may be used it may:

- o Remove the right amount of dead skin
- o Remove excess oils
- o Add missing oils
- o Apply the right amounts of natural moisturising compounds

Achieve the elusive goal of deep pore cleaning by actually reaching   down into pores and cleaning them out.

Dental Robots:

Four remote-controlled nanorobots examine and clean the subocclusal surfaces of a patient's teeth, near the gumline.
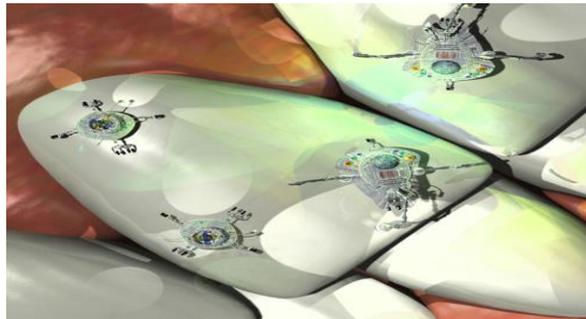
Copyright 2001 American Dental Association

Medical nanodevices could augment the immune system by finding and disabling unwanted bacteria and viruses.
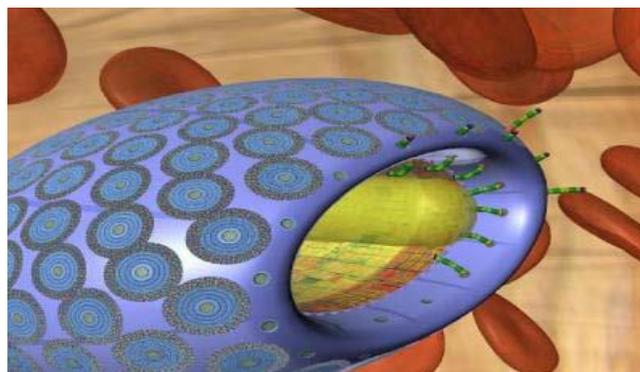
Devices working in the bloodstream could nibble away at atherosclerotic deposits, widening the affected blood vessels.It may be prevented most heart attach

GOALS

- Construction of a nano-assembler
    - o A machine capable of building nanoprobes on a grand scale

- The next step would be self-replication of nanoprobes- mitosis
- Rough estimates say that this will be reached in about 10-20 years

PREDICTIONS

- Predicting the future of nanotechnology is much like trying to predict the remainder of a motion picture from a single frame
- Although the future of medicine lies unclear, it is certain that nanotechnology will have a significant impact

Nanotechnology in Diagnostic:

Several nanoparticles have been used for diagnostics. Of these, the most frequently used are gold nanoparticles, QDs, and magnetic nanoparticles. Nanodiagnostics is the new term that describes use of methods and techniques of nanotechnology and its principles for diagnostics purposes. It includes, although not limited to, the manipulation and assessment of single molecule, size reduction of systems and platforms to make use of nanoscale properties obtainable from interactions between surfaces and biomolecules.

Nanodiagnostics is an evolving application of nanoscale technology to meet the demand of clinical diagnostics, determining disease state, any predisposition to such, the pathology of the condition and the identification of causative organisms. With nanotechnology, diagnosis is being carried out on a nano-scale leading to a trend of the use of hand held devices that are easy to use and marketable

Nanodiagnostics as surging new field of molecular diagnostics, have been positively changing laboratory procedures, providing new ways for patient's sample assessment and early detection of disease biomarkers with increased sensitivity and specificity. Nanoparticle platforms have been developed and optimized for the detection of pathogens and cancer biomarkers such that diagnostic proceedures now become less cumbersome but more sensitive because most of the complex proceedures are now integrated onto a simple device having the capacity to be used for on the spot diagnosis.

Gold particles (AuNPs) find significant exploitations in biomedical field due to

(i) their comparative chemical stability, making them less hazardous, (ii) simple and straightforward synthesis and fabrication process, and (iii) genuine biocompatibility and noninterference with other labeled biomaterials (e.g., antibody and other biomarkers)

Colloidal Au has been playing an important role for curing various diseases although the exact mechanism of action is still poorly understood. Today, the applications of AuNPs are increasing day by day in pharmaceutical sciences for human welfare. It can be used to understand more about the nature of diseases like cancer and HIV by providing significant target with nanovehicle.

Unique Properties of Gold Nanoparticles for Diagnostic Purpose:

Tuning the Optical Properties of Gold for Biodiagnosis:

The size-dependent absorbance of AuNPs was explored to demonstrate how alloying affects the chemical stability of NPs and also how composition, size, and nanostructure can be employed to adjust the optical properties. The absorbance and scattering properties of AuNPs can be tuned in accordance with their size parameter.

NPs less than 20 nm show only their surface plasma resonance (SPR), but scattering properties of such materials is negligible. In the case of large NPs (20–80 nm), the scattering properties of the materials increase. The large AuNPs show relatively high-scattering properties making them more applicable for biomedical applications, whereas those having relatively high-absorption properties are widely used in colorimetric detection of analytes as well as for biological analysis by changing refractive index of AuNP's environment.

Gold Nanoparticles and Surface Plasmon Resonance (SPR):

Surface plasmon resonance (SPR) is a phenomenon occurring at the metal surface when a beam of light is incident on the surface of the molecules at a particular angle and distance (typically in case of gold (Au) and silver (Ag) metals or spherical NPs). Application of biosensing SPR instruments is the determination of affinity parameters for biomolecular interaction.

This technique holds utility not only for measurement in real-time kinetics of ligand-receptor interactions but also in screening of lead compound identification in pharmaceutical drug development as well as in detection of small molecules, DNA hybridization, enzymesubstrate interactions, antibody characterization, studying antigen-antibody interaction, characterization of antibody orientations, epitope mapping, protein conformational studies, and labelfree immunoassays.

Unique properties of AuNPs along with their applications in clinical diagnosis and different biological studies

Surface plasmon resonance

- Ligand-receptor interaction
- DNA hybridization
- Antibody characterization
- Epitope mapping
- Label-free immunoassay
- Screening of lead compound
- Identification of disease biomarker

Surface plasmon resonance

- Single-molecule detection
- Actual biological system and catalysis analytical assay
- *In situ* ambient analysis
- Protein and nucleic acid biosensors
- Protein characterization studies

Magnetic resonance properties

- MRI
- CT-MRI
- MRI-contrast agent
- Diagnosis of malignant and solid tumors
- Bimodal contrast agents

Fluorescence properties

- Imaging
- Analytical genomic and proteomic studies
- Drug screening
- Immunological assay
- Identification of reactive oxygen species (ROS)

Magnetic Resonance Properties of AuNPs for MRI

The new era of molecular imaging, in vivo characterization, and measurement of biological processes at cellular and molecular level aims at quantifying molecular changes associated with the onset and development of pathological states, thereby, providing early diagnosis and prognosis of diseases like cancer. The imaging of cells, cellular and subcellular structures, requires imaging agents of high relaxivity and density endowed with targeting ability to specific cellular receptors.

AuNPs are especially attractive for imaging and therapy due to their SPR, enhanced light scattering, and absorption. In the field of MRI, AuNPs can be used as a template agent in place of Gadolinium (Gd) chelates for use as MRI contrast agents due to their high sensitivity and also in diagnosis.

PEG-coated iron oxide gold is a type of core-shell nanoparticles (PEG-AuIONs), measuring approximately 25 nm in diameter, which reveals high specificity to solid tumors as they accumulate mostly within the tumor mass along with low nonspecific accumulation in the liver and spleen. PEG-AuIONs as promising MRI contrast agents for diagnosis of malignant tumors including pancreatic cancer.

Fluorescence Behavior of Gold Nanoparticles:

Fluorescence-based assays and detection techniques are among the most highly sensitive and popular biological tests in clinical diagnosis. AuNPs show excellent behavior of antiphotobleaching under the presence of strong light illumination

A new fluorescence method has been developed for cell imaging, when the cells stained with AuNPs are illuminated with strong light, the fluorescence of AuNPs on cell membrane or inside cells can be collected for cell imaging. Au nanoprobes immobilized with fluorescein-hyaluronic acid (HA) conjugates which are fabricated and utilized for monitoring intracellular reactive oxygen species (ROS) generation in live cells via NP surface energy transfer.

AuNPs as fluorescent labels for optical imaging and sensing for analytical genomics and proteomics. Fluorescence resonance energy transfer (FRET) is a spectroscopic technique whereby the excitation energy of the donor electron is transferred to the acceptor via an induced-dipole movement interaction. AuNP-based FRET monitors DNA hybridization, and DNA cleavage by nucleobases after hybridization has been developed by varying the DNA length

Large molecules such as proteins can be sensed with 20 nm AuNPs stabilized by Cy5.5-Gly-PoLeu-Gly-Val-Arg-Gly-Cys-(amide) showing selectivity for a matrix metalloprotease served as fluorescent imaging probe for in vivo drug screening and protease activity.

Quantum Dots:

QDs are inorganic fluorophores that offer significant advantages over conventionally used fluorescent markers. Inorganic crystals of CdSe (cadmium selenide 200-10000 atoms wide), coated with ZnS (zinc sulphide). They emit fluorescent light when irradiated with low energy light. The size of the dots (< 10 nm) determines the frequency of light emitted (i.e. colour). The dots usually have a polymer coating with multivalent bio-conjugate attached, or are embedded into microbeads.

Collection of dots of different size embedded to a given microbead emits distinct spectrum of colours - spectral bar code specific for this bead.Detection technique with the use of 10 intensity levels and 6 colours could theoretically provide 106 distinct codes. Quantum dots, for example CdSe-ZnS nanocrystals, do no emit in the near infrared, so they cannot be used for analysis in blood. QDs have a wide range of applications for molecular diagnostics and genotyping.

What is nanoscale?

There is no fixed definition for what nanoscale is, but there are a couple of things that are very important – small size and different properties.

The size of nanoparticles is at least one dimension (height, length or depth) less than 100 nm. A nanotube can be much longer than 100 nm, but it is still called a nanoparticle because it is only about 3 nm wide. A very thin film of material can be many centimetres wide, but if it is less than 100 nm thick, it is still called a nanofilm.

Nanoparticle properties

To many scientists, things are at the nanoscale if they are so small that they display different properties to the large scale material. This mostly happens when particles are only a few nanometres across. For example, you may know that water boils at 100 ºC (at a pressure of 1 atmosphere), but that is only true for large amounts of water. A drop of water only 5 nm across boils at 95.9 ºC. One nanoparticle can behave differently to another nanoparticle even if it is only slightly a different size. It may be a different colour, it may have a different melting point, or it may conduct electricity differently.

The study of objects and phenomena at a very small scale, roughly 1 to 100 nanometers (nm)

- 10 hydrogen atoms lined up measure about 1 nm

- A grain of sand is 1 million nm, or 1 millimeter, wide

What's interesting about the nanoscale?

- Nanosized particles exhibit different properties than larger particles of the same substance

- As we study phenomena at this scale we…

Learn more about the nature of matter

Develop new theories

Discover new questions and answers in many areas, including health care, energy, and technology

Figure out how to make new products and technologies that can improve people's lives

- The naked eye can see to about 20 microns
- A human hair is about 50-100 microns thick
- Light microscopes let us see to about 1 micron

Scanning electron microscopes (SEMs), invented in the 1930s, let us see objects as small as 10 nanometers

Higher resolution due to small size of electrons

Atomic Force Microscope (AFM)

A tiny tip moves up and down in response to the electromagnetic forces between the atoms of the surface and the tip

The motion is recorded and used to create an image of the atomic surface

Scanning Tunneling Microscope (STM)

A flow of electrical current occurs between the tip and the surface

The strength of this current is used to create an image of the atomic surface

Nano means a billionth (a billion is a thousand million) so

- A nanometre is a billionth of a metre

- A nanosecond is a billionth of a second.

Nanoscale_Properties

The fundamental properties of matter change at the nanoscale. The properties of atoms and molecules are not governed by the same physical laws as larger objects, but by quantum mechanics the physical and chemical properties of nanoparticles can be quite different from those of larger particles of the same substance. Altered properties can include but are not limited to colour, solubility, material strength, electrical conductivity, magnetic behavior, mobility (within the environment and within the human body), chemical reactivity and biological activity.

The Size of Atom:

An atom is important because it designates the ultimate particles in which matter exists. The smallest unit into which matter can be divided and building blocks of all matter comprised of a nucleus (at it's center) and an electron cloud.

A human hair is about 1 million carbon atoms wide.

A typical human cell contains roughly 1 trillion atoms.

A speck of dust might contain 3x10^{12} (3 trillion) atoms.

It would take you around 500 years to count the number of atoms in a grain of salt.

Physics at the Nanoscale:

Nanomaterials are closer in size to single atoms and molecules than to bulk materials. Molecule is the smallest part of a substance that retains all the properties of the substance without losing its chemical identity and is composed of one or more atoms. Quantum mechanics is a scientific model that was developed for describing the motion and energy of atoms and electrons. Due to the smallness of nanomaterials, their mass is extremely small and gravitational forces become negligible. Instead, electromagnetic forces are dominant in determining the behavior of atoms and molecules.

One of the consequences is a phenomenon called tunnelling. Tunnelling is a fundamental quantum effect and it is the basis of a very important instrument for imaging nanostructured surfaces called the Scanning Tunnelling Microscope (STM).

Quantum confinement: in a nanomaterial, such as a metal, electrons are confined in space rather than free to move in the bulk of the material.

Quantisation of energy: electrons can only exist at discrete energy levels. Quantum dots are nanomaterials that display the effect of quantisation of energy.

Random molecular motion: molecules move due to their kinetic energy. This is called random molecular motion and is always present. At the macroscale, this motion is very small compared to the sizes of the objects and thus is not influential on how the object moves. At the nanoscale, however, these motions can be of the same scale as the size of the particles and thus have an important influence on how they behave. One example of a random kinetic motion is Brownian motion.

Chemistry at the nanoscale:

It has already been stated that a nanomaterial is formed of at least a cluster of atoms, often a cluster of molecules. It follows that all types of bonding that are important in chemistry are also important in nanoscience.

They are generally classified as:

Intramolecular bonding (chemical interactions): these are bondings that involve changes in the chemical structure of the molecules and include ionic, covalent and metallic bonds;

Intermolecular bonding (physical interaction): these are bondings that do not involve changes in the chemical structure of the molecules and include ion-ion and ion-dipole interactions; van der Waals interactions; hydrogen bonds; hydrophobic interactions; repulsive forces (such as steric repulsions).

Nanomaterials often arise from a number of molecules held together or large molecules that assume specific three-dimensional structures through intermolecular bonding (macromolecules). Therefore, nanoscience also deals with supramolecular chemistry -- i.e. the chemistry that deals with interactions among molecules.

Intermolecular bondings, such as hydrogen bonding and van der Waals bonding are weak interactions but in a large number they can have a total energy that can be quite significant.

For instance, the structure of DNA (which has a cross-section of 2 nm): the two helixes are held together by numerous hydrogen bonds. One type of intermolecular bonding particularly significant in nanoscience is the hydrophobic effect. This is a process basically driven by entropy and which has a major role in biological materials. In simple terms, it is the property by which non-polar molecules (e.g. oil) tend to form aggregates of like molecules in water.

Material Properties:

Regardless of whether we consider a bulk material or a nanoscale material, its physical and chemical properties depend on many of its surface properties. Surfaces perform numerous functions: they keep things in or out; they allow the flow of a material or energy across an interface; they can initiate or terminate a chemical reaction, as in the case of catalysts.

The branch of science that deals with the chemical, physical and biological properties of surfaces is called surface science.

The importance of surface atoms:

In surface science, the chemical groups that are at the material interface determine its properties. Properties like catalytic reactivity, electrical resistivity, adhesion, gas storage and chemical reactivity depend on the nature of the interface. Nanomaterials have a significant proportion of atoms existing at the surface. The fact that in a nanomaterial a larger fraction of the atoms is at the surface influences some physical properties such as the melting point.

Surface energy: Atoms and molecules that exist at the surface or at an interface are different from the same atoms or molecules that exist in the interior of a material. Atoms and molecules at the interface have enhanced reactivity and a greater tendency to agglomerate: surface atoms and molecules are unstable, they have high surface energy. One of the ways of reducing the surface energy innanoparticles is agglomeration. The surface of 10 identical nanoparticles is equal to the sum of the surface energy of each individual nanoparticle. If these were to agglomerate, and become one large particle, the overall surface energy would be reduced.
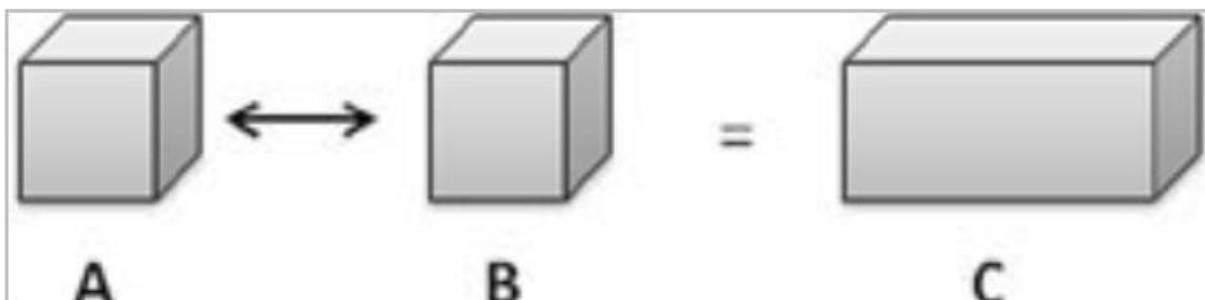
The surface energy of two separate cubes is higher than the surface energy of the two cubes agglomerated. Nanoparticles have a strong intrinsic tendency to agglomerate. To avoid this, surfactants can be used. This also explains why when nanoparticles are used in research and industry they are often immobilised on a solid support

or mixed within a matrix. Even in commercial products that claim to contain nanoparticles (such as sunscreens) microscope images show that they are actually present in the form of agglomerates of > 100 nm dimensions.

Shape also matters:

Given the same volume, the extent of the surface area depends on the shape of the material. A simple example is a sphere and a cube having the same volume. The cube has a larger surface area than the sphere. For this reason, in nanoscience, not only the size of a nanomaterial is important, but also its shape. Figure 4 illustrates this concept. In the section on catalysis, an example is given of a nanomaterial whose properties are determined not only by size but also by shape.

Figure 4: The ratio between the height (h) and the diameter (d) determines whether a shape is like a wire or a disc: shape influences surface area.
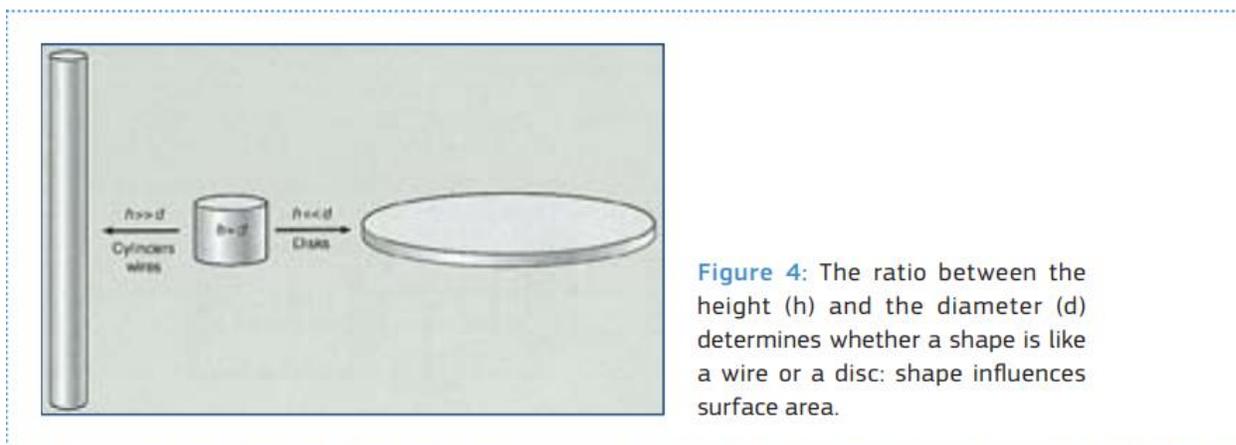
Electrical Properties:

There are three categories of materials based on their electrical properties: (a) conductors; (b) semiconductors; and (c) insulators. The energy separation between the valence band and the conduction band is called Eg (band gap). The ability to fill the conduction band with electrons and the energy of the band gap determine whether a material is a conductor, a semiconductor or an insulator.

In conducting materials like metals, the valence band and the conducting band overlap, so the value of Eg is small: thermal energy is enough to stimulate electrons to move to the conduction band. In semiconductors, the band gap is a few electron volts.

Quantum confinement:

The general principle is that confinement occurs if a characteristic size is less than or equal to the electron coherence length. Quantum confinement causes the energy of the band gap to increase. At very small dimensions when the energy levels are quantified, the band overlap present in metals disappears and is actually transformed into a band gap.

This explains why some metals become semiconductors as their size is decreased.The increase in band gap energy due to quantum confinement means that more energy will be needed in order to be absorbed by the band gap of

the material. The quantum confinement effect is observed when the size of the particle is too small to be comparable to the wavelength of the electron.

To understand this effect we break the words like quantum and confinement, the word confinement means to confine the motion of randomly moving electron to restrict its motion in specific energy levels(discreteness) and quantum reflects the atomic realm of particles. As the size of a particle decrease till we a reach a nano scale the decrease in confining dimension makes the energy levels discrete and this increases or widens up the band gap and ultimately the band gap energy also increases.

Optical properties:

Some nanomaterials display very different optical properties, such as colour and transparency, compared to bulk materials. The 'colour' of a material is a function of the interaction between the light and the object. If a material absorbs light of certain wavelengths, an observer will not see these colours in the reflected light. Only reflected wavelengths reach our eyes and this makes an object appear a certain colour. In general light (I) incident on a material can be transmitted (T), absorbed (A) or reflected (R):

I = T+A+R

As the size of the materials is reduced, scattering (S) of light can also contribute to its colour.

Reflection (R) occurs when light strikes a smooth surface and the incident wave is directed back into the original medium. The reflected wave has same geometrical structure as the incident wave.

Absorption (A) is a process that involves energy transformation. The energy levels of a substance determine the wavelengths of light that can be absorbed. It is a molecular phenomenon, dependent on the chemical identity and structure of the substance (not on the size of the molecules or clusters), and involves electronic transitions, vibrations and rotations. Chromophores and fluorephores are examples of organic materials that have specific electronic transitions.

Transmission (T) is the ability of light to pass through a material: it is complementary to absorption. Transmission of light is what is left after reflection, scattering and absorption have occurred.

Scattering (S) is the phenomenon that occurs when radiation hits a structure with dimensions comparable to the incident wavelength.

LSPR energy is sensitive to the dielectric function of the material and the surroundings, and to the shape and size of the nanoparticle. This means that if a ligand, such a protein, attaches to the surface of the metal nanoparticle, its LSPR energy changes. Similarly, the LSPR effect is sensitive to other variations such as the distance between the nanoparticles, which can be changed by the presence of surfactants or ions. The LSPR effect has been observed not only on metal nanoparticles but also in nanorings, voids in metal films and other nanostructures.

Magnetic properties:

The magnetic properties of a magnet are described by its magnetisation curve. In general terms, the magnetisation curve of a ferromagnetic material is a plot of the total magnetisation of the sample versus the applied DC field with strength H.

