•Eukaryotic cells are about 1000 times larger than bacteria cells and also have a membrane enclosed nucleus containing their DNA, and several other internal structures known as organelles.

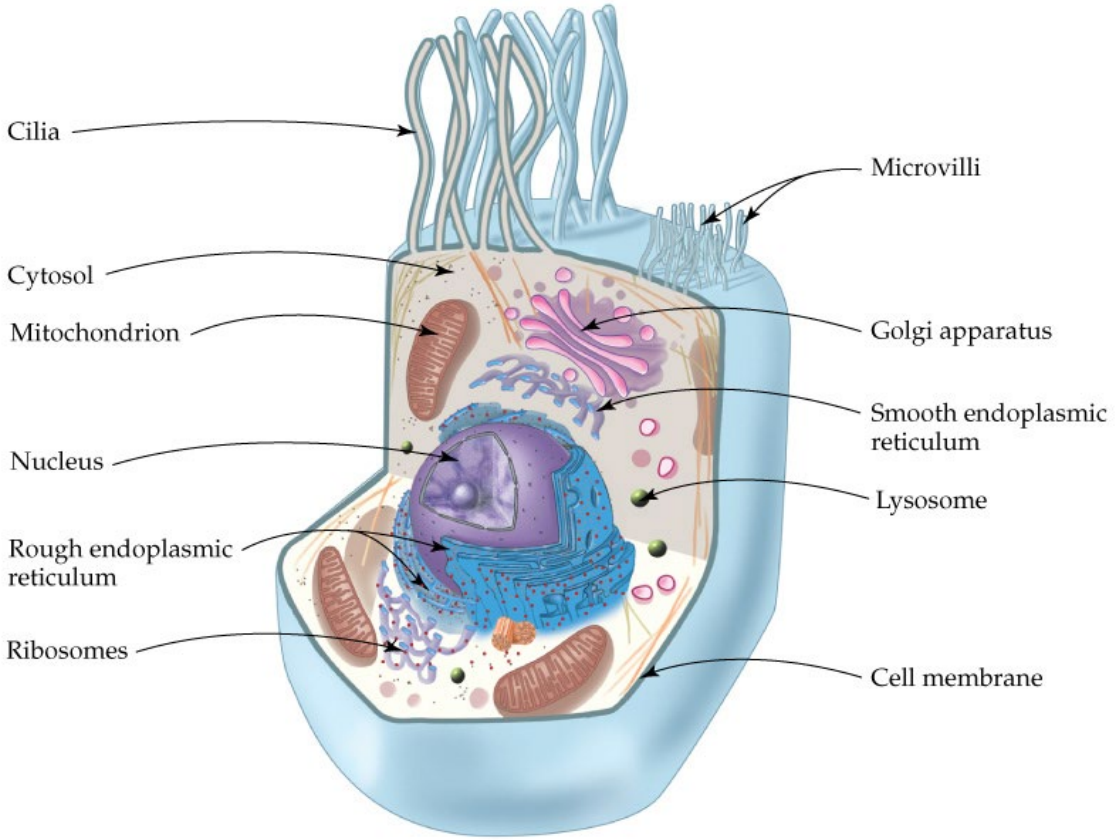
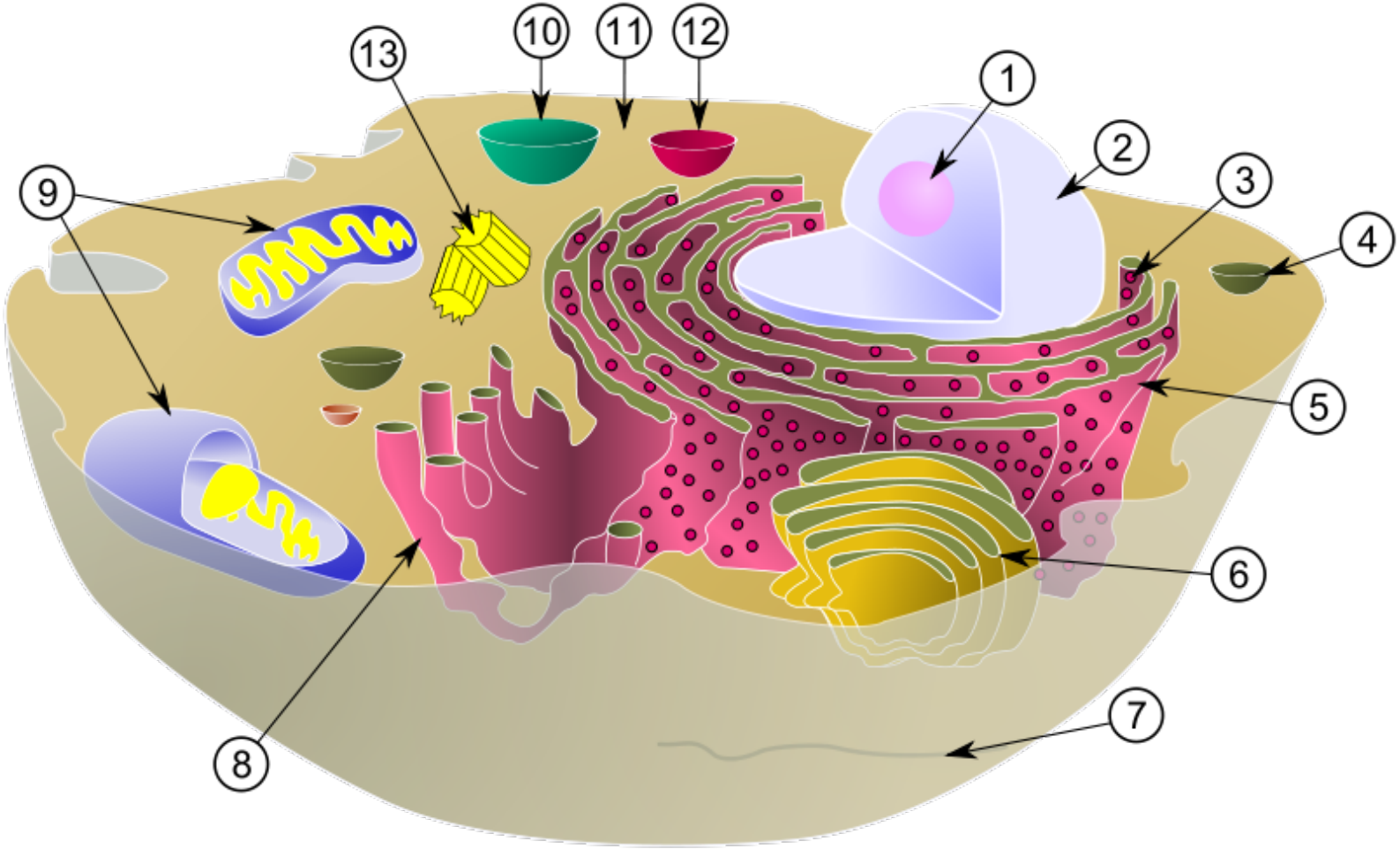
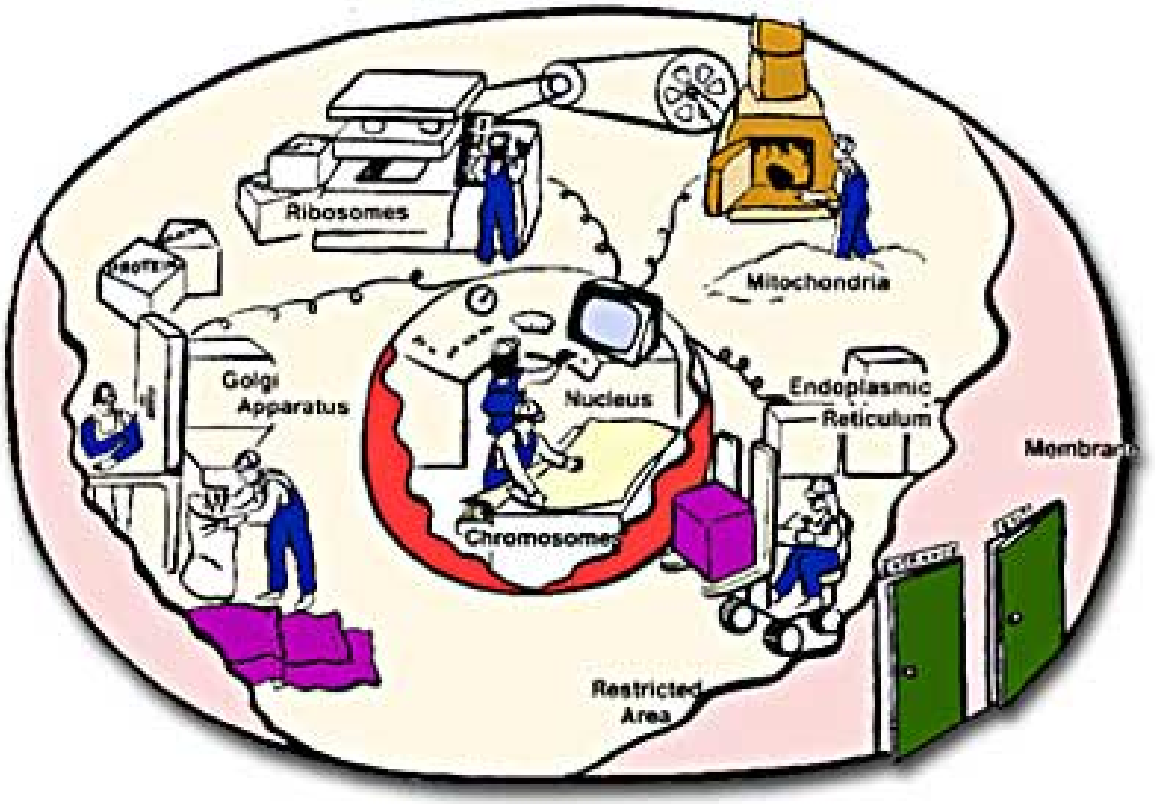


Fig 21.3 A generalized eukaryotic cell.



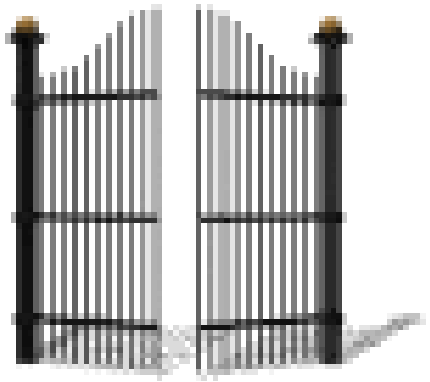
•Schematic showing the cytoplasm, with its components (or *organelles*), of a typical animal cell. Organelles: (1) nucleolus (2) nucleus (3) ribosome (4) vesicle (5) rough endoplasmic reticulum (6) Golgi apparatus (7) cytoskeleton (8) smooth endoplasmic reticulum (9) mitochondria (10) vacuole (11) cytosol (12) lysosome (13) centriole.

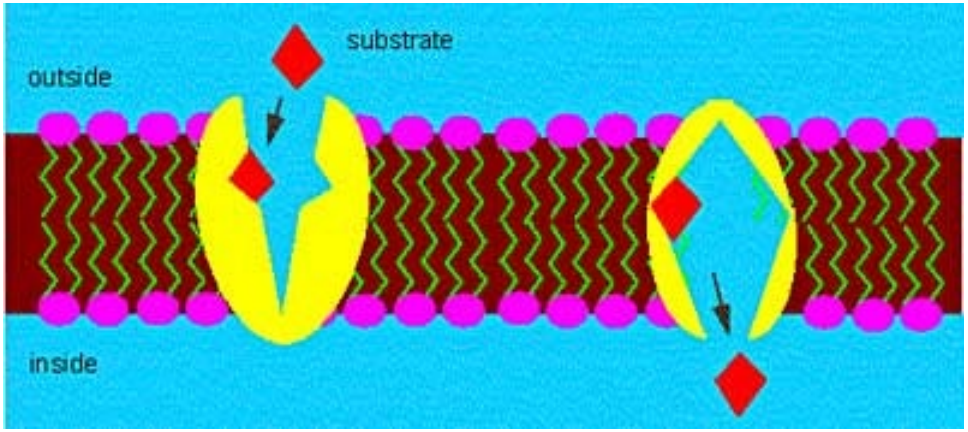
A Busy Factory



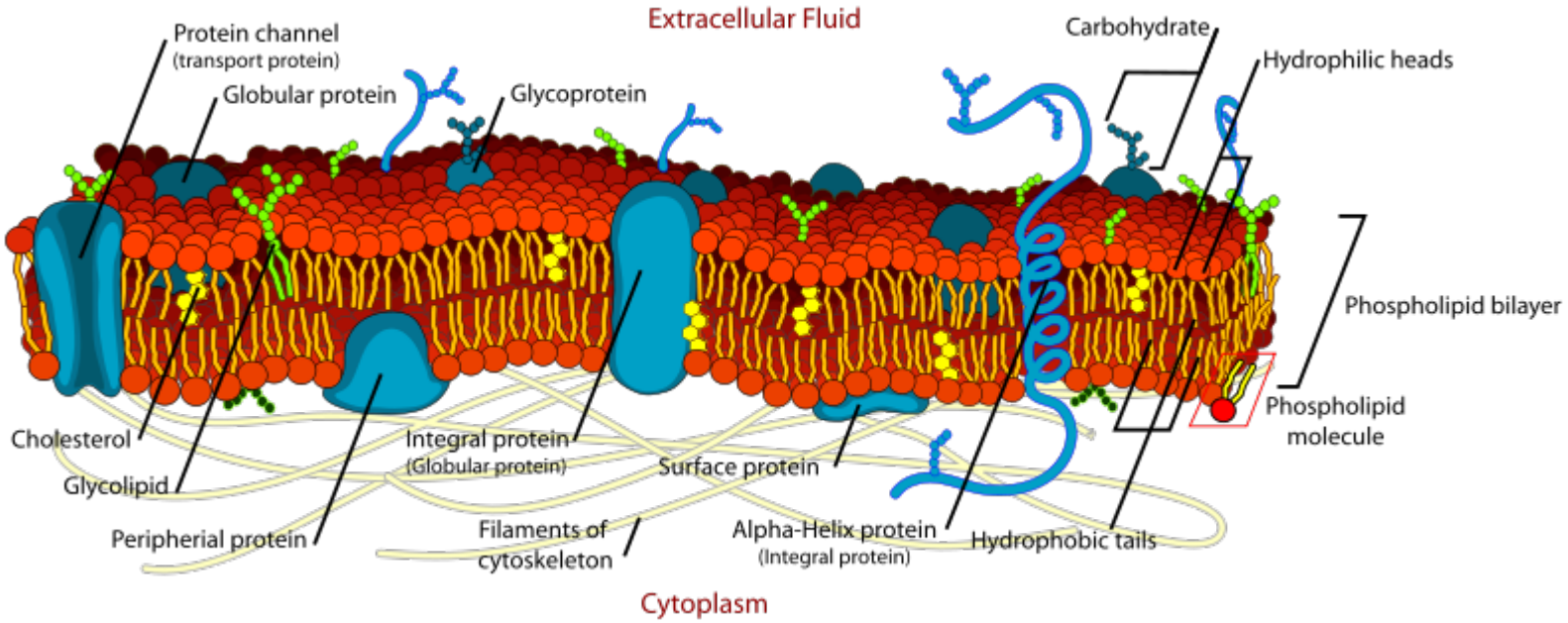
A cell can be thought of as a "factory," with different departments each performing specialized tasks.

