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قسم التقنيات الاحيائية

تقنيات احيائية نانوية

المرحلة الثالثة

الفصل الثاني

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Nanotechnology

The study of the controlling of matter on an atomic and molecular scale. Generally, nanotechnology deals with structures sized between (1 to 100) nanometers in at least one dimension and involves developing or modifying materials or devices within that size.

Nanoscience (Nano is a Greek word Nanos which mean dwarf), 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

WHAT IS NANO?

The word "*nano*" originates from the Greek word "*Nanos*" which means "*dwarf*" (i.e. an abnormally short person). However, in the scientific language, it is a prefix that has a value equal to "*one billionth*, i.e. 10^{-9} from the meter".

Following examples helps to understand a sense of nano-scaled objects gives a qualitative idea.

1) Human hair is around 20,000 nm in diameter.
2) Size of the diameter of the DNA molecule is about 2 nm.
3) Space between carbon-carbon atoms in a molecule (Cs, bond length) are in the range of (0.12–0.15 nm)

History

- In 1959, the great physicist Richard Feynman described the ability to use one set of precise tools to construct and operate another proportionally smaller set by manipulating and developing the individual atoms and molecules.

- In the late 1970s, Eric Drexler realized that molecular machines could control the chemical manufacture of complex products and it would be a powerful technology.

- In 1974, Professor Norio Taniguchi defined the term "Nano-technology" in his paper which mainly consists of the processing of separation and deformation of materials by one atom or by one molecule.

- The birth of cluster science (a small group or bunch of something) and the invention of the scanning tunneling microscope (STM) in the early 1980s are the major developments toward starting nanotechnology and nanoscience.

- This development led to the discovery of fullerene (which is any molecule composed entirely of carbon) in 1986 and a few years later carbon nanotubes (which are allotropes of carbon with a cylindrical nanostructure) were discovered.

- In the early 1990s Huffman and Kraetscher, discovered the way of synthesizing and purifying large quantities of fullerenes.

A **fullerene** is any molecule composed entirely of carbon, in the form of a hollow sphere, ellipsoid, tube, and many other shapes. Spherical fullerenes are also called **buckyballs**, and they resemble the balls used in football (soccer). Cylindrical ones are called carbon nanotubes or buckytubes. Fullerenes are similar in structure to graphite, which is composed of stacked graphene sheets of linked hexagonal rings; but they may also contain pentagonal (or sometimes heptagonal) rings.

- In 1992, the synthesis of carbon nanotube on a large–scale was established by Dr. Ebbesen.

- In 2000, the use of nanotechnology commercially was begun, and the rapid growth was recorded in the market, which is found in food packaging, sunscreen cream, cosmetics, clothing, and household uses. In 2009 Samsung declared the large scale production of devices built with 30 nm technology as proposed by Feynman

Properties of nanomaterials:

Depending on the physical and chemical properties of nanomaterial's products are:

- Light
- Strong
- Smaller
- More Durable

General Introduction

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.

Nanotechnologies: Are the design, characterization, production and application of structures, devices and systems by controlling shape and size at the nanometer scale. Nanotechnology is interdisciplinary which needs physics, chemistry, engineering, biology, etc.

The aims of nanotechnology:

Once we can control feature size, we can enhance material properties and device functions beyond those that we currently know *or* even imagine. Nanotechnology aims to gain control of structures and devices at the atomic, molecular and supramolecular levels, and to learn how to efficiently manufacture and use these devices.

Particles at nanoscale different than the on a larger scale:
Physics is different on the nanometer scale. Properties not seen on a macroscopic scale now become important such as quantum mechanical and thermodynamic properties. Rather than working with bulk materials, one works with individual atoms and molecules. By learning about an individual molecule's properties, we can put them together in very well-defined ways to produce new materials with new and amazing characteristics.

Importance of nanoscale:

Nanotechnology is not only a simple continuation of miniaturization from micron meter scale down to nanometer scale. Materials in the micrometer scale mostly exhibit physical properties the same as that of bulk form; however, materials in the nanometer scale may exhibit physical properties distinctively different from that of bulk. When at least one of the dimensions of any type of material is reduced below ~ 100 nm, then it's mechanical, thermal, optical, magnetic and other properties change at some size characteristics of that material

Important aspects of nanotechnology:

Nanotechnology has three important aspects: size, structure, and resulting novel properties.

1- Size: To imagine how small the nanoscale is see the following figure.