Ferromagnetism: Magnetic hysteresis

M_s – Saturation magnetization

M_{rs} – Saturation remanent magnetization

H_c – Coercive force (*the field needed to bring the magnetization back to zero*)
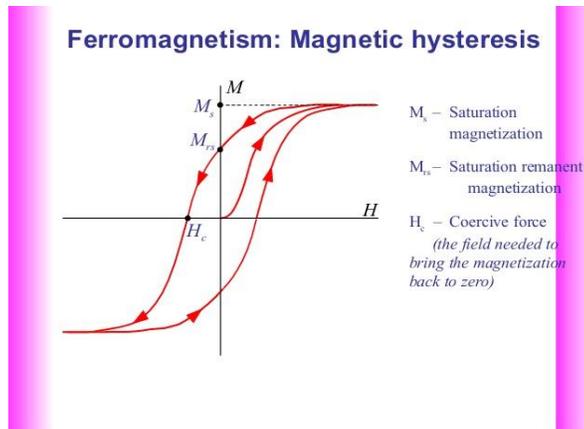
Initially, as H increases, M increases until a saturation point Ms is reached. When H is decreased from the saturation point, M does not decrease to the same value it had before: rather, it is higher on the curve of the decreasing field. This is called hysteresis.

When the applied field H is returned to zero, the magnet still has a magnetisation, referred to as remnant magnetisation M_r. In order to remove the remnant magnetisation, a field Hc has to be applied in the direction opposite to the field applied the first time. This field is called the coercive field.

The diverse applications of magnets require the magnetisation curves to have different properties. In general, for soft magnetic materials (e.g. those used in transformers and rotating electrical machinery), which are subject to rapidly alternating AC magnetic fields (so that they repeat the magnetisation curve many times), small or zero coercive fields are required to minimise the energy loss (in the form of heating) during operation. In the case of permanent magnets (hard magnets) used as part of high-field systems, large coercive fields are required and large hysteresis loops are sought, as well as high saturation magnetisations.

Mechanical properties:

Some nanomaterials have inherent exceptional mechanical properties which are connected to their structure. One such material is carbon nanotubes: these are extremely small tubes having the same honeycomb structure of graphite, but with different properties compared to graphite. Carbon nanotubes are 100 times stronger than steel but six times lighter. Nanomaterials can also be used to improve the mechanical properties of existing materials.

 In this case, nanocomposites are formed

Nanocrystalline materials, which are polycrystalline (i.e. made of many crystals which are identical but connected without orientation) and defined as materials with grain sizes from a few nanometres up to 100 nm. In contrast, the grain size in industrial metallic materials is about 10, 000 nm or greater. These materials generally show improved mechanical properties (toughness, hardness, etc.).

Overview of Nanomaterials:

Nanoscience will impact the design and fabrication of new materials with innovative properties and functions. Contributions to this field are very widespread, and include enhancing the properties of plastics, ceramics, coatings, composites, fibres and many more. Nanoscience also introduces an entirely new concept in material

design, the bottom-up approach of material self-assembly, which is directly inspired from how organic and inorganic materials are created in nature.

Nanostructured materials are solids or semi-solids (e.g. hydrogels, liquid crystals) characterised by a nano-sized inner structure. They vary differ from crystalline, microstructured and amorphous solids because of the scale order. In crystalline solids, the atoms are neatly arranged in a grid where the distance between neighbouring atoms is well defined, and this order extends to macroscopic dimensions. In contrast, microstructured materials show structural variation only on a micron scale, whereas amorphous materials exhibit short-range order only.

In nanostructured materials, the spatial order is at the nanoscale, which lies between the microscopic and the atomic scale. The size of the nanostructures and the scale order within them in the solid impacts the properties of a material. Nanostructured materials differ from conventional polycrystalline materials in the size of the structural units of which they are composed. Due to the large surface area, bulk properties become governed by surface properties. This surface — also called an interface — can form a border with the embedding matrix, a nanoparticle, air or vacuum in the case of a pore or defect.

Examples of nanostructured materials are nanoporous, nanocrystalline, nanocomposite and hybrid materials. **Nanoporous** materials have nano-sized pores. **Nanocrystalline** material consists of many nano-sized crystalline domains. One example is nanocrystalline materials, which are polycrystalline (i.e. made of many crystals which are identical but connected without orientation) and defined as materials with grain sizes from a few nanometres up to 100 nm. In contrast, the grain size in industrial metallic materials is about 10 000 nm or greater. These materials generally show improved mechanical properties (toughness, hardness, etc.).

Nanocomposite material contains two or more phaseseparated components with morphology of spheres, cylinders or networks with nano-sized dimensions (further divided into inorganic and polymer nanocomposites). **Hybrid** materials are made of a combination of organic and inorganic components interconnected at a molecular level (e.g. block copolymers).

One of the distinguishing features of nanostructured materials is that they can have properties that differ significantly from those displayed in bulk. This means that scientists have the opportunity to design new materials with specific functions by exploiting the intrinsic properties of nanomaterials. As a result, coatings, plastics and metals with new properties can be made to fulfil specific functions.

Biomimetic nanomaterials:

Biomimetics, also known as bionics, biognosis, or biomimicry, is the use and implementation of concepts and principles from nature to creating new materials, devices and systems. Nature is the best nanotechnology platform. Biomimetic materials are materials developed using inspiration from nature.

Biomimetics is the study of the formation, structure, or function of biologically produced substances and materials and biological mechanisms and processes especially for the purpose of synthesizing similar products by artificial mechanisms which mimic natural ones. There is significant current interest in bio-mimetic synthesis as technologies to underpin the development of processes which are modular, scalable and crucially accessible to the broad materials community.

The state of the art research, such as DNA nanotechnology (nanoscale fabrication using DNA building blocks) and DNA templated synthesis (in vitro replication, transcription and translation using DNA templates) currently all have a complete reliance on biological polymers. Knowing the structure and functions of biological molecules, we can synthesise hybrid molecules, including peptides, lipids and organic polymers, and develop biomimetic nanofibres, bioinorganic composites and nanoporous coatings for tissue engineering.

Biomimetic nanoparticles are under active development. For example, ferritin, a protein that transports and stores iron in an organism, forms nanocavities with an inner diameter of 8 nm. Magnetic nanoparticles of iron oxide and cobalt oxide with a mean size of 6 nm can be encapsulated in these nanocavities. Aapproaches employ "growing" nanoparticles of specific sizes inside bacteria or the biomass of plants (oats, wheat or alfalfa). Metal salts are added to these biological objects, and after biocatalitic reduction to metals they form nanoparticles. Methods of growing metallic nanoparticles in plants by adding metal salts to the irrigation water have been described. Nanoparticles are formed in the stems and other parts of plants and can be extracted. Utilizes biological mechanisms to create materials

   - Mimicking biological self-assembly processes

   - Using single biological units as a building block along with inorganic materials

Mimics biology at the molecular level

   - Synthesizing structures that mimic biological structures

Atom-precise manipulation yields composite materials and nano-scale structures with desirable properties

Parallel self-assembly processes achieve precision with high speed and reproducibility.
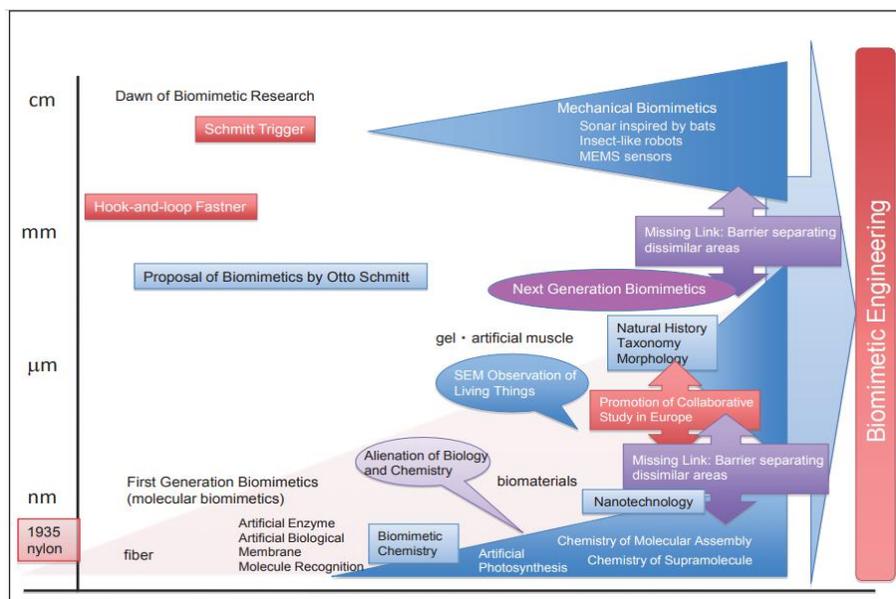
Biomimetic membranes, capsules and bioreactors

The bilipid membrane has served as a biomimetic model for decades. A simple example is liposomes (lipid vesicles) which are easily formed by shaking oil vigorously in water. Planar-supported bilayers are also inspired by the lipid membrane and are formed by simply 'dipping' a suitable substrate inside an organic aqueous phase.

> Inside the cell, there are numerous self-assembled structures that encapsulate specific biomolecules and release them as a consequence of molecular signalling. These structures are inspiring a wide range of nanocapsules for application in drug delivery. In some cases, bacteria or viruses are used as templates for fabricating these nanocapsules.

Gecko-inspired adhesive (or bio-rubber):

The adhesive properties of the gecko foot will discuss here. Specifically, how these are not related to a glue in the foot, but rather to van der Waals and capillary forces exerted by millions of nanostructures (called setae) that make up the foot. This allows the animal to walk upside down, against gravity and on many different surfaces, including those which are wet.

Scientists have been inspired by this animal to design and fabricate adhesives for numerous applications. A group of researchers at the University of California, Berkeley, has developed adhesive gecko-foot-like surfaces for use in climbing robots. The adhesive is made of patches of microfibre arrays with 42 million polypropylene microfibre per square centimetre. The patches can support up to 9 N cm-2: a 2 cm2 patch can support a load of 400 g. This result is very close to the loads supported by a gecko, which are about 10 N cm-2. This gecko-like adhesive is very similar in functionality to the natural gecko foot, but not as good—yet

Self-healing adhesives:

Diatoms are a type of algae with nanostructured amorphous silica surfaces. Diatoms are unicellular algae that have the capability to colonize any natural and man-made submerged surfaces. Diatoms are a large group of eukaryotic microalgae that have a rigid cell wall made of silica (SiO_2). Diatoms are often among the first organisms to colonize underwater surfaces, because their adhesive mucilage enables the cells to attach to substrata of a very wide range of chemical composition (organic, inorganic, natural or man-made).

Surface adhesion of diatoms belonging to the raphid pennate type requires the secretion of so-called adhesive mucilage strands through a dedicated slit in the silica cell wall, which is termed the raphe. Adhering cells can then move across the surface, which is accomplished through an actin-myosin dependent cytoskeletal motor that translocates the adhesive mucilage strands in a rearward direction through the raphe, thereby moving the cell forward. Some diatom species have evolved strong self-healing underwater adhesives. Some are free-floating, others have adhesive properties in water: for instance, diatoms in the Antarctic seas can attach to ice.

Others secrete viscous mucilage which binds colonies together while protecting the silica shells from wear as they rub against each other. Molluscs are another species that have adhesive properties under water. Both diatoms and molluscs have strong underwater glues that can also resist stress and self-heal. They serve as a biomimetic model for self-healing materials. These natural adhesives and their self-healing properties are due to the properties of the proteins contained in them. These proteins have sacrificial bonds that allow the molecule to be reversibly stretched by breaking and re-bonding.

This sacrificial bond behaviour has been observed in many other materials, such as wool. Closing the wounds with sticky materials has been introduced to prevent bleeding and induce the wound healing process. Many types of surgical adhesives including tissue adhesives have been developed to be a suitable alternative for sutures and staples. A new approach which aims at producing bio-adhesives by mimicking the nature along with applying nanotechnology methods. Engineering stable underwater adhesives currently poses a major technical challenge, because most man-made adhesives fail in wet conditions, owing to chemical modification of the adhesive or its substrate.

Diatoms produce adhesives that are extremely strong and robust, in both fresh- and seawater environments.

AFM (Atomic Force Microscopy) study of living diatoms, phase imaging and force spectroscopy experiments revealed characteristics of these natural adhesives that may be of use in designing man-made adhesive analogues that function in wet environments. The AFM allows for investigations of micromechanical properties of the cell surface, for example viscoeleastic properties, adhesion forces and hardness measurements, in physiological conditions. Experiments with three diatom species that produce outstanding natural adhesives: *Eunotia sudetica*, *Navicula seminulum* and an unidentified species

Self-assembled nanomaterials:

The concept of self-assembly derives from the observation that, in natural biological processes, molecules self-assemble to create complex structures with nanoscale precision. Examples are the formation of the DNA double helix or the formation of the membrane cell from phospholipids. Self-assembly is a process that builds an ordered structure, brick-by-brick, starting from disordered building blocks, using simple key ingredients.

Self-assembly is commonly controlled by certain intrinsic material parameters e.g., composition, strain, thickness, phase transformation, structural changes and results from the interaction between different factors e.g., deposit/substrate, liquid/gas/solid phases, crystals. A number of extrinsic factors, including thermal treatment, chemical and electrochemical reactions, mechanical stress, electric or magnetic fields, can strongly influence the self-assembled morphologies.

 In self assembly, sub-units spontaneously organise and aggregate into stable, well-defined structures through non-covalent interaction. This process is guided by information that is coded into the characteristics of the sub-units and the final structure is reached by equilibrating to the form of the lowest free energy. An external factor, such as a change in temperature or a change in pH, can disrupt this organisation. For instance, a protein self-assembles into a specific structure but, if exposed to conditions such as high heat or high acidity, it can denature, which means that its structure is damaged, and the protein unfolds. This means that the protein loses its function as its structure is damaged. So, in nature, self-organised structures have specific functions.

Nanoparticles have the ability to assemble chemically through covalent or noncovalent interactions with their capping ligand. The terminal functional group on the particle are known as capping ligands. These ligands tend to be complex and sophisticated, self-assembly can provide a simpler pathway for nanoparticle organization by synthesizing efficient functional groups.

DNA oligomers have been a key ligand for nanoparticle building blocks to be self-assembling via sequence-based specific organization.The successful design of ligand-building block units can play an essential role in manufacturing a wide-range of new nano systems, such as nanosensor systems, nanomachines/nanobots, nanocomputers.

Biomimetic membranes:

Mode of thinking that has given rise to the research and advancement of biomimetic membranes, an innovation in water filtration technology that aims to replicate a natural process occurring at the cell level - specifically, the highly-selective and efficient transport of water molecules across a cell membrane.

A promising approach to this concept is based on the use of aquaporin molecules, a naturally-existing protein that serves the important function of maintaining osmoregulation in living organisms by facilitating water transport through cell walls. Aquaporin molecule is the ability to restrict the passage of contaminants including bacteria, viruses, minerals, proteins, DNA, dissolved gases, salts, detergents, and even protons without encumbering the passage of water.

For the past several years, a number of research efforts have been underway in an attempt to utilize aquaporins in the development of a new biomimetic membrane technology. Biomimetic membranes hold considerable promise as a low-energy option and a more effective alternative to desalination, industrial water treatment and other water purification applications.

The Aquaporin Inside technology is essentially a thin film coating that hosts aquaporin proteins in an environment that retains the molecules natural activity of moving water molecules. The coating can be applied to both flat-sheet membranes and hollow fiber modules. The design approach to Applied Biomimetic's technology involves controlling the amount of integrated aquaporin proteins in order to design membranes to a specific permeability

Polyelectrolyte - Supported Lipid Bilayers:

Phospholipid membranes, as an important component of cell structures, can naturally create a boundary to separate the internal environment from the external environment of cells. To better understand the structure, function, and properties of biological membranes, researchers have attempted to develop various biomimetic models, well known as lipid vesicles (liposomes).

Due to the amphiphilic nature of lipid molecules, they can spontaneously form hollow spherical closed bilayers in water. Such biomimetic vesicles have not only served as model biological membranes in our outstanding of basic cell physiology, but have also been expanded to numerous applications such as drug vehicles, gene therapy, and nanoreactors.

Biomimetic energy nanomaterials:

Many challenges that we are now facing in the energy area (improvements needed in solar panels, hydrogen fuel cells, rechargeable batteries, etc.) can be solved through the use of nano-engineered materials. Some of these materials have been developed following direct inspiration from nature, such as the new types of solar photovoltaic cells, which try to imitate the natural nanomachinery of photosynthesis. Another interesting example is that of using battery electrodes with self-assembling nanostructures grown by genetic engineered viruses.

Self-assembled monolayers (SAMs):

Some organic molecules, when exposed from solution or vapour to a suitable substrate, self-assemble to produce homogeneous, densely packed layers of monomolecular thickness. These organic molecules have long chains with two different end groups. The monolayer is formed when one of the two end groups of the organic molecule reacts with a particular surface forming a chemical bond. The surface properties of the substrate are then defined by the exposed functional groups of the monolayer. For example, alkyl-silane or alkane thiol molecules exposed to a silica or metal surface assemble into organised layers.

SAM-forming materials may be physisorbed layers,

Langmuir-Blodgett films

Chemisorbed layers,

 - such as organosilanes bonded to silica or organothiols bonded to gold.

Films of mixed SAMs with tailored surface properties can be fabricated by mixing two (or more) precursor molecules and photosensitive SAM layers can be produced by molecularly engineering the precursor to include a photoreactive species. Whitesides and his co-workers from Harvard University have introduced the use of mixed SAMs of alkanethiols on gold surfaces to control protein and cell adhesion. SAMs of alkanethiol on gold are formed when a gold surface is exposed to a solution or to the vapour of an alkanethiol

Application:

SAMs are extremely useful in thin-film technology since they provide a simple, versatile and relatively inexpensive way of producing coatings with specific functionalities. Thin coatings are used in many applications, for example to control surface wetting and adhesion properties; to provide chemical resistance or specific biocompatibility; to confer antibacterial properties; and for sensors. SAMs are particularly interesting for developing DNA and protein micro and nanoarrays for medical and for future electronic components in computer chips and other ICT (Information and Communication Technologies) developments.

The sulphur atoms of the alkanethiols coordinate with the gold surface, while the alkyl chains are closely pack and tilted to 30° from the surface normal. The terminal end group of a ω-substituted alkanethiol determines the surface properties of the monolayer.
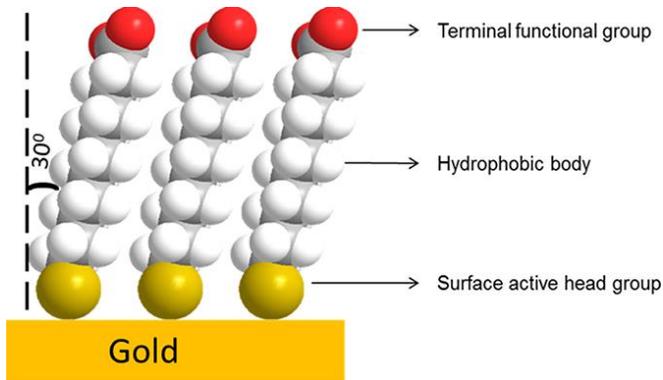
Surfaces with micron and nanopatterns of SAMs are interesting since they allow the creation of metallic hybrid circuits where biomolecules can be selectively attached (and released) to patterns of gold. Different methods exist for creating micro and nanopatterns of SAMs, such as microcontact printing (µCP), nanocontact printing (nCP), conventional lithography and Dip Pen Nanolithography.

Liquid crystals

A liquid crystal is a fourth state of matter: it has properties between those of a conventional liquid and those of a solid crystal. Like a liquid, it flows, and, like a crystal, it can display long-range molecular order (Figure 2).
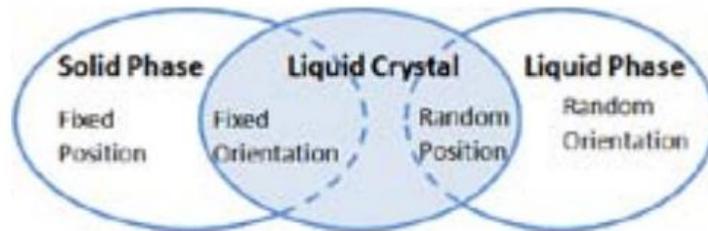
Figure 2: The liquid crystal phase is in between a solid and a liquid phase

Image: L. Filipponi, iNANO, Aarhus University, Creative Commons Attribution ShareAlike 3.0

In terms of classifications, liquid crystals (together with polymers and colloids), are often classified as soft matter and treated under the branch of physical chemistry of condensed matter. A stable phase of matter characterized by anisotropic properties without the existence of a 3-dimensional crystal lattice – generally lying between the solid and isotropic (liquid) phase.
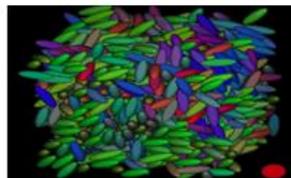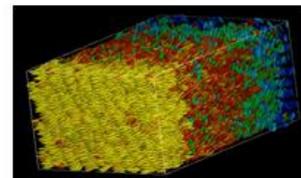
Liquid crystals Phase:

A fluid phase in which a liquid crystal flows and will take the shape of its container. It differs from liquid that there are still some orientation order possessed by the molecules.
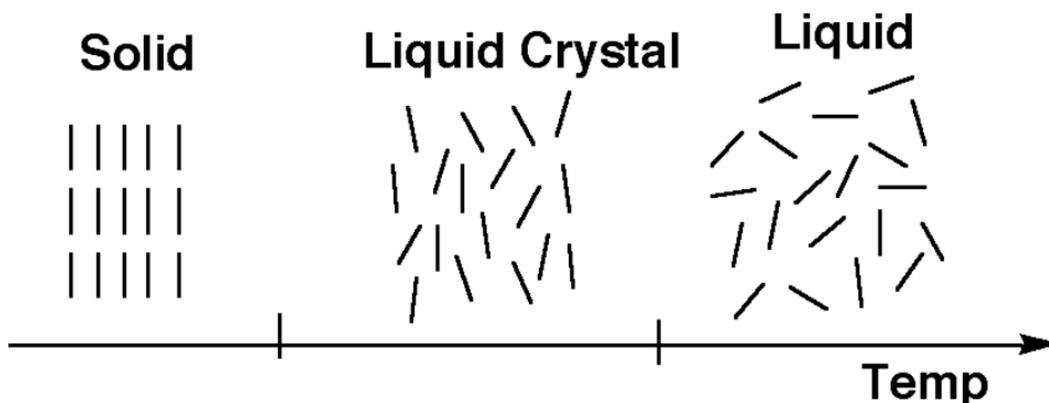
A phase that exists between solid and liquid. Discovered in 19th century when studying a cholesterol derivative.
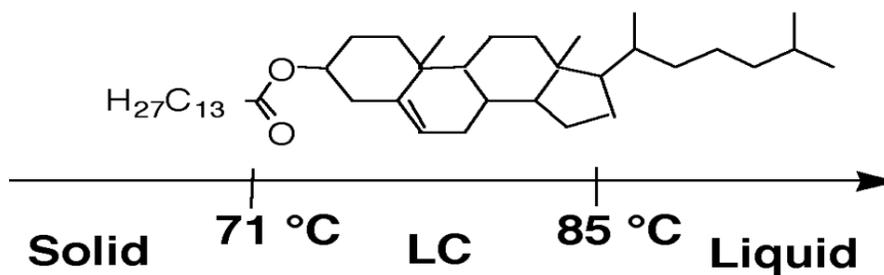
Nematic, Smectic & Cholesteric
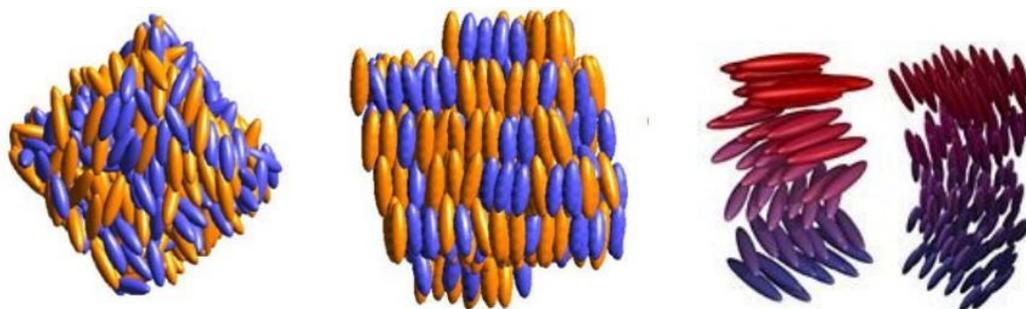
Anisotropic substances may go through one or several Liquid Crystal Phases

Nematic Phase: Molecules in this phase are long and rod-like in shape. They are free to move in space.