The Plasma Membrane





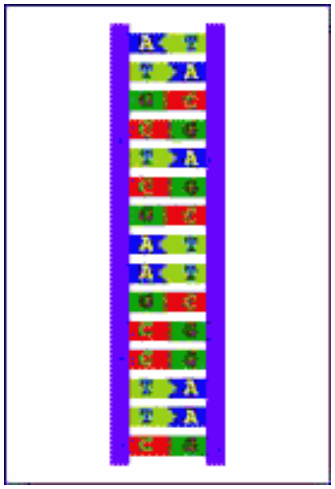
Cell Membrane



Characteristic diffusivities

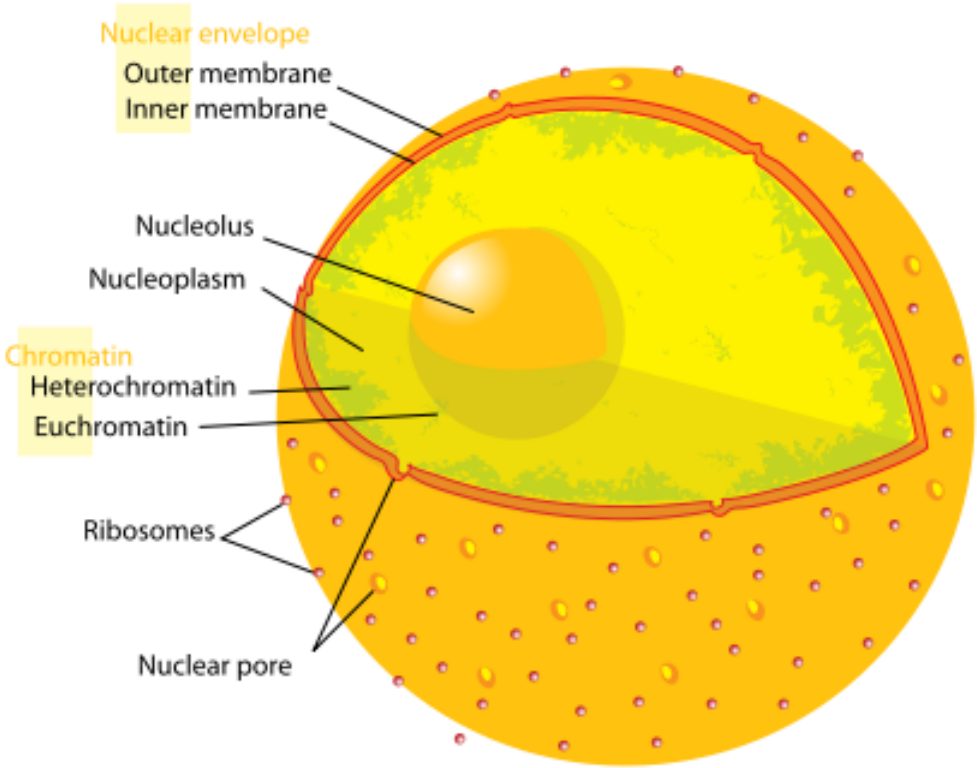
Particle	Typical size	Diffusion constant
Solute ion	10^{-1} nm	2×10^3 $\mu m^2/s$
Small protein	5 nm	40 $\mu m^2/s$
Virus	100 nm	2 $\mu m^2/s$
Bacterium	1 μm	0.2 $\mu m^2/s$
Mammalian/human cell	10 μm	0.02 $\mu m^2/s$

The Nucleus



The cell factory contains a large inventory of blueprints dating all the way to its founding. Some of these blueprints are out of date, and some are for parts and products that are no longer made. Part of your job would entail sorting through everything, finding the correct blueprints, copying them, and sending the copies out to the assembly line at the correct time.

Nucleus

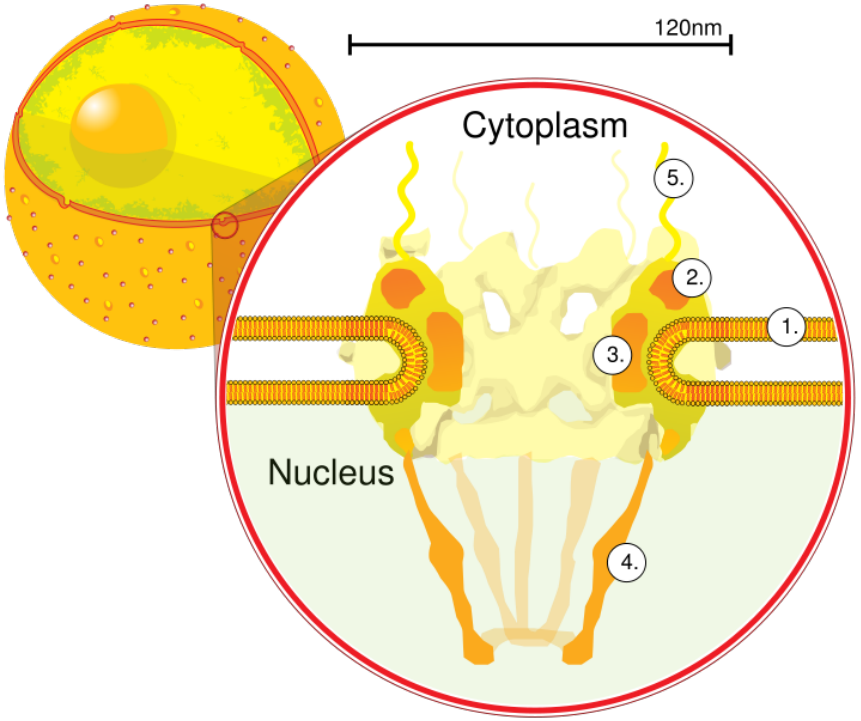


•In cell biology, the **nucleus** is a membrane-enclosed organelle found in most eukaryotic cells. It contains most of the cell's genetic material, organized as multiple long linear DNA molecules in complex with a large variety of proteins such as histones to form chromosomes. The genes within these chromosomes make up the cell's nuclear genome. The function of the nucleus is to maintain the integrity of these genes and to control the activities of the cell by regulating gene expression.

In cell biology, the **nucleolus** (plural *nucleoli*) is a "sub-organelle" of the cell nucleus, which itself is an organelle. A main function of the nucleolus is the production and assembly of ribosome components

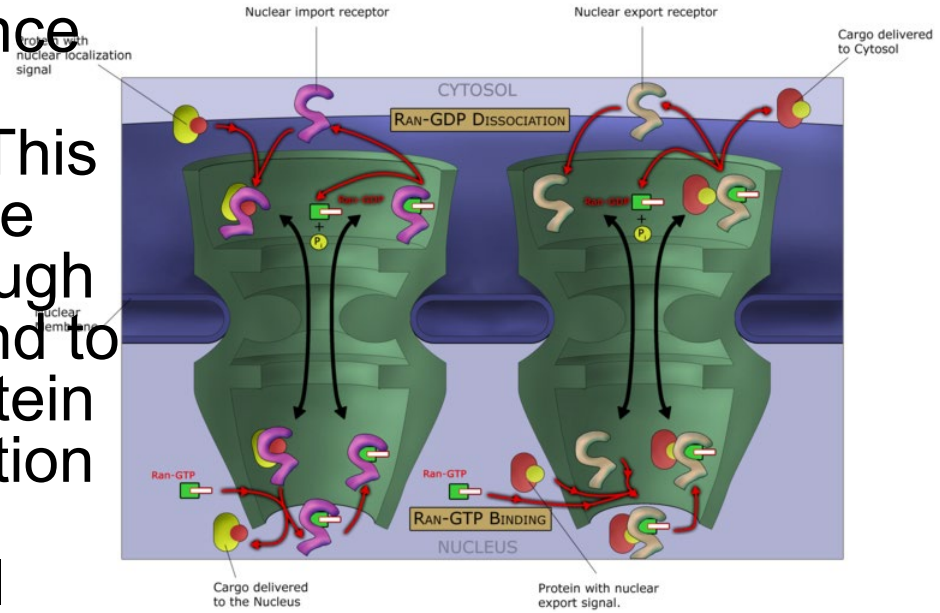
Nuclear pores

Nuclear pores, which provide aqueous channels through the envelope, are composed of multiple proteins, collectively referred to as nucleoporins. The pores are 100 nm in total diameter; however, the gap through which molecules freely diffuse is only about 9 nm wide, due to the presence of regulatory systems within the center of the pore. This size allows the free passage of small water-soluble molecules while preventing larger molecules, such as nucleic acids and proteins, from inappropriately entering or exiting the nucleus. These large molecules must be actively transported into the nucleus instead. The nucleus of a typical mammalian cell will have about 3000 to 4000 pores throughout its envelope

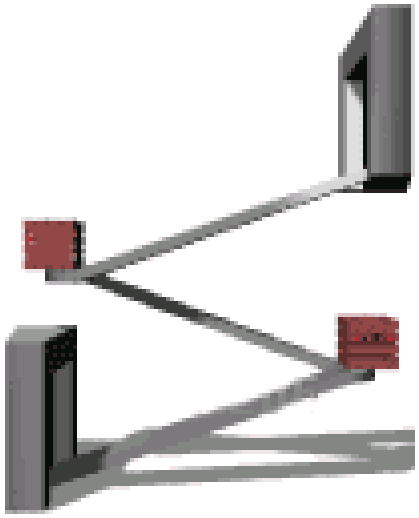


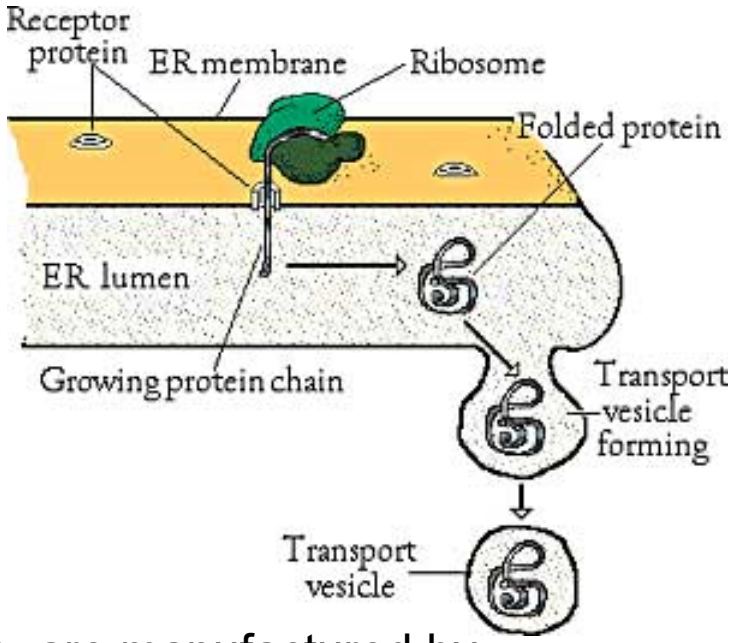
Nuclear localizing sequence (NLS)

- A **nuclear localizing sequence** (**NLS**) is an amino acid sequence which acts like a 'tag' on the exposed surface of a protein. This sequence is used to confine the protein to the cell nucleus through the **Nuclear Pore Complex** and to direct a newly synthesized protein into the nucleus via its recognition by cytosolic nuclear transport receptors. Typically, this signal consists of a few short sequences of positively charged lysines or arginines. Typically the NLS will have a sequence (NH2)-Pro-Pro-Lys-Lys-Lys-Arg-Lys-Val-(COOH).



The Ribosomes and the ER



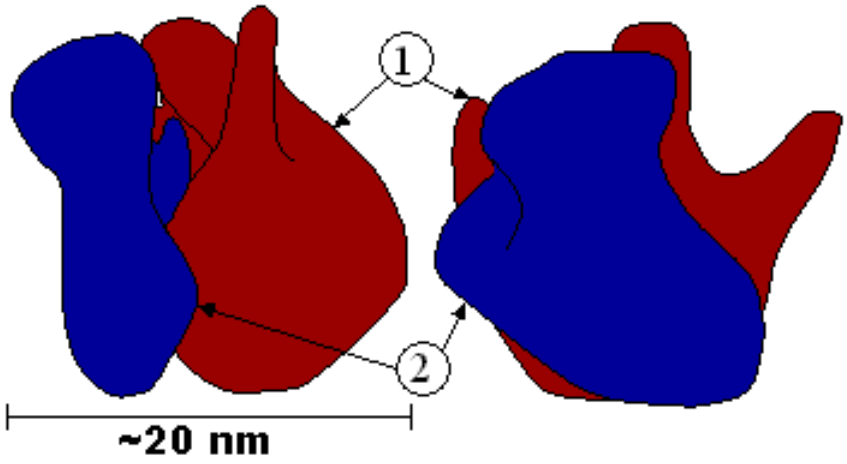


Ribosomes, the workers that build proteins, are manufactured by the nucleolus. They consist of two separate subunits: a large, lower subunit and a small, upper subunit. Ribosomes attach to the rough ER . Now let's take a look at how final processing occurs

The cell has its own assembly line and workers. Within the cytoplasm is a series of large, flattened membranes that fold back and forth on each other and have a very large surface area. This collection of membranes is called the **ENDOPLASMIC RETICULUM**, or**ER**.

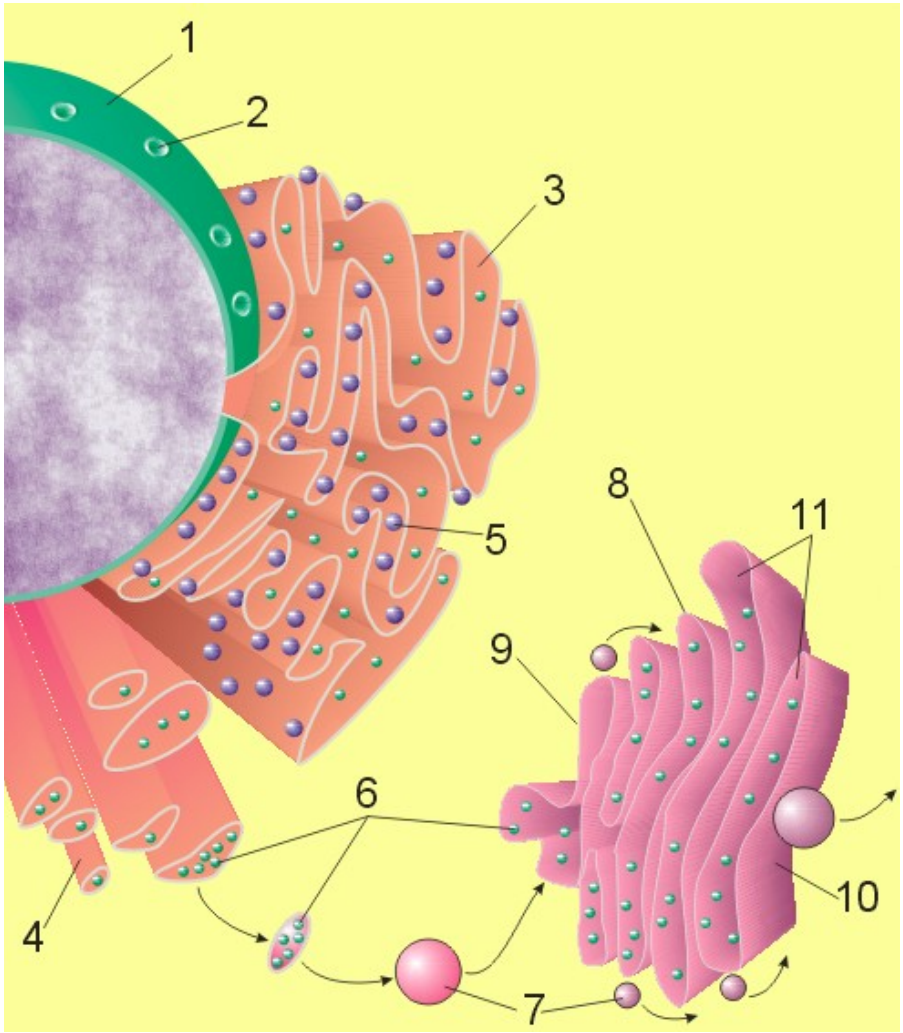
Ribosome

A **ribosome** is a small, dense organelle in cells that assembles proteins. Ribosomes are about 20nm in diameter and are composed of 65% ribosomal RNA and 35% ribosomal proteins (known as a Ribonucleoprotein or RNP). It translates messenger RNA (mRNA) to build a polypeptide chain (e.g., a protein) using amino acids delivered by Transfer RNA (tRNA). It can be thought of as a giant enzyme that builds a protein from a set of genetic instructions. Ribosomes can float freely in the cytoplasm (the internal fluid of the cell) or bound to the endoplasmic reticulum, or to the nuclear envelope.