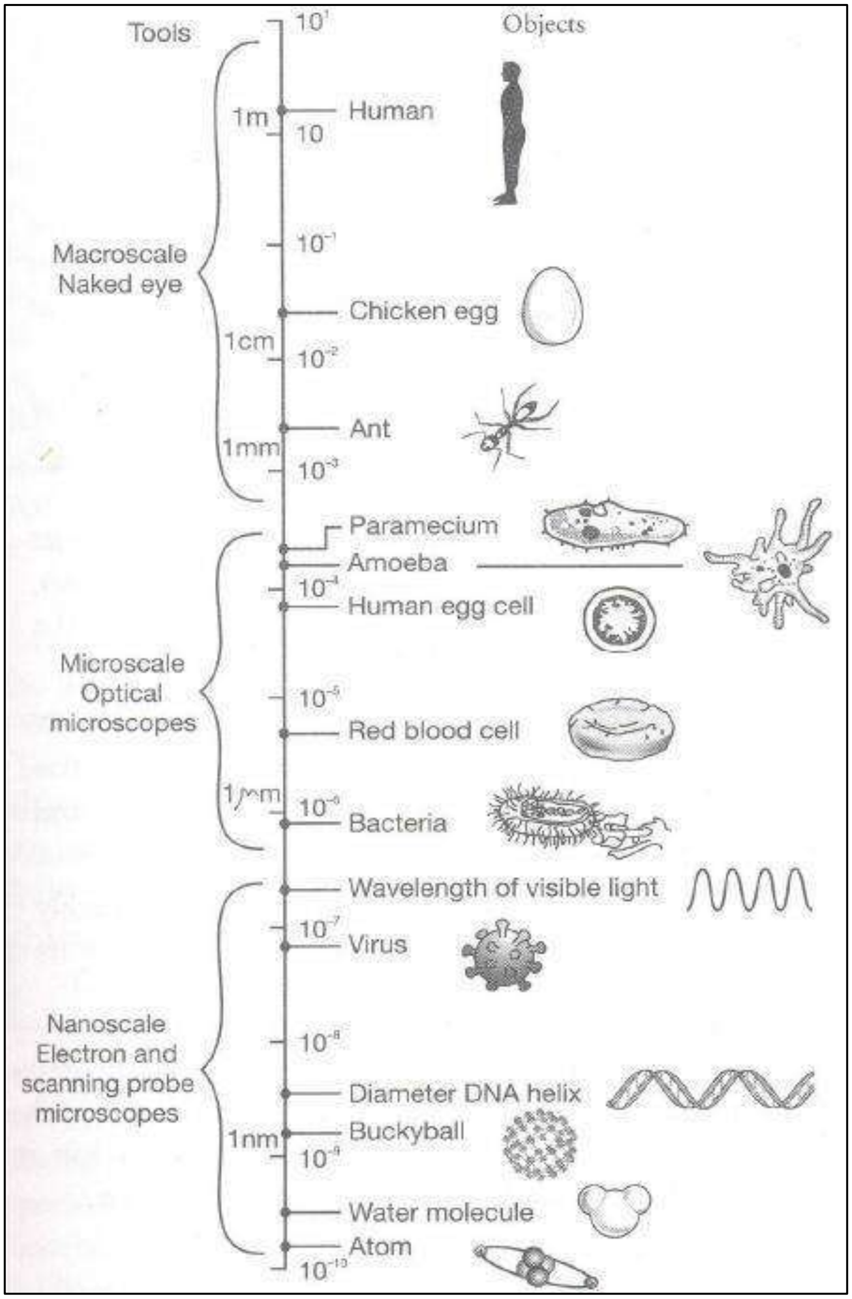

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Figure: Size comparison from macroscale objects to nanoscale objects.

2- **Structure:** Nanotechnology is not just about the size of looking at very small things, it is about structure, or how things are put together, arranged, or assembled. It is the ability to work observes, manipulate, and build at the atomic or molecular level.

3- **Novel properties:** Nanotechnology produces materials and systems that exhibit novel and significantly changed physical, chemical, and biological properties because of their size and structure. When a substance consists only of clusters of a few hundred atoms, the laws of quantum mechanics influence dramatic changes in its mechanical, optical, and electronic properties. These properties include improved catalysts, tunable photo activity, increased strength, etc.

Properties of materials can be different at the nanoscale for two main reasons:

1. **Nanomaterials have a relatively larger surface area or surface area to volume ratio** when compared to the same mass of material produced in a bulk form. This can make materials more chemically reactive (in some cases materials that are inert in their bulk form become reactive Blue Green to Light Green or Yellow Red when produced in their nanoscale form), and affect their strength *or* electrical properties. ***For example***, gold is chemically inert at the macroscopic scale. However, gold becomes reactive and catalytic at the nanoscale, and even melts at a lower temperature. The larger surface area permits simultaneous interaction of chemicals with catalysts, which makes the catalyst more effective.

2. **Quantum mechanical effects** become significant at nano regime - affecting the optical, electrical and magnetic behavior of materials. One example is the "*quantum size effect*" where the electronic properties of solids are altered with great reductions in particle size. This effect does not come into play by going from macro to micro dimensions. However, it becomes pronounced when the nanometer size range is reached.

Quantum mechanics (QM):

Also known as quantum physics or quantum theory is a branch of physics that deals with physical phenomena at nanoscopic scales. Interactions of energy and matter. Quantum mechanics provides a largely useful structure for many features of the modern periodic table of elements including the behavior of atoms during chemical bonding and has played a significant role in the development of many modern technologies.

In advanced topics of quantum mechanics, some of these behaviors are macroscopic and appear at only extreme (i.e., very low or very high) energies or temperatures (such as in the use of superconducting magnets).

Diameter, surface area and volume

Nanoparticles have unique properties due to their small size. All nanoparticles regardless of their chemical constituents have a surface area: extremely high volume ratios. Thus, many of the physical properties of the nanoparticles such as solubility and stability are dominated by the nature of the nanoparticle surface. While high surface areas to volume ratios are important for applications such as catalysis.

The volume of a sphere:

Nano sphere Diameter (nm)	Surface area (nm^2)	Volume (nm^3)	Ratio Surface Area: Volume
10	314	523	0.60
20	1260	4190	0.30
30	2830	14100	0.20
40	5030	33500	0.15
50	7850	65500	0.12
60	11300	113000	0.10

Properties of Nanomaterials

Nanomaterials have properties that are different from those of bulk materials**.** Nanomaterials are of interest because at this scale unique optical, magnetic, electrical, and other properties emerge. These emergent properties have the potential for great impacts in electronics, medicine, and other fields. Nano carbons such as fullerenes and carbon nanotubes are excellent examples of nanomaterials. Most nanostructure materials are crystalline and have unique properties.

1. **Physical Properties:** The inter-atomic spacing decreases with size and this is due to long-range electrostatic forces and the short-range core-core repulsion**.** The melting point of nanoparticles decreases with size.

2. **Chemical Properties:** A large fraction of the atoms are located at the surface of the nanomaterial which increases its reactivity and catalytic activity. The large surface area to volume ratio, the variations in geometry, and the electronic structure of nanoparticles have a strong effect on catalytic properties.

3. **Electrical properties:** The energy band structure and charge carrier density in the materials can be modified quite differently from their bulk and in turn will modify the electronic properties of the materials. Nanoparticles made of semiconducting materials like Germanium, Silicon and Cadmium are not a semiconductor. Nanoclusters of different sizes will have different electronic structures and different energy level separations. So they show diverse electronic properties which depend on their size.

4. **Magnetic Properties:** The magnetic moment of nanoparticles is found to be very less when compared with its bulk size**.** It should be possible that non-ferromagnetic bulk exhibits ferromagnetic-like behavior when prepared in the nano range. Bulk Gold and Pt are non-magnetic, but at the nano size, they are magnetic.

Nanomaterials features:

Nanomaterials have structural features in between those of atoms and the bulk materials. While most microstructured materials have similar properties to the corresponding bulk materials, the properties of materials with nanometer dimensions are significantly different from those of atoms and bulks materials.