Smectic Phase: This phase can be reached at lower temperatures than the nematic phase. Molecules align themselves in layers. More order and higher viscosity

Cholestric Liquid Crystal: Molecules with intermolecular forces that favor alignment between molecules at a slight angle to one another. The director is not fixed in space as in a nematic phase, it rotates throughout the sample

pitch

Structure of the chiral nematic phase.
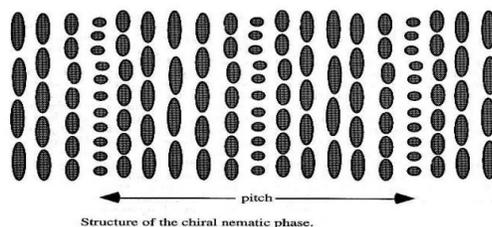
A fascinating and characteristic feature of liquid-crystalline systems is that they change their molecular and supermolecular organisation drastically as a result of very small external disturbances. The molecules in liquid crystal displays, for instance, are reoriented by relatively weak electrical fields.

If a small amount of chiral molecules are dissolved in an achiral liquid-crystalline host phase, remarkable macroscopic chirality effects occur, ranging from helical superstructures to the appearance of ferroelectricity.

Liquid crystal self-assembly:

Liquid crystals are partly ordered materials, somewhere between their solid and liquid phases. This means that liquid crystals combine the fluidity of ordinary liquids with the interesting electrical and optical properties of crystalline solids. Molecules of liquid crystals are often shaped like rods or plates or some other form that encourages them to align collectively along a certain direction.

Liquid crystals are temperature sensitive since they turn to solid if it is too cold and to liquid if it is too hot.

Example of the self-organisation of anisometric molecules in liquid-crystalline phases
Left: Rod-like molecules form a nematic liquid, in which the longitudinal axes of the molecules are aligned parallel to a common preferred direction (director).
Right: Disc-like (discotic) molecules arrange to molecule-stacks (columns), in which the longitudinal axes are also aligned parallel to the director. As a result of their orientational order, liquid crystals exhibit anisotropic physical properties, just like crystals.
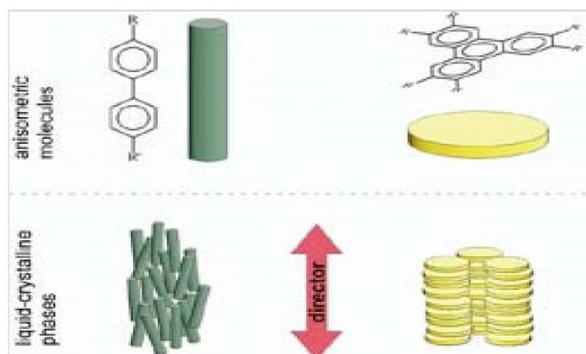
Phases of liquid crystals and their properties:

A liquid crystal is formed by the self-assembly of molecules into ordered structures, or phases. An external disturbance, such as a change in temperature or magnetic field, even very small, can induce the liquid crystal to assume a different phase. Different phases can be distinguished by their different optical properties.

Liquid crystals are divided into three groups:

thermotropic liquid crystals consist of organic molecules, typically having coupled double bonds, and exhibit a phase transition as temperature is changed (Figure 5, left)

lyotropic liquid crystals consist of organic molecules, typically amphiphilic (water-loving) and exhibit a phase transition as a function of both temperature and concentration of the liquid crystal molecules in a solvent (typically water) (Figure 5, right, and Figure 6)

metallotropic liquid crystals are composed of both organic and inorganic molecules, and their liquid crystal transition depends not only on temperature and concentration but also on the organic-inorganic composition ratio.

Liquid crystal applications:

The order of liquid crystals can be manipulated with mechanical, magnetic or electric forces. What is interesting is that this change of order can be obtained with very small variations of these forces.

The properties of liquid crystals are useful in many applications.

The colour of some liquid crystals depends on the orientation of its molecules, so any influence that disturbs this orientation (e.g. a difference in magnetic or electric field, temperature, or the presence of certain chemicals) can be detected with a colour change.

Liquid crystals are routinely used in displays for cell phones, cameras, laptop computers and other electronics. In these displays, an electric field changes the orientation of the molecules in the liquid crystal, and affects the polarisation of light passing through them.

Because of their sensitivity to temperature, and the property of changing colour, they are also used in thermometers. In miniaturised sensors, liquid crystals can detect certain chemicals, electric fields and changes in temperature.

Nanostructured metals and alloys:

Nanostructuring is the new and promising way to enhance the properties of metals and alloys for advanced structural and functional application. A nanostructured material is made of grains or other microstructural entities that have average size 100 nm or less in length at least in one dimension. Other entities include precipitates, second phase, a third phase, etc.

Gold	~ 35,000 years ago
Copper	~ 4,000 BC
Bronze (Cu–Sn)	~ 1,200 BC
Brass (Cu-Zn)	2,000 – 1,000 BC
Iron	~ 1,200 BC
Steel	~ 500 BC

Metal nanoparticles _ MNPs:

The term metal nanoparticleis used to described nanosizedmetals with dimensions (length, width or thickness) within the size range 1-100 nm.
The existence of metallic nanoparticlesin solution was first recognized by Faraday in 1857 and a quantitative explanation of their colourwas given by Mie in 1908. Metal nanoparticles are a clear example of how the properties of matter can change at the nanometre scale.

For instance, metal gold is notably yellow in colour and used for jewellery. As the noblest of all metals, gold is very stable. However, if gold is shrunk to a nanoparticle, it changes colour, becoming red if it is spherical and even colourless if it is shaped in a ring. Moreover, gold nanoparticles become very reactive and can be used as new catalysts

The main characteristics of MNPs:

large surface-area-to-volume ratio as compared to the bulk equivalents;

large surface energies

the transition between molecular and metallic states providing specific electronic structure (local density of states LDOS);

plasmon excitation;

quantum confinement;

short range ordering;

increased number of kinks;

a large number of lowcoordination sites such as corners and edges, having a large number of dangling bonds and consequently specific and chemical properties and the ability to store excess electrons.

Plasmonic structures:

Noble metal nanoparticles, meaning gold, silver, platinum and palladium nanoparticles, show localised surface plasmon-resonances (LSPR).The energy of the LSPR depends on the particle shape, size, composition, inter-particle spacing and dielectric environment.

The surface of the nanoparticles can be functionalised with numerous chemical and biochemical molecules enabling specific binding of organic molecules such as antibodies, making them useful in sensors. Special interest for optical detection and sensing in analytical chemistry and molecular biology.

 The refractive index can be used as the sensing parameter: changes in the local dielectric environment, induced by the sensing process, are used to detect the binding of molecules in the particle nano-environment.

The change in aggregation between the nanoparticles as a result of analyte attachment affects the LSPR energy, so this effect can be used for highly miniaturised sensors.

Reinforcements:

Metal nanoparticles are used as reinforcement in alloys for applications in lightweight construction within the aerospace sector and, increasingly, the automotive sector. The method is used, for example, to harden steel. Titanium nanoparticles are used as an alloy compound in steel, and the resulting material shows improved properties with respect to robustness, ductility, corrosion and temperature resistance. Particles of iron carbide are also precipitated in steel to make it harder. The nanoparticles block the movement of the dislocations in the crystalline material increasing the hardness.

Polymer:

A polymer is a large molecule made of a chain of individual basic units called monomers joined together in sequence. A copolymer is a macromolecule containing two or more types of monomers. When the polymer is a good conductor of electricity, it is referred to as conductive polymer (or organic metal).

Conductive polymers:

Polymers that are good conductors of electricity are called conductive polymers and include polyacetylene, polyaniline, polypyrrole, polythiophene. Characterised by their alternating double-single chemical bonds, so they are π-conjugated. They are responsible for the good electrical conduction properties of the material. Conductive polymers have revealed that these are made of a sequence of metallic nanoparticles about 10 nm in diameter. The high conductivity of polymers such as polyacetylene and polyaniline is related to the nanostructure of the polymer.

Block copolymers:

A copolymer is a macromolecule containing two or more types of monomers and a block copolymer comprises these basic units or monomer types joined together in long individual sequences called blocks. An example is the

diblock polymer (A)m(B)n, which is made of a linear sequence of m monomers of type A joined together to a linear sequence of n monomers of type B. Block copolymers are made of a hydrophilic (water-attractive) block, and a hydrophobic (water-repellent) block.

In general, macromolecules having hydrophilic and hydrophobic regions, such as lipids, self-assemble in ordered structures when in water, the hydrophobic region packs together, avoiding the water molecules, leaving the hydrophilic molecules to the exterior of the structure. The block copolymer can form spherical micelles (nanospheres), cylindrical micelles and membranes.

Both cylindrical and spherical micelles consist of a non-soluble (hydrophobic) core surrounded by a soluble corona. Membranes are made up of two monolayers of block copolymer aligned to form a sandwich-like membrane, soluble block-insoluble block-soluble block.
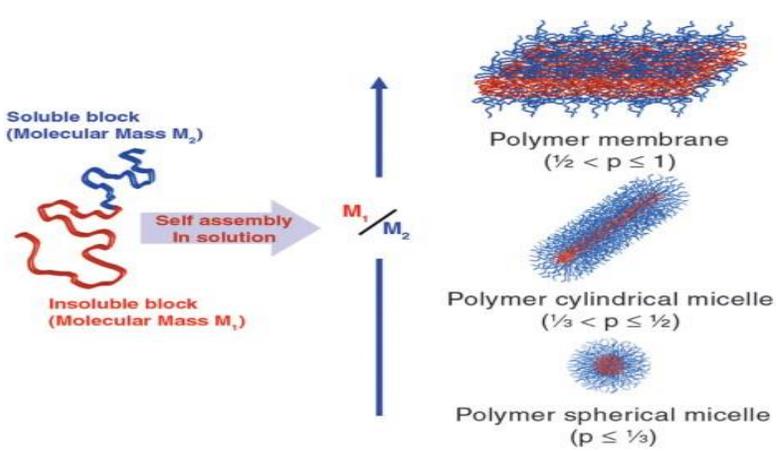
Biomedical applications:

The ability of block copolymers to form nanoparticles and nanostructures in aqueous solutions makes them particularly useful for biomedical applications, such as therapeutics delivery, tissue engineering and medical imaging. In the field of therapeutic delivery, materials that can encapsulate and release drugs are needed.

Hydrogels are very useful for the controlled release of drugs and block copolymer hydrogels are particularly advantageous for the possibility of conferring some stimuli-activated properties, such as temperature-sensitivity.

Block copolymers form nanostructures with both hydrophilic and hydrophobic areas, so they can form vesicles that can encapsulate and carry both hydrophobic and hydrophilic therapeutic agents. Micelles formed using block copolymers have a hydrophilic corona that makes them more resistant to the interaction of proteins, in particular plasma proteins; therefore, these types of micelles exhibit long circulation times in vivo.

Polymeric Nanofibers:

They are fiber with diameter in nanometer range. Many types of polymers were processed into nanofibers of 50 to 1000 nanometers in diameter, several orders of magnitude smaller than conventional fiber spinning. Nanostructured fibrous materials, or nanofibres, are an important class of nanomaterials, now readily available due to recent developments in electrospinning and related fabrication technologies.

Nanofibres have some unique properties:

they are highly porous. It is possible to increase the mechanical stability of nanofibrous structures by annealing the fabric so to join together the crossing points of those fibres. These properties make nanofibrous scaffolds useful for many biomedical and industrial applications.

Nanofibers:

➢   Properties

-large specific surface area

-high porosity

-small pore size

-diameter range (50 – 1000) nm

➢   Material

- Polymer solutions or melts

-More than 30 polymers, including polyethylene oxide, DNA, polyaramids, and polyaniline, have been electrospun.

- These fibers can be made of variety organic (nylon, polyester, acryl) or biological polymers (proteins, collagens).

- Peptide amphiphiles or cellulose.

Nanofiber Applications:

- Air and liquid filters
- Wound dressings
- Tissue enginnering
- Surface modifications
- Sound absorptive materials
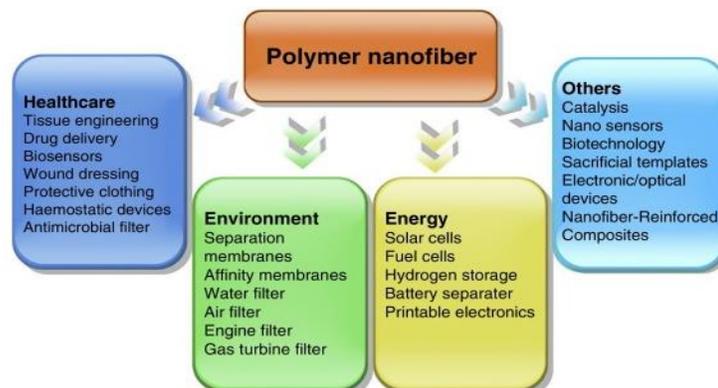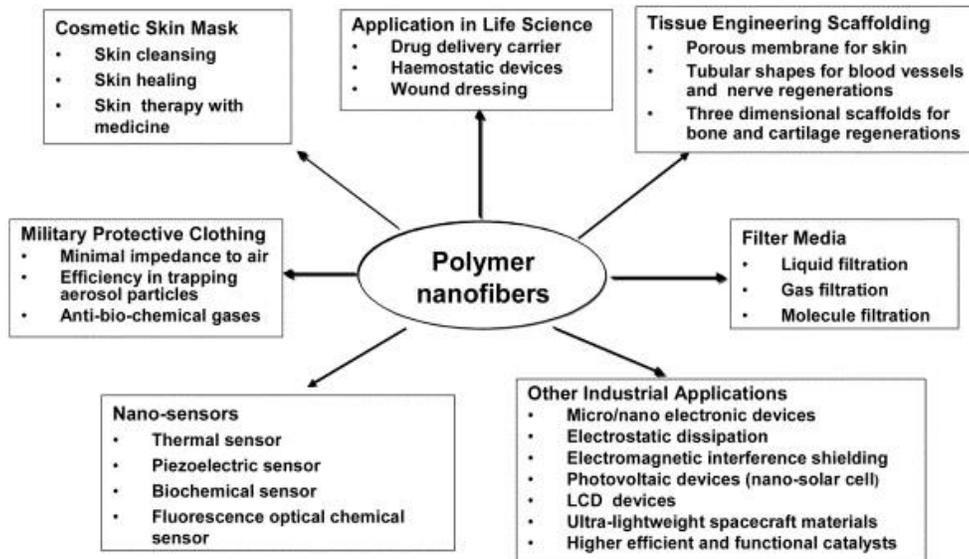
Semiconductors:

Semiconductors, unlike metals, have a band gap. The band gap is between the valence band and the conduction band. In intrinsic semiconductors which possess no impurities (e.g. boron, germanium, indium, silicon), there are no electronic states in the band gap. The properties of semiconductors, in particular the band gap, are manipulated by the addition of dopants — impurities able to donate charge carriers in the form of electrons (n-type) or holes (p-type).

Quantum dots:

Quantum dots are made of semiconductor materials, such as CdSe, ZnSe and CdTe. 10 nm in size

A quantum dot (QD) has a discrete quantised energy spectrum, so it can absorb a specific wavelength and emit a monochromatic colour. Depending on their size, QDs emit different colours.

Semiconducting oxides:

Semiconducting oxides like TiO2 and ZnO in bulk (macro) form are widely used in industry in many products.

Titanium dioxide:

Titanium dioxide (TiO2) is a mineral mainly found in two forms: rutile and anatase. Titanium dioxide is the most widely used white pigment because of its brightness (white colour) and very high refractive index (n = 2.4). It is used in paints, plastics, toothpastes, papers, inks, foods and medicines. In sunscreens with a physical blocker,

titanium dioxide is used both because of its high refractive index and its resistance to discolouration under ultraviolet light.

Titanium nanoparticles:

Titanium nanoparticles (30–50 nm, often referred to as nano-TiO2) are at the centre of much attention due to their optical and catalytic properties: they retain the ability to absorb UV light but light scattering is dramatically reduced, so that TiO2 goes from appearing white to transparent. Nano-TiO2 is thus suitable for transparent coatings, and for new-generation sunscreens, which are characterised by a high protective factor but transparent appearance. The catalytic properties of TiO2 when nanosized are also greatly enhanced by the large surface-to-volume ratio. This property is increasingly used for chemical catalysis applications such as photocatalytic purification of water and air to decompose organic pollutants (solar photocatalytic remediation). Thin films of TiO2 are used on windows to confer self-cleaning properties on the glass (this application of nano-TiO2 nanoparticles is reviewed in the section on nanocoatings).

Zinc dioxide:

Zinc oxide (ZnO) has some similar properties to TiO2 (i.e. its nanoparticles scatter light so it can be used for transparent UV filters, in creams or coatings). Like TiO2, it is used for solar photocatalytic remediation but, compared to TiO2, it has a weaker photocatalytic effect. ZnO is that it has a tendency to grow in self-organised nanostructures. Zinc oxide nanocolumns are of particular interest since low-temperature photoluminescence measurements have revealed intense and detailed ultraviolet light emission near the optical band gap of ZnO at 3.37 eV. ZnO can act as an optical amplification medium and as a laser resonator.

Indium tin oxide:

Indium tin oxide (ITO) is a semiconducting material whose main feature is the combination of electrical conductivity and optical transparency. ITO is typically around 90 % indium(III)-oxide (In2O3) and 10 % tin(V)-oxide (SnO2). It is widely used in its thin-film form as transparent electrodes in liquid crystal displays, touch screens, LEDs, thin-film solar cells, semiconducting sensors, etc.

ITO is an infrared absorber and is currently used as a thermal insulation coating on window glass. Its anti-static properties make it additionally useful in applications such as the packaging and storage of electronic equipment.

Ceramic and Glassy Materials:

Ceramic materials by definition are ionically bound; they are hard materials, both electrically and thermally very stable. Included in this category are, for example, Al2O3, Si3N4, MgO, SiO2, Na2O, CaO and ZrO2. Ceramics are characterised by being **hard yet brittle**, therefore, in many cases, they are used as **composites** where they are mixed with other materials (e.g. metals) to increase their mechanical performance. Ceramics exist both in a crystalline and non-crystalline

Porous alumina:

Porous alumina membranes produced by anodic aluminium oxidation are characterised by having hexagonally close-packed channels with diameters ranging from 10 to 250 nm or greater. This material is often used as a template for the synthesis of other materials.

Zeolites:

Zeolites are natural crystalline materials with pores having regular arrangements. They are also often used in the template synthesis of nanomaterial. Selenium can be incorporated into the channels of mordenite - a natural zeolite

Aerogels:

Silicon dioxide (SiO2) is the main component of quartz. It is chemically robust and finds widespread applications. Aerogels are manufactured with a sol-gel technique and can be made of carbon, metal oxide, polymers or silicates.

Due to their high porosity, aerogels have an extremely high surface area and very low thermal conductivity.

- Suitable for thermal insulation and as filter materials.
- Low specific weight _ making them interesting for lightweight construction.
- High optical transparencies.
- Silica aerogels are made of pores of about 10 nm arranged in distances between 10 and 100 nm.
- They are resistant and chemically inert to liquid metals, heat resistant up to 1 200 °C and non-toxic.
- Biomedical applications, such as substrates for cell growth and analysis.

Carbon based Materials:

➢ Carbon is the most important element for all living organisms in Earth, as most of the organic elements are made out of it.

➢ Carbon has attracted a great deal of interest in the scientific community due to the discovery of several allotropes (i.e., fullerenes, carbon nanotubes, graphene).

➢ Carbon-based nanomaterials demonstrate unprecedented physical and chemical properties such as

 - high strength,

 - excellent resistance to corrosion and exceptional electrical

 - thermal conduction and stability.

➢ Nano-carbon materials are used in a wide range of fields, including biology, energy storage and medicine.

➢ Graphite and diamond: two very popular materials, one used conventionally in pencils and the other in jewellery.

➢ These two materials could not be more different:

- graphite is soft, light, flexible, and conducts electricity

- while diamond is extremely strong, hard and does not conduct electricity.

> Both materials are made of carbon atoms linked through strong bonds (covalent).

> In graphite, each carbon atom uses three out of its four electrons to form single bonds with its neighbours, forming a linear sheet,

> Whereas, in diamond, each carbon atom uses all its four electrons to form four single bonds, resulting in a 3D structure.

Who found first nanotube?

1970: Morinobu Endo-- First carbon filaments of nanometer dimensions, as part of his PhD studies at the University of Orleans in France.

He grew carbon fibers about 7 nm in diameter using a vapor-growth technique. Filaments were not recognized as nanotubes and were not studied.

1991:Sumio Iijima-- NEC Laboratory in Tsukuba-- used high-resolution transmission electron microscopy to observe carbon nanotubes.

Carbon nanotube:

Carbon nanotubes are large molecules of pure carbon that are long and thin and shaped like tubes, about 1-3 nanometers (1 nm = 1 billionth of a meter) in diameter, and hundreds to thousands of nanometers long.

As individual molecules, nanotubes are 100 times stronger-than-steel and one-sixth its weight. Some carbon nanotubes can be extremely efficient conductors of electricity and heat; depending on their configuration, some act as semiconductors. A significant nanoparticle discovery that came to light in 1991 was carbon nanotubes. Where buckyballs are round, nanotubes are cylinders that haven't folded around to create a sphere. Carbon nanotubes are composed of carbon atoms linked in hexagonal shapes, with each carbon atom covalently bonded to three other carbon atoms.

Carbon Nanotubes (CNT) Properties:

- CNTs have High Electrical Conductivity
- CNTs have Very High Tensile Strength
- CNTs are Highly Flexible- can be bent considerably without damage
- CNTs are Very Elastic ~18% elongation to failure
- CNTs have High Thermal Conductivity
- CNTs have a Low Thermal Expansion Coefficient
- CNTs are Good Electron Field Emitters
- CNTs Aspect Ratio

Carbon Nanotubes (CNT):

Carbon nanotubes (CNTs) are allotropes of carbon. Carbon nanotubes can appear as single-wall nanotubes (SWNTs), with a diameter of approximately 1.4 nm. Multi-wall nanotubes (MWNTs), consisting of 2–30 concentric tubes with an outer diameter of 30–50 nm. The structure of an SWNT can be conceptualised by wrapping a one-atom-thick layer of graphite sheet (grapheme) into a cylinder.