Endoplasmic Reticulum

The **endoplasmic reticulum** or **ER** is an organelle found in all eukaryotic cells that is an interconnected network of tubules, vesicles and cisternae that is responsible for several specialized functions: Protein translation, folding, and transport of proteins to be used in the cell membrane (e.g., transmembrane receptors and other integral membrane proteins), or to be secreted (exocytosed) from the cell (e.g., digestive enzymes); sequestration of calcium; and production and storage of glycogen, steroids, and other macromolecules.[1] The endoplasmic reticulum is part of the endomembrane system. The basic structure and composition of the ER membrane is similar to the plasma membrane.



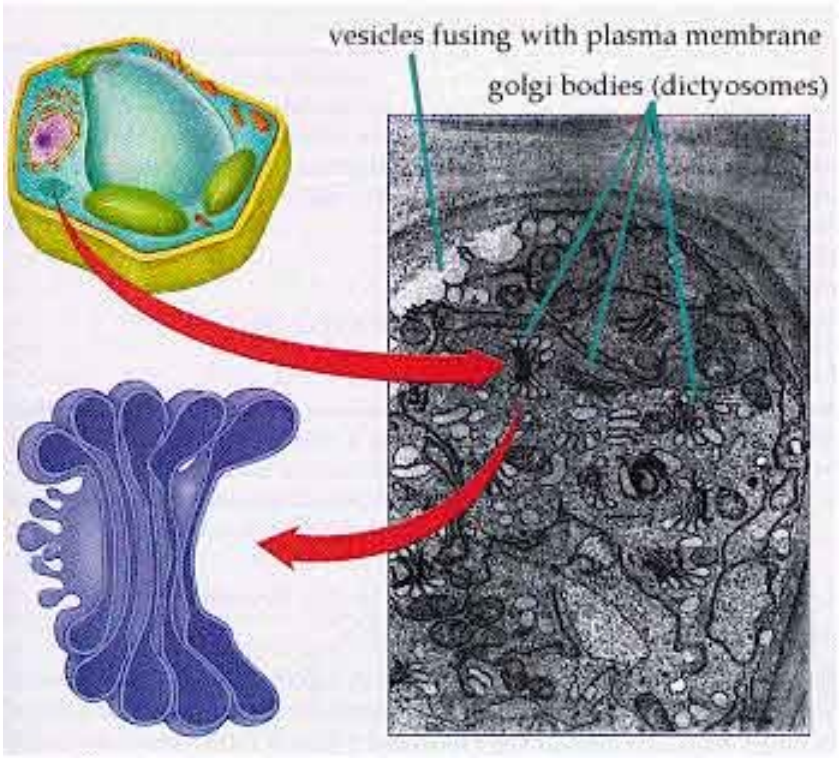
Rough endoplasmic reticulum

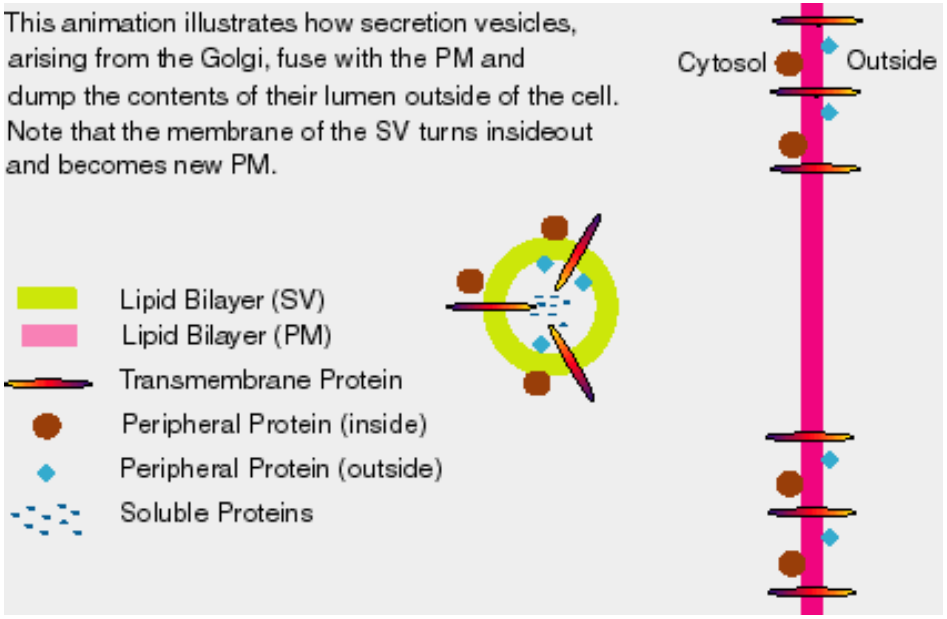
- The surface of the rough endoplasmic reticulum is studded with protein-manufacturing ribosomes giving it a "rough" appearance. But it should be noted that these ribosomes are not resident of the endoplasmic reticulum incessantly. The ribosomes only bind to the ER once it begins to synthesize a protein destined for sorting. The membrane of the rough endoplasmic reticulum is continuous with the outer layer of the nuclear envelope. Although there is no continuous membrane between the rough ER and the Golgi apparatus, membrane bound vesicles shuttle proteins between these two compartments. The rough endoplasmic reticulum works in concert with the Golgi complex to target new proteins to their proper destinations

Smooth endoplasmic reticulum

- The smooth endoplasmic reticulum has functions in several metabolic processes, including synthesis of lipids, metabolism of carbohydrates and calcium concentration, and attachment of receptors on cell membrane proteins. It is connected to the nuclear envelope. Smooth endoplasmic reticulum is found in a variety of cell types (both animal and plant) and it serves different functions in each. It consists of tubules and vesicles that branch forming a network. In some cells there are dilated areas like the sacs of rough endoplasmic reticulum. The network of smooth endoplasmic reticulum allows increased surface area for the action or storage of key enzymes and the products of these enzymes. The smooth endoplasmic reticulum is known for its storage of calcium ions in muscle cells.

The Golgi Apparatus

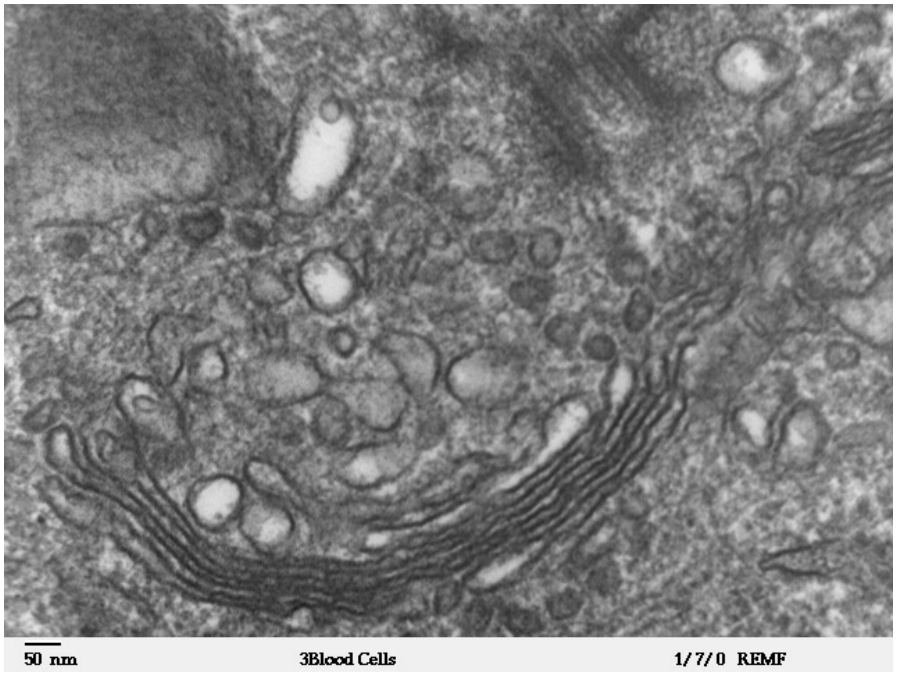




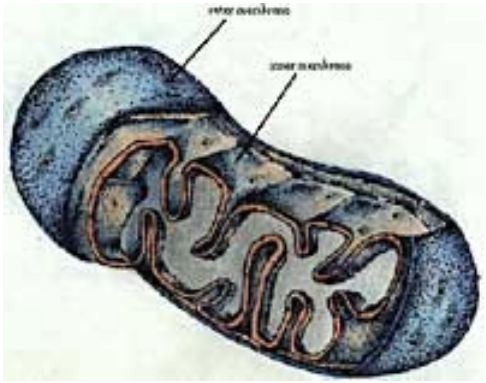
The Golgi apparatus is analogous to the finishing and packing room in a factory. Once the ribosome finishes manufacturing a protein in the rough ER, the protein needs to be prepared for use or export. Special enzymes will trim off any extra amino acids, and then the unfinished protein moves through channels in the smooth ER.

Golgi apparatus

The **Golgi apparatus** (also called the **Golgi body**, **Golgi complex**, or **dictyosome**) is an organelle found in typical eukaryotic cells. It was identified in 1898 by the Italian physician Camillo Golgi and was named after him. The primary function of the Golgi apparatus is to process and package macromolecules synthesised by the cell, primarily proteins and lipids. The Golgi apparatus forms a part of the endomembrane system present in eukaryotic cells.



Mitochondria

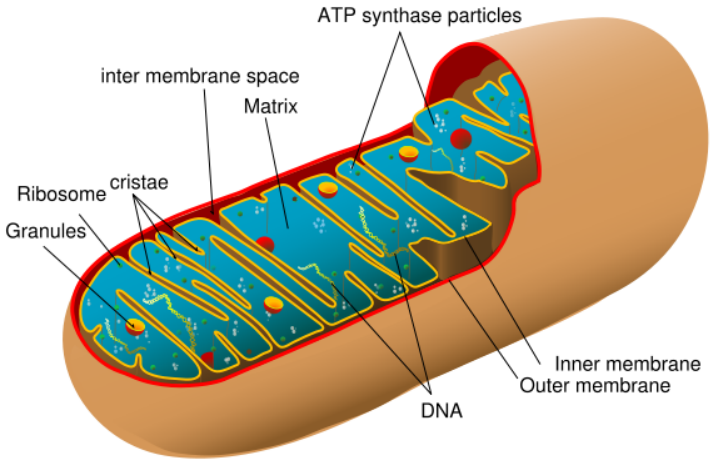


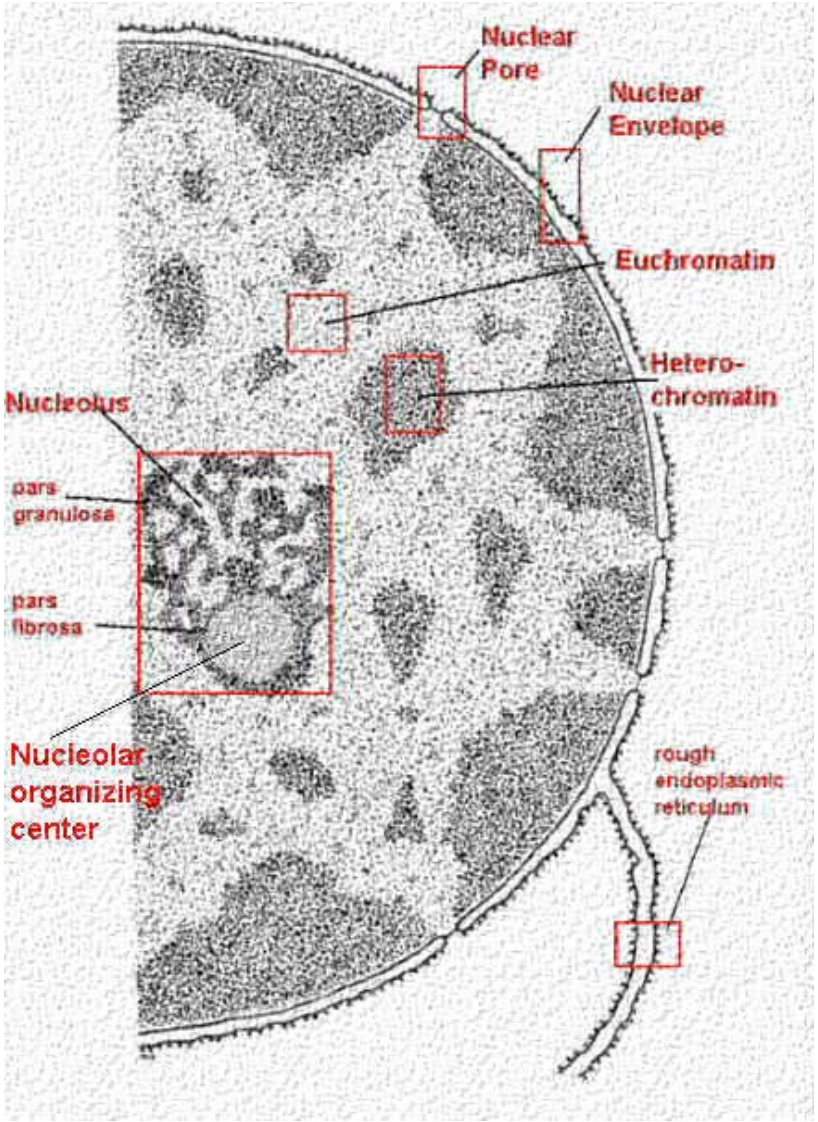
- ATP -
a Source of
ENERGY

Like our factory's power plant, mitochondria and chloroplasts transform one form of energy to another. Remember that nearly all the energy used by living things on Earth comes from the Sun. This section discusses how energy is made available for cell processes.

Mitochondrion

- In cell biology, a **mitochondrion** is a membrane-enclosed organelle, found in most eukaryotic cells.Mitochondria are sometimes described as "cellular power plants," because they convert NADH and NADPH into energy in the form of ATP via the process of oxidative phosphorylation. A typical eukaryotic cell contains about 2,000 mitochondria, which occupy roughly one fifth of its total volume. Mitochondria contain DNA that is independent of the DNA located in the cell nucleus. According to the endosymbiotic theory, mitochondria are descended from free-living prokaryotes.