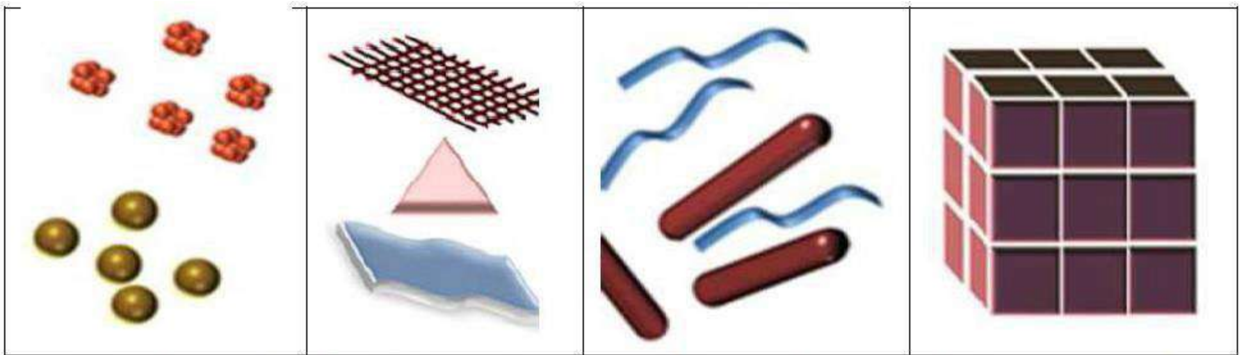
This is mainly due to the nanometer size of the materials which render them: Large fraction of surface atoms, high surface energy, and reduced limitation which do not exist in the corresponding bulk materials.Due to their small dimensions, nanomaterials have a n extremely large surface area to volume ratio, which makes a large to be the surface or interfacial atoms, resulting in more "surface" dependent material properties. Especially when the sizes of nanomaterials are comparable to length, the entire material will be affected by the surface properties of nanomaterials. This in turn may enhance or modify the properties of the bulk materials. For example, metallic nanoparticles can be used as very active catalysts. Chemical sensors from nanoparticles enhanced the sensitivity and sensor selectivity.

Classification of Nanomaterials:

Nanomaterials can be nanoscale in one dimension (e.g., surface films), two dimensions (e.g., strands or fibers), or three dimensions (e.g., precipitates, colloids). They can exist in a single, fused, aggregated, or agglomerated forms with spherical, tubular, and irregular shapes.

Nanostructures (dimensions of the nanomaterials)

Are the ordered system of one dimension, two dimensions, or three dimensions of nanomaterials, assembled with nanometer-scale in a certain pattern which includes nanosphere, nanotubes, nanorods, nanowires, and nanobelt. Nano-structured materials are classified as zero- dimensional, one- dimensional, two-dimensional, three-dimensional nanostructures.



(a) 0D spheres and clusters	(b) 1D films, plates, and networks	(c) 2D nanofibers, wires, and rods,	(d) 3D nanomaterials or nanocrystallite

The **Clusters** are particles containing a very small number of atoms or simply a few hundred atoms or smaller. A **Nanocrystallite** is generally understood to possess crystalline order in addition to nanoscale size.

Note: If one dimension of the three-dimensional nanostructure is at the nanoscale, then it is called a **Quantum Well**. If two dimension of the three-dimensional nanostructure is at the nanoscale, then it is called a **Quantum Wire**. If all the three dimensions of the nanostructure are at the nanoscale, then it is called a **Quantum Dot**. Nanocrystallites are also called quantum dots.

The ***seven main nanomaterial categories*** are

(1)) Carbon-based nanomaterials
(2) Nano-composites
(3) Nano-metals & Nano-alloys
(4) Biological nanomaterials
(5) Nano-polymers
(6) Nano-glasses
(7) Nano-ceramics.

Quantum Confinement: In nanocrystals, the electronic energy levels are not continuous as in the bulk but are discrete (finite density of states), because of the confinement of the electronic Wave function to the physical dimensions of the particles**.** This phenomenon is called Quantum confinement.

There are two ways of approaching the properties of nanoscale objects: the ***Bottom-up*** approach and the ***Top-down*** approach. In the **Bottom-up** approach (or ***Atom-Atom Assembly***), one assembles atoms and molecules into objects whose properties vary discretely with the number of constituent entities, and then increases the size of the object until this discretization gives way to the limit to continuous variation. The relevant parameter becomes the size rather than the exact number of atoms contained in the object. In the **Top-down** approach, one considers the evolution of the properties of a sample as its size is whittled down from macroscopic toward nanometric lengths.

Carbon-based Nanomaterials (or Nano carbons): They are defined as materials in which the nano component is pure carbon. Fullerenes and carbon nanotubes are excellent examples of it. When graphite was vaporized using a laser beam a molecule that contained 60 carbon atoms as the major product called ***Fullerenes*** the molecule was based on rings of 5 and 6 carbon atoms, looking just like a soccer ball**.** ***Carbon nanotubes (CNTs)*** are molecular tubes having diameters of a few nanometers (as low as 1 nm) made up of lattices of carbon atoms. CNTs were discovered in 1991 by the Japanese electron microscopist Sumio Iijima who was studying the material deposited on the cathode during the arc-evaporation synthesis of fullerenes.

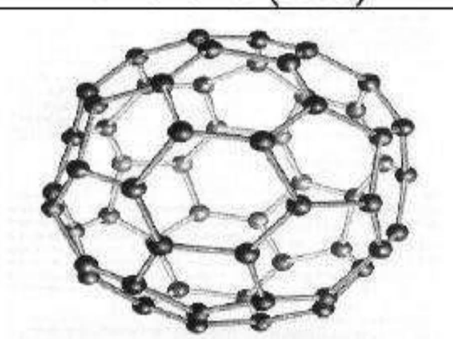
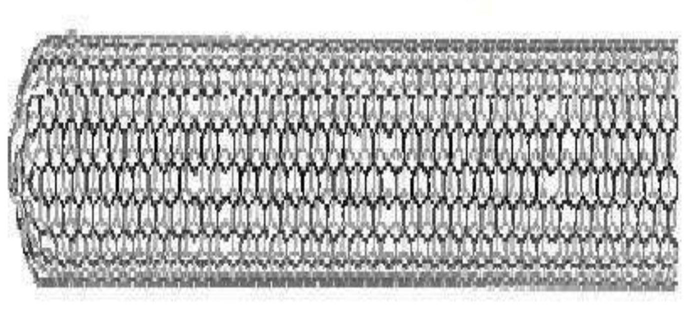
Fullerenes are made by the heating of graphite in an electric arc in the presence of inert gases such as helium or argon. Fullerenes are the only pure form of carbon because they have a smooth structure without having „dangling‟ bonds. Fullerenes are cage-like molecules. C**60** molecule has a shape like a soccer ball and Spherical fullerenes are called ***Buckyballs*** in short.

Fullerenes are a class of cage-like carbon compounds that contained 60 carbon atoms, composed of fused pentagonal and hexagonal carbon rings, looking just like a soccer ball. It contains twenty carbons ring from five carbon atoms and twelve carbons ring from six carbon atoms. A six-membered ring is fused with six or five-membered rings but a five- membered ring can only fuse with six-membered rings. C-60 can be used as excellent microscopic ball bearings, lubricant, and catalyst. They can cage other molecules, so in the future, this may be used to deliver drugs in small amounts for slow release**,** e.g., cancer treatment.

Carbon Nanotubes (CNT)

Carbon Nanotubes (CNT)

They are molecular tubes (cylindrical nanostructure) having diameters of a few nanometers made up of lattices of carbon atoms. CNTs are at least 100 times stronger than steel. In addition, they conduct heat and electricity far better than copper. So, CNTs can be used in tiny, physically strong conducting devices. CNTs have been filled with potassium atoms, making them even better electrical conductors.