To complete the nanotube, imagine adding two half fullerenes on each end of the nanotube. Nanotubes can be characterized by their number of concentric cylinders, cylinder radius and cylinder length. Some nanotubes have a property called chirality, an expression of longitudinal twisting. Multiple nanotubes can be assembled into microscopic mechanical systems called nanomachines.
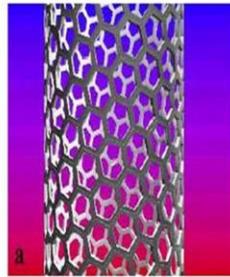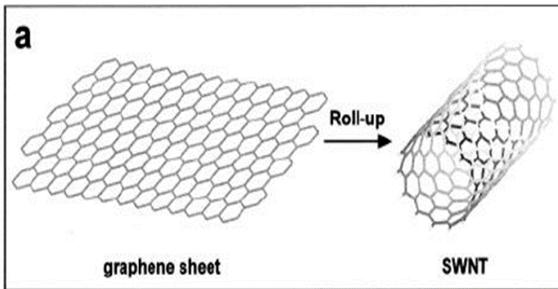
Schematic of a CNT
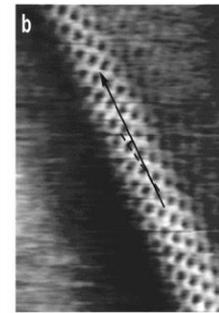
STM image of CNT

Nanotubes are formed by rolling up a graphene sheet into a cylinder and capping each end with half of a fullerene molecule.

Shown here is a (5, 5) armchair nanotube (top), a (9, 0) zigzag nanotube (middle) and a (10, 5) chiral nanotube.

The diameter of the nanotubes depends on the values of *n* and *m*.
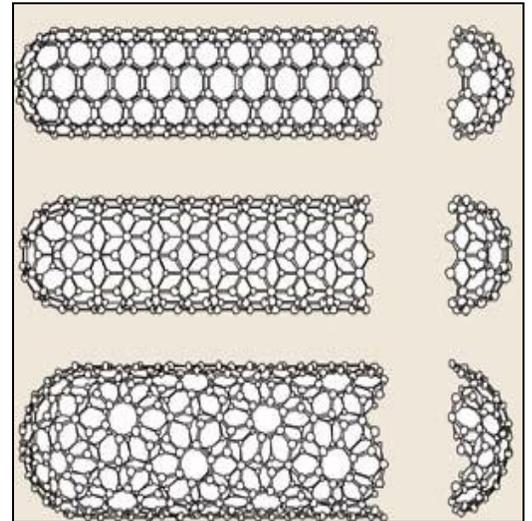
Carbon nanotube Properties:

Carbon Nanotubes are an example of true nanotechnology: they are less than 100 nanometers in diameter and can be as thin as 1 or 2 nm. They are molecules that can be manipulated chemically and physically in very useful ways. They open an incredible range of applications in materials science, electronics, chemical processing, energy management, and many other fields. Some properties include Extraordinary electrical conductivity, heat conductivity, and mechanical properties. They are probably the best electron field-emitter known, largely due to their high length-todiameter ratios.

As pure carbon polymers, they can be manipulated using the well-known and the tremendously rich chemistry of that element. Some of the above properties provide opportunity to modify their structure, and to optimize their solubility and dispersion.

Electrical Properties:

If the nanotube structure is armchair then the electrical properties are metallic. If the nanotube structure is chiral then the electrical properties can be either semiconducting with a very small band gap, otherwise the nanotube is a moderate semiconductor. In theory, metallic nanotubes can carry an electrical current density of $4{\times}10^9$ A/cm^2 which is more than 1,000 times greater than metals such as copper.
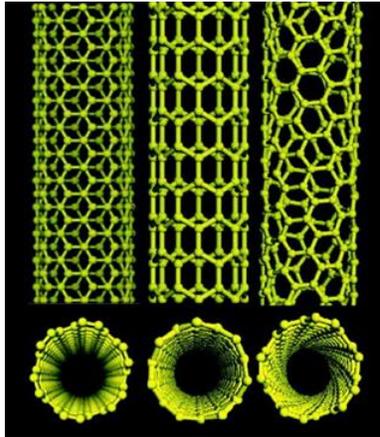
Thermal Properties:

All nanotubes are expected to be very good thermal conductors along the tube, but good insulators laterally to the tube axis. It is predicted that carbon nanotubes will be able to transmit up to 6000 watts per meter per Kelvin at room temperature; compare this to copper, a metal well-known for its good thermal conductivity, which transmits 385 watts per meter per K. The temperature stability of carbon nanotubes is estimated to be up to 2800°C in vacuum and about 750°C in air.

Strength and Elasticity:

Each carbon atom in a single sheet of graphite is connected via strong chemical bond to three neighboring atoms. CNTs can exhibit the strongest basal plane elastic modulus and hence are expected to be an ultimate high strength fiber. The elastic modulus of SWNTs is much higher than steel that makes them highly resistant.

Defects:

Defects can occur in the form of atomic vacancies. High levels of such defects can lower the tensile strength by up to 85%. Because of the very small structure of CNTs, the tensile strength of the tube is dependent on its weakest segment in a similar manner to a chain, where the strength of the weakest link becomes the maximum strength of the chain.

Health Hazards:

According to scientists at the National Institute of Standards and Technology, carbon nanotubes shorter than about 200 nanometers readily enter into human lung cells similar to the way asbestos does, and may pose an increased risk to health. Carbon nanotubes along with the majority of nanotechnology, are an unexplored matter, and many of the possible health hazards are still unknown.

Carbon nanotube Applications:

CNTs have not only unique atomic arrangements but also have unique properties that include large current carrying capability

- long ballistic transport length
- high thermal conductivity
- mechanical strength

These extraordinary properties of CNTs qualifies them exciting prospects and variety of applications in the area of microelectronics/nanoelectronics

- spintronics
- optics
- material science
- mechanical
- biological fields

Particularly, in the area of nanoelectronics, CNTs and graphene nanoribbons (GNRs) demonstrates wide range of applications such as

- -energy storage devices
- -energy conversion devices that includes thermoelectric
- -photovoltaic devices
- -field emission displays and radiation sources
- -nanometer semiconductor transistors
- -nanoelectromechanical systems (NEMS
- -electrostatic discharge (ESD) protection
- -interconnects and passive

Carbon nanotube Applications - Structural:

CNTs possesses remarkable properties and qualities as structural materials. Their potential applications include:

(a) Textiles—CNTs can produce waterproof and tear-resistant fabrics.

(b) Body armor—CNT fibers are being used as combat jackets. The jackets are used to monitor the condition of the wearer and to provide protection from bullets.

(c) Concrete—CNTs in concrete increases its tensile strength and halt crack propagation.

(d) Polyethylene—CNT fibers can be used as polyethylene. The CNT based polyethylene can increase the elastic modulus of the polymers by 30 %.

(e) Sports equipment—Golf balls, golf clubs, stronger and lighter tennis rackets, bicycle parts, and baseball bats.

(f) Bridges—CNTs may be able to replace steel in suspension and bridges.

(g) Flywheels—The high strength/weight ratios of CNTs enable very high rotational speeds.

(h) Fire protection—Thin layers of buckypaper can potentially protect the object from fire. The dense, compact layer of CNT or carbon fibers in the form of buckypaper can efficiently reflect the heat.

Carbon nanotube Applications - Electromagnetic:

CNTs can be fabricated as electrical conductors, semiconductors and insulators. Such applications include:

(a) Buckypaper—Thin nanotube sheets are 250 times stronger and 10 times lighter than steel. They can be used as heat sink for chipboards, backlight for LCD screens, or Faraday cage to protect electrical devices/aeroplanes.

(b) Light bulb filament—CNTs can be used as alternative to tungsten filaments in incandescent lamps

(c) Magnets—A strong magnetic field can be generated using multi-walled CNTs coated with magnetite

(d) Solar cells—Germanium CNT diode exploits the photovoltaic effect. In some solar cells, nanotubes are used to replace the ITO (indium tin-oxide) to allow the light to pass to the active layers and generate photocurrent

(e) Electromagnetic antenna—CNTs can act as an antenna for radio and other electromagnetic devices due to its durability, light weight and conductive properties.

Carbon nanotube Applications - Chemical:

CNTs finds tremendous applications in the chemical field also, few of them are as follows:

   (a) Air pollution filter—CNTs are one of the best materials for air filters because they possess high adsorption capacity and large specific area. The conductance of CNTs changes when polluted gas comes in its contact. This helps in detecting and filtering the polluted air. CNT membranes can successfully filter carbon dioxide from power plant emissions

(b) Water filter—CNT membranes can aid in filtration. It can reduce distillation costs by 75 %. These tubes are so thin that small particles (like water molecules) can pass through them, while blocking larger particles (such as the chloride ions in salt). CNTs have high active site and controlled distribution of pore size on their surface. This increases not only its sorption capabilities, but also its sorption efficiency. CNTs have effective sorption capacity over broad pH range (particularly for 7 to 10 pH).

(c) Chemical Nanowires—The CNTs finds their applications in nanowire manufacturing using materials such as gold, zinc oxide, gallium arsenide, etc. The gold based CNT nanowires are very selective and sensitive to hydrogen sulphide (H2S) detection. The zinc oxide (ZnO) based CNT nanowires can be used in applications for light emitting devices and harvesters of vibrational energy.

(d) Sensors—CNT based sensors can detect temperature, air pressure, chemical gases (such as carbon monoxide, ammonia), molecular pressure, strain, etc. The operation of a CNT based sensor is primarily dependent on the generation of current/voltage. The electric current is generated by the flow of free charged carrier induced in any material. This charge is typically modulated by the adsorption of a target on the CNT surface.

Composite:

The idea behind nanocomposites is to use building blocks with dimensions in the nanometre range to design and create new materials with unprecedented flexibility and improvements in their physical properties. This concept is exemplified in many naturally occurring materials, such as bone, which is a hierarchical nanocomposite built from ceramic tablets and organic binders. When designing the nanocomposite, scientists can choose constituents with different structures and composition and, hence, properties, so that materials built from them can be multifunctional.

Nanocomposites typically consist of an inorganic (host) solid containing an organic component or vice versa or two (or more) inorganic/organic phases in some combinatorial form. At least one component must be nano-sized. In general, nanocomposite materials can demonstrate different mechanical, electrical, optical, electrochemical, catalytic and structural properties which are different from those of the individual components.

 Apart from the properties of the individual components, interfaces in a nanocomposite play an important role in determining the overall properties of the material. Due to the high surface area of nanostructures, nanocomposites present many interfaces between the intermixed phases and, often, the special properties of the nanocomposite are a consequence of the interaction of its phases at interfaces.

Inorganic nanocomposites:

High-performance ceramics are sought in many applications, such as highly efficient gas turbines, aerospace materials, cars, etc. The field of ceramics that focuses on improving their mechanical properties is referred to as structural ceramics.

Nanocomposite technology is also applicable to functional ceramics such as ferroelectric, piezoelectric, varistor and ion-conducting materials. In this case, the properties of these nanocomposites relate to the dynamic behaviour of ionic and electronic species in electro-ceramic materials. Among these materials,in this document, the review is limited to nanocomposite with enhanced magnetic properties.

Polymer nanocomposites:

Polymer composites are materials where a polymer is filled with an inorganic synthetic and/or natural compound in order to increase several properties, such as heat resistance or mechanical strength, or to decrease other properties, such as electrical conductivity or permeability for gases like oxygen or water vapour.

Materials with synergistic properties are used to prepare composites with tailored characteristics; for instance, high-modulus but brittle carbon fibres are added to low-modulus polymers to create a stiff, lightweight polymer composite with some degree of toughness.

Current polymer composites are really filled polymers, since these materials lack an intense interaction at the interface between the two mixed partners. Although some nano-filled composites have been used for more than a century, such as carbon-black and fumed-silica-filled polymers, researchers have only recently started to systematically produce and study these materials.

One of the most common reasons for adding fillers to polymers is to improve their mechanical performance. Although the scientific community has made remarkable progress in this field in the last years, polymer nanocomposites have just started to be explored, and many research questions still need to be addressed.

What is clear so far is that the use of nanoscale fillers opens the way for the development of materials with exceptional properties. For instance, nanoparticles do not scatter light significantly, thus it is possible to make polymer composites with altered electrical or mechanical properties that remain optically clear. Nanoparticles are also of interest not just for their small size, but for their inherent unique properties.

Nanocoating:

Nanocoatings are a type of nanocomposite. The layer thickness of a nanocoating is usually 1–100 nm. A nanocoating refers to very fine, thin layers of polymeric chemical substances used to impart specific corrosion resistance, chemical and physical properties to a substrate surface.

Nanocomposite films include multilayer thinfilms, in which the phases are separated along the thickness of the film, or granular films, in which the different phases are distributed within each plane of the film. A nanocoating is the sealing of a material at the atomic level through methods such as atomic layer deposition (ALD). A nanocoating is a consistent network of molecules which arrange themselves to form a nanostructured network that is used to protect the material it is covering.

A nanocoating can be produced with utmost precision through a process which involves atomic building blocks, where atoms are deposited in a controlled fashion to produce a layer that conforms uniformly on every distinct feature of the surface.

There is a growing interest in the application of nanomaterials in building industry mainly because of their positively perceived characteristics including thermal properties, moisture behavior, energy efficiency, air quality improvement, self-cleaning, and anti-bactericidal effects. Nanocoatings make it possible to change the properties of some materials, for example to change the transmission of visible and IR radiation in glass, or to introduce new properties such as 'self-cleaning' effects.

Nano coatings are used on a wide variety of substrates, including metals, glass, ceramics and polymers. Some benefits of nanocoatings are:

- Reduced need for substrate maintenance activities to prevent corrosion
- Reduced labor and material costs
- Prolonged substrate lifespan and application use
- Increased substrate resistance to temperature fluctuations
- Substrate waterproofing
- Ultraviolet (UV) stability and abrasion resistance

Coating properties :

- Highly effective dirt-repellent, non-stick coatings resembling glass-ceramic or Teflon
- Hydrophilic, conductive, coloured, transparent or decorative ("soft feel") and corrosion-proof coatings
- High adhesion to the coating's chemical bond with the workpiece's surface
- High chemical and temperature resistance (up to 600°C)
- Diffusion barrier for certain metal ions
- Can be cleaned with very little effort

Nano-Particles for Coatings :

■ Inorganics
   ■ Colloidal Silica
   ■ Fumed Silica
   ■ Silicates
   ■ Titania
   ■ Alumina
   ■ Zinc Oxide
   ■ POSS

■ Organics
   ■ Acrylics
   ■ Urethanes
■ Carbon Black
■ Organo-Clay
■ Other

Nanocoating Applications:

Current applications for its technology are in the categories of Electronics, Lifestyle, Life Sciences, Filtration & Energy and Military & Institutional. Important area of application of nanocoatings is tribological coatings. Tribology is the science and technology of interacting surfaces in relative motion. Tribological properties include friction, lubrication and wear.

Tribological coatings are those coatings that are applied to the surface of a component in order to control its friction and wear. In this area, the term 'thin films' is often used as an alternative to nanocoatings. Traditional materials used in coatings for tribological applications are carbides, cemented carbides, metal ceramic oxides, nitrides and carbon-based coatings.

Responsive nanocoatings:

Responsive nanocoatings are those where the properties of the material in the coating react to environmental conditions, such as light or heat, either in a passive or an active way. These coatings allow the properties of some materials to change, such as glass, by conferring new or improved properties. The use of glass is very common in modern buildings, since it allows the construction of transparent and seemingly lightweight structures.

Low-e coatings are a type of passive nanocoatings, since the properties of the layers are undisturbed during its operation. Another class of coatings used in glasses are those often described as dynamic or smart coatings.

Smart coatings can also be passive in the sense of changing their optical properties due to a change of external temperature (thermochromic) or light incidence (photochromic).

Another example of nanotechnology applied to smart coatings is the use of a family of wavelength-selective films for manufacturing heat mirrors. One of these materials is indium tin oxide (ITO), an infrared absorber. A 300 nm ITO coating on glass provides more than 80 % transmission for the wavelengths predominant in sunlight.

Superhydrophilic coatings:

Photocatalytic coatings (commercialized as self cleaning glass) which use the catalytic properties of titanium dioxide (TiO2). When irradiated with UV light, the coating becomes superhydrophilic: therefore, rain water adheres to the glass providing 'selfcleaning'. Pilkington Activ™ Self-cleaning Glass is a commercial example of a glass with a photocatalytic coating that renders the material easier to clean.

Superhydrophilic coatings are also useful for rendering a surface fog-resistant. Substances that can be used as anti-fog agents include surfactants (e.g. soap), hydrogels, hydrophilic nanoparticles and colloids. The anti-fog agent creates a thin film that does not allow the formation of water droplets but rather 'forces' the water molecules to spread on the surface.

Superhydrophobic coatings:

Nanocoating is hydrophobic (water repellent), oleo phobic (oil repellent) surface layer that repels water, oil, dirt, and other dry particles.High hydrophobicity eco-friendly nano coating can be applied onto objects to make them waterproof for the long-term.The opposite to superhydrophilc coatings are superhydrophobic coatings, which totally repel water. Droplets of water on these surfaces have very high contact angles and 'bead-up' forming nearly spherical droplets. Superhydrophobic coatings have surfaces that mimic the surface found in the lotus leaf and are being developed for many applications that require resistance to dirt and ease of cleaning.
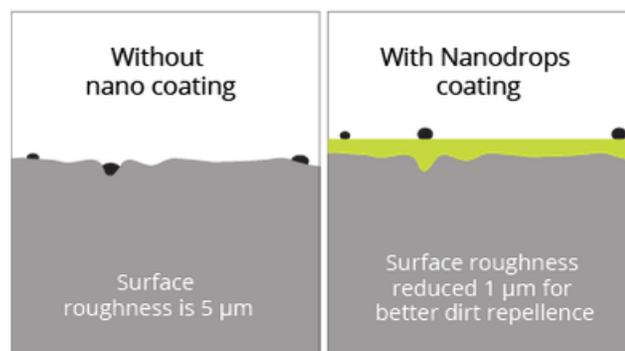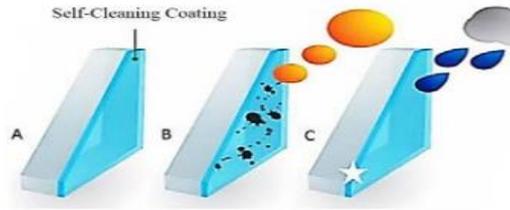
A Self-cleaning Glass System Based on Titanium Oxide (TiO$_2$) Thin Film Coating.
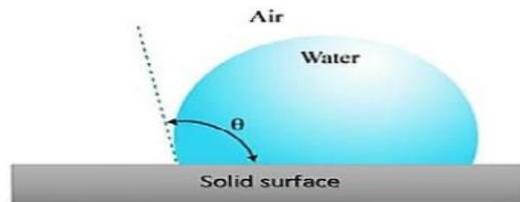
A Hydrophobic System Based on Silicon Oxide (SiO$_2$) Coated Surface.

Surface Engineering for Mechanical Enhancement of Cell Sheet by Nanocoatings:

Cell sheet technology is becoming increasingly popular in tissue engineering and regenerative medicine, due to integrity into versatile organ and manageable cell and tissue type from the bank, and no needs of large volume organ for transplantation. Cell-based therapies and tissue engineering are widely used in regenerative medicine.

Three-dimensional (3-D) biodegradable polymer scaffolds seeded with cells have been used for the regeneration of various host tissues, including bone, skin, cartilage, and heart tissues. However, artificial polymer scaffolds can lead to inflammatory responses and pathological fibrosis. Excessive connective tissue formation and insufficient cell-seeding are considered to be additional limitations to the use of scaffolds in regenerative medicine. Layer-by-layer (LbL) assembly of nanometer scaled film coating method was introduced to inter-planar cell sheet for multilayered cell sheet and a single cell before sheet formation.

LbL self-assembly technique is a widespread method of thin film fabrication that is based on alternate immersion into solutions of interactive materials. Nano-films with collagen and alginate increased mechanical property of cell sheets without altering cell functions, viability, and proliferation.

This integration with biological materials to cell sheet has a still room to be controlled with defined molecular layer in nano-meter scale, as regarding that oxygen transportation is limited due to the sheet thickness and its permeability after *in vivo* transplantation. The LbL assembly not only allows for nanometer-scale control over film thickness, but also can be performed on virtually any kind of substrate, even cell membranes. Through the LbL technique, multi-functional films can be manufactured from diverse materials, such as polymers, proteins, nanoparticles and therapeutics.

Characterization Method_ Microscope:

An optical microscope uses visible light (i.e. electromagnetic radiation) and a system of lenses to magnify images of small samples. For this reason, it is also called a light microscope. Optical microscopes are the oldest and simplest of the microscopes.

The resolution limit of an optical microscope is governed by the wavelength of visible light. Visible light is the part of the electromagnetic spectrum with wavelengths between 400 and 700 nm. The resolving power of an optical microscope is around 0.2 µm or 200 nm: thus, for two objects to be distinguishable, they need to be separated by at least 200 nm.

Single objects smaller than this limit are not distinguishable: they are seen as fuzzy objects. This is known as the diffraction limit of visible light. Other microscopes have been designed which use other beams: rather than light, they use electron beams to illuminate the sample.

Electron microscopes have much greater resolving power than light microscopes that use electromagnetic radiation and can obtain much higher magnifications of up to two million times, while the best light microscopes are limited to magnifications of 2 000 times.

There are various types of electron microscopes, such as the scanning electron microscope (SEM) and or the transmission electron microscope (TEM).

Scanning Tunnelling Microscope (STM) can create detailed 3D images of a sample with atomic resolution.

Scanning electron microscope (SEM)
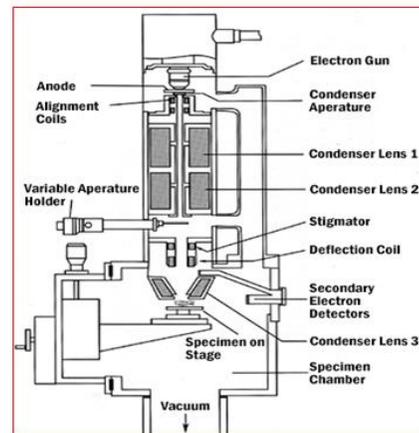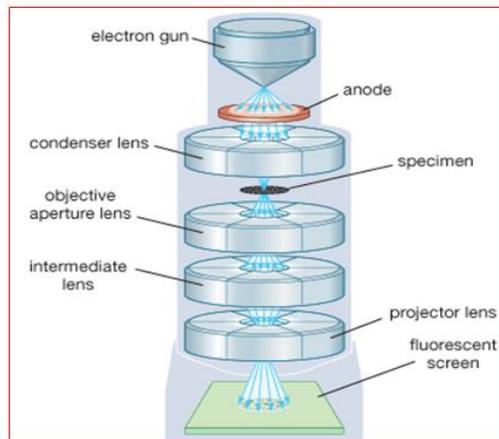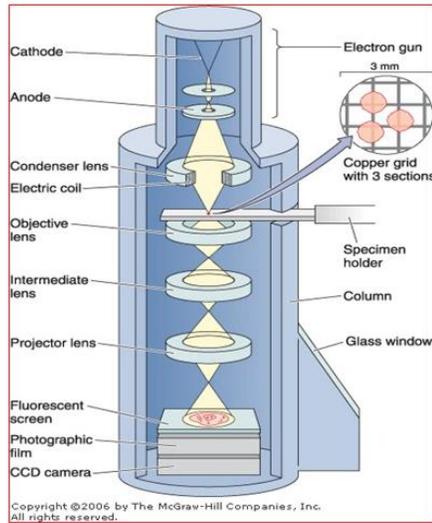
Transmission electron microscope (TEM)

Labels in diagram: Cathode, Anode, Condenser lens, Electric coil, Objective lens, Intermediate lens, Projector lens, Fluorescent screen, Photographic film, CCD camera, Electron gun, 3 mm, Copper grid with 3 sections, Specimen holder, Column, Glass window

There are various types of electron microscopes, such as the scanning electron microscope (SEM) and or the transmission electron microscope (TEM).