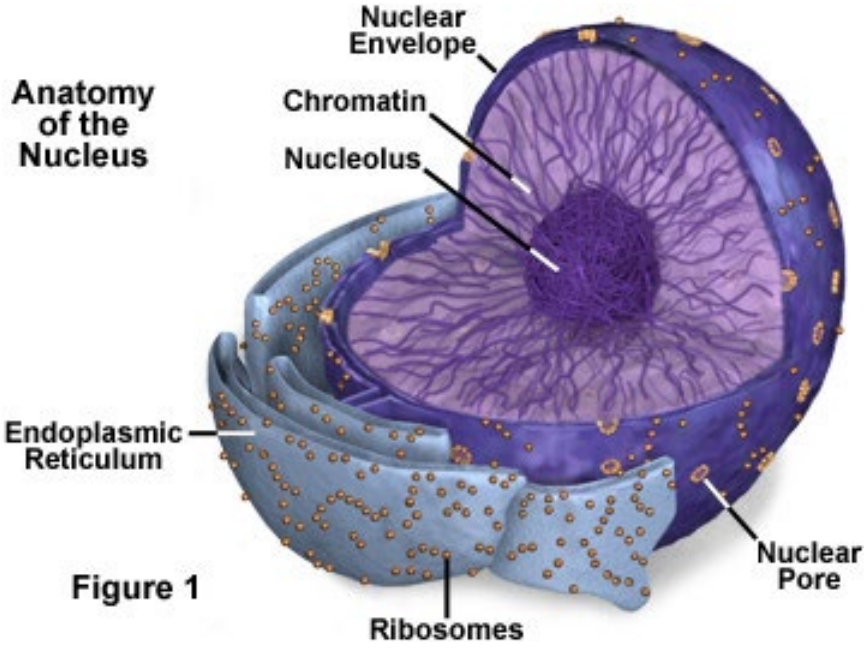


Figure 1

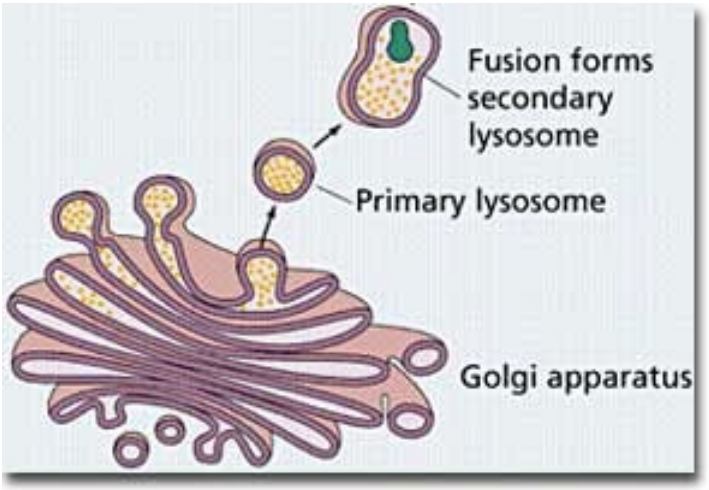
The main roles of the nucleolus are to synthesize rRNA and assemble ribosomes

The main function of the cell nucleus is to control gene expression and mediate the replication of DNA during the cell cycle

Lysosomes

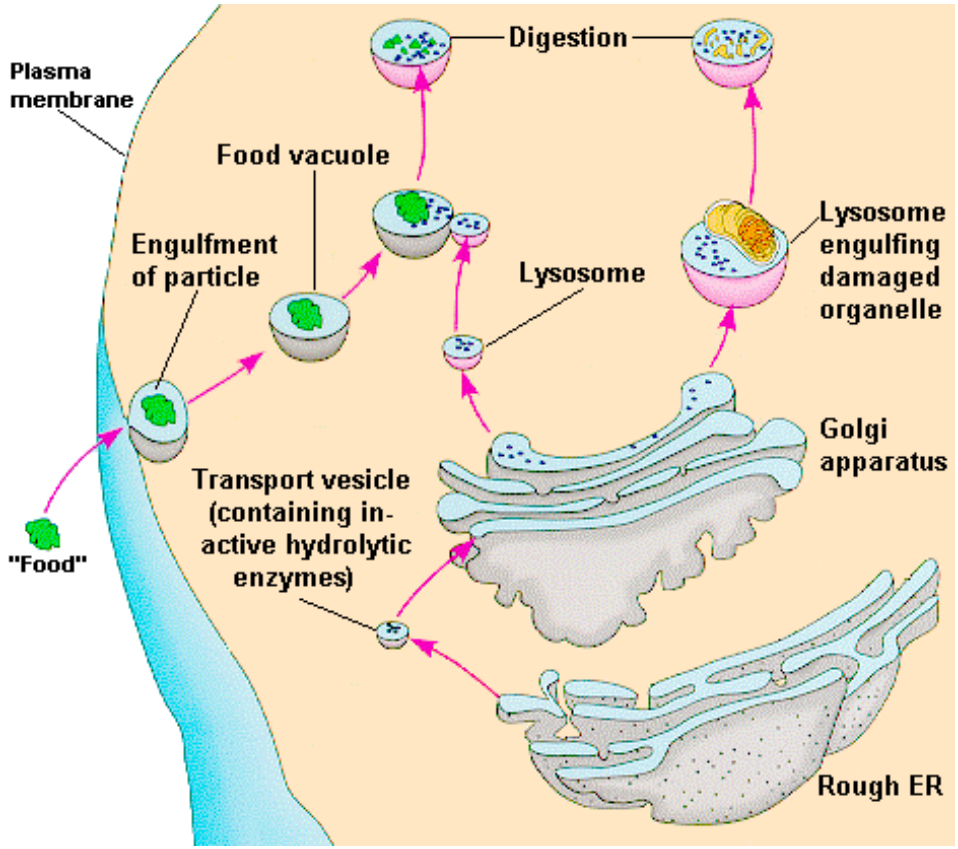
- **Lysosomes** are organelles that contain digestive enzymes (acid hydrolases). They digest excess or worn out organelles, food particles, and engulfed viruses or bacteria. The membrane surrounding a lysosome prevents the digestive enzymes inside from destroying the cell. Lysosomes fuse with vacuoles and dispense their enzymes into the vacuoles, digesting their contents. They are built in the Golgi apparatus. The name *lysosome* derives from the Greek words *lysis*, which means dissolution or destruction, and *soma*, which means body. They are frequently nicknamed "suicide-bags" or "suicide-sacs" by cell biologists due to their role in autolysis.

Lysosomes



Lysosomes are responsible for the breakdown and absorption of materials taken in by the cell. Often, a cell engulfs a foreign substance through **ENDOCYTOSIS**, another form of active transport. During endocytosis, the cell membrane puckers up, forms a pouch around materials outside the cell, and pinches off to become a vesicle. If the contents need to be destroyed, lysosomes combine with the vesicle and release their enzymes.

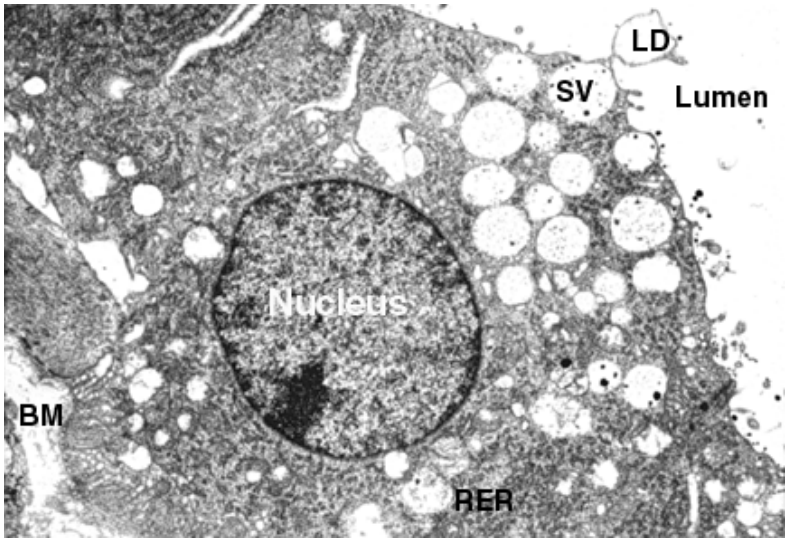
Lysosome


Digestion
Plasma membrane
Food vacuole
Engulfment of particle
Lysosome
Lysosome engulfing damaged organelle
Golgi apparatus
Transport vesicle (containing in-active hydrolytic enzymes)
"Food"
Rough ER

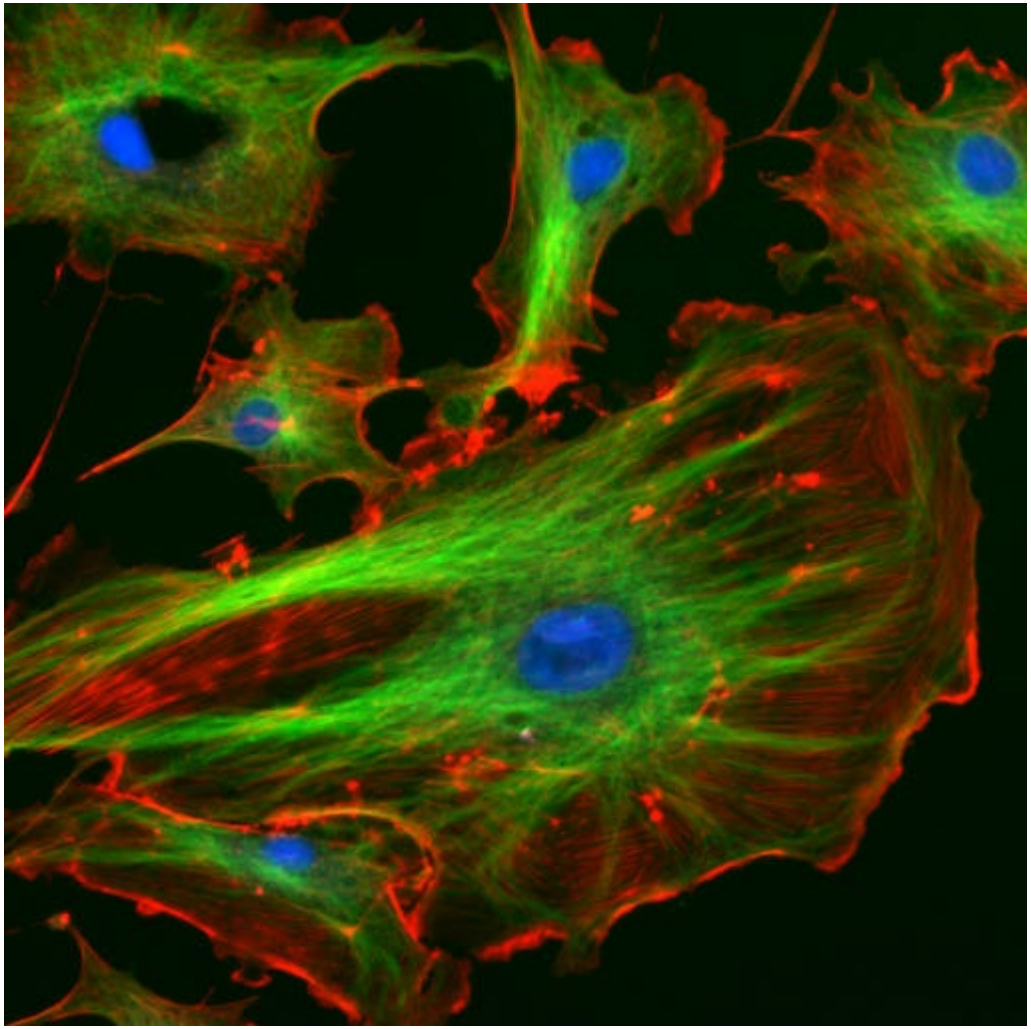
Vesicle

In cell biology, a **vesicle** is a relatively small and enclosed compartment, separated from the cytosol by at least one lipid bilayer. If there is only one lipid bilayer, they are called *unilamellar* vesicles; otherwise they are called *multilamellar*. Vesicles store, transport, or digest cellular products and waste.

This biomembrane enclosing the vesicle is similar to that of the plasma membrane. Because it is separated from the cytosol, the intravesicular environment can be made to be different from the cytosolic environment. Vesicles are a basic tool of the cell for organizing metabolism, transport, enzyme storage, as well as being chemical reaction chambers. Many vesicles are made in the Golgi apparatus, but also in the endoplasmic reticulum, or are made from parts of the plasma membrane.

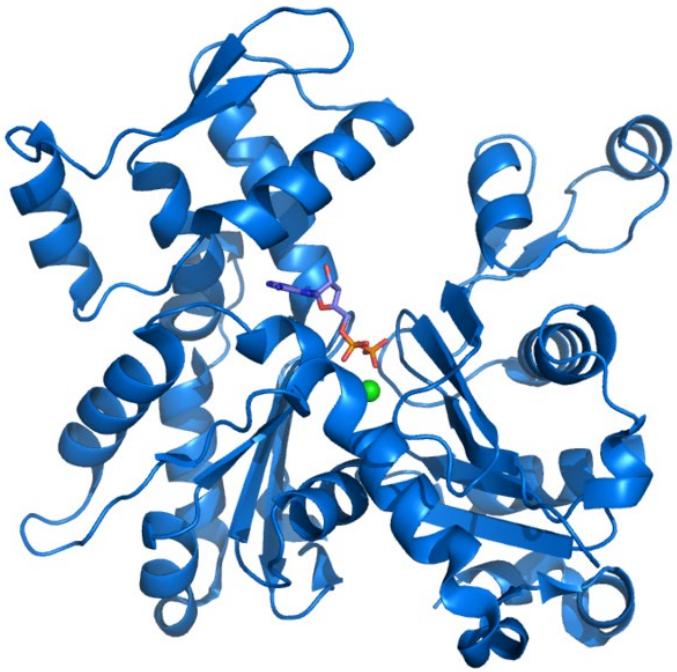


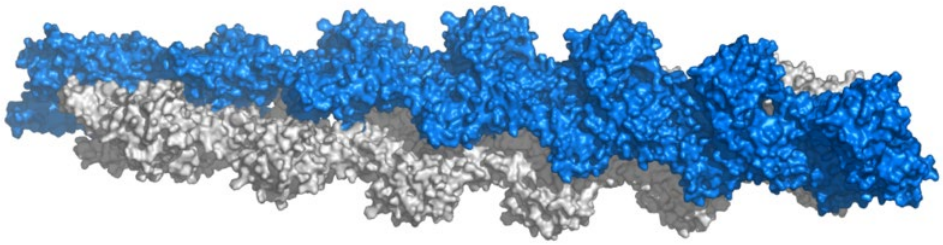
Cytoskeleton



The eukaryotic cytoskeleton. Actin filaments are shown in red, microtubules in green, and the nuclei are in blue.