Fullerene (C60)	Carbon nanotube (CNT)
	

Synthesis of Nanoparticles (NPs)

In general, NPs can be synthesized by using the chemical, physical or mechanical method, depending on either the principle of a bottom-up or top-down approach. The bottom-up approach fabricates NPs by atom-atom or molecule or cluster-cluster pairs. The top-down approach takes a large-scaled substance and modifies it to Nanometric dimensions. Nanomaterials deal with very fine structures: a nanometer is a billionth of a meter. This indeed allows us to think in both the ‘ bottom up’ or the‘ top down’ approaches to synthesize nanomaterials, i.e. either to assemble atoms or to dis-assemble (break, or dissociate) bulk solids into finer pieces until they are constituted of only a few atoms. This domain is a pure example of interdisciplinary work encompassing physics, chemistry, and engineering up to medicine.

Meanwhile, there are other ways to classify preparation methods in terms of medium phase for preparation Gas-phase/ Liquid phase/ Aerosol phase/ Solid-phase. There are a variety of physical techniques, typically a 'top-down' approach which can yield sub-10nm particles, but the major drawbacks are surface contamination and the introduction of structural defects that cannot achieve the high size uniformity. Producing metal nanoparticles of good stability is a wild job due to their high surface energy and have a great tendency to aggregate, also it is an expensive method Whereas, chemical techniques are regarded as better, cheaper with no need for sophisticated instruments, and provide a larger yield

Techniques of synthesis Nanomaterials:

There are a large number of techniques available to synthesize different types of Nanomaterials in the form of colloids, clusters, powders, etc. that some important methods are:

1. Physical method.
2. Chemical method.
3. Biological method.
4. Hybrid technique.

Mechanical grinding

Mechanical attrition is a typical example of a 'top-down' method of synthesis of nanomaterials, where the material is prepared not by cluster assembly but by the structural decomposition of coarser-grained structures as the result of severe plastic deformation.

This has become a popular method to make Nano crystalline materials because of its simplicity, the relatively inexpensive equipment needed, and the applicability to essentially the synthesis of all classes of materials. The major advantage often quoted is the possibility for easily scaling up to capacity quantities of material for various applications. Similarly, the serious problems that are usually cited are;

1. Contamination from milling media and/or atmosphere
2. To consolidate the powder product without coarsening the Nano crystalline microstructure. The contamination problem is often given as a reason to dismiss the method, at least for some materials.

Mechanical milling is typically achieved using a high-energy shaker, earthly ball. The energy transferred to the powder from refractory or steel balls depends on the rotational (vibrational) speed, size and number of the balls, ratio of the ball to powder mass, the time of milling, and the milling atmosphere. Nanoparticles are produced by the shear action during grinding.

Milling in cryogenic liquids can greatly increase the brittleness of the powders influencing the fracture process. As with any process that produces fine particles, an adequate step to prevent oxidation is necessary. Hence this process is very restrictive for the production of non-oxide materials since then it requires that the milling take place in an inert atmosphere and that the powder particles be handled in an appropriate vacuum system or glove box.

This method of synthesis is suitable for producing Nano crystalline alloy particles, elemental or compound powders.

If the mechanical milling imparts sufficient energy to the constituent powders a homogeneous alloy can be formed. Based on the energy of the milling process and thermodynamic properties of the constituents the alloy can be rendered amorphous by this processing.

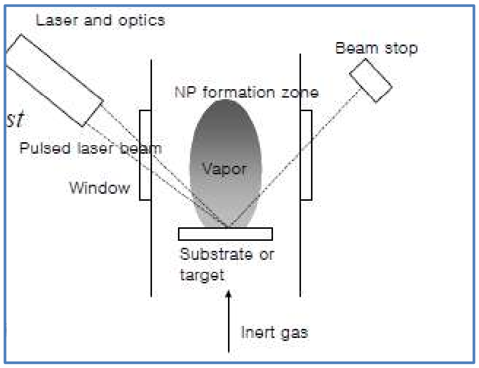
Classification of preparation methods

- In terms of the method of "monomer" preparation

A monomer is a molecule that forms the basic unit for polymers, which are the building blocks of proteins.

Physical / Chemical

aser ablation of solids



- Laser ablation is a technique in which a pulsed laser rapidly heats
- A very thin (<100 nm) layer of substrate material, resulting in the formation of an energetic plasma above the substrate.

- This technique should be distinguished from laser vaporization, as apart from atoms and ions also fragments of solid or liquid material are ablated from the substrate surface which varies in size from sub-nanometric to micrometric. Therefore it cannot be considered as a pure homogeneous nucleation process.
- The pulse duration and energy determine the relative amounts of ablated atoms and particles.
- Typically used lasers are the ND: YAG (532 nm) and excimer (191, 248, and 308 nm) lasers. The material removal rate by laser ablation decreases with longer target exposure times, therefore the target is usually rotated. When used for producing films, this technique is called pulsed laser deposition (PLD).
- Typical production rates are in the order of micrograms per pulse with pulse frequencies of about 50 Hz, yielding 10-100 mg powder per hour. Reactive laser ablation in which a reaction of the ablated material with the reactor gas occurs is also used ablated an Al target in an O_2 atmosphere, producing Al_2O_3 nanoparticles.

ials Synthesis of Nanomaterial By the biological method:

Synthesis of Nanomaterials using biological ingredients can be roughly divided into the following three types:

1. Use of microorganisms.
2. Use of plant extracts or enzymes.
3. Use of templates like DNA, membranes, viruses, and diatoms.

- Microorganisms are the organisms that are detectable under a microscope such as bacteria, fungi, yeasts, etc.
- Some bacteria are quite useful and are used in the processing of cheese, curds, bread, alcohol, vaccines, etc.
- Some are harmful and are responsible for spoiling food or causing diseases.
- Microorganisms are capable of interacting with metals coming in contact with them through their cell and form nanoparticles.

Prokaryotic and Eukaryotic cells.

- The prokaryote cell is simpler and therefore smaller, than a eukaryote cell, lacking a nucleus and most of the other organelles of eukaryotes.
- Eukaryotic cells are about 15 times wider than a typical prokaryote and can be as much as 1000 times greater in volume.
- The major difference between prokaryotes and eukaryotes is that eukaryotic cells contain membrane-bound compartments in which specific metabolic activities take place.
- Some microorganisms produce H_2S. It can oxidize organic matter forming sulfate, which in turn acts like an electron acceptor for metabolism.
- This H_2S can in presence of metal salt, convert metal ions into metal sulfide, which deposits extracellular.
- Metal ions form a metal salt enters the cell body. The metal ions are then converted into a nontoxic form and covered with certain proteins to protect the cell from a toxic environment.
- Microorganisms are capable of secreting some polymeric materials like polysaccharides; they have phosphate, hydroxyl, and carboxyl anionic groups which complex with metal ions and bind extracellularly Cells are capable of reacting with metals or ions by processes like oxidation, reduction, methylation, and demethylation.