The resolution is actually so high that it is possible to see and distinguish the individual atoms (0.2 nm = 2 * 10-10 m) on the surface. Scanning tunnelling microscope is a fundamental tool in nanoscience and nanotechnologies. It is used in both industrial and fundamental research to obtain atomic-scale images of metal and semiconducting surfaces. STM can be used to manipulate (move!) individual atoms, trigger chemical reactions, as well as performing electronic spectroscopy.

STM is a Scanning Probe Microscopy (SPM) technique provides images of surfaces by scanning the surface line by line with a probe. The tip of an STM is about 3 mm (3 * 10-3 m) long and should be located very close to the surface to be scanned. In practice, the distance between the end of the tip and the surface must be less than 0.1 nm (10-10 m), without the tip actually hitting the surface.

To visualise how small and precise this actually is, it corresponds to placing the 300 m tall Eiffel Tower (3 * 102 m) top down with a distance of 0.01 mm (1 * 10-5 m) over a neighborhood and scanning across it without actually touching it.
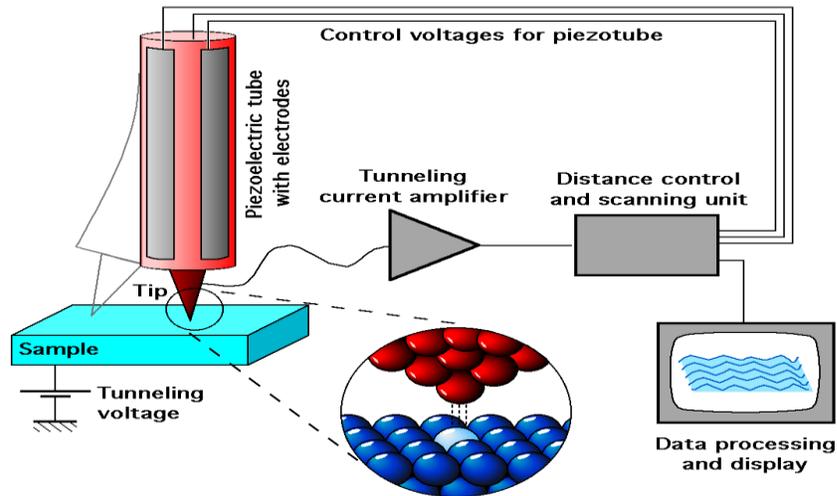
The Atomic Force Microscope (AFM) was developed specifically to overcome the intrinsic limitations of the STM, which is not suitable for imaging surfaces coated with biological entities such as DNA or proteins.

The AFM operates in air and not under a vacuum. The AFM measures the interaction force (attractive or repulsive) between the probe and the surface. The probe is continuously moved along the surface and the cantilever deflection is constantly monitored. The vertical movement of the probe is recorded to create a topographic map of the surface under study.

The AFM probe tip is very sharp, with a radius of curvature in the range of tens of nanometres. If the surface under analysis is soft, the probe can penetrate it, with the risk of damaging it and degrading the spatial resolution of the resulting micrograph.
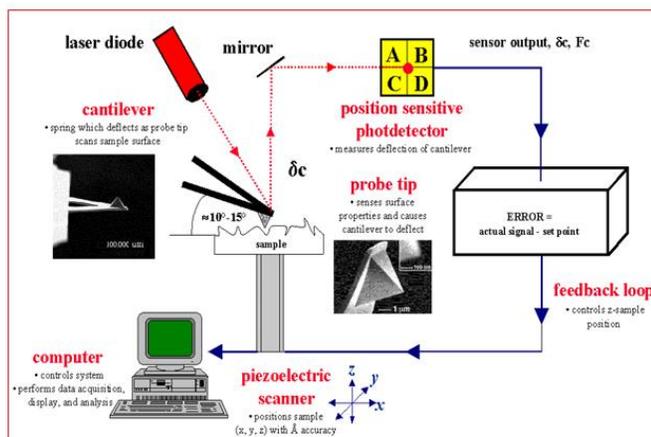
Atomic Force Microscopy (AFM)
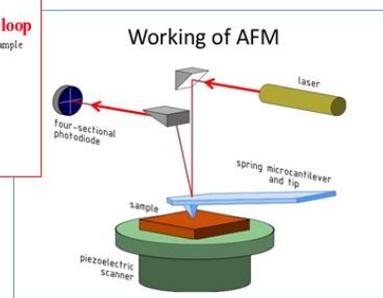
Characterization Method_ Spectroscopy:

Spectroscopy is defined as the branch of science that is concerned with the investigation and measurement of spectra produced when matter interacts with or emits electromagnetic (EM) radiation. Spectroscopy is a technique that uses the interaction of energy with a sample to perform an analysis.

Depending on the wavelength of the electromagnetic used and the type of interaction with matter that occurs (absorption, scattering, etc.), different spectra are measured from which much information can be inferred.
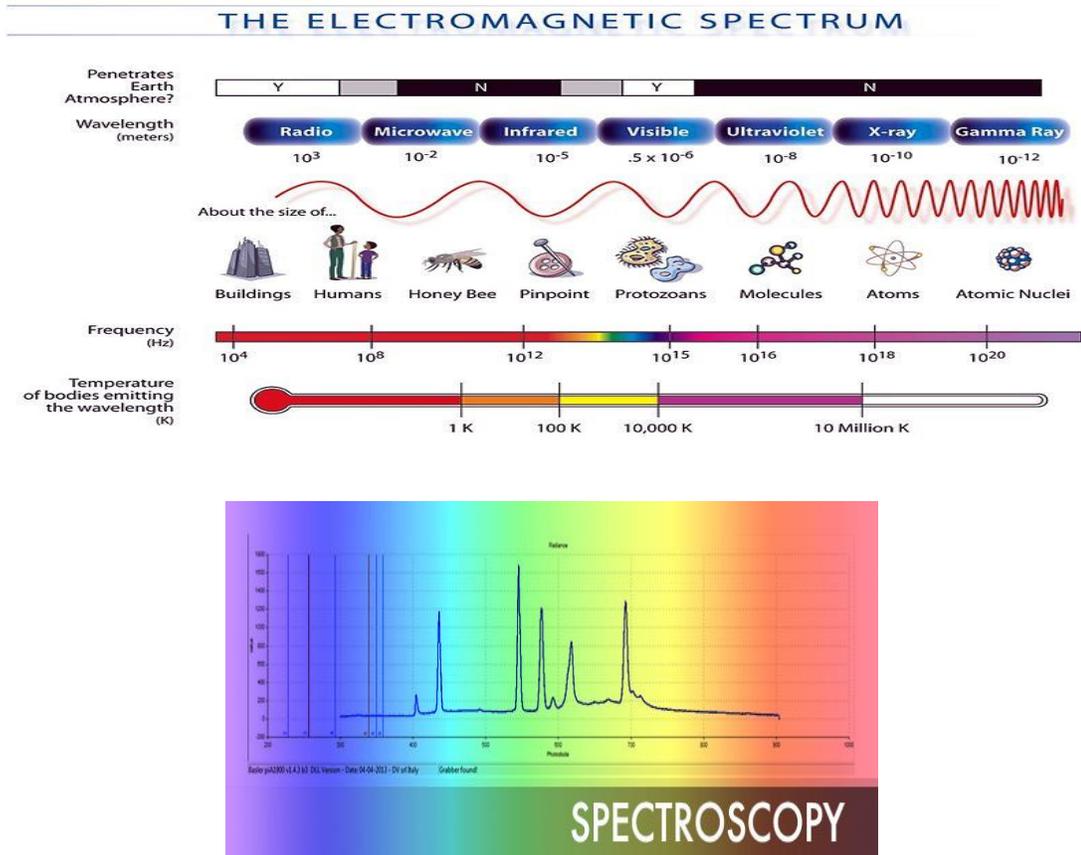
X-ray method:

X-rays were discovered in 1895 by German physicist Roentgen. X-ray methods involve exciting a sample either with X-rays (creating more X-rays) or with electrons (creating X-rays). X-rays can be also generated by bombarding a sample with alpha particles. The energy of emitted X-rays is equal to the difference between the binding energies of the electrons involved in the transition.

There are various methods that use X-rays: X-ray fluorescence (XRF), X-ray diffraction (XRD), etc. In the context of nanomaterials, the most important method is small-angle X-ray scattering (SAXS) analysis. Like XRD, this method is based on the principle of scattering of X-rays.

X-ray System

Produces X-rays from electrical energy

Tailors X-ray spectrum

Converts X-rays to light and records

Source

Restrictor (Collimator)

Filter

Subject

Anti-scatter

Detector

Determines size and shape of beam

Selectively removes scattered photons
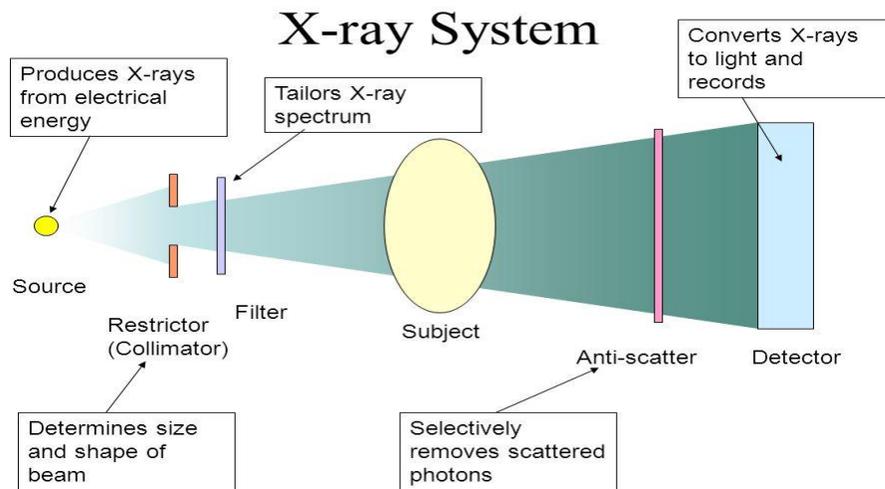
Spanning a wide range of research fields, such as biology, chemistry, physics, and engineering, nanotechnology is uniquely interdisciplinary in character. The common factor in nanotechnology is the lateral dimension of the structures studied. Defined as materials being in, or having components in, the one billionth (10-9) of a meter range, nanotechnology research and development relies on accurate measurement of atomic and molecular distances within structures ranging from semiconductor devices to nano-powders.

The dimensions of X-ray wavelengths are of the same magnitude as the size of nanostructures, X-ray diffraction (XRD) and associated techniques are primary tools for the nanotechnology researcher. X-ray reflectometry (XRR) determines layer thickness, roughness, and density. High-resolution X-ray diffraction can measure layer thickness, roughness, chemical composition, lattice spacing, relaxation and more.

X-ray diffuse scattering is used to determine lateral and transversal correlations, distortions, density, and porosity. A new advance in X-ray imaging has revealed the dramatic three-dimensional shape of gold nanocrystals, and is likely to shine a light on the structure other nano-scale materials. The new technique improves the quality of nanomaterial images, made using X-ray diffraction, by accurately correcting distortions in the X-ray light.

Most nanomaterial imaging has been done using electron microscopy. X-ray imaging is an attractive alternative as X-rays penetrate further into the material than electrons and can be used in ambient or controlled environments.

SENSORS:

A sensor is a device capable of recognizing a specific chemical species and signaling the presence, activity or concentration of that species in solution through some chemical change. A sensor is a device that detects and responds to some type of input from the physical environment.

The specific input could be light, heat, motion, moisture, pressure, or any one of a great number of other environmental phenomena. The output is generally a signal that is converted to human-readable display at the sensor location or transmitted electronically over a network for reading or further processing.

Sensors are sophisticated devices that are frequently used to detect and respond to electrical or optical signals. A Sensor converts the physical parameter (for example: temperature, blood pressure, humidity, speed, etc.) into a signal which can be measured electrically.
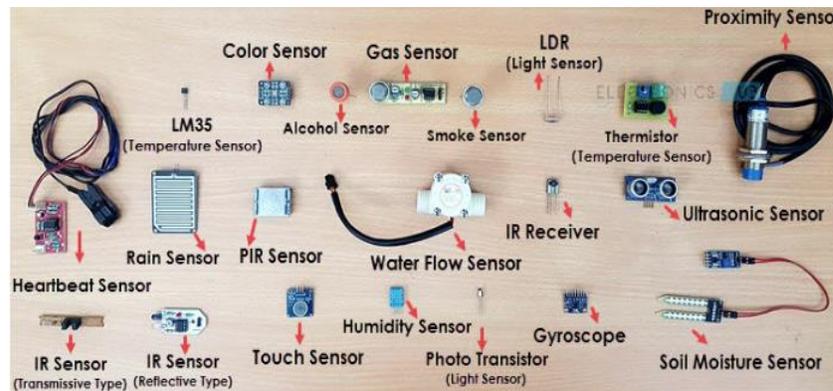
Criteria to choose a Sensor

There are certain features which have to be considered when we choose a sensor. They are as given below:

1. Accuracy

2. Environmental condition - usually has limits for temperature/ humidity

3. Range - Measurement limit of sensor

4. Calibration - Essential for most of the measuring devices as the readings   changes with time

5. Resolution - Smallest increment detected by the sensor

6. Cost

7. Repeatability - The reading that varies is repeatedly measured under the same environment

BIOSENSORS:

Biosensor = bioreceptor + transducer.

A device that utilizes biological components e.g. enzymes to indicate the amount of a biomaterial. A biosensor is an analytical device, used for the detection of an analyte, that combines a biological component with a physicochemical detector.

The bioreceptor is a biomolecule that recognizes the target analyte whereas the transducer converts the recognition event into a measurable signal. The sensitive biological element (e.g. tissue, microorganisms, organelles, cell receptors, enzymes, antibodies, nucleic acids, etc.) is a biologically derived material or biomimetic component that interacts (binds or recognizes) with the analyte under study.

Parts of a biosensor:

Every biosensor comprises:

- -A biological component that acts as the sensor
- -An electronic component that detects and transmits the signal

Biosensor elements:

-A variety of substances may be used as the bioelement in a biosensor. Examples of these include:

- Nucleic acids
- Proteins including enzymes and antibodies. Antibody-based biosensors are also called immunosensors.
- Plant proteins or lectins
- Complex materials like tissue slices, microorganisms and organelles

Enzyme is a Bioreceptor:

When we eat food such as a hamburger and French fries, they are broken down into small molecules in our body via many reaction steps (these breakdown reactions are called catabolism). These small molecules are then used to make building blocks of our body such as proteins (these synthesis reactions are called anabolism).

 Each of these catabolism and anabolism reactions (the combination is called metabolism) are catalyzed by a specific enzyme. Therefore, an enzyme is capable of recognizing a specific target molecule. This bio recognition capability of the enzyme is used in biosensors. Other bio recognizing molecules (= bio receptors) include antibodies, nucleic acids, and receptors.
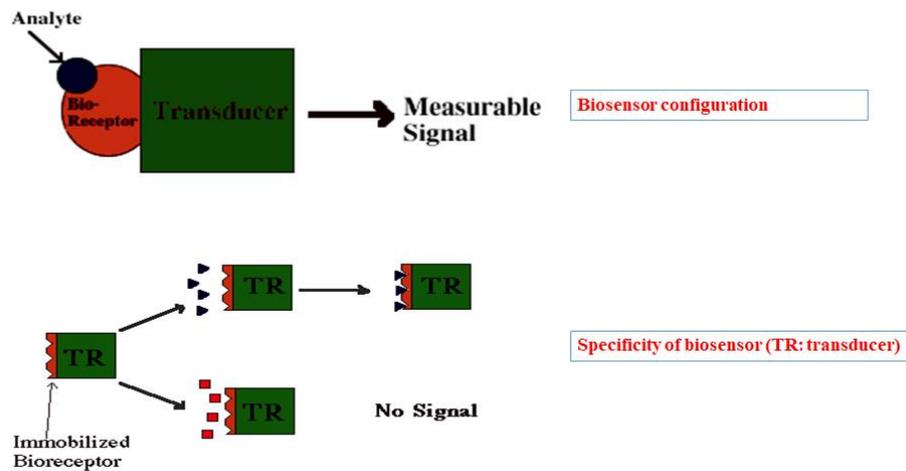
Immobilization of Bioreceptor:

One major requirement for a biosensor is that the bioreceptor molecule has to be immobilized in the vicinity of the transducer. The immobilization is done either by physical entrapment or chemical attachment.

Note that only minute quantities of bioreceptor molecules are needed, and they are used repeatedly for measurements.

Transducer:

A transducer should be capable of converting the biorecognition event into a measurable. Typically, this is done by measuring the change that occur in the bioreceptor reaction.

For example, the enzyme glucose oxidase (used as a bioreceptor in a glucose biosensor) catalyzes the following reaction:

Glucose + O2 --------> Glucosnic acid + H2O2

To measure the glucose concentration, three different transducers can be used:

- An oxygen sensor that measures oxygen concentration
- A pH sensor that measures the acid (gluconic acid) production
- A peroxide sensor that measures H_2O_2 concentration.
- An oxygen sensor is a transducer that converts oxygen concentration into electrical current.
- pH sensor is a transducer that converts pH change into voltage change.
- A peroxidase sensor is a transducer that converts peroxidase concentration into an electrical current.

Cholesterol monitoring:

1) Low incentive to use (effects are long term)

2) Cost high

3) What do you do with the information?

4) Learnt nothing from the Glucose industries development.

Considerations in Biosensor Development:

Once a target analyte has been identified, the major tasks in developing a biosensor involves:

1. Selection of a suitable bioreceptor molecule

2. Selection of a suitable immobilization method

3. Selection of a suitable transducer

4. Designing of biosensor considering measurement range, linearity, and minimization of interference

5. Packaging of biosensor

There are numerous nanoparticles that can be used as biosensor components.

These work as probes recognizing an analyte or differentiating between analytes of interest. In such applications, some biological molecular species are attached to the surface of the nanoparticles to recognize the target of interest through a lock-and-key mechanism.

The probes then signal the presence of the target by a change in colour, mass or other physical change. Nanoparticles used as elements for biosensors include quantum dots, metallic nanoparticles, silica nanoparticles, magnetic beads and fullerenes, which are hollow cages of carbon atoms, shaped like footballs.

Carbon nanotubes and nanowires are also employed for sensing. The latter can be fabricated out of a semiconductor material and their size tuned to have a specific conducting property. This, together with the ability to bind a specific analyte on their surface, yields a direct, label-free electrical read-out. These nanowire biosensors allow the detection of a wide range of chemical and biological species, including low concentrations of protein and viruses, and their application ranges from the medical to the environmental sector.

Other biosensors use nanostructured particles as nano-sieves through which charged molecules are transported in an electric field. In this case, particles with engineered nanopores are used. Nanoscale biosensors have the potential to greatly aid in the diagnosis of diseases and monitoring of therapies.

A large number of approaches have been developed in recent years while relatively few have so far been converted into clinical diagnostic tools — their wide application in patient care is foreseen in the next 5–10 years.

Basic Characteristics of a Biosensor:

1. LINEARITY: Linearity of the sensor should be high for the detection of high substrate concentration.

2. SENSITIVITY: Value of the electrode response per substrate concentration.

3. SELECTIVITY: Chemicals Interference must be minimized for obtaining the correct result.

4. RESPONSE TIME: Time necessary for having 95% of the response

Selectivity:

Selectivity is perhaps the most important feature of a biosensor. Selectivity is the ability of a bioreceptor to detect a specific analyte in a sample containing other admixtures and contaminants. The best example of selectivity is depicted by the interaction of an antigen with the antibody.

Classically, antibodies act as bioreceptors and are immobilised on the surface of the transducer. A solution (usually a buffer containing salts) containing the antigen is then exposed to the transducer where antibodies interact only with the antigens. To construct a biosensor, selectivity is the main consideration when choosing bioreceptors.

Reproducibility:

Reproducibility is the ability of the biosensor to generate identical responses for a duplicated experimental set-up. The reproducibility is characterized by the precision and accuracy of the transducer and electronics in a biosensor.

Precision is the ability of the sensor to provide alike results every time a sample is measured and accuracy indicates the sensor's capacity to provide a mean value close to the true value when a sample is measured more than once. Reproducible signals provide high reliability and robustness to the inference made on the response of a biosensor.

Stability:

Stability is the degree of susceptibility to ambient disturbances in and around the biosensing system. These disturbances can cause a drift in the output signals of a biosensor under measurement. This can cause an error in the meas-ured concentration and can affect the precision and accuracy of the biosensor. Stability is the most crucial feature in applications where a biosensor requires long incubation steps or continuous monitoring. The response of transducers and electronics can be temperature-sensitive, which may influence the stability of a biosensor.

Sensitivity:

Value of the electrode response per substrate concentration. The minimum amount of analyte that can be detected by a biosensor defines its limit of detection (LOD) or sensitivity. In a number of medical and environmental monitoring applications, a biosensor is required to detect analyte concentration of as low as ng/ml or even fg/ml to confirm the presence of traces of analytes in a sample.

For instance, a prostate-specific antigen (PSA) concentration of 4 ng/ml in blood is associated with prostate cancer for which doctors suggest biopsy tests. Hence, sensitivity is considered to be an important property of a biosensor.

Linearity:

Linearity is the attribute that shows the accuracy of the measured response (for a set of measurements with different concentrations of analyte) to a straight line, mathematically represented as $y=mc$, where c is the concentration of the analyte, y is the output signal, and m is the sensitivity of the biosensor.

Linearity of the biosensor can be associated with the resolution of the biosensor and range of analyte concentrations under test. The resolution of the biosensor is defined as the smallest change in the concentration of an analyte that is required to bring a change in the response of the biosensor.

Depending on the application, a good resolution is required as most biosensor applications require not only analyte detection but also measurement of concentrations of analyte over a wide working range.

Biosensors: Classification based on transducers

There are different types of Biosensors based on the sensor devices and the biological materials and some of them are discussed in this class.

Optical sensors:

An optical sensor converts light rays into an electronic signal. The purpose of an optical sensor is to measure a physical quantity of light and, depending on the type of sensor, then translates it into a form that is readable by an integrated measuring device.

Optical Sensors are used for contact-less detection, counting or positioning of parts. Optical sensors can be either internal or external. External sensors gather and transmit a required quantity of light, while internal sensors are most often used to measure the bends and other small changes in direction.

The measured possible by different optical sensors are Temperature, Velocity Liquid level, Pressure, Displacement (position), Vibrations, Chemical species, Force radiation, pH- value, Strain, Acoustic field and Electric field.

Types of Optical Sensors:

There are different kinds of optical sensors, the most common types which we have been using in our real world applications as given below. Photoconductive devices used to measure the resistance by converting a change of incident light into a change of resistance. The photovoltaic cell (solar cell) converts an amount of incident light into an output voltage. The Photodiodes convert an amount of incident light into an output current.
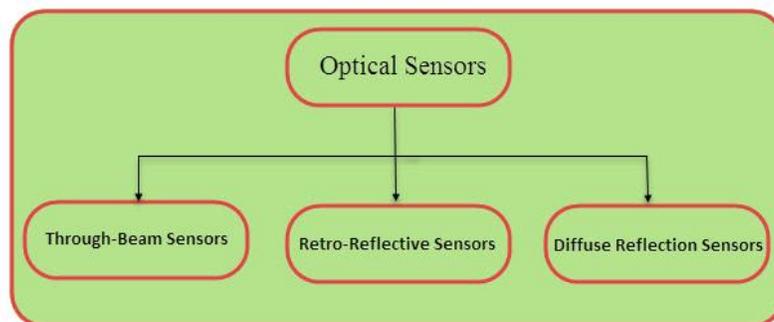

Through-Beam Sensors:

The system consists of two separate components the transmitter and the receiver are placed opposite to each other. The transmitter projects a light beam onto the receiver. An interruption of the light beam is interpreted as a switch signal by the receiver. It is irrelevant where the interruption occurs.