Actin

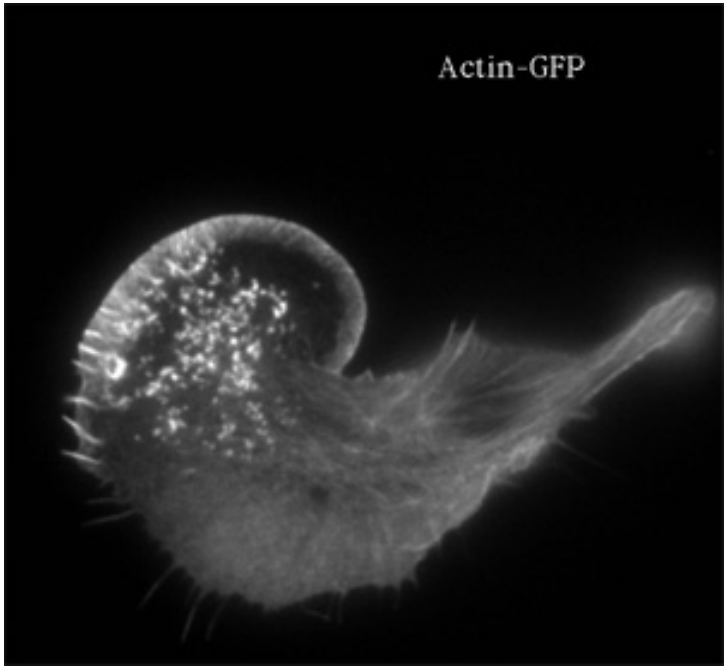


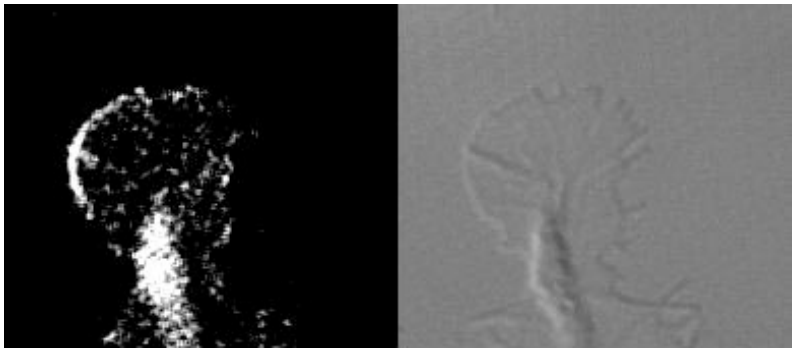


- **Actin** is a globular structural, 42 kDa, protein that polymerizes in a helical fashion to form **actin filaments** (or **microfilaments**). These form the cytoskeleton, a three-dimensional network inside the eukaryotic cell. Actin filaments provide mechanical support for the cell, determine its shape, and enable movement of the cell through lamellipodia, filopodia, or pseudopodia. Actin filaments, along with myosin, have an essential role in muscular contraction. In the cytosol, actin is predominantly bound to ATP, but can also bind to ADP. An ATP-actin complex polymerizes faster and dissociates slower than an ADP-actin complex.

Lamellipodia

- The **lamellipodium** is a cytoskeletal actin projection on the mobile edge of the cell. It contains a two-dimensional actin mesh; the whole structure pulls the cell across a substrate. Within the lamellipodia are ribs of actin called microspikes, which, when they spread beyond the lamellipodium frontier, are called filopodia (Small, et all, 2002). The lamellipodium is born of actin nucleation in the plasma membrane of the cell (Alberts, et al, 2002) and is the primary area of actin incorporation or microfilament formation of the cell. Lamellipodia range from 1µm to 5µm in breadth and are approximately 0.2µm thick.Lamellipodia are found primarily in very mobile cells, crawling at a speeds of 10-20µm/minute over epithelial surfaces..
- The tip of the lamellipodium is the site where exocytosis occurs in migrating mammalian cells as part of their clathrin-mediated endocytic cycle.

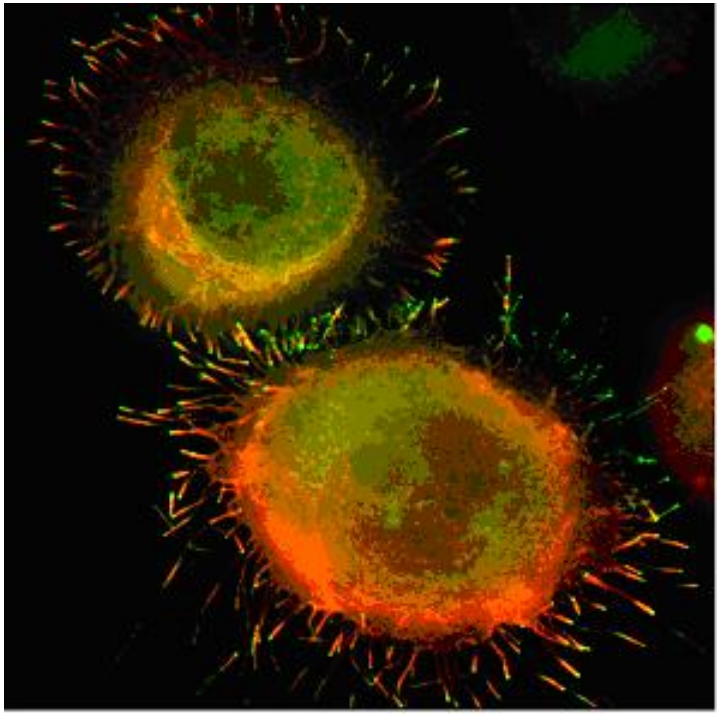




http://www.microscopyu.com/moviegallery/livecellimaging/3t3/t1/3t3-dslwmp1.html

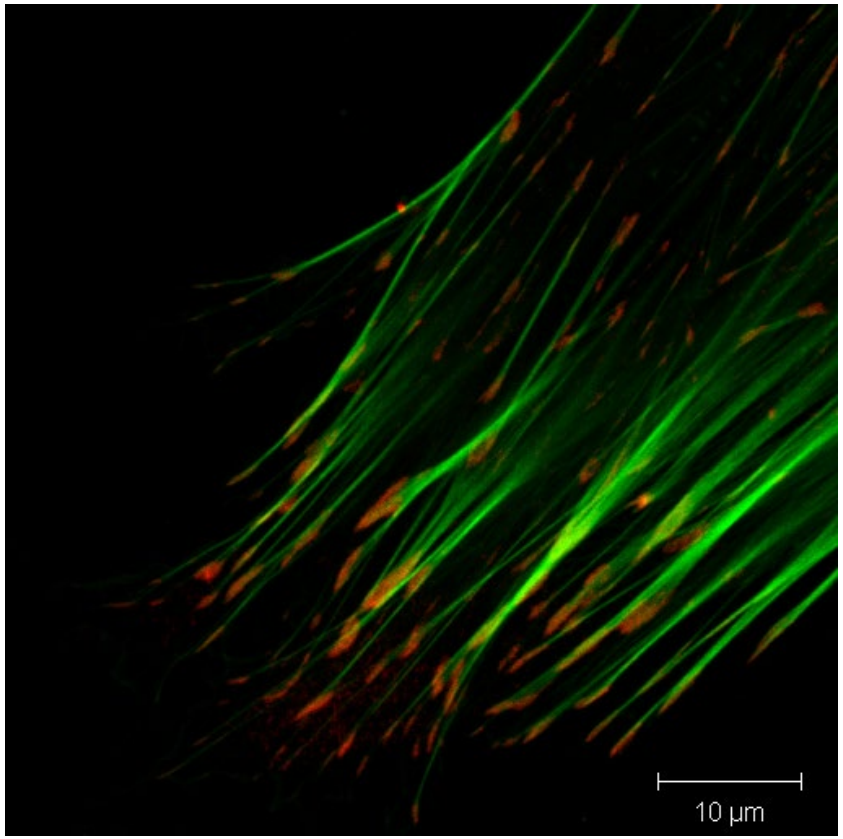
Filopodia

The **filopodia** are slender cytoplasmic projections, similar to lamellipodia, which extend from the leading edge of migrating cells. They contain actin filaments cross-linked into bundles by actin-binding proteins, e.g. fimbrin. Filopodia form focal adhesions with the substratum, linking it to the cell surface. A cell migrates along a surface by extending filopodia at the leading edge. The filopodia attach to the substratum further down the migratory pathway, then contraction of stress fibres retracts the rear of the cell to move the cell forwards.



Focal adhesion

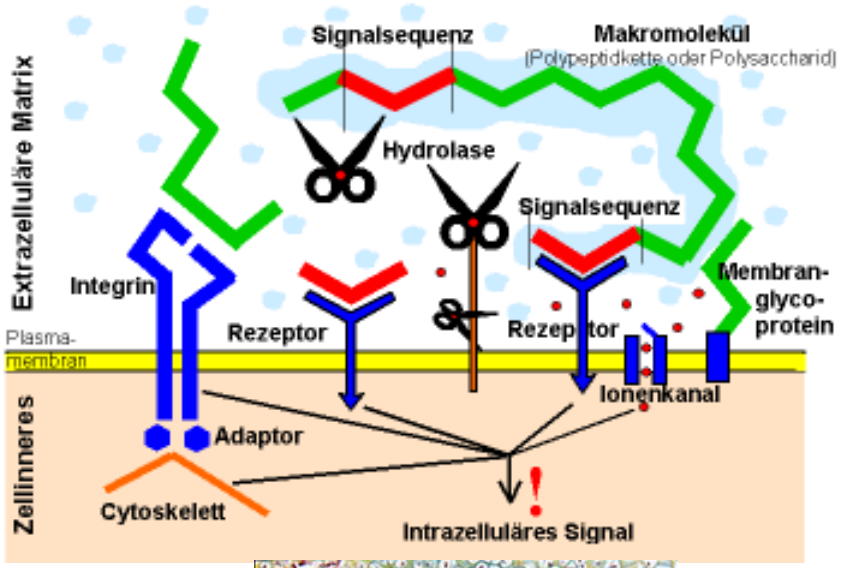
- In cell biology, '**Focal Adhesions'** are specific types of large macromolecular assemblies through which both mechanical force and regulatory signals are transmitted. More precisely, **FAs** can be considered as sub-cellular macromolecules that mediate the regulatory effects (e.g. cell anchorage) of extracellular matrix (ECM) adhesion on cell behavior.

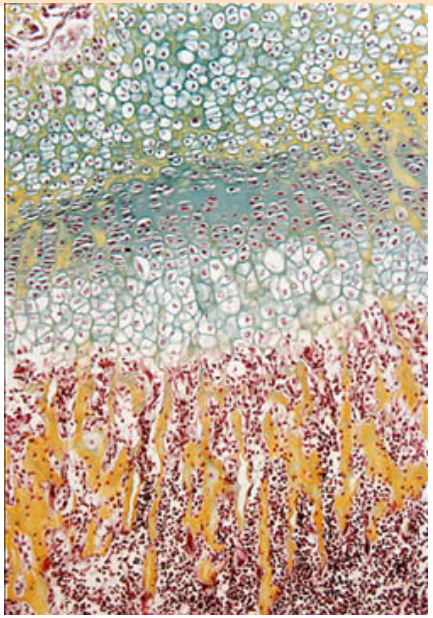


Extra Cellular Matrix

The ECM's main components are various glycoproteins, proteoglycans and hyaluronic acid. In most animals, the most abundant glycoproteins in the ECM are collagens.

ECM also contains many other components: proteins such as fibrin, elastin, fibronectins, laminins, and nidogens, and minerals such as hydroxylapatite, or fluids such as blood plasma or serum with secreted free flowing antigens.



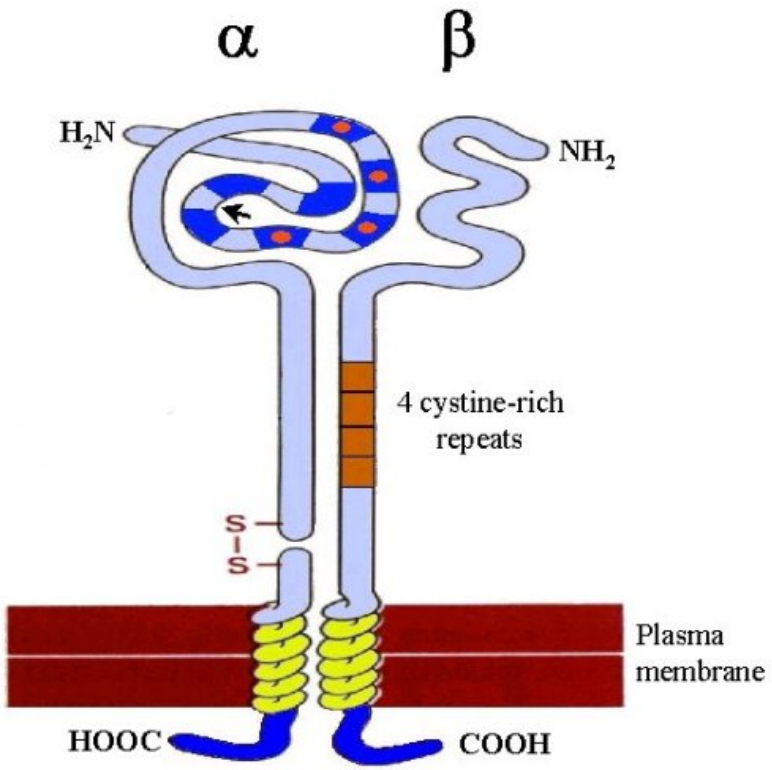


Integrin

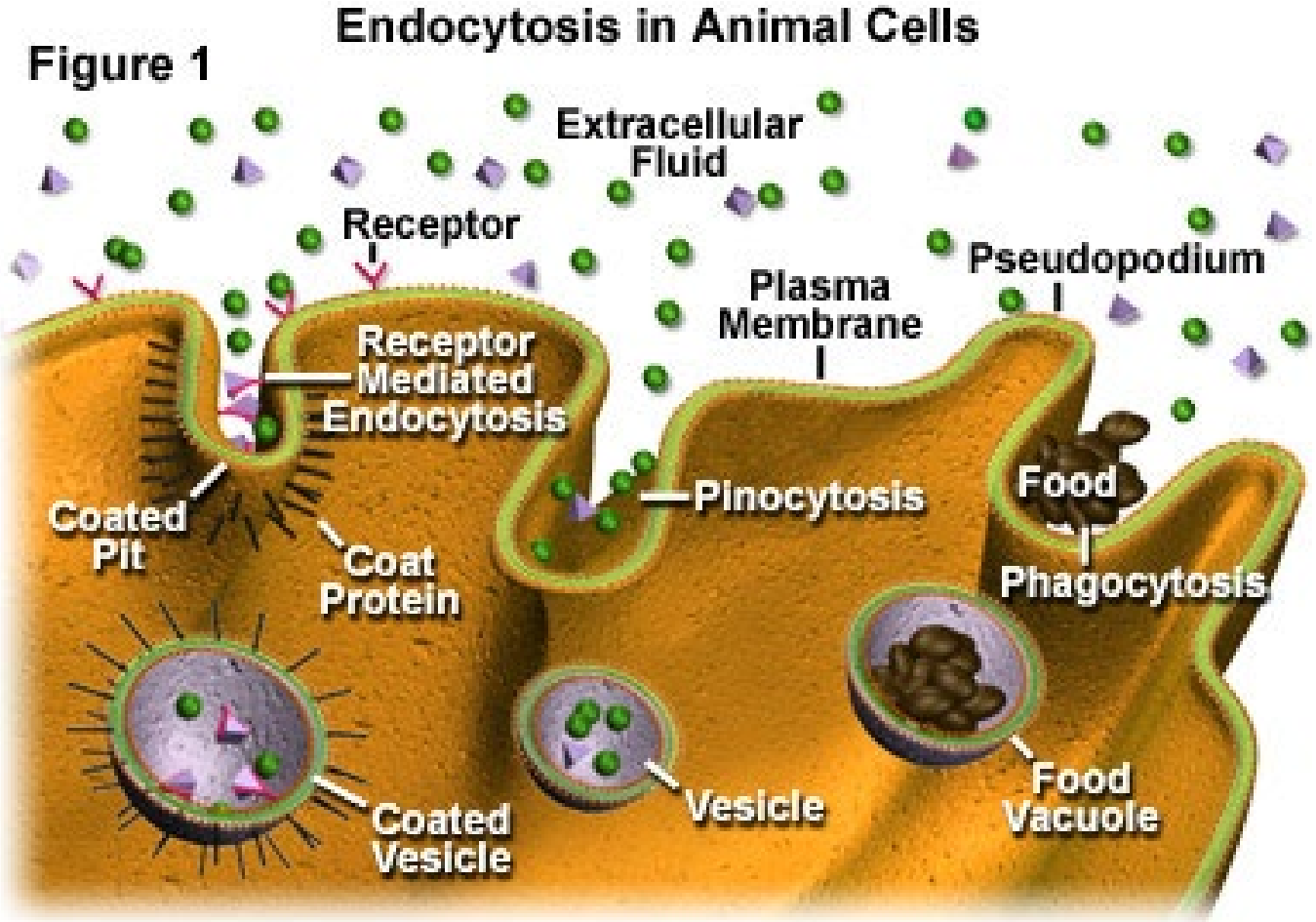
An **integrin**, or **integrin receptor**, is an integral membrane protein in the plasma membrane of cells. It plays a role in the attachment of a cell to the extracellular matrix (ECM) and to other cells, and in signal transduction from the ECM to the cell. There are many types of integrin, and many cells have multiple types on their surface. Integrins are of vital importance to all metazoans, from humans to sponges.