Classification of preparation methods

- In terms of phase of medium for preparation

Gas-phase/ Liquid phase/ Aerosol phase/ Solid phase Gas-
Phase Physical Preparation

Characteristics of gas-phase preparation Formation in the less dense and more mobile phase:

- Requires large-V and high -T process
- High equipment cost
- exclude additional sintering process
- Aggregation: less and weak but still some
- Properties: quite different between gas and NP produced
- No solubility problems for precursors in gas media
- Sulfide, nitride, carbide, and boride: easily obtainable
- Less number of chemical species and processes involved
- High purity product/ environmentally friendly
- No washing, no additional sintering, and easier recovery
- No effective stabilizers and less controllable Liquid-phase Preparation In general, liquid-phase preparation has an advantage
- Highly developed
- High controllability
- Produce very progressing products
- But has disadvantages, too.
- Requires lots of chemical species and process steps, e.g. aging, filtration, washing, drying, sintering (thermal treatment) Droplet-to-Particle Conversion-Aerosol-phase preparation Advantage of aerosol preparation.
- Media: both liquid + gas
- Use of advantage of gas-phase preparation
- Continuous, simple processes, less number of chemical species, no sintering process
- Gas-to-droplet interaction Evaporation (drying)/condensation, droplet-surface interaction
- Confined growth
- Methods of atomization
- Disintegration (nebulization) of liquid or suspension by
- Pressure atomizer
- Two-fluid atomizer
- Rotating disk atomizer
- Ultrasonic nebulizer
- Electrospray

Types of Nanomaterials (NMs)

Nanomaterials can be metals, ceramics, polymeric materials, or composite materials. For biomedical applications there are two major types:

1- Organic Nanomaterials

Particles with organic molecules as a major constructing material e.g., liposomes and dendrimers.

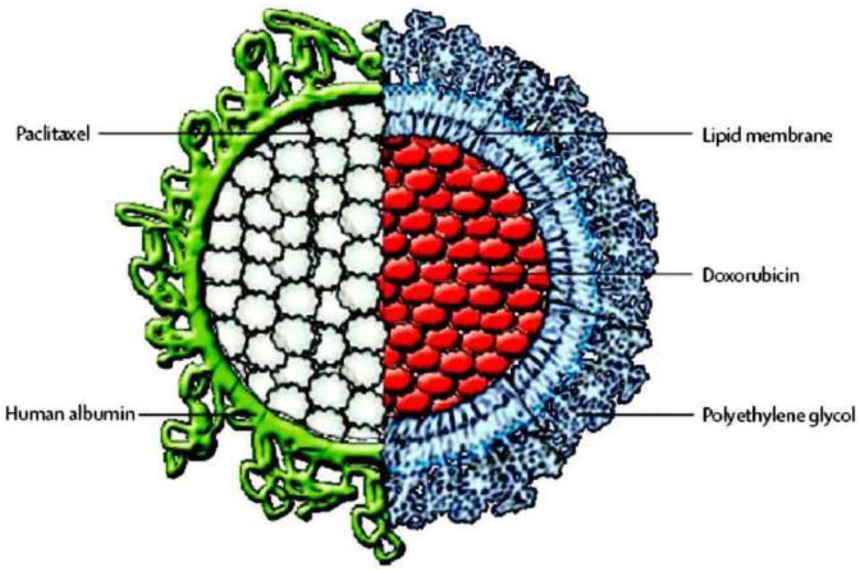
A- Liposome is an artificially-prepared spherical vesicle composed of a lipid bilayer. The liposome can be used as a vehicle for the administration of nutrients and pharmaceutical drugs. Liposomes can be prepared by disrupting biological membranes (such as by sonication).

• Liposomes are often composed of phosphatidylcholine-enriched phospholipids and may also contain mixed lipid chains with surfactant Surfactants are usually amphiphilic organic compounds, meaning they contain both hydrophobic groups (their *tails*) and hydrophilic groups (their *heads*). Therefore, a surfactant contains both a water-insoluble (or oil soluble) component and a water-soluble component. A liposome design may employ surface ligands for attaching to unhealthy tissue.

• The major types of liposomes are the multilamellar vesicle (MLV), the small unilamellar vesicle (SUV), the large unilamellar vesicle (LUV), and the cochleate vesicle.

• Liposomes have spherical shape NMs made of lipid bilayer membranes that have an aqueous interior. They are being used as vehicles for drug delivery in different human tumors.

B- Dendrimers are synthetic molecules that contain high functional groups, nearly spherical structures, nanometer sizes, large numbers of reactive end group functionalities, shielded interior voids, with low systemic toxicity used as drug and gene delivery. Exciting results are produced by using organic nanoparticles.



The basic structure of organic nanoparticles

***Paclitaxel** is a mitotic inhibitor used in cancer chemotherapy

***Albumin** is emerging as a versatile protein carrier for drug targeting protein-based drugs

2- Inorganic Nanomaterials

- This kind of Nanomaterials consists of inorganic elements, usually metals, as a core.
- The most popular examples are quantum dots (QDs), gold and silver, metal oxides, iron oxide magnetics NPs, and carbon nanotube.

- Quantum dots are fluorescent nanoparticles of 2–10 nm in size that contain a core of hundreds to thousands of atoms of group II and VI elements (e.g., Cadmium, Technetium, Zinc, and Selenide) or group III (e.g., Tantalum) and V elements (e.g., Indium).

- To make them more soluble in water, QDs capped with coordinating ligand and an amphiphilic polymer.

- The typical structure of QDs enables them to have unique characterization which includes emitting powerful fluorescence (differs in nature from organic dyes) with minimum overlap between spectra and they can be turned to emit between 450nm and 850nm by changing the size or chemical composition of the nanoparticle.

- These and other advantages of QDs make it possible to label multiple molecular targets simultaneously by the use of quantum dots both *in vitro* and *in vivo*.
- However, the use of quantum dots in imaging and therapeutics *in vivo* is limited by the toxic effects of the heavy metal core.