Through-beam sensor
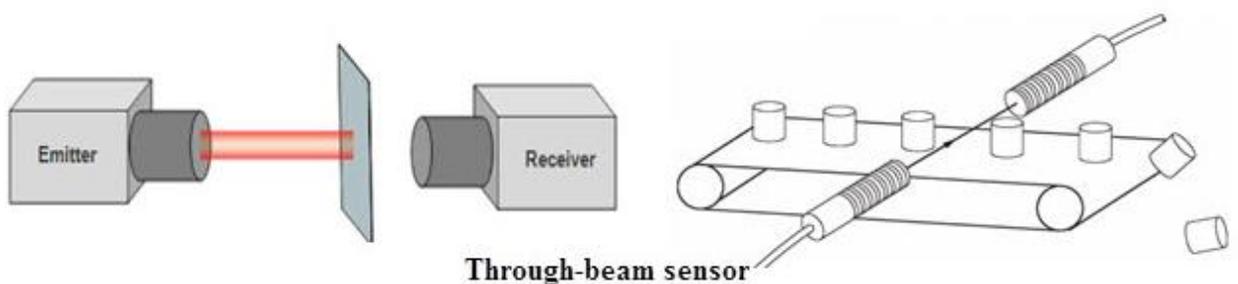
Retro-Reflective Sensors:

Transmitter and receiver are both in the same house, through a reflector the emitted light beam is directed back to the receiver. An interruption of the light beam initiates a switching operation. Where the interruption occurs is of no importance.
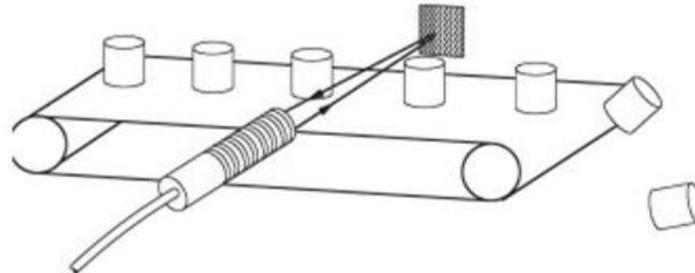
Retro-Reflective Sensors

➢

Diffuse Reflection Sensors:

Both transmitter and receiver are in one housing. The transmitted light is reflected by the object to be detected.


Diffuse Reflection Sensor

blind range   range
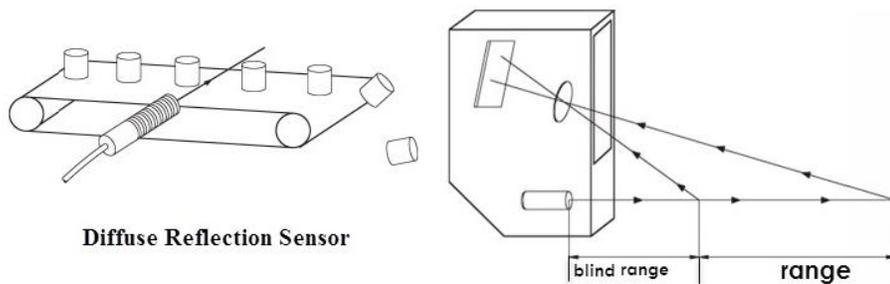
Electrochemical Biosensor:

Electrochemical Biosensors is a simple device. It measures the measurement of electronic current, ionic or by conductance changes carried by bio-electrodes. These sensors employ redox reactions to quantify the amount of an analyte. The current flowing through the system or the potential difference between the electrodes as a result of the oxidation and reduction reactions involving the analyte are used for its quantification in the sample.

The various electrochemical parametes that could be monitored are:

- **Conductometric measurements**, which measures changes in the conductance of the system due to the presence of the analyte.

- **Potentiometric measurements**, which measures the electrical potential difference between a working and reference electrode.

- **Amperometric measurements,** which involves measuring the current generated by electrochemical oxidation or reduction of electroactive species at a constant applied potential.
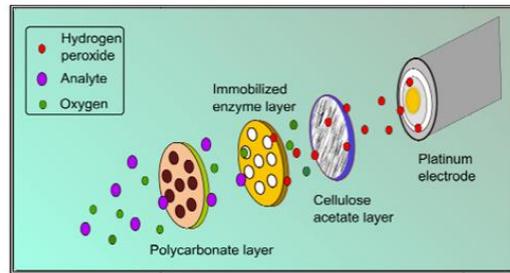
Depicts the principle of a simple electrochemical sensor

The working electrode is a platinum electrode that is in contact with a cellulose acetate and a polycarbonate layer sandwiching an enzyme layer. enzyme catalyzes the redox reaction involving the leading to the formation of hydrogen peroxide current flowing through the electrode
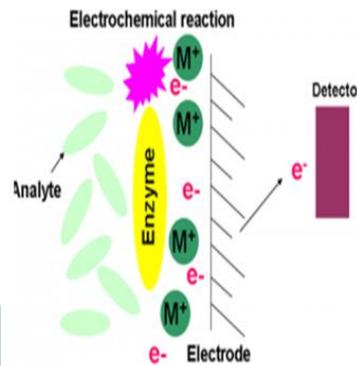
Cantilever biosensor:

A cantilever biosensor is a biosensor made of numerous arms, which are tens of micrometres long but very thin. The surface of the cantilever is functionalized with a nanometre-thick layer of coating which ensures anchorage of the probe material (which can be a DNA strand or a protein, for example).

Each cantilever is different and can probe for a different target. In this type of sensor, the adsorption of the analyte to the specific targets on a cantilever causes a surface stress and bends the cantilever. Microcantilevers based-biosensors are a new label-free technique that allows the direct detection of biomolecular interactions in a label-less way and with great accuracy by translating the biointeraction into a nanomechanical motion.

Over the last years, the number of applications of these sensors has shown a fast growth in diverse fields, such as genomic or proteomic, because of the biosensor flexibility, the low sample consumption, and the non-pretreated samples required. Microcantilevers are sensitive enough to detect single base-pair mismatch in DNA hybridization. They are able to detect pH and temperature changes, the formation of self-assembled monolayers, DNA hybridization, antibody-antigen interactions, or the adsorption of bacteria.
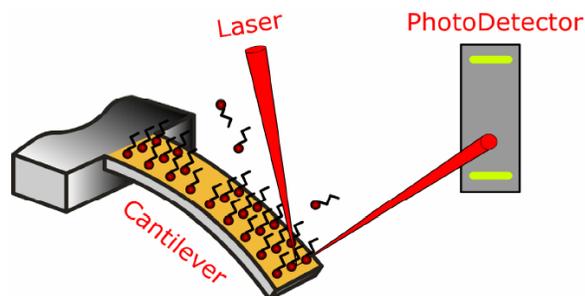
Plasmonic biosensors:

The most common plasmonic biosensor principle is refractometric detection. When a molecule binds to the surface, the refractive index changes. All molecules of interest have a refractive index which is higher than water. The properties of the plasmon are changed because they depend on the refractive index close to the metal.

By optical spectroscopy, changes in intensity of light for different wavelengths can then be detected. The resonance shifts in the spectrum. The optical properties of noble metal nanoparticles have received significant research attention in recent years for their potential as components in many applications, including chemical/biochemical sensors. The optical properties of noble metal nanoparticles are dominated by an effect called localized surface Plasmon resonance (SPR).

One of the consequences of the LSPR effect in metal nanoparticles is that they have very strong visible absorption due to the resonant coherent oscillation of the plasmons. As a result, colloids of metal nanoparticles such as gold or silver can display colours that are not found in their bulk form, such as red, purple or orange, depending on the shape, size and surrounding media of the nanoparticles.

The energy of SPR is sensitive to the dielectric function of the material and the surroundings and to the shape and size of the nanoparticle. This means that if a ligand such as a protein attaches to the surface of the metal nanoparticle, its SPR energy changes. Similarly, the SPR effect is sensitive to other variations such as the distance between the nanoparticles, which can be changed by the presence of surfactants or ions.

In a plasmonic biosensor, the nanoparticles can be dispersed in a medium (in which case the biosensor is a colloidal plasmonic biosensor) or supported on a surface (surface plasmonic biosensor).

This Kretschmann Experimental System uses a metal film thin enough to monitor the plasmon

A plasmon can be thought of as a ray of light bound onto a surface - propagating among the surface and presenting itself as an electromagnetic field.
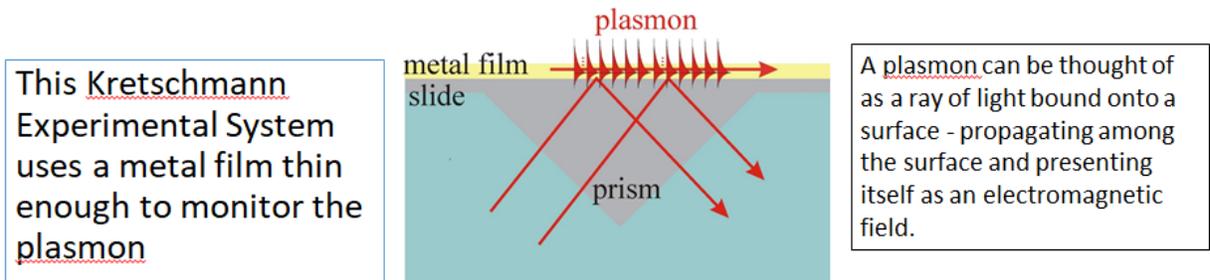
Plasmonic biosensors_Applications:

- SPR imaging used to obtain images of thio-oligonucleotides linked onto a gold surface
- Detection of DNA hybridization using liquid phase SPR imaging techniques
- Identification of binding events with label-free molecules
- High speed and sensitivity with real-time reaction monitoring
- High spatial resolutions
- Identity specific vs. non-specific adsorption processes
- In-situ capabilities

Types of Biosensors:

The Analyte (What do you want to detect)
Molecule - Protein, toxin, peptide, vitamin, sugar, metal ion

Sample handling How to deliver the analyte to the sensitive region?
 (Micro) fluidics - Concentration increase/decrease), Filtration/selection
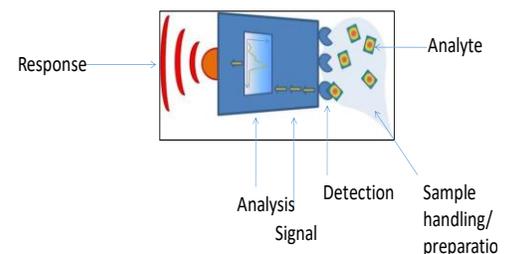
Detection/Recognition (How do you specifically recognize the analyte?)

**Signal** (How do you know there was a detection)

Example of biosensors:

Pregnancy test
Detects the hCG protein in urine.

Glucose monitoring device (for diabetes patients)
Monitors the glucose level in the blood.

Infectous disease biosensor from RBS

Old time coal miners' biosensor

Amperometric Biosensor:

The Biosensors are based on the electrons movement, i.e. electronic current determination as a reaction of enzyme-catalyzed redox reaction. Generally a normal contact voltage passes through the electrodes to analyze. In the enzymatic reaction which produces the substrate or product can transfer the electrons with the surface of electrodes to be reduced.

As a result an alternate current flow can be measured. The substrate concentration is directly proportional to the magnitude of the current. The reduction of oxygen is acquired through the oxygen electrodes and it is a simple way to from an Amperometric biosensor. The example is the determination of glucose by glucose.
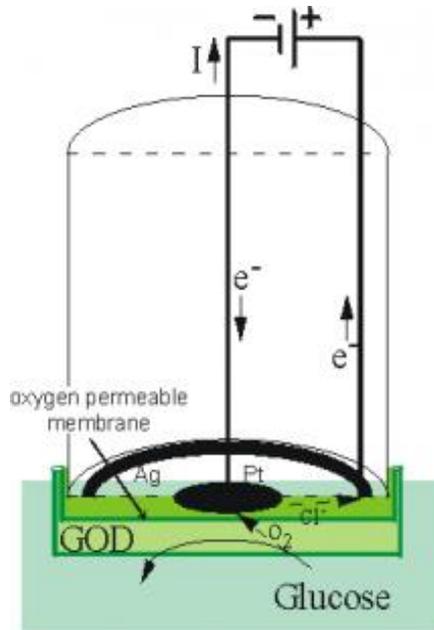
Blood Glucose Biosensor:

The blood glucose Biosensors are used widely throughout the world for diabetic patients. It has a single use disposable electrodes with glucose oxide and derivatives of a mediator (Ferrocence) and the shape of the blood glucose Biosensor looks like a watch pen.

With the help of hydrophilic mesh electrodes are converted. The Blood glucose Biosensor is a good example of Amperometric Biosensor.


Blood Glucose Biosensor

Potentiometric Biosensor:

In this type of Biosensors changes the concentration of ionic is determined by the ion-selective electrodes in this pH electrodes are used most commonly. Hence a large amount of enzymatic reactions is involved in the release of hydrogen ions. Ammonia-selective and Corbondioxide selective electrodes are some other important

electrodes. The Potentiometric Biosensors is the sensitivity of enzymes to ionic concentration like H+ and NH+4.

The example of the ISFET Biosensor is to monitor intra-myocardial for open heart surgery.
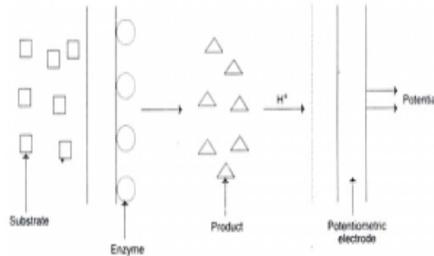
Immuno–Biosensors:

The immune Biosensors works on the principle of immunological specificity and mostly coupled with measurement on the Potentiometric Biosensors. There are different configuration of probabilities for immune Biosensors some of them are given below and the figure shows the description.

- The immobilized antibody can directly combine through the antigen
- The immobilized antigen can combine with the antibody which can twist to a second free antigen.
- The immobilized antibody combined with the free antigens and enzyme labeled antigen in opposition.
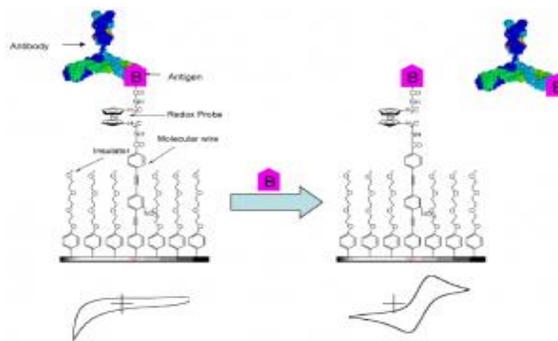
DNA biosensors:

In the future, DNA will find use as a versatile material from which scientists can craft biosensors. DNA biosensors can theoretically be used for medical diagnostics, forensic science, agriculture, or even environmental clean-up efforts. No external monitoring is needed for DNA-based sensing devises.

DNA biosensors are complicated mini-machines—consisting of sensing elements, micro lasers, and a signal generator. At the heart of DNA biosensor function is the fact that two strands of DNA stick to each other by virtue of chemical attractive forces. On such a sensor, only an exact fit—that is, two strands that match up at every nucleotide position—gives rise to a fluorescent signal (a glow) that is then transmitted to a signal generator.

Metastatic cancer cell biosensors:

Metastasis is the spread of cancer from one part of the body to another via either the circulatory system or lymphatic system.Unlike radiology imaging tests (mammograms), which send forms of energy (x-rays, magnetic fields) through the body to only take interior pictures, biosensors have the potential to directly test the malignant power of the tumor.

The combination of a biological and detector element allows for a small sample requirement, a compact design, rapid signals, rapid detection, high selectivity and high sensitivity for the analyte being studied. Compared to the usual radiology imaging tests biosensors have the advantage of not only finding out how far the cancer has spread and checking if treatment is effective, but also are cheaper, more efficient (in time, cost and productivity) ways to assess metastaticity in early stages of cancer.

Calorimetric Sensors:

Calorimetric sensors (Note the spelling; Colorimetric sensors will refer to optical sensors!!), involve the measurement of heat that is generated (Calorie: unit of heat; Calorimetric: Measurement of heat). These sensors typically utilize thermistors that transform heat generated or loss during a reaction into an electrical signal.

The entire sensing set-up is surrounded by an insulated jacket to ensure no loss of heat generated during the reaction. The enzyme is immobilized in a packed bed column that is placed in the centre of the insulated chamber. The sample is allowed to pass through a coiled column of aluminum that serves as a heat exchanger to ensure uniform temperature of the sample entering the reaction chamber.

A thermistor is placed at the inlet of the reactor containing the immobilized enzyme and another thermistor is placed at the exit of the reactor to measure the temperature after the conversion of the substrate to product. A thermistor records temperature changes by altering its resistance. Higher temperatures will causereduction in the resistance of the thermistor. The difference in resistance between thermistors located at the entry and exit points to the reactor is recorded as a measure of the temperature change produced as a result of the passage of the sample.

List of enzymes with their substrate and enthalpy change

Enzyme	Substrate	Heat output $-\Delta H$ (kJ /mol)
Catalase	Hydrogen peroxide	100
Glucose oxidase	Glucose	80
Penicillinase	Penicillin G	67
Urease	Urea	61
Cholesterol oxidase	Cholesterol	53
Uricase	Uric acid	49
Invertase	Sucrose	20
Trypsin	Peptides	10 - 30
Amylase	Starch	8
Chymotrypsin	Esters	4 - 16
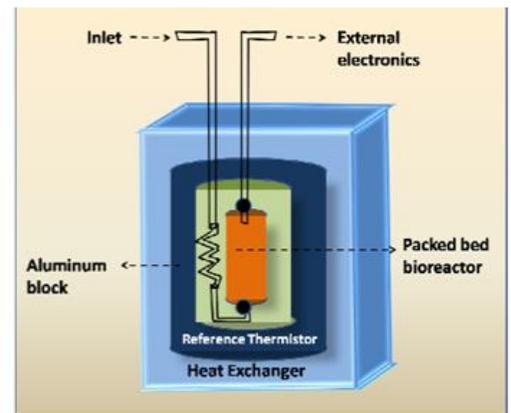
Bio receptors:

➢ A typical biosensor is represented; it consists of the following components.

Analyte:

A substance of interest that needs detection. For instance, glucose is an 'analyte' in a biosensor designed to detect glucose.

Bioreceptor:

A molecule that specifically recognizes the analyte is known as a bioreceptor.

Enzymes, cells, aptamers, deoxyribonucleic acid (DNA) and antibodies are some examples of bioreceptors.

The process of signal generation (in the form of light, heat, pH, charge or mass change, etc.) upon interaction of the bioreceptor with the analyte is termed bio-recognition.

Transducer:

The transducer is an element that converts one form of energy into another.

In a biosensor the role of the transducer is to convert the bio-recognition event into a measurable signal.

This process of energy conversion is known as signalization.

Most transducers produce either optical or electrical signals that are usually proportional to the amount of analyte–bioreceptor interactions.

Electronics:

This is the part of a biosensor that processes the transduced signal and prepares it for display.

It consists of complex electronic circuitry that performs signal conditioning such as amplification and conversion of signals from analogue into the digital form.

The processed signals are then quantified by the display unit of the biosensor.

Display:

The display consists of a user interpretation system such as the liquid crystal display of a computer or a direct printer that generates numbers or curves understandable by the user.

This part often consists of a combination of hardware and software that generates results of the biosensor in a user-friendly manner.

 The output signal on the display can be numeric, graphic, tabular or an image, depending on the requirements of the end user. In a biosensor, the bioreceptor is designed to interact with the specific analyte of interest to produce an effect measurable by the transducer.

Antibody/antigen interactions

An immunosensor utilizes the very specific binding affinity of antibodies for a specific compound or antigen.

The specific nature of the antibody-antigen interaction is analogous to a lock and key fit in that the antigen will only bind to the antibody if it has the correct conformation. Binding events result in a physicochemical change

that in combination with a tracer, such as a fluorescent molecules, enzymes, or radioisotopes, can generate a signal.

There are limitations with using antibodies in sensors:

- The antibody binding capacity is strongly dependent on assay conditions (e.g. pH and temperature) and
- The antibody-antigen interaction is generally irreversible. However, it has been shown that binding can be disrupted by chaotropic reagents, organic solvents, or even ultrasonic radiation.

Artificial binding proteins:

The use of antibodies as the bio-recognition component of biosensors has several drawbacks. *They have high molecular weights and limited stability, contain essential disulfide bonds and are expensive to produce.*

Recombinant binding fragments (Fab, Fv or scFv) or domains (VH, VHH) of antibodies have been engineered. Small protein scaffolds with favorable biophysical properties have been engineered to generate artificial families of Antigen Binding Proteins (AgBP), capable of specific binding to different target proteins while retaining the favorable properties of the parent molecule. The elements of the family that specifically bind to a given target antigen, are often selected in vitro by display techniques: *phage display, ribosome display, yeast display or mRNA display*.

The artificial binding proteins are much smaller than antibodies (usually less than 100 amino-acid residues), have a strong stability, lack disulfide bonds and can be expressed in high yield in reducing cellular environments like the bacterial cytoplasm, contrary to antibodies and their derivatives. They are thus especially suitable to create biosensors.

Enzymatic interactions:

The specific binding capabilities and catalytic activity of enzymes make them popular bioreceptors. Analyte recognition is enabled through several possible mechanisms:

- the enzyme converting the analyte into a product that is sensor-detectable,
- detecting enzyme inhibition or activation by the analyte,
- monitoring modification of enzyme properties resulting from interaction with the analyte.

The main reasons for the common use of enzymes in biosensors are:

- ability to catalyze a large number of reactions
- potential to detect a group of analytes (substrates, products, inhibitors, and modulators of the catalytic activity)
- suitability with several different transduction methods for detecting the analyte.

The catalytic activity of enzymes also allows lower limits of detection compared to common binding techniques. However, the sensor's lifetime is limited by the stability of the enzyme.

Affinity binding receptors:

Antibodies have a high binding constant in excess of 10^8 L/mol, which stands for a nearly irreversible association once the antigen-antibody couple has formed. For certain analyte molecules like glucose affinity binding proteins exist that bind their ligand with a high specificity like an antibody, but with a much smaller binding constant on the order of 10^2 to 10^4 L/mol.

The association between analyte and receptor then is of reversible nature and next to the couple between both also their free molecules occur in a measurable concentration. In case of glucose, for instance, concanavalin A may function as affinity receptor exhibiting a binding constant of 4x10^2 L/mol

The use of affinity binding receptors for purposes of biosensing has been proposed by Schultz and Sims in 1979 and was subsequently configured into a fluorescent assay for measuring glucose in the relevant physiological range between 4.4 and 6.1 mmol/L.

Nucleic acid interactions:

Biosensors that employ nucleic acid interactions can be referred to as genosensors. The recognition process is based on the principle of complementary base pairing, adenine:thymine and cytosine:guanine in DNA. If the target nucleic acid sequence is known, complementary sequences can be synthesized, labeled, and then immobilized on the sensor. The hybridization probes can then base pair with the target sequences, generating an optical signal. The favored transduction principle employed in this type of sensor has been optical detection.