Schematic drawing of a typical integrin dimer

Arrow shows the region where an I domain is inserted in some α subunits. Not all α subunits are posttranslationally cleaved. Internal disulphide bonds within subunits are not shown. Dark blue regions in the head segment of the α subunit represent homologous repeats. Those with the EF-hand consensus sequence are marked with red circles to denote binding sites for divalent metal ion.



Endocytosis



Nanoparticles for Biomedical Applications

Nanoparticles have been extensively explored for various biomedical applications, ranging from drug delivery and diagnostic imaging to therapy and regenerative medicine. The diversity in their composition, size, shape, and surface properties allows for their tailored application in different biomedical fields. Here are some of the key types of nanoparticles used in biomedical applications:

Metal Nanoparticles:

- **Silver nanoparticles, Gold nanoparticles, Iron oxide nanoparticles:**.

Quantum Dots:

Lipid-Based Nanoparticles:

- **Liposomes**

Polymeric Nanoparticles:

Dendrimers:

Carbon-Based Nanoparticles:

- **Carbon nanotubes and graphene:**
- **Nanodiamond**
- **Carbon dot**

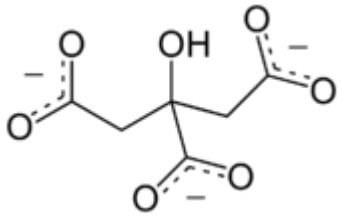
Silica Nanoparticles:

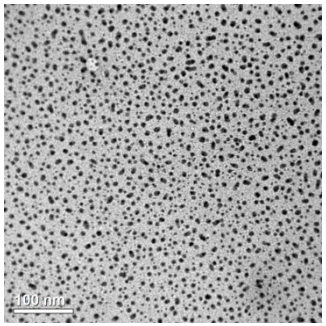
Porous Nanoparticles

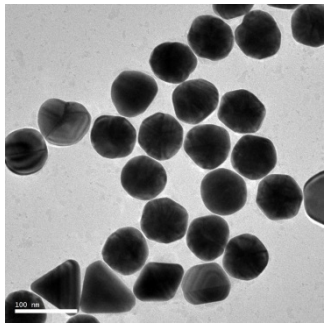
Synthesis of Nanoparticles and Surface Modifications

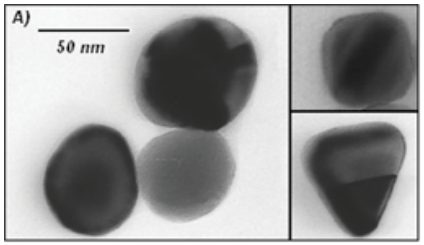
Synthesis of Silver Nanoparticles

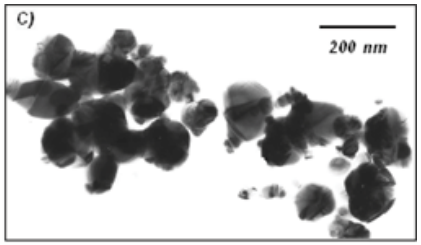
1. *A solution of **$AgNO_3$** (1.0×10^{-3} M) in deionized water was heated until it began to boil.*
2. ***Sodium citrate** solution was added dropwise to the silver nitrate solution as soon as the boiling commenced. The color of the solution slowly turned into grayish yellow, indicating the reduction of the Ag+ ions.*
3. *Heating was continued for an additional 15 min, and then the solution was cooled to room temperature before employing for further experimentation.*

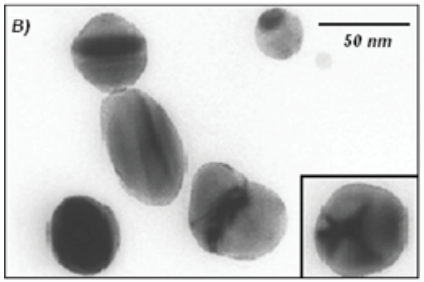


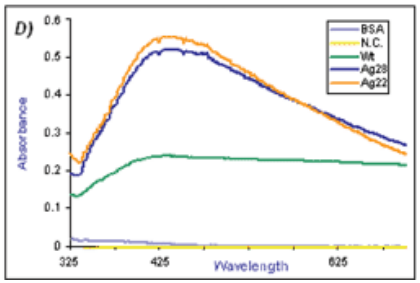






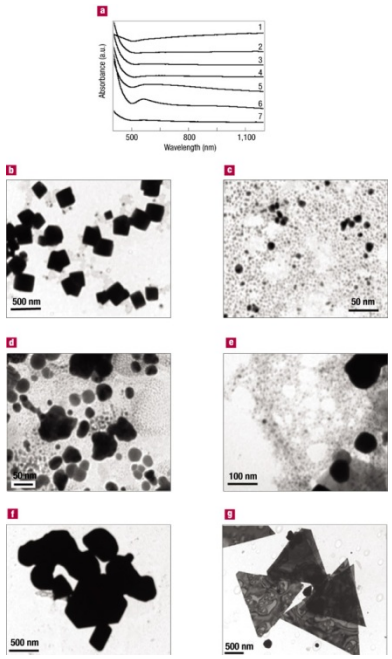






Synthesis of Gold Nanoparticles

1. Add 20 mL of 1.0 mM **$HAuCl_4$** to a 50 mL round bottom flask on a stirring hot plate.
2. Add a magnetic stir bar and bring the solution to a boil.
3. To the boiling solution, add 2 mL of a 1% solution of **trisodium citrate dihydrate**
4. The gold sol gradually forms as the citrate reduces the gold(III). Stop heating when a deep red color is obtained.



$$(1)\quad M_xO_y \xrightarrow[(\text{medium})\ \Delta_T]{\text{Reducing Agent}} M_n + H_2O$$

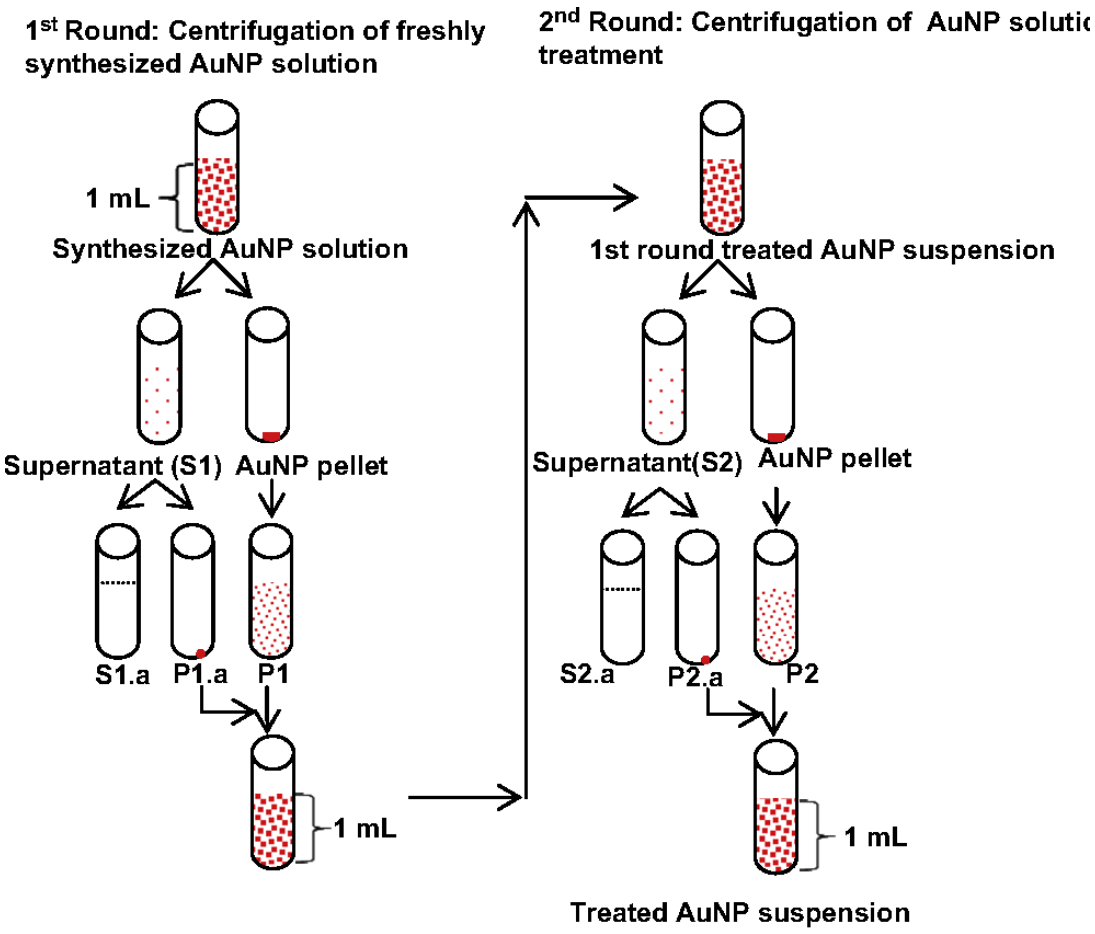
(Reducing Agent = R - COH)

$$(2)\quad M(L)_x \xrightarrow[(\text{medium})\ \Delta_T]{\text{Reducing Agent}} M_n + L^-$$

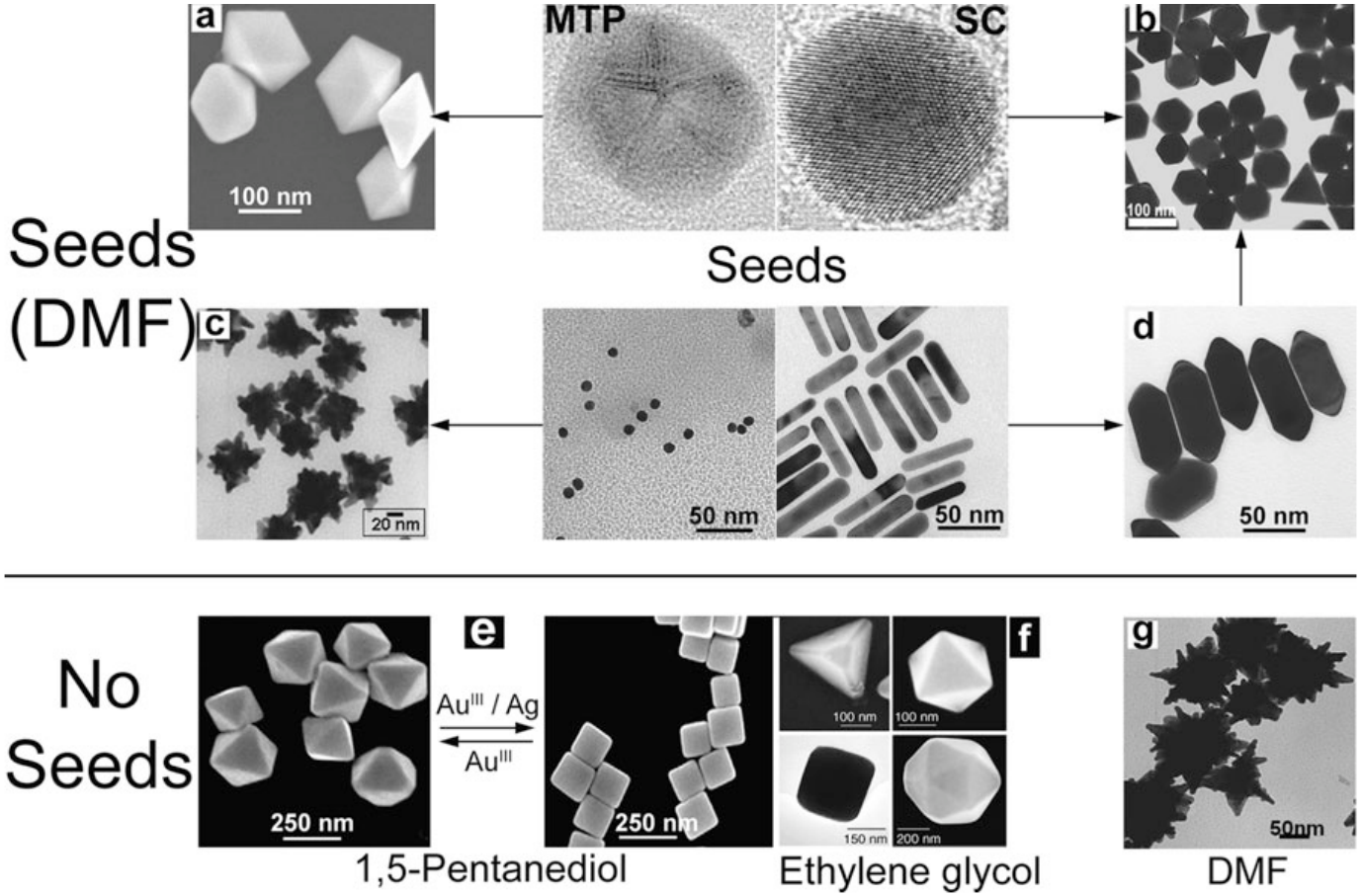
$(L=NO_3^-, C_2H_5O^-)$

(Reducing Agent = R - COH)