• Gold Nanoparticles (Au NPs) has unique chemical and physical properties in addition to the high surface-to-volume ratio depending on their size, shape, and degree of aggregating gold nanoparticles that can appear red, blue, or in other colors

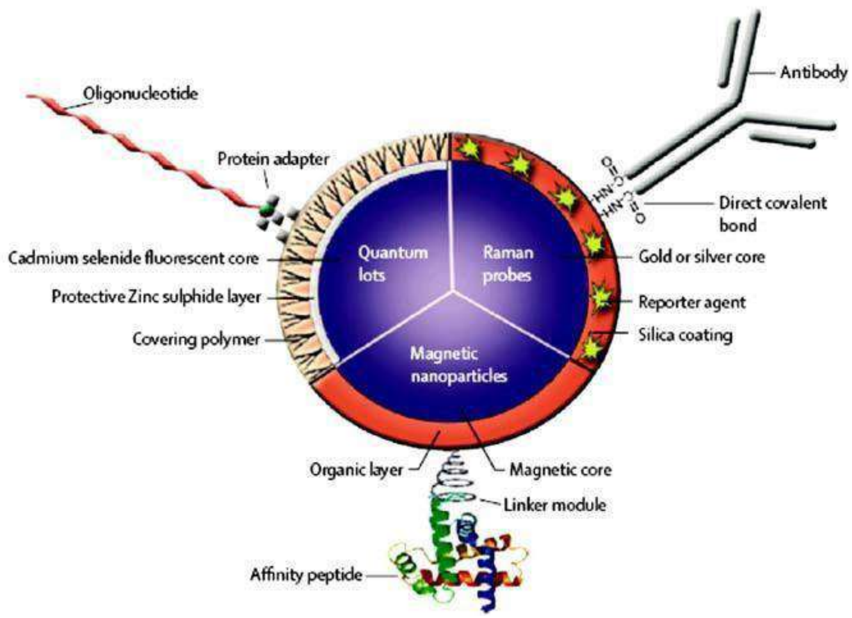


Figure: shows the basic structure of inorganic nanoparticles.

Functionalization strategies and chemistry

Successful conjugation of biological molecules on nanoparticles is a critical point for nanomaterials (NMs) use in biomedical applications, therefore it is necessary to control the strategy of incorporating a specific biomolecule on the surface of NMs or inside the NMs. It is worth mentioning that an efficient functionalization is influenced by several parameters such as nanoparticles shape, structure, size, charge, chemistry, and surface modification

Two major ways have been utilized to achieve this purpose, as follows:

1- Covalent immobilization techniques

This kind of immobilization depends on the chemically modified surfaces of nanoparticles used to provide a covalent bond without the addition of a spacer. Upon covalent linkage of amino groups on the biological molecules with carboxyl groups at the free ends of stabilizer (NHS esters are formed). Using this protocol, almost all kinds of biological molecules can be attached to the surface of nanoparticles

2- Non-covalent immobilization techniques

These interactions generally involve non-covalent bonding (i.e. ionic, hydrogen bonding, hydrophobic interactions). Hydrophobic interactions are taking place due to attraction between hydrophobic parts of the antibody and the metal surface. Typically, the bonding of biomolecules by this technique is unstable because the biomolecule can be fully done from nanoparticles

Characterization of nanoparticles

Detection, characterization, and isolation

The detection and characterization of nanoparticles present scientists with particular challenges. Being of a size that is at least four to seven times smaller than the wavelength of light means that individual nanoparticles cannot be detected by the human eye, and they are observable under optical microscopes only in liquid samples under certain conditions. Thus, in general, specialized techniques are required to see them, and none of these approaches is currently field-deployable.

Techniques to detect and characterize nanoparticles fall into two categories: direct and indirect.

- ❖ Direct techniques include transmission electron microscopy (TEM), scanning electron microscopy (SEM), and atomic force microscopy (AFM).

These techniques can image nanoparticles, directly measure sizes, and infer shape information, but they are limited to studying only a few particles at a time. There are also significant issues surrounding sample preparation for electron microscopy. In general, however, these techniques can be quite effective for obtaining basic information about a nanoparticle.

- ❖ Indirect techniques use X-rays or neutron beams and obtain their information by mathematically analyzing the radiation scattered or diffracted by the nanoparticles.

The advantage of these techniques is that they can simultaneously sample and average very large numbers of nanoparticles and often do not require any particular sample preparation.

Nanoparticles in the environment

Nanoparticles occur naturally in the environment. For example, the sea emits an aerosol of salt that ends up floating around in the atmosphere in a range of sizes, from a few nanometers upward, and smoke from volcanoes and fires contains a huge variety of nanoparticles, many of which could be classified as dangerous to human health.

Dust from deserts, fields, and so on also has a range of sizes and types of particles, and even trees emit nanoparticles of hydrocarbon compounds such as terpenes (which produce the familiar blue haze seen in forests).To understand the potential of nanoparticles, a deeper knowledge of their synthesis and applications is needed. Characterization is done by using a variety of different techniques

Nanoparticle characterization

Nanoparticle characterization parameters include:

1. Surface area and porosity
2. Solubility
3. Particle size distribution
4. Aggregation
5. Hydrated surface analysis
6. Wettability
7. Adsorption potential
8. Shape and size of interactive surface

Understanding nanoparticle characterization parameters

There are several techniques used to understand these characterization parameters in nanoparticles.

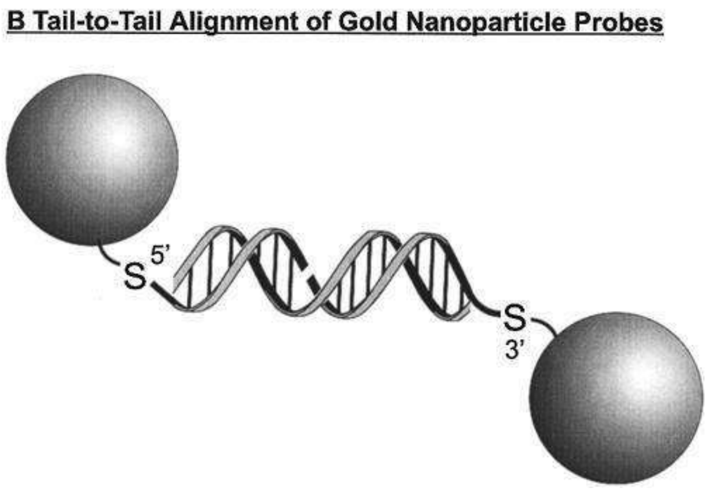
For example, they include:

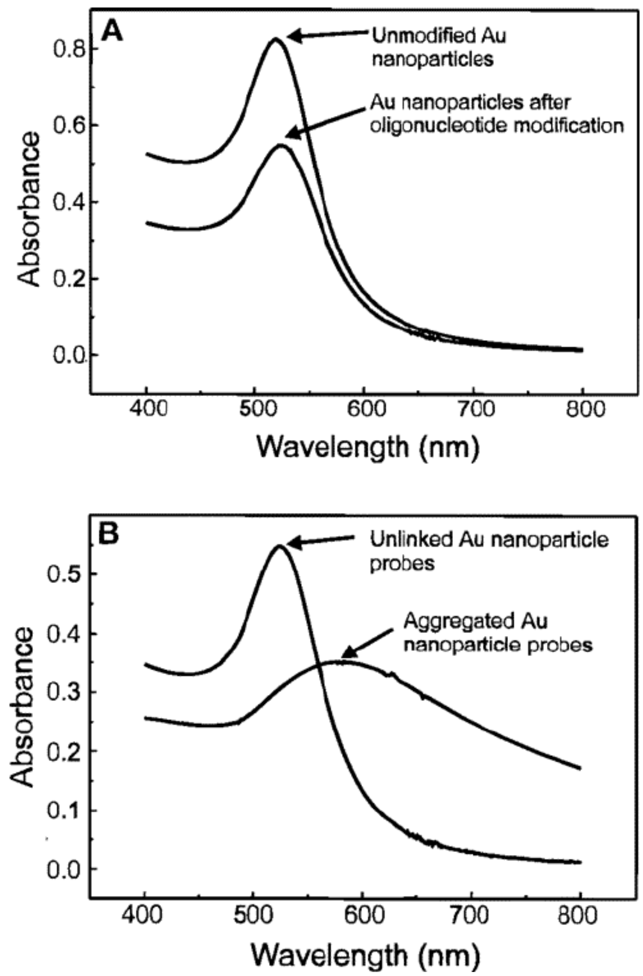
1. -Electron microscopy including TEM and SEM
2. -Atomic force microscopy (AFM)
3. -Dynamic light scattering (DLS)
4. -X-ray photoelectron spectroscopy (XPS)
5. -Powder X-ray diffraction (XRD)
6. -Fourier transform infrared spectroscopy (FTIR)
7. -Ultraviolet-visible spectroscopy
8. -Dual polarisation interferometry
9. -Nuclear magnetic resonance (NMR)

Plasmon Absorbance - Factors

- Surface functionality, temperature, and the solvent
- Particle concentration and particle size

Plasmon absorbance – Applications





Nanoscale Imaging

- Scanning Electron Microscope (SEM)
- Transmission Electron Microscope (TEM)
- Scanning Probe Microscopy (SPM)
- Scanning tunneling microscopy
- Atomic force microscopy (AFM)

❖ **Transmission Electron Microscope (TEM)**

- Specimens for examination under the transmission electron microscope (TEM) must be specially prepared to a thickness that permits the passage of electrons (50-500 nm).

- As the wavelength of electrons is much smaller than that of light, the resolution attainable in TEM images is many orders of magnitude better than that of a light microscope.
- Transmission electron microscopes can reveal the finest internal details of a cell.
- For biological samples, cell structure and morphology are commonly determined whilst the localization of antigens or other specific components within cells is readily undertaken using specialized preparative techniques. Atomic resolution is possible.

❖ Scanning Electron Microscope (SEM)

- By scanning an electron beam across a specimen and collecting electrons emitted from the irradiated spot we can obtain topographical and chemical information on materials from the macroscopic scale to very high magnifications with great depth of field in focus.

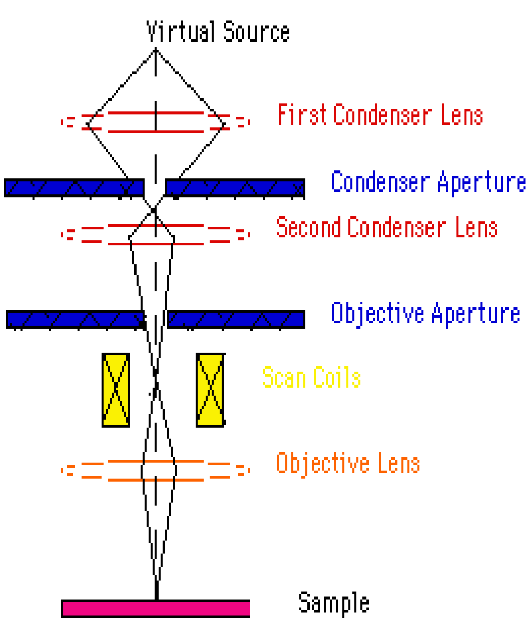


Figure: Scanning Electron Microscope

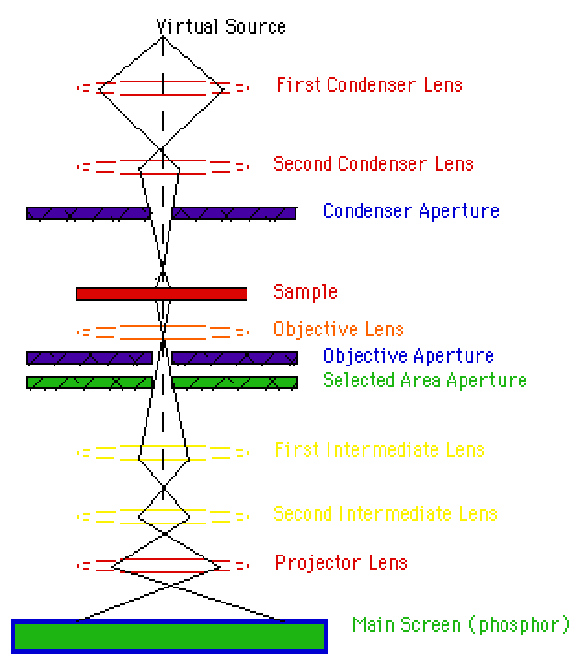


Figure: Transmission Electron Microscope

SEM

-High Resolution of bulk specimens (no need to make sample thin)

-20 - 50 Å: most commercial instruments (less than 10 Å for research instruments)

-3-D appearance of the specimen image as a result of the large depth of field (depth of focus)

-Capable of very low magnifications complementing the information available from the optical image

TEM

-High Resolution of thin specimens

-1.2 - 1.5 Å: most commercial instruments

-No 3-D appearance of the specimen image

-Technique that provides crystallographic/structural information (lattice arrangement, orientation relationships, dislocations, twins...)

Scanning Probe Microscopy (SPM)

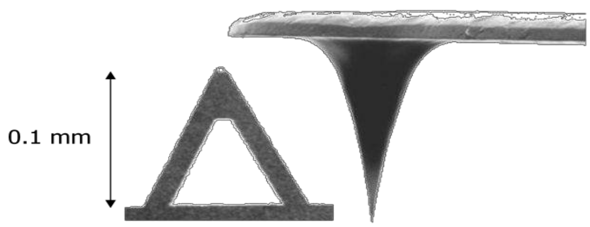
SPMs are a family of instruments used for studying the properties of materials from the atomic to the micron level.