Cells:

Cells are often used in bioreceptors because they are sensitive to surrounding environment and they can respond to all kinds of stimulants. Cells tend to attach to the surface so they can be easily immobilized.

Compared to organelles they remain active for longer period and the reproducibility makes them reusable.They are commonly used to detect global parameter like stress condition, toxicity and organic derivatives.

They can also be used to monitor the treatment effect of drugs. One application is to use cells to determine herbicides which are main aquatic contaminant. Microalgae are entrapped on a quartz microfiber and the chlorophyll fluorescence modified by herbicides is collected at the tip of an optical fiber bundle and transmitted to a fluorimeter.

Applications of Biosensors:

- Biosensors are devices comprising a biological element and a physiochemical detector that are used to detect analytes.
- These instruments have a wide range of applications ranging from clinical through to environmental and agricultural.
- The devices are also used in the food industry.
- Some examples of the fields that use biosensor technology include:
- General healthcare monitoring
- Screening for disease
- Clinical analysis and diagnosis of disease
- Veterinary and agricultural applications

- Industrial processing and monitoring
- Environmental pollution control

Potential Applications of Biosensors
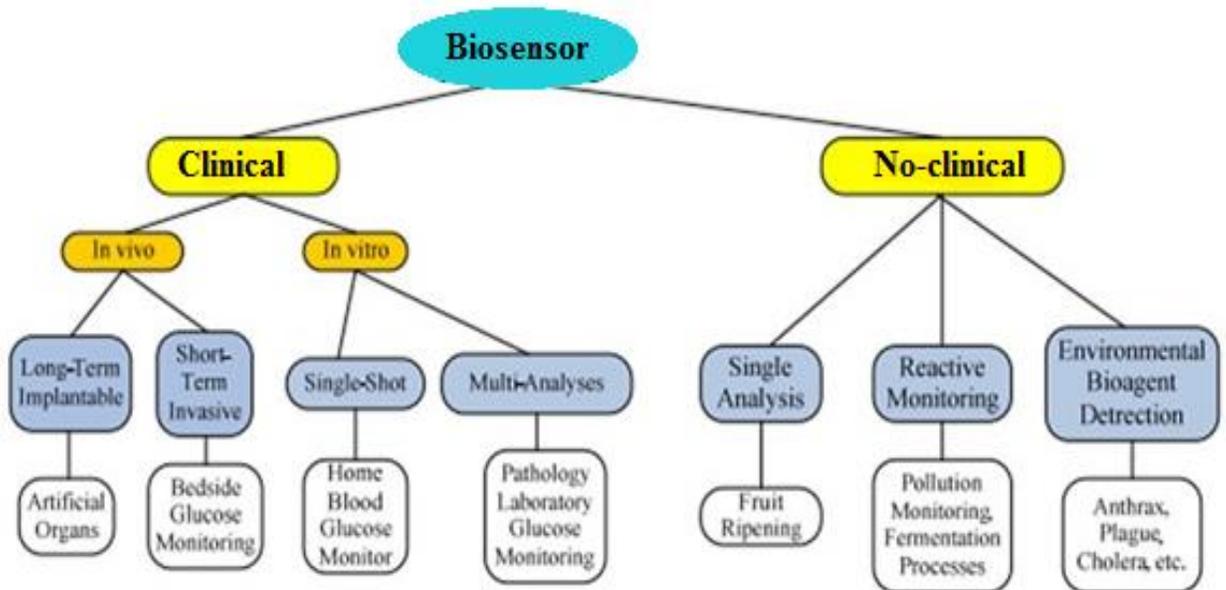
In food processing, monitoring, food authenticity, quality and safety

Quality and safety, maintenance of food products and processing

Food authentication and monitoring with objective and consistent measurement of food products, in a cost effective manner, are desirable for the food industry. Thus development of biosensors in response to the demand for simple, real-time, selective and inexpensive techniques is seemingly propitious.

Monitoring of ageing of beer using enzymatic biosensors, based on cobalt phthalocyanine – during storage

Biosensors are used for the detection of pathogens in food. Presence of Escherichia coli in vegetables, is a bioindicator of faecal contamination in food. E. coli has been measured by detecting variation in pH caused by ammonia (produced by urease–E. coli antibody conjugate) using potentiometric alternating biosensing systems.

In fermentation processes:

In fermentation industries, process safety and product quality are crucial. Thus effective monitoring of the fermentation process is imperative to develop, optimize and maintain biological reactors at maximum efficacy.

Biosensors can be utilized to monitor the presence of products, biomass, enzyme, antibody or by-products of the process to indirectly measure the process conditions. Biosensors precisely control the fermentation industry and produce reproducible results due to their simple instrumentation, formidable selectivity, low prices and easy automation.

Biosensing technology for sustainable food safety:

The term food quality refers to the appearance, taste, smell, nutritional value, freshness, flavour, texture and chemicals. Smart monitoring of nutrients and fast screening of biological and chemical contaminants are of paramount importance, when it comes to food quality and safety.

Glutamine is the nitty-gritty of crucial functions such as (signalling, transport and precursor in biosynthesis of nucleic acids, amino sugars and proteins). Patients deficient in glutamine suffer from pathologies such as malabsorptive disorders and have to be supplemented, to improve immune functions.

Glutaminase-based microfluidic biosensor chip with a flow-injection analysis for electrochemical detection has been used for detection in fermentation process.

In medical field:

In the discipline of medical science, the applications of biosensors are growing rapidly. Glucose biosensors are widely used in clinical applications for diagnosis of diabetes mellitus, which requires precise control over blood-glucose levels. Blood-glucose biosensors usage at home accounts for 85% of the gigantic world market.

Biosensors are being used pervasively in the medical field to diagnose infectious diseases. A promising biosensor technology for urinary tract infection (UTI) diagnosis along with pathogen identification and anti-microbial susceptibility is under study. A novel biosensor, based on hafnium oxide (HfO_2), has been used for early stage detection of human interleukin (IL)-10.

Biosensor Applications in Medical:

Blood Glucose Monitoring:

Blood Glucose Monitoring is a way of checking the concentration of glucose in the blood using a glucometer.

Purpose:

- Provides quick response to tell if the sugar is high or low indicating a change in diet, exercise or insulin.
- Over time, it reveals individual of blood glucose changes.

Biosensors for diabetes applications

Glucose as diabetes biomarker:

About 3% of the population worldwide suffers from diabetes, a leading cause of death, and its incidence is growing fast. Diabetes is a syndrome of disordered metabolism resulting in abnormally high blood sugar levels.

Optimal management of diabetes involves patients measuring and recording their own blood glucose levels. Under normal physiological condition, the concentration of fasting plasma glucose is in the range 6.1–6.9 mmolL−1, so the variation of the blood glucose level can indicate diabetes mellitus, besides other conditions.

Association recommends that insulin-dependent type 1 diabetics self monitor blood glucose 3–4 times daily, while insulin-dependent type 2 diabetics monitor once-daily. Therefore it is necessary to develop a simple,

sensitive, accurate, micro-volume and low-cost approach for glucose analysis which is appropriate for rapid field tests and is also effective as an alternative to the existing methods.

Types of Glucose Biosensors

Enzymatic glucose biosensors

First generation glucose biosensor
Second generation glucose biosensor
Third generation glucose biosensor

Non-enzymatic glucose biosensors

### First-generation of glucose biosensors (Clark enzyme electrode)

First proposed in 1962 by Clark and Lyons :

These sensors were initially based on an electrochemical approach, which used the enzyme glucose oxidase (GOx). Electrochemical sensors were chosen for blood-glucose measurements due to their high sensitivity, on the order of µM to mM, good reproducibility and ease of fabrication at relatively low cost. GOx catalyses the oxidation of glucose to gluconolactone in the presence of oxygen, while producing hydrogen peroxide (H2O2) and water as by-products.

Measurements of peroxide formation have the advantage of being simpler, especially when miniature devices are being considered. The first commercially successful glucose biosensor using Clark's technology was the Yellow Springs Instrument Company analyzer (Model 23A YSI analyzer) for the direct measurement of glucose in 1975, which was based on the amperometric detection of hydrogen peroxide.

This analyzer was almost exclusively used in clinical laboratories because of its high cost due to the expensive platinum electrode. In the sensor design presented by Clark and Lyons, indirect quantification of glucose concentrations was achieved by placing a thin layer of the GOx enzyme on a platinum electrode via a semipermeable dialysis membrane.

This sensor measured the decrease in oxygen concentration and the liberation of hydrogen peroxide, which was proportional to the glucose concentration.
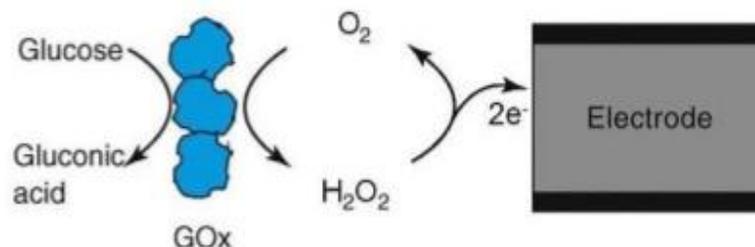
Second-generation of Glucose Biosensors (Mediated Biosensors):

Limitations of the first generation glucose biosensors were over come by using mediated glucose biosensors, second generation glucose sensors. The improvements were achieved by replacing oxygen with non-physiological electron acceptors, called redox mediators that were able to carry electrons from the enzyme to the surface of the working electrode.

A reduced mediator is formed instead of hydrogen peroxide and then reoxidized at the electrode, providing an amperometric signal and regenerating the oxidized form of the mediator. A variety of electron mediators, such as ferrocene, ferricyanide, quinines, tetrathialfulvalene (TTF), tetracyanoquinodimethane (TCNQ), thionine, methylene blue, and methyl viologen were used to improve sensor performance.

During the 1980s, mediator-based second-generation glucose biosensors, the introduction of commercial screen-printed strips for SMBG (Self-monitoring of blood glucose), were developed and implemented.

The first electrochemical blood glucose monitor for self-monitoring of diabetic patients was pen-sized and was launched in 1987 as ExacTech by Medisense Inc.

Various self-monitoring glucose biosensors are based on the use of ferrocene or ferricyanide mediators.

Device Name	Mediator
Precision	Ferrocene
Elite	Ferricyanide
Sure Step	Ferricyanide
AccuCheck	Ferricyanide
FreeStyle	Osmium

Third-generation of Glucose Biosensors:

This feature allows a 3rd generation glucose sensing mechanism, which is independent of mediators or oxygen.

The third-generation glucose biosensors are reagentless and based on direct transfer between the enzyme and the electrode without mediators. Instead of mediators with high toxicity, the electrode can perform direct electron transfers using organic conducting materials based on charge-transfer complexes. The absence of mediators is the main advantage of third generation biosensors, leading to a very high selectivity.

1st generation	2nd generation	3rd generation

In first-generation biosensors, the electrons are transferred to molecular oxygen and the resulting decrease in the oxygen concentration and/or the produced hydrogen peroxide is measured.	Second-generation biosensors use artificial, partially toxic mediators or nanomaterials to transport the electrons to the electrode.	In third-generation biosensors, the electrons are transferred directly from the enzyme to the electrode without any intermediate stages or use of nanoparticles.

Continuous Glucose Monitoring Systems (CGMS):

A CGM is an FDA-approved device that provides continuous insight into glucose levels throughout the day and night. A device that provides "real-time" glucose readings and data about trends in glucose levels

- Reads the glucose levels under the skin every 1-5 minutes (10-15 minute delay)
- Provides alarms for high and low glucose levels and trend information
- The 3rd era in diabetes management
- Continuous Glucose Monitoring systems use a tiny sensor inserted under the skin to check glucose levels in tissue fluid.
- The sensor stays in place for several days to a week and then must be replaced.
- A transmitter sends information about glucose levels via radio waves from the sensor to a wireless device.

How It Works

- A: Insulin Pump that is set up to receive radio transmissions, from label D, and controls the administration of insulin.
- B: Insulin Transfusion Set that is attached to the body and remains in use for up to three days before requiring replacement.
- C: A tiny glucose sensor that is inserted into subcutaneous tissue, also requires replacement after three days of use.
- D: Small light weight device attached to the glucose sensor and is used to transmit the collected data to a digital read out, in this case the insulin pump.
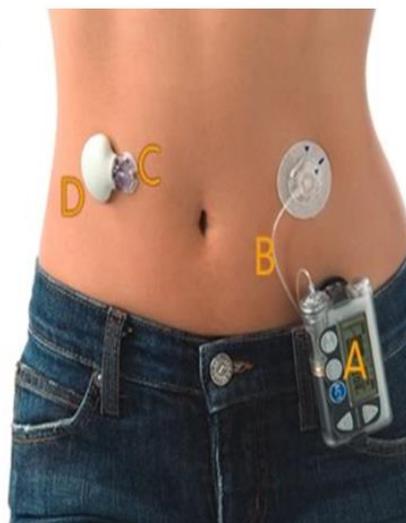
Applications of Biosensors in Environment:

A biosensor is defined by IUPAC as a self-contained integrated device that is capable of providing specific quantitative or semi-quantitative analytical information using a biological recognition element (biochemical receptor), which is retained in direct spatial contact with a transduction element. Protection of human health and the environment requires the rapid, sensitive detection of pollutants and pathogens with molecular precision.

Accurate sensors are needed for in situ detection, both as miniaturised portable devices and as remote sensors, for real-time monitoring of large areas in the field. Generally speaking, a sensor is a device built to detect a specific biological or chemical compound, usually producing a digital electronic signal on detection.

Sensors are now being used for the identification of toxic chemical compounds at ultra-low levels (ppm and ppb) in industrial products, chemical substances, water, air and soil samples, or in biological systems. With high specificity and sensitivity, biosensors provide an exceptional analytical system for the monitoring of environmental pollutants.

They are inexpensive and attractive alternative to the conventional analytical techniques, which are capable of providing real-time online monitoring. With the diverse effect of these pollutants on the biological system, a number of biosensors have been developed and are still in progress. Among toxic compounds, determination of heavy metals, phenolic compounds, mercury, organophosphorus, and carbamate pesticides is the major concern, considering their extensive contribution in increased pollutant level.

Biosensors for determination of organic and inorganic compounds and relevant parameters in the environment:

Environmentally relevant compounds or parameters	Transducing element	Biorecognition element	Features
Toxicity	Optical (bioluminescence)	Recombinant bioluminescent bacteria	Cell array to classify toxicity
Biochemical oxygen demand	Electrochemical (amperometric)	Multispecies culture	Minimum measurable BOD=0.088 mg/L O2; (biosensor BOD/BOD5) ratio=0.80
Chlamydia trachomatis (DNA)	Electrochemical	DNA (hybridisation)	Previous PCR amplification LOD: 0.2 mg/L
Salmonella enteriditis, Lysteria monocytogene	Optical (SPR)	Antibodies	106 cell/mL
Organic compounds Isoproturon, diuron simazine	Optical (fluorescence)	Chlorella vulgaris (Algae cells)	0.025 µg/L
Bisphenol A	Optical (fluorescence)	Antibodies	Monitoring in a waterworks
Surfactants	Electrochemical	Pseudomonas and Achromobacter	LOD: 0.25 mg/L (SDS)

Biosensor or biodevices can used as environmental quality monitoring tools in the assessment of physical, chemical and biological monitoring of pollutants. The major applications of biosensors are monitoring of various pollutants including heavy metals, organic and inorganic pollutants, toxins, antibiotics and contaminating microorganisms.

Heavy metals:

Heavy metals, i.e. copper (Cu), cadmium (Cd), mercury (Hg), lead (Pb), zinc (Zn), etc., are recently the major cause of serious environmental pollution problems. These are known for their high toxicity and bioaccumulation attribute in the food chain. A number of bacterial biosensors have been developed for the determination of heavy metals in different environmental samples using enzyme and DNA as biorecptor and optical and electrochemical as transduction system.

Biochemical oxygen demand (BOD):

Biochemical oxygen demand is one of the significant parameters used in the estimation of the concentration of biodegradable organic pollutants present in a water sample. In routine practice, BOD determination of any sample is a time consuming process, i.e. 5 days, therefore it is not suitable for online process monitoring.

Its rapid determination of could be possible only by using BOD biosensors. Cells of recombinant Escherichia coli with Vibrio fisheri gene lux AE based biosensor was developed for measuring BOD. Recently, a BOD biosensor has been developed using yeast with oxygen probe and able to detect organic pollutants within 15 minutes.

Nitrogen compounds:

Nitrogen compounds, i.e. nitrates, are widely used by food manufacturing industries as preservatives (increase shelf-life) and chemical fertilizer industries as fertilizer (increase the fertility of the soil). The excess uses of

these compounds can cause adverse effects on human health and also contaminating the surface and groundwater, later which can be toxic for aquatic environment.

Nitrogen compounds can react irreversibly with hemoglobin hence, decreasing oxygen carrying capacity. To determine the concentration of nitrogen compounds in water samples, several biosensors have been developed by researchers. Amperometric based biosensor has been developed, using an enzyme (cytochrome c nitrate reductase) obtained from Desulfovibrio desulfuricans for determination of nitrate. Another rapid, highly sensitive and stable conductimetric enzymatic based biosensor has been described for the estimation of nitrate in water.

Polychlorinated biphenyls (PCBs):

PCBs are toxic organic compounds, universal environment pollutants; hence several countries banned their production long time ago. Such compounds are highly lypophilic nature, therefore abundant chances of accumulating in the food chain.

Numerous biosensors have been developed to detect PCBs in the environment including:

i. Nucleic acid (DNA) based biosensor with chronopotentiometric detection
ii. Immunosensors with fluorescence
iii. Electrochemical sensors

Phenolic compounds:

Phenols and their derivatives, i.e. chlorophenol are distributed commonly in the environment. Such compounds are mainly used in the production of dyes, drugs, plastics, pesticides, detergents, etc. Since, phenolics having high toxicity and possible accumulation in the environment and therefore, their detection and monitoring is essential to protect the environment.

Most commonly used biosensors for detection and monitoring of phenolics are:

1. Amperometric biosensor with enzyme (tyrosinase) as bioreceptor for selective detection of phenol in effluent.
2. A flow-injection chemiluninnescence fiberoptic biosensor detection of chlorophenols.

Organophosphrous (OP):

Organophosphrous (OP) compounds Organophosphorous compounds are a group of organic chemicals that are commonly used as insecticides, herbicides and pesticides in modern agriculture for controlling pests, weeds and vectors. Pesticides are the substances meant for preventing, destroying or repelling of pest. Pesticides are most widely distributed in water, soil and food.

Toxicity and persistence of pesticides in the environment are a matter of concern. Enzyme based sensors are most extensively used for detection of these compounds.Immunological based amperometric biosensors have also been developed for detection pesticides in water. For detection of herbicides like phenylureas and triazines (inhibit photosynthesis), amperometric and optical transducers have been developed and employed.

Dioxins are polychlorinated compounds discharged as byproducts during several chemical processes involving chlorine.

Applications of Biosensors in Food Industry:

Food processing industry faces various challenges; one of the foremost challenges is the need for quick and cost effective methods to detect the presence of allergenic components and pathogens in the food. Biosensors pave way for the rapid detection of pathogens, allergens as well as pesticide residues in food.

Detection of contaminants, verification of product contents, product freshness and monitoring of raw materials conversion are the areas of potential biosensor applications. Biosensors have the potential to produce an analytical revolution to resolve the challenges in the agricultural and the food industries.

The determination of chemical and biological contaminants in foods is of paramount importance to the health of food because, unlike the contamination of a physical nature, they cannot be displayed. Development of biosensors to the analysis of the quality of food, since they have proven to be an extremely viable alternative to traditional analytical techniques such as chromatography.

In the area of food the interest in the development of biosensors mainly focuses on analysis of food security (detection of compound contaminants, allergens, toxins, pathogens, and additives etc.) Food composition and online process control.

Main areas applying biosensors technologies in food industry

Food safety		
Xenobiotic compounds	Bacterial toxins:	Pathogenic microorganisms:
• Additives	• Mycotoxins	• Virus
• Drugs	• Marine Toxins	• Bacteria
• Pesticides and fertilizers		• Protozoa
• Other contaminants: dioxins, PCB's, PAH's, heavy metals and biotoxins		

Food quality	
Composition of food:	Lifetime:
• Sugars	• Polyphenols and fatty acids (rancid)
• Amino acids	• Sugars and organic acids (maturation)
• Alcohols	• Biogenic Amines (index freshness)
• Organic acids	• Aliina (garlic and onions)
• Cholesterol	

The concept of food safety involves ensuring the production and marketing of harmless food, and by that way ensure the health of the consumer. On the other hand, foods can naturally present anti-nutritional compounds that can generate disorders in the consumer, given that they hinder absorption and metabolize distinct nutrients causing them to have a deficiency.

Antinutritional components (oxalate and glycoalkaloids) or allergen (gluten) can be contained naturally in foods. First mentioned are mostly detected by enzymatic amperometric biosensors, while for allergens are described imunosensors.

Oxalic acid is of great importance in food industries and clinical analysis. An increase in oxalate excretion through urine indicates hyperoxaluria, renal failure, kidney lesions and pancreatic insufficiency. The ingestion of a large quantity of food rich in oxalic acid can cause loss of calcium in the blood as well as injury to the kidneys.

Biosensors used in anti-nutrients detection

Biological component	Transductor	Analyte
oxalate oxidase immobilized on chitosan	Potenciometric	Oxalate
oxalate oxidase and peroxidase	Amperometry	Oxalate in urine
oxalate oxidase immobilized on gold nanoparticles	Amperometry	Oxalate
β-glucosidase	Potenciometric	amygdalin
Peroxidase	Potenciometric	amygdalin

Commercially available biosensors for food industry

Despite the large number of publications on biosensors used in food analysis, only a few systems are commercially available.

Biosensors for benzoic acid detection

The concept of food security implies the production and marketing of food products that offer no risk to consumer health. The use of additives has become an increasingly common practice in the food industry seeking greater lifetime favoring storage and long distance transport. Due to the growing demand for processed food, the use of preservatives has been gaining importance in modern food technology. Benzoic acid as well as salts, benzoates Na and K, are among the most widely used preservatives to inhibit microbial growth, depending on the cost benefit.