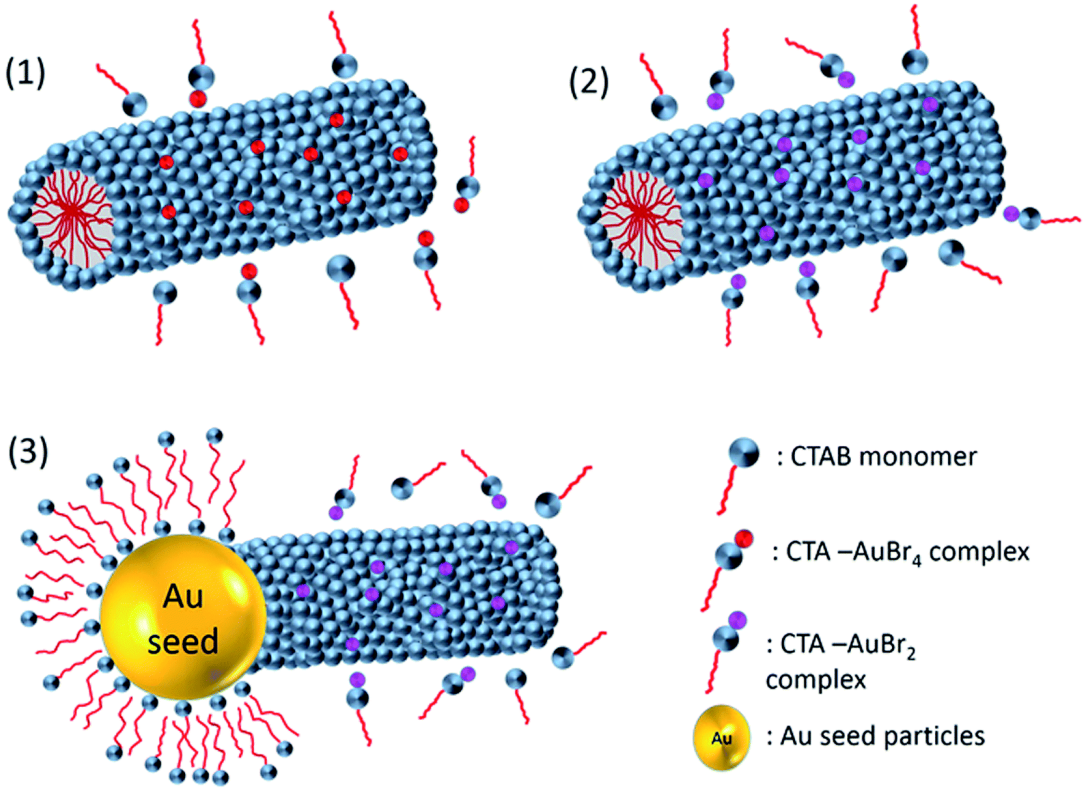
Purification of Au nanoparticles



Shape Control

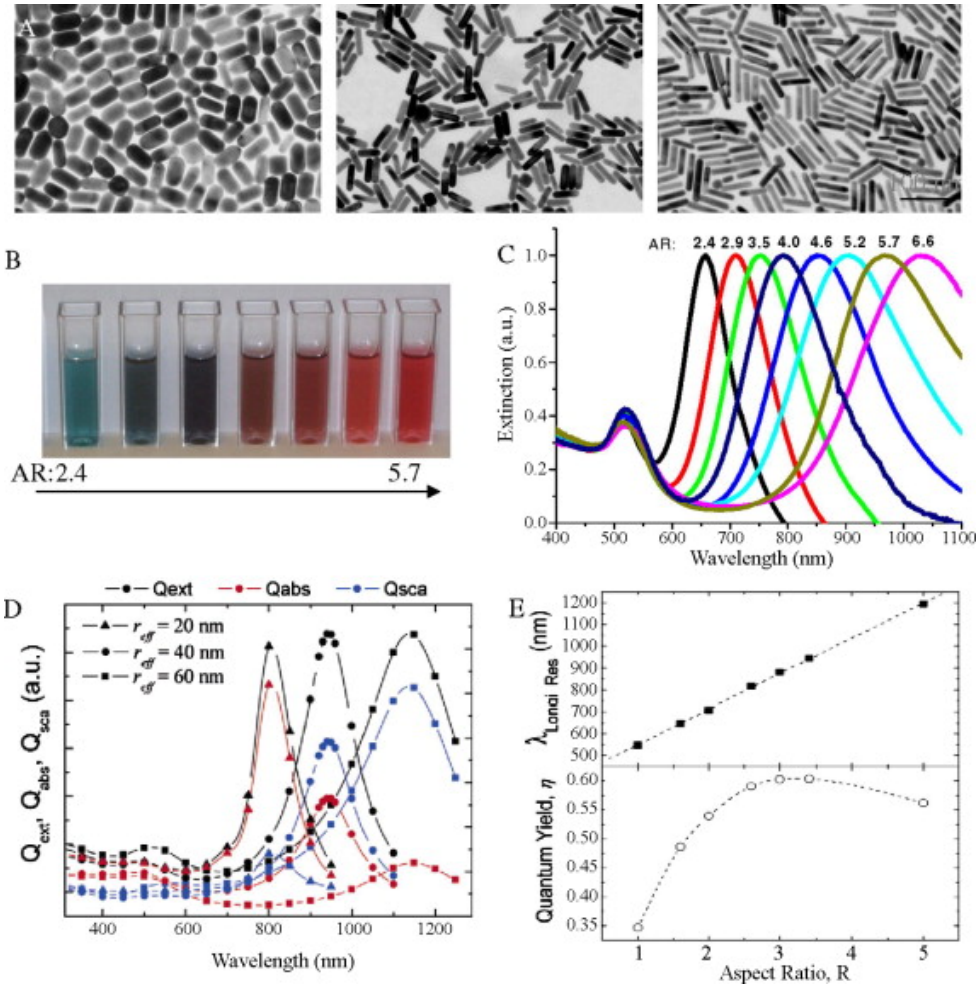


ographs of Au nanoparticles with various shapes, synthesised through DMF/polyol reduction in the pr

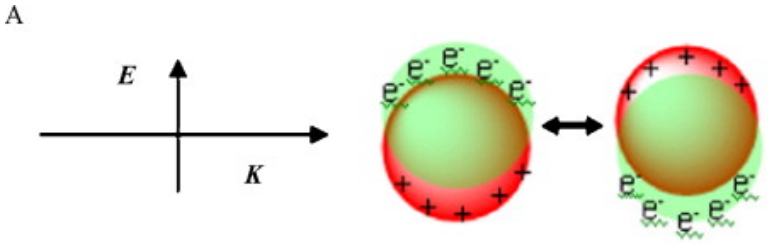

(1)
(2)
(3)
Au
seed
: CTAB monomer
: CTA –AuBr4 complex
: CTA –AuBr2
complex
Au
: Au seed particles
Electric
field
Electron
cloud
Metal rod
Longitudinal electrons oscillation
Electric
field
Metal rod
Electron
cloud
Transverse electrons oscillation
Absorbance (AU)
Wavelength (nm)
Longitudinal
plasmon band
Tansverse
plasmon band
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
400
500
600
700
800
900
1000
1100

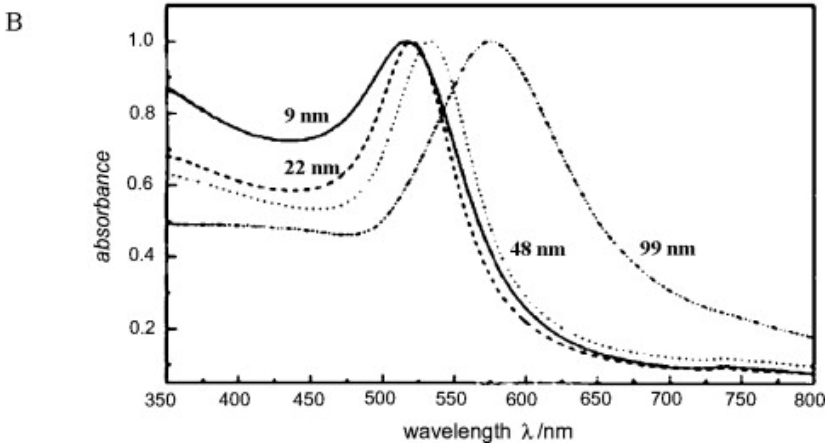
(a) (b)

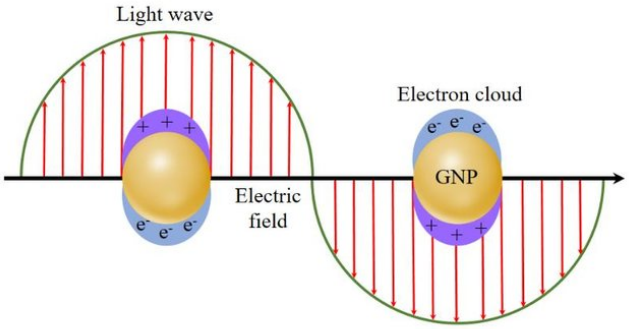
Nanorods


A
B
AR:2.4
5.7
C
AR: 2.4 2.9 3.5 4.0 4.6 5.2 5.7 6.6
Extinction (a.u.)
Wavelength (nm)
D
Qext
Qabs
Qsca
r_{eff} = 20 nm
r_{eff} = 40 nm
r_{eff} = 60 nm
Q_{ext}, Q_{abs}, Q_{sca} (a.u.)
Wavelength (nm)
E
$\lambda_{Longi\ Res}$ (nm)
Quantum Yield, η
Aspect Ratio, R

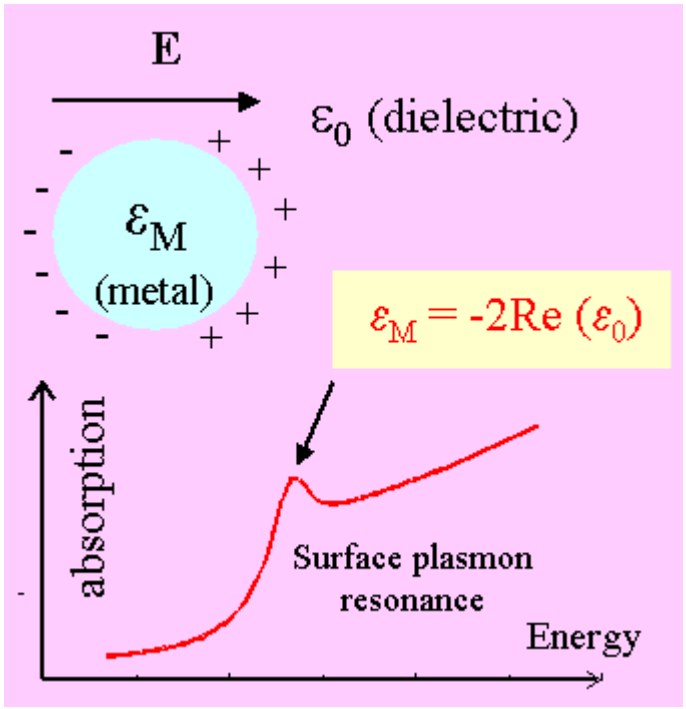
Localized Surface Plasomon

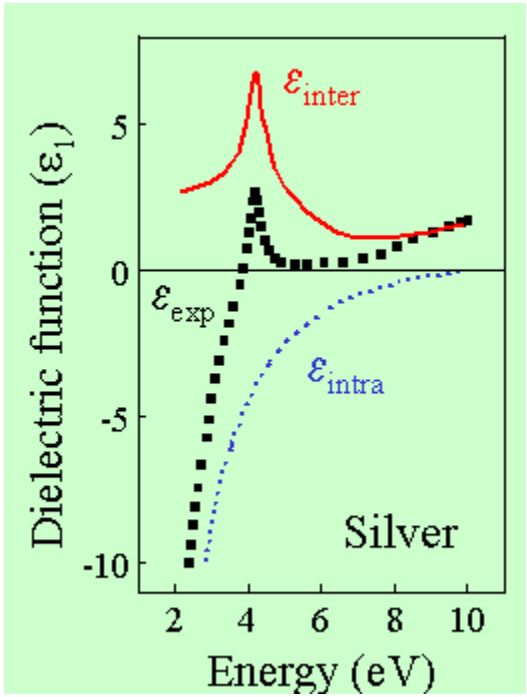






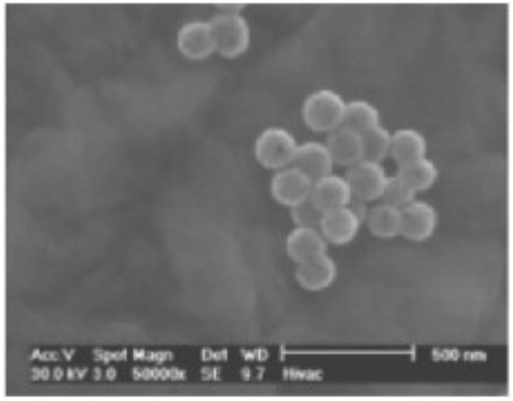
$$\varepsilon_{eff} = \varepsilon_0 + 3N\varepsilon_0 \frac{\varepsilon_M - \varepsilon_0}{\varepsilon_M + 2\varepsilon_0}$$

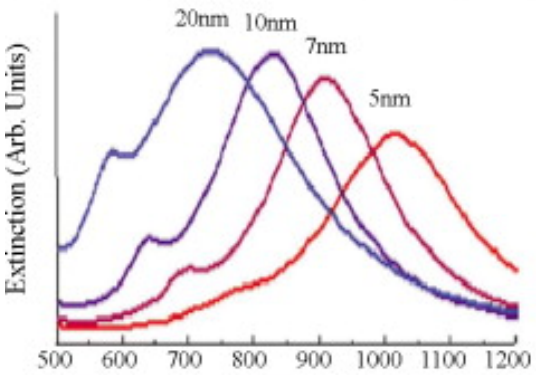




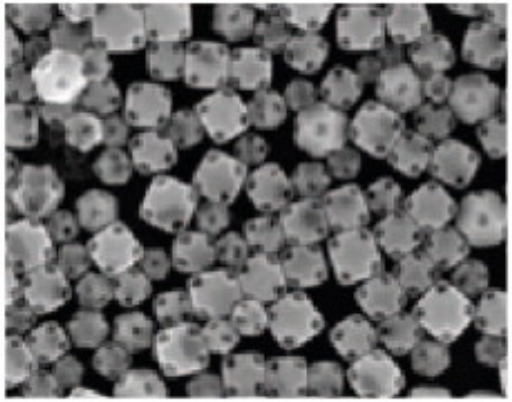
Shape Dependence

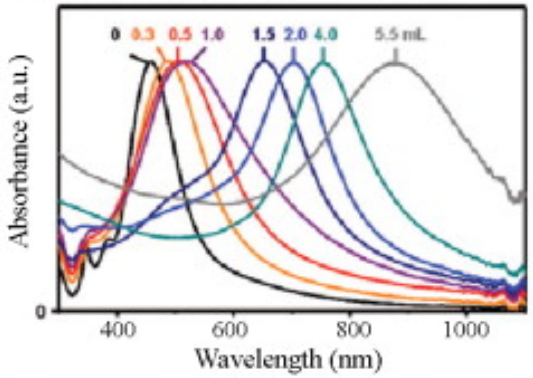
A. gold nanoshell





B. gold nanocage





Surface Plasmons and Localized Surface Plasmons

Surface Plasmons (SPs):
Definition: Surface plasmons are coherent delocalized electron oscillations that exist at the interface between a metal and a dielectric material, propagating along the interface. They are excited by electromagnetic waves under specific conditions, facilitating energy transfer across the interface.
Nature: SPs are propagating waves that can travel along the metal-dielectric interface over relatively long distances compared to the wavelength of light, depending on the materials and the interface quality.
Dependency: The existence and properties of SPs depend on the dielectric constants of the metal and the adjacent dielectric material, as well as the geometry of the interface.

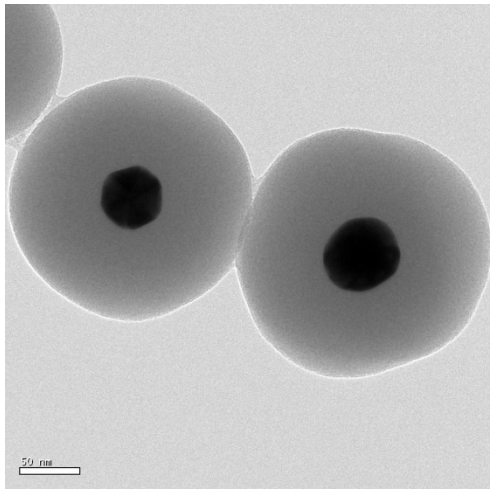
Localized Surface Plasmons (LSPs):
Definition: Localized surface plasmons are confined electron oscillations in metallic nanoparticles or nanostructures that occur when the conduction electrons collectively oscillate relative to the fixed positive ions, in response to an external electromagnetic field.
Nature: LSPs are localized around the nanoparticle and do not propagate along an interface. Their resonance frequency depends on the particle's size, shape, and the dielectric environment.
Dependency: The resonance condition for LSPs is determined by the nanoparticle's geometry and the dielectric properties of both the particle and its surrounding medium. Unlike SPs, LSPs can be excited in isolated nanoparticles, not requiring a continuous interface.

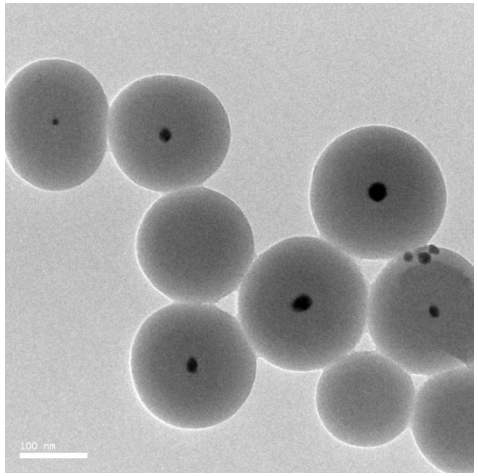
Key Differences

Propagation: SPs propagate along the interface between a metal and a dielectric, while LSPs are confined to the vicinity of metallic nanoparticles or nanostructures.
Geometry Dependence: The behavior of SPs is influenced by the interface's properties, whereas LSPs are strongly affected by the size, shape, and material of the nanoparticles, as well as the surrounding dielectric environment.
Localization: SPs are delocalized and can extend over large distances along the interface, whereas LSPs are inherently localized around the nanostructure.
Excitation: LSPs can be excited in individual nanoparticles without the need for a continuous metal-dielectric interface, whereas SPs require a planar or curved interface for their propagation.

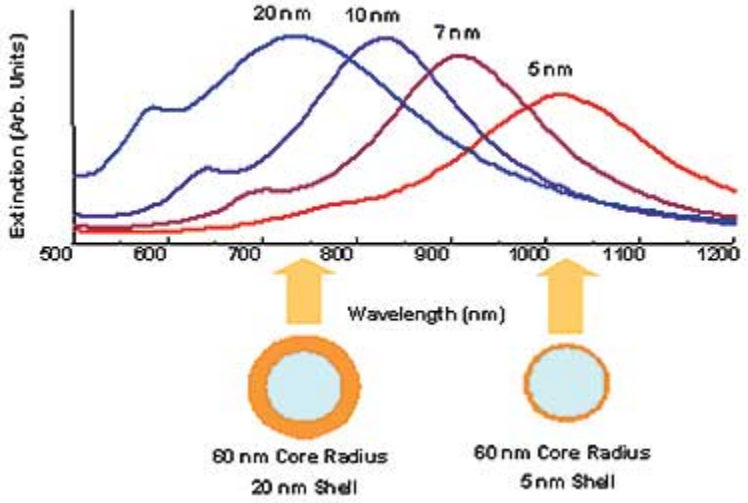
Construction of Core Shell Ag/Au@SiO_2 Nanoparticles

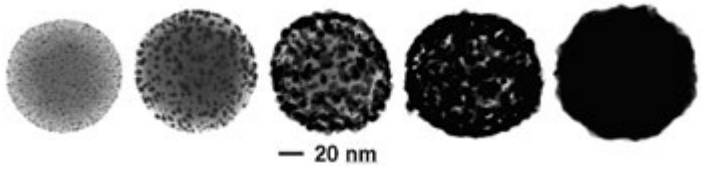
1. *Under vigorous stirring, 1 ml of the silver/ gold colloids solution was mixed with 250 mL of isopropanol and 25 mL of deionized water.*
2. *Immediately after the addition of 4 mL of 30% ammonium hydroxide, different amounts of tetraethoxysilane (TEOS) were added to the reaction mixture.*
3. *To obtain different silica layer thicknesses, TEOS solutions with a concentration between 50% and 100% was added to the suspension. The reaction was stirred at room temperature for 30 minutes and then was allowed to age without agitation at 4 ℃ overnight.*
4. *Each suspension of silica-coated silver/gold nanoparticles was washed and centrifuged, followed by re-suspension in water. The thickness of the silica layers was determined from TEM images .*





Core-Shell Nanoparticles





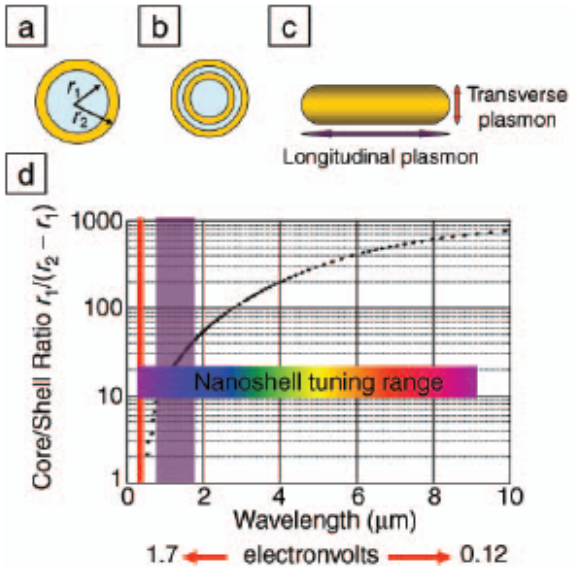


Figure 1. (a) Schematic illustration of a silica-core, gold-shell nanoshell, indicating inner (r_1) and outer (r_2) radii of the shell layers. (b) Depiction of a four-layer, concentric nanoshell. (c) Schematic illustration of a metallic nanorod. (d) Plot of nanoshell resonance as a function of core and shell dimensions, overlaid with reported spectral ranges of nanorod resonances (red, transverse plasmon; purple, longitudinal plasmon), and reported nanoshell and concentric nanoshell combined spectral range of plasmon response.

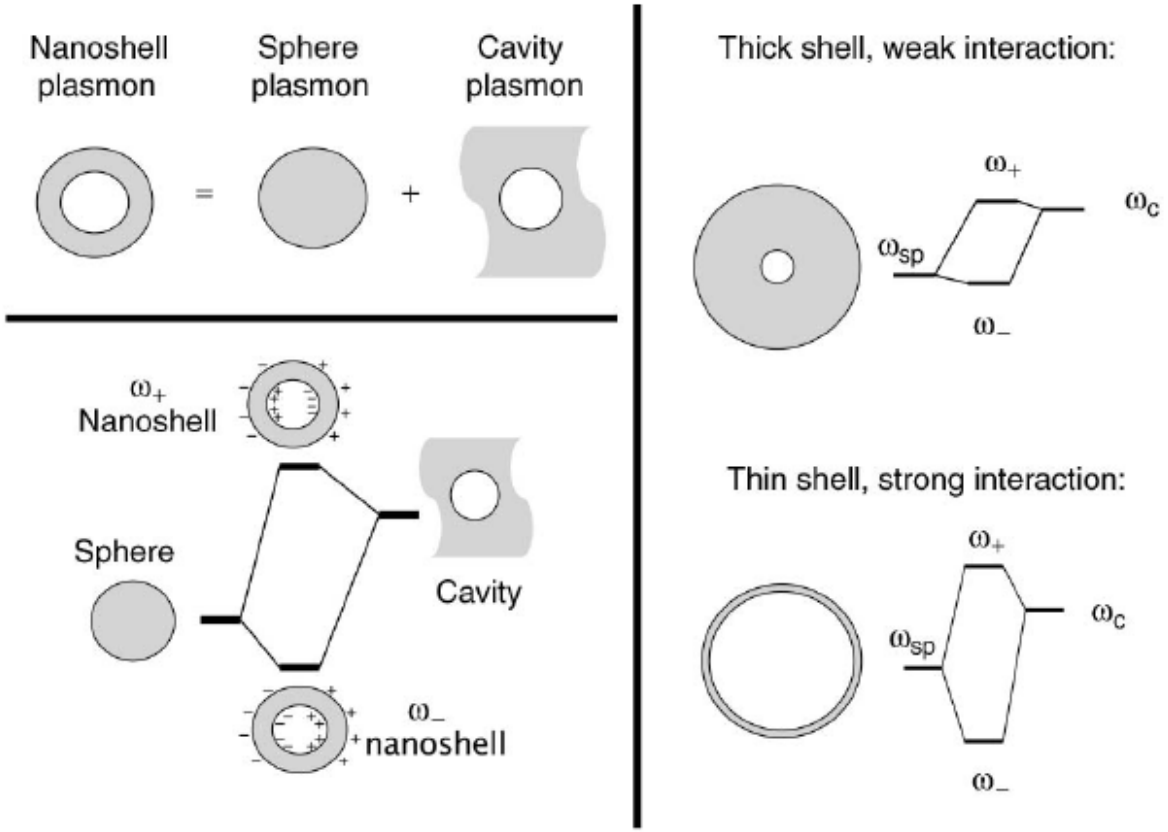


Figure 2. Plasmon hybridization and the sphere–cavity model for nanoshells: the interaction between a sphere (resonance frequency, ω_{sp}) and a cavity plasmon (resonance frequency, ω_c) is tuned by varying the thickness of the shell layer of the nanoparticle. Two hybrid plasmon resonances, the ω_- "bright," or "bonding," plasmon and the ω_+ "dark," or "anti-bonding," plasmon resonances are formed. The lower-energy plasmon couples most strongly to the optical field.

Preparation of Fe_3O_4@Ag/Au

1. *To the magnetic nanoparticle suspension obtained from commercial company, add 50 ml of a solution of Au (III) salt or Ag (I) salt at concentration of 0.01–1% mmol/L , shaking for 30 minutes, allowing Au (III) or Ag (I) ion to absorb on the surface of magnetic nanoparticle sufficiently,*
2. *Then adding 15–40 ml of reducing agent, such as hydroxylamine hydrochloride at concentration of 40 mmol/L, reacting for 5–40 minutes.*
3. *Further adding 1–10 ml of a solution of Au (III) salt or Ag (I) salt at concentration of 0.01–1%, shaking for 10 minutes, coating a reduced layer of gold or silver on the surface of the magnetic nanoparticle, forming super-paramagnetic composite particles having core/shell structure, separating magnetically, washing repeatedly with distilled water.*

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Quantum Dots

Quantum dots are tiny semiconductor particles only a few nanometers in size, so small that their optical and electronic properties differ from those of larger particles due to quantum mechanics. Here's a breakdown of what makes quantum dots unique and their significant applications:

Definition and Properties
Size: Quantum dots typically range from 2 to 10 nanometers in diameter. At these small sizes, quantum dots contain only a few thousand atoms.

Quantum Confinement: Because of their size, electrons in quantum dots are confined in three spatial dimensions, leading to discrete energy levels. This confinement affects the absorption and emission of light, making quantum dots tunable by changing their size.

Tunability: The color of light emitted by a quantum dot can be adjusted by changing its size. Smaller dots emit shorter wavelengths (blue light), while larger dots emit longer wavelengths (red light).

Brightness and Stability: Quantum dots have high brightness and photostability, outperforming many traditional dyes and fluorescent proteins, which is particularly beneficial in imaging applications.

The Nobel Prize in Chemistry 2023

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry 2023 to

Moungi G. Bawendi
Massachusetts Institute of Technology (MIT), Cambridge, MA, USA

Louis E. Brus
Columbia University, New York, NY, USA

Aleksey Yekimov
Nanocrystals Technology Inc., New York, NY, USA

"for the discovery and synthesis of quantum dots"

They planted an important seed for nanotechnology

The Nobel Prize in Chemistry 2023 rewards the discovery and development of *quantum dots*, nanoparticles so tiny that their size determines their properties. These smallest components of nanotechnology now spread their light from televisions and LED lamps, and can also guide surgeons when they remove tumour tissue, among many other things.

Everyone who studies chemistry learns that an element's properties are governed by how many electrons it has. However, when matter shrinks to nano-dimensions quantum phenomena arise; these are governed by the size of the matter. The Nobel Laureates in Chemistry 2023 have succeeded in producing particles so small that their properties are determined by quantum phenomena. The particles, which are called quantum dots, are now of great importance in nanotechnology.

"Quantum dots have many fascinating and unusual properties. Importantly, they have different colours depending on their size," says Johan Åqvist, Chair of the Nobel Committee for Chemistry.

Physicists had long known that in theory size-dependent quantum effects could arise in nanoparticles, but at that time it was almost impossible to sculpt in nano-dimensions. Therefore, few people believed that this knowledge would be put to practical use.

However, in the early 1980s, **Aleksey Yekimov** succeeded in creating size-dependent quantum effects in coloured glass. The colour came from nanoparticles of copper chloride and Yekimov demonstrated that the particle size affected the colour of the glass via quantum effects.

A few years later, **Louis Brus** was the first scientist in the world to prove size-dependent quantum effects in particles floating freely in a fluid.

In 1993, **Moungi Bawendi** revolutionised the chemical production of quantum dots, resulting in almost perfect particles. This high quality was necessary for them to be utilised in applications.

Quantum dots now illuminate computer monitors and television screens based on QLED technology. They also add nuance to the light of some LED lamps, and biochemists and doctors use them to map biological tissue.

Quantum dots are thus bringing the greatest benefit to humankind. Researchers believe that in the future they could contribute to flexible electronics, tiny sensors, thinner solar cells and encrypted quantum communication – so we have just started exploring the potential of these tiny particles.

Moungi G. Bawendi, born 1961 in Paris, France. PhD 1988 from University of Chicago, IL, USA. Professor at Massachusetts Institute of Technology (MIT), Cambridge, MA, USA.

Louis E. Brus, born 1943 in Cleveland, OH, USA. PhD 1969 from Columbia University, New York, NY, USA. Professor at Columbia University, New York, NY, USA.

Aleksey Yekimov, born 1945 in the former USSR. PhD 1974 from Ioffe Physical-Technical Institute, Saint Petersburg, Russia. Formerly Chief Scientist at Nanocrystals Technology Inc., New York, NY, USA.

Synthesis of Quantum Dots