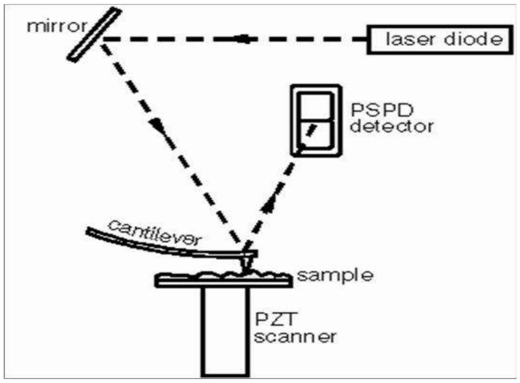
Atomic Force Microscopy (AFM)

- An AFM probes the surface of a sample with a sharp tip. Tip located at the free end of a cantilever that is 100-200 μm long.
- Forces between the tip and cantilever cause the cantilever to bend and/or twist.
- This deflection is measured as the tip is scanned over the surface, providing a map of the surface topography.
- AFMs can be used to study insulators and conductors.

AFMs can be operated in air, vacuum, and liquids. Biological measurements, in particular, are often carried out *in vitro* in biological fluids

Atomic Force Microscopy





Contact (Repulsive) Mode AFM

- AFM tip makes soft physical contact with the sample.
- Contact force causes the cantilever to bend to accommodate changes in topography.

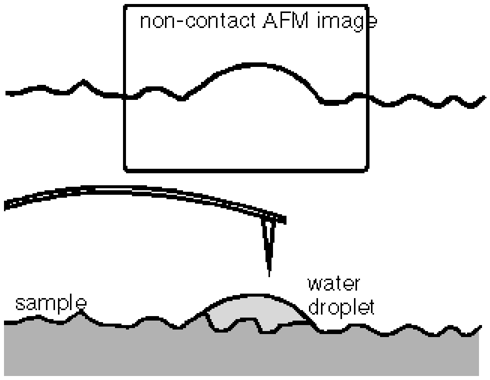
Non-Contact (Attractive) Mode

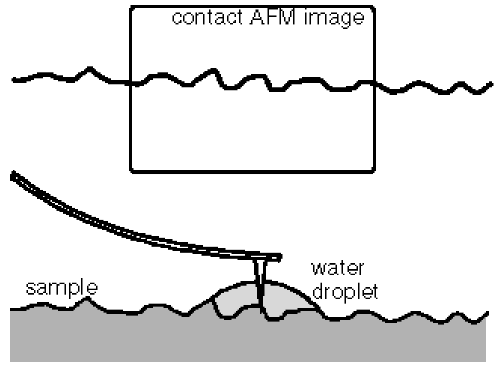
- Vibrating stiff cantilever (100 – 400 Hz).
- Detect changes in frequency or amplitude of the cantilever caused by changes in the force gradient (slope of the force-distance curve).
- Height resolution better than 0.1nm.
- Good for soft and/or elastic samples.
- No contamination of the sample by a tip.

Comparison

- Non-Contact
  - Low damage
  - Less sensitive to fine topographical detail

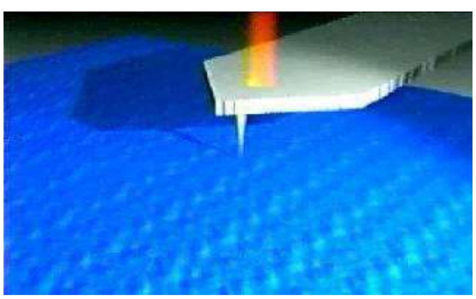
- Contact
  - Can damage soft samples through lateral forces (dragging material)

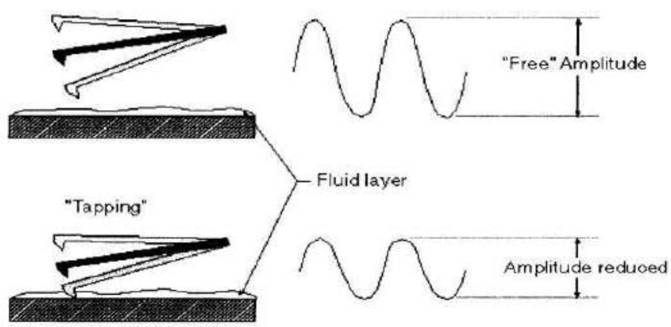




Tapping Mode AFM

- Similar to non-contact mode, but at bottom of travel the tip just ‘taps’ the Sample surface.
- Oscillation amplitude is monitored.
- Excellent for soft samples (e.g. biological samples, etc.).
- Tapping Mode overcomes problems associated with friction, adhesion, and electrostatic forces.





AFM in the Life Sciences

- Fundamental Challenges of Microscopy in Biology:
  - To preserve the specimen accurately in the native state
  - To achieve sufficient resolution to learn something useful about the structure/function of the specimen
  - AFM is a breakthrough technology that allows three-dimensional imaging and measurement of unstained and uncoated structures in air or fluid from molecular to micron scales Scanners can now be

immersed in liquids without damage, allowing direct examination of samples in biological fluids, water, or fixation media such as glutaraldehyde.

- In addition to topographic imaging, the AFM can be used simultaneously to measure forces on active biological specimens, offering insight into cellular and even molecular dynamics.
  - Countless biological processes - muscle contraction, cell motility, DNA replication, protein synthesis, drug-receptor interactions, and many others - are largely governed by intermolecular forces.
  - And with its sensitivity at the piconewton level, the AFM is an excellent tool for probing such interactions.

Characterization

Technique	Information
TEM/SEM	Size/Shape/Size Distribution
UV/vis	Size/Size Distribution
AFM	Size/Shape/Size Distribution
X-ray	Composition

Nano-Applications

Nanomedicine is the monitoring, repair, construction, and control of human biological systems at the molecular level using engineered Nano devices and nanostructures.

Nanomedicine is an inter in field of science, even a simple project needs contributions from physicists, engineers, material chemists, biologist, and end-users such as an orthopedic surgeon.

Molecular nanotechnology and molecular manufacturing are key enabling technologies.

Analyzing and repairing the human body just as we repair any other machine

Nanotechnology can be used that can be added to the fabric and make them stain resistant.

Using nanoparticles in the manufacture of solar cells is beneficial because:- They can reduce manufacturing costs by using a low-temperature process instead of the high-temperature vacuum deposition process typically used to produce conventional cells made with crystalline semiconductor material.

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.

Self-cleaning glassworks two ways: These two processes are introduced using a coating of titanium dioxide on the outside surface of the glass

1. A process called photo-catalysis is the action of light onto the surface of the glass to basically “eat” the dirt on the surface.

2. A process is known as hydrophilicity. This means that the glass “loves water” and any rainwater impacting on the surface will form sheets that will wash down any dirt in a uniform fashion.

Nanostructured devices have the potential to serve as the basis for next- generation energy systems that make use of densely packed interfaces and thin films.

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.

Pancreatic cancer 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 visible under magnetic resonance imaging (MRI).

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.