Company	Biosensor
Oriental electric	Fish deterioration tracking
Massachusetts Institute of Technology	Detection of *Escherichia coli* 0157:H7 in lettuce (Canary)
Michigan State University's Electrochemical Biosensor	Detection of *Escherichia coli* O157:H7 and *Salmonella* in meat products in USA
Georgia Research Tech Institute	Detection of *Salmonella* and *Campylobacter* in pork industry
Naval Research Laboratory	Detection of *Staphylococcal* enterotoxin B and *Botuminum* toxin A in tomatoes, sweet corn, beans and mushrooms
Universitat Autònoma de Barcelona in collaboration with CSIC	Detection of atrazine traces
Molecular Circuitry Inc.	*Escherichia coli* 0157, *Salmonella, Listeria* and *Campylobacter*
Research International	Proteins, toxins, virus, bacteria, spores and fungi (simultaneous analysis)
Universal Sensors	Ethanol, methanol, glucose, sucrose, lactose, L-aas, glutamine, ascorbic acid and oxalate
Texas Instruments Inc.	Penaut Allergens, antibiotics
Yellow Springs Instruments Co	Glucose, sucrose, lactose, L-lactate, galactose, L-glutamate, ethanol, H_2O_2, starch, glutamine and choline
Affinity Sensors	*Staphylococcus aureus* and cholera toxin
Ambri Limited	Pathogens such as *Salmonella e Enterococcus*

Given the wide use of benzoic acid and its salts (benzoates) as preservatives in the food industry, detection and quantify cation of these are of great importance in controlling product quality

- In order to prevent fraud and improper manufacturing practices,
- Considering the possible adverse effects those including preservatives,
- Exacerbation of symptoms of chronic rhinitis,
- Asthmatic reactions,
- Hyperactivity in children,
- Genotocixidade,
- Clastogenicity and mutagenicity (in human lymphocytes)

Biosensors for detection benzoate/benzoic acid in food samples

Biosensor/principle	Detection range/sample
Mushroom tissue homogenate/ enzyme inhibition	25–100 µM (non-alcoholic)
PPO-PANI/enzyme inhibition	0.0366 mg/L (non-alcoholic)
PPO-PANI- Pan/enzyme inhibition	2×10^{-7} M (milk, yogurth andnon-alcoholic beverages)
PPO-Teflon/grafite/enzyme inhibition	9.0×10^{-7} M (mayonnaiseand non-alcoholic beverages)
Carbon Electrode modified with PPO-nano-CaCO3/enzyme inhibition	5.6×10^{-7} - 9.2×10^{-5} M (yogurth, and non-alcoholic beverages)
Glassy Carbon Electrodemodified with PPO/CaHPO$_4$enzyme inhibition	119.6-132 mg/L (non-alcoholic beverages, mayonnaise)
PPO-Gel made of Titanium modifiedwith carbon nanotubes /enzyme inhibition	0.03 mM – 1.06 mM (non-alcoholic beverages)

Biosensors for heavy metals:

Heavy metals are the most dangerous environmental contaminants, which present a serious threat to human health, even in trace quantities. Contamination of soils due to discharge of industrial effluents is one of the most significant problems faced by man. Heavy metals are widely existent in these contaminated environments.

Moreover, fertilizer has become one of the polluting sources of heavy metals. So repetitive applications of commercial fertilizers and pesticides continually for agriculture have contributed to a continuous accumulation of heavy metals in soils. The majority of existing techniques used for trace analysis of heavy metals includes spectroscopic, voltammetric and chromatographic methods, which can detect species at low concentrations or even in single elements. biosensor composter a differential pair of planar thin-film interdigitated electrodes, deposited on a ceramic pad, (used as a conductometric transducer) together with the three-enzyme system (invertase, mutarotase, glucose oxidase), immobilized on the transducer surface, (used as a bioselective element). The developed biosensor demonstrated the best sensitivity toward ions Hg2+ and Ag+.

The modern environmental and food analysis requires sensitive, accurate, and express methods. The growing field of the biosensors represents an answer to this demand. Biosensors for potential environmental and food applications continue to show advances in areas such as genetic modification of enzymes and microorganisms, improvement of recognition element immobilization and sensor interfaces.

Gene chip:

There are different names for the microarrays, like DNA/RNA Chips, BioChips or GeneChips. The array can be defined as an ordered collection of microspots, each spot containing a single defined species of a nucleic acid. The microarray technique is based on hybridisation of nucleic acids. There exist two variants of the chips:

- cDNA microarrays
- oligonucleotide arrays

Although both the DNA and oligonucleotide chips can be used to analyse patterns of gene expression, fundamental differences exist between these methods. Two commonly used types of chips differ in the size of the arrayed nucleic acids.

The Gene Chip System consists of arrays, hybridization ovens, fluidics stations, scanners, and software for data analysis. All of these pieces of equipment are used in a full experiment with a microarray and how the results are analyzed.
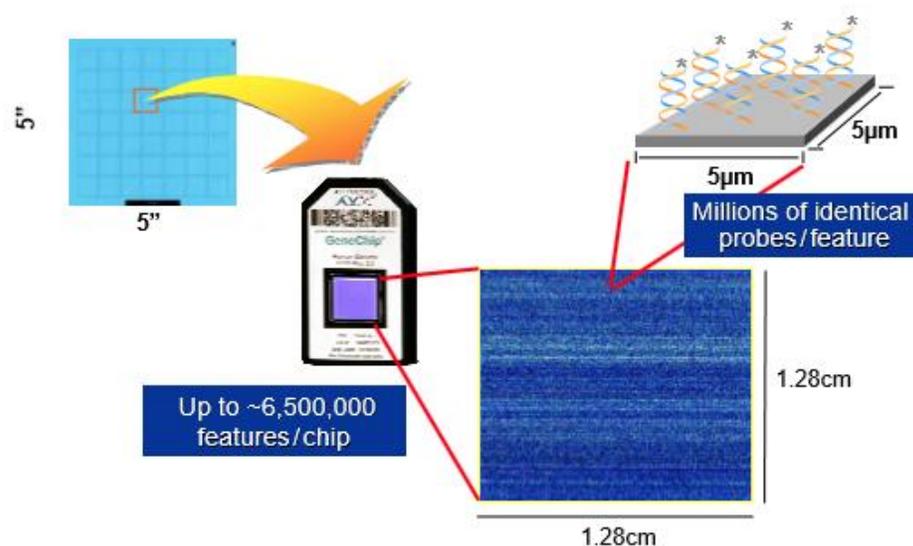
These GeneChip microarrays are a fusion of the technology of the semiconductor industry with life sciences – this is why these arrays are called "chips". The chips are manufactured on wafers. These wafers are 5-inch-by-5-inch pieces of glass. You can get anywhere from 49 to 900 individual chips out of each wafer, depending on the overall size of the final chip to be made

A standard chip is 1.28 cm X 1.28 cm, the size of a thumbnail. On each one of those chips there are now over 6.5 million sections (squares) known as features. In each feature there are millions of identical DNA probes on them. In the diagram above, the probes are represented by the blue spiral connected to the feature. A probe is a 25 base pair (25-mer) length piece of DNA that is attached to the chip.

Each feature has millions of identical probes attached to them. The probes are used to probe the sample for certain DNA or RNA segments. The orange spirals with the stars at the end are RNA from a sample applied to the chip. Probes are the essential part of how the GeneChip functions
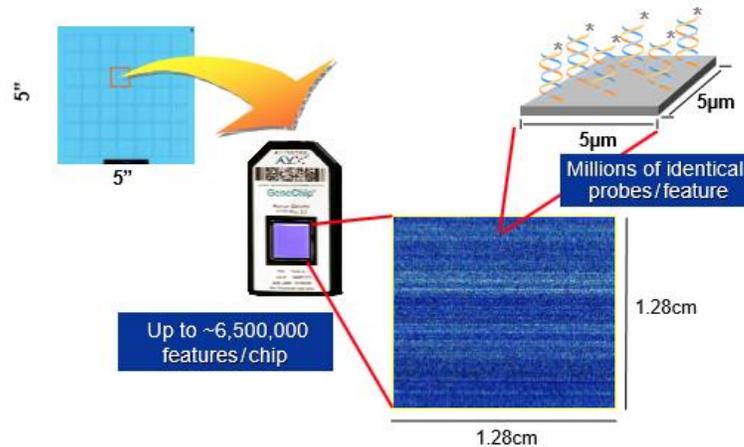
Hybridization:

Hybridization is the basis for the function of microarrays.

Hybridization: The process of joining two complementary strands of DNA to form a double -stranded molecule. The two strands are known as complimentary. This hybridization occurs because of complimentary base pairing rules (A – T, and C – G).

The hybridization of the probes on the features to RNA in sample from a cell being studied is the key to the function of the genechip

Microarrays:

A snapshot that captures the activity pattern of thousands of genes at once. These devices are used for diagnostic purposes such as DNA analysis (DNA microarray), protein detection (protein microarrays) as well as whole cell analysis.

Microarrays are platforms made of hundreds of detection sites that have micron-sized dimensions and allow the specific detection of a (bio)chemical within a mixture or the simultaneous detection of many (bio)chemicals. The detection is related to the chemical functionality on the micron-sized spots in the array and it leads to a single chemical 'yes/no' reaction per spot.

Microarrays are used as screening tools, not only for diagnostic purposes but also for screening new drugs. Nanotechnology can impact microarray technology by creating densely packed, smaller, nano-sized arrays (nanoarrays) that could allow faster screening of a larger number of (bio) chemicals. This technique uses fluorescent probes made of organic molecules attached to the species to be detected (e.g. a protein or a fragment of DNA)

When reaction occurs, this is attached to the detection spot, which becomes fluorescent in a 'colour' corresponding to the emission of the fluorescent probe. Nanoparticles in the form of quantum dots (QD) can be used as an alternative to conventional organic dyes, being more stable, sensitive and monochromatic. A substantial (tenfold) enhancement in sensitivity compared to common fluorescent markers has been accomplished through the use of gold and silver particles of uniform dimensions in the range 40 to 120 nm.

Signal amplification is also obtained using metal nanoparticle labels, such as DNA-modified gold nanoparticles. These nano-sized probes have molecules attached to their surface that ensure the selectivity of the detection, while the nano-properties of the probe are responsible for enhancing the signal.
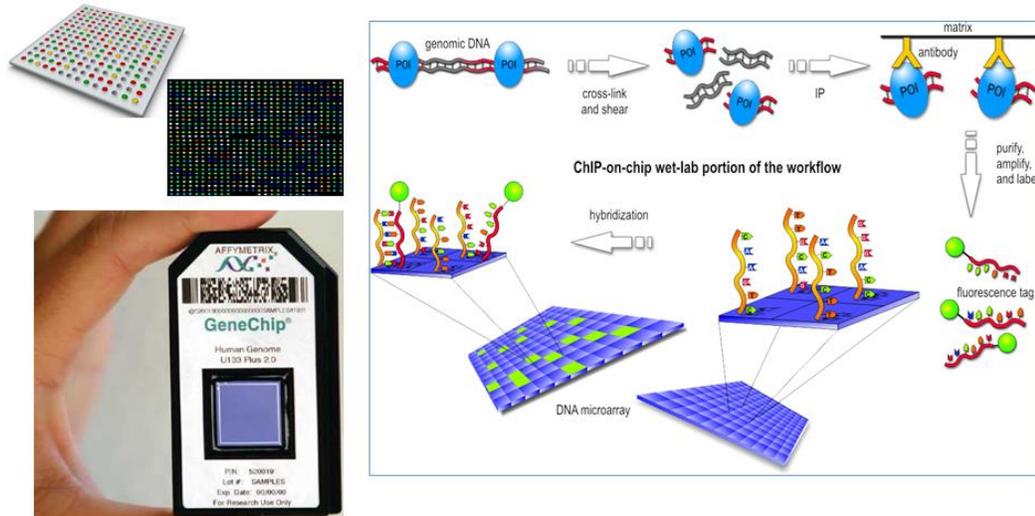
Therapy:

A therapy normally involves a pharmaceutical route (drugs) to treat the disease from the inside of the body. Nanotechnologies are making a tremendous impact in this field, with new drugs and new types of treatments under development, some of which have already proven clinically effective and have entered the market.
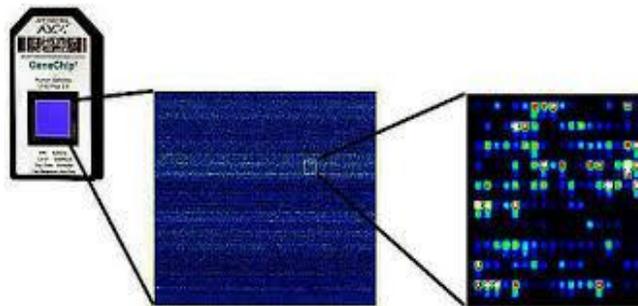
Drug development and targeted drug delivery:

Advances in the field of pharmacology stem from two main concepts:

- the development of new biologically active drugs
- the development of new drug delivery systems able to reach the specific site of the disease.

Drug delivery systems (DDS) are not a new concept: research in this field started in the mid 1960s and resulted in the type of drugs used today. Drug delivery systems are in the same form as the pills that are frequently taken and that release their active component gradually in time or that dissolve based on some physiological conditions. Drug delivery systems also exist in the form of implants, inserts or other drug-releasing systems.

Drug design and screening:

The structure of biological macromolecules defines a three-dimensional nano-environment that mediates specific functions in the cell.

The design of new drugs requires a very detailed understanding of this nano-environment. Gaining insight into the structure of macromolecules on the nanoscale through electron microscopy, nuclear magnetic resonance spectroscopy (NMR) and X-ray crystallography is of fundamental importance tounderstanding biological processes and for the development of new medicines.

Targeted drug delivery:

Pharmaceutical drugs developed using conventional synthesis routes are limited by problems such as low efficacy, low solubility in water and lack of selectivity. Physiological barriers often prevent the drug from reaching and acting at the target site — a phenomenon called drug resistance.

The efficacy of drugs is also dependent on the dose used, but dose-dependent side effects often limit their acceptable usage. Delivery systems need to be miniaturized to much smaller than the target, and specific in composition to elicit a certain response. With the use of nanotechnologies, targeted drugs are becoming a reality.

The aim is to design and deliver drugs in such a way that they can recognise the bad cells at a molecular level, pene trate the cell membrane, and act inside the infected cell. This is often crucial for the efficacy of a drug, since most virus replication and other disease conditions take place across the cell membrane and inside the cell. This way, the treatment will be delivered where it is needed and will be specific, eliminating the problem of the drug killing healthy cells.

An example of this approach is siRNA drug delivery.

siRNA drug delivery:

RNA interference is a natural, fundamental mechanism in gene regulation that occurs in both plants and animals, humans included. DNA in the nucleus of a cell, when genes are express, the genetic information is copied from DNA messenger RNA (mRNA), which then orchestrate the formation of proteins.

In 1998, Andrew Fire and Craig Mello discovered that double stranded RNA (dsRNA) can interfere with and break down the mRNA for a specific gene, thus stopping the production of a specific protein. The gene is, therefore, 'silenced' and the production of the protein is turned off.

RNA interference plays an important role in switching off genes during an organism's development and controlling cellular functions. Developing nanocarriers for the targeted delivery of siRNA. They are studying a novel chitosan-based siRNA nanoparticle delivery system for RNA interference in vitro and in vivo. Chitosan is a naturally occurring that has been widely used in drug delivery systems. cationic polysaccharide.

It contains positively charged amine groups that can interact with the negatively charged backbone of siRNA and form polyplexes in the form of nanoparticles about 200 nm in size.The protonated amine groups allow transport across cellular membranes and subsequent endocytosis into cells. It has been shown that a

chitosan/siRNA nanoparticle delivery system silences genes both in vivo and in vitro. Moreover, this delivery system has been shown to be biocompatible, non-toxic and biodegradable.

Stimuli-activated drug delivery:

Activated on reaching the target and the active component released at a controlled rate, this is called stimuli-activated drug delivery. In gene therapy, one of the biggest challenges is the targeted delivery of the nuclei acid load to the target (e.g. plasmid-DNA or siRNA) either to silence (RNA silencing) or to activate the expression of a protein as a way to treat a number of diseases.

The idea is to utilize a nanocarrier that passively accumulates in the diseased tissues (e.g. tumours), followed by stimuli-induced activation at the required site. In the case of thermoresponsive systems, the application of heat in precise locations of the tissue can induce the deposition of the nanocarrier in the extracellular target region.

Current and future nano-drug carriers

Nano-sized drug carriers currently under development include either materials that self-assemble, or conjugated multicomponent systems, for instance a drug linked to a protein and a polymer (called a polymer-drug conjugate.

Numerous nanosystems are now being investigated and include micelles, nanoemulsions, nanotubes, nanofibres, liposomes, dendrimers, polymer therapeutics, nanoparticles, nanocapsules, nanospheres and hydrogels. Some of these nano-sized drug carriers are established in the field of drug delivery, such as liposomes.

Many are now used for treating some forms of cancer, hepatitis, and leukaemia. An example is an anticancer drug called DOXIL.

Regenerative Medicine:

At times, the only way to treat a disease is the removal of the infected organ or tissue. Such loss can also derive from an injury or a congenital condition (e.g. vision or hearing impairment). To compensate for the lost or impaired body function, an artificial construct is implanted in the body. Depending on the type, site and extent of the loss, this construct can be in the form of an engineered tissue or an implant.

Regenerative Disease

A degenerative disease is a type of a medical condition that causes a tissue or organ to deteriorate over time. There are quite a number of degenerative diseases and many of them are associated with aging, or gets worse during the aging process.

Degenerative diseases refer to medical problems that worsen over time. These degenerative diseases may affect the central nervous system (brain and spinal cord), bones, blood vessels or heart. Sometimes, certain medications and therapies can treat these degenerative diseases. Unfortunately, some degenerative diseases have no cure. Degenerative diseases are classified into three main groups: cardiovascular, neoplastic, and nervous system.

The most common cardiovascular diseases are hypertension, coronary disease, and myocardial infarction. Neoplastic diseases include tumors and cancer. Diseases that affect the nervous system include Parkinson's and Alzheimer's.

Tissue and biomaterial engineering

Tissue engineering deals with the fabrication of artificial scaffolds to support the growth of donor cells, which differentiate and grow into a tissue that mimics the lost natural one. This tissue engineered construct is then implanted in the patient and, in time, resorbed by the body and fully integrated by the host tissue. The scaffold that supports cell growth is the core of this technique.

In the body, cells are supported in their growth and function by a natural scaffold, called the extracellular matrix (ECM). This is a very complex and intricate web of nanofibres that provide the mechanical architecture for cellular growth. Moreover, the ECM is filled with small molecules (e.g. growth factors) and proteins that direct many cell processes, such as adhesion, migration, growth, differentiation, secretion and gene expression.

The biggest challenge in regenerative medicine is the artificial replication of this perfect nano-scaffold. Close to the field of tissue engineering, and in many cases an integral part of it, is biomaterial engineering. Materials used in regenerative medicine are called biomaterials in the sense of being able to trigger and support a biological response. One of the distinguishing features of nanotechnologies is their ability to create new functional materials.

Biomaterials for Tissue Engineering

Biomaterials serve as an integral component of tissue engineering. They are designed to provide architectural framework reminiscent of native extracellular matrix in order to encourage cell growth and eventual tissue regeneration.

Bone and cartilage represent two distinct tissues with varying compositional and mechanical properties. Typically, three individual groups of biomaterials, ceramics, synthetic polymers and natural polymers, are used in the fabrication of scaffolds for tissue engineering.

Widespread use of ceramic scaffolds, such as hydroxyapatite (HA) and tri-calcium phosphate (TCP), for bone regeneration applications. Ceramic scaffolds are typically characterized by high mechanical stiffness (Young's modulus), very low elasticity, and a hard brittle surface.

Nanotechnologies

Nanotechnologies are also employed in the fabrication of biomaterials that are responsive to the environment, for this reason, are called smart biomaterials. Finally, nano-sized sensors could be inserted inside a biomaterial (e.g. nanowire biosensors) functionalised with receptors that can monitor the presence of small organic molecules, proteins, cells (e.g. cancer cells) and viruses.

This could be used to collect information on the implant status and activity. Tissue and biomaterial engineering have applications in basically all aspects of regenerative medicine (i.e. neuroprosthetics and neuron regeneration (e.g. spinal cord repair), bone restoration, hearing and vision restoration, motor restoration, etc.).

Diagnostic Imaging

Techniques such as X-ray, computer tomography (CT), ultrasound (US), magnetic resonance imaging (MRI) and nuclear medicine (NM) are well established imaging techniques, widely used in both medicine and biochemical research.Imaging techniques could only detect changes in the appearance of a tissue when the symptoms of the disease were relatively advanced.

It is in this specific area that nanotechnologies are making their greatest contribution by developing better contrast agents for nearly all imaging techniques. The physiochemical characteristics of the nanoparticles (particle size, surface charge, surface coating and stability) allow the redirection and concentration of the marker at the site of interest.

An example of nanoparticles used in research for imaging is perfluorocarbon nanoparticles employed as contrast agents for nuclear imaging, magnetic resonance imaging and ultrasound, with applications in the imaging of blood clots, angiogenesis, cancer metastases and other pathogenic changes in blood vessels.

Diagnostic imaging refers to a variety of non-invasive methods for identifying and monitoring diseases or injuries via the generation of images representing internal anatomic structures and organs of the patient's body.

In X-ray imaging, to enhance the signal, an agent must deliver a detectable number of heavy atoms into targeted tissue without toxic effects. Nanoparticles of heavy metals have the highest density of surface atoms but they must be inert and stable. Nanoparticles of inert metals like silver and gold are too expensive and would render the technique not cost-effective. A solution has been proposed by General Electric in the form of nanoparticles made of heavy metal compounds encapsulated in gold shells.

By targeting receptors unique to a certain type of cancer cell, gold nanoparticles can enhance an X-ray image of a suspected cancer tissue by many orders of magnitude. Gold nanoshells are a promising material for the optical imaging of cancer. Optical technologies could provide high resolution, non-invasive functional imaging of tissue at competitive costs.

Magnetic resonance imaging (MRI) uses a large magnet and radio waves to look at organs and structures inside your body. Health care professionals use MRI scans to diagnose a variety of conditions, from torn ligaments to tumors. MRIs are very useful for examining the brain and spinal cord. Nuclear scans use radioactive substances to see structures and functions inside your body. They use a special camera that detects radioactivity. X-rays are a type of radiation called electromagnetic waves. X-ray imaging creates pictures of the inside of your body.

Remediation and Mitigation:

Simply stated, remediation is the process of clean up and disinfection. Mitigation is structural and non-structural measures undertaken to limit the adverse impact of natural hazards, environmental degradation and technological hazards. In other words, help in reducing the cause of problem to prevent further damage.

Soil and groundwater contamination arising from manufacturing processes are a matter of great complexity and concern. Affected sites include contaminated industrial sites (including lakes and rivers in their vicinity), underground storage tank leakages, landfills and abandoned mines.

Pollutants in these areas include heavy metals (e.g. mercury, lead, cadmium) and organic compounds (e.g. benzene, chlorinated solvents, creosote). Nanotechnology can develop techniques that will allow for more specific and cost-effective remediation tools. Currently, many of the methods employed to remove toxic contaminants involve laborious, time-consuming and expensive techniques.

Nanotechnology facilitates developing technologies that can perform in situ remediation and reach inaccessible areas such as crevices and aquifers, thus eliminating the necessity for costly 'pump-andtreat' operations.

In addition, as a result of its ability to manipulate matter at a molecular level, nanoscience can be used to develop remediation tools that are specific to a certain pollutant (e.g. metal), therefore increasing affinity and selectivity, as well as improving the sensitivity of the technique. Drinking water quality and its contamination from pollutants is another matter of concern.

Mercury and arsenic are, in particular, two extremely toxic metals that pose very high health risks. Remediation methods that allow the fast, economic and effective treatment of water polluted with such contaminants is urgently needed.

Remediation using metal nanoparticles:

The use of zero-valent (Fe0) iron nanoparticles for the remediation of contaminated groundwater and soil is a good example of how environmental remediation can be improved with nanotechnology. When exposed to air, iron oxidises easily to rust; however, when it oxidises around contaminants such as trichloroethylene (TCE), carbon tetrachloride, dioxins, or PCBs, these organic molecules are broken down into simple, far less toxic carbon compounds.

Since iron is non-toxic and is abundant in the natural envir onment (rocks, soil, water, etc.). Some industries have started using an 'iron powder' to clean up their new industrial wastes. Nanotechnology has offered a solution to this remediation technology in the form of iron nanoparticles. These nanoparticles are 10 to 1 000 times more reactive than commonly used iron powders.

They have a larger surface area available for reacting with the organic contaminant and their small size (1–100 nm) allows them to be much more mobile, so they can be transported effectively by the flow of groundwater.When nano-sized iron powders are used, no toxic by-products are formed, a result of the increased reactivity and stability of the nanoparticles compared to the granular iron powder. Bimetallic iron nanoparticles, such as iron/palladium, have been shown to be even more active and stable than zero-valent iron nanoparticles, thus further improving this remediation technology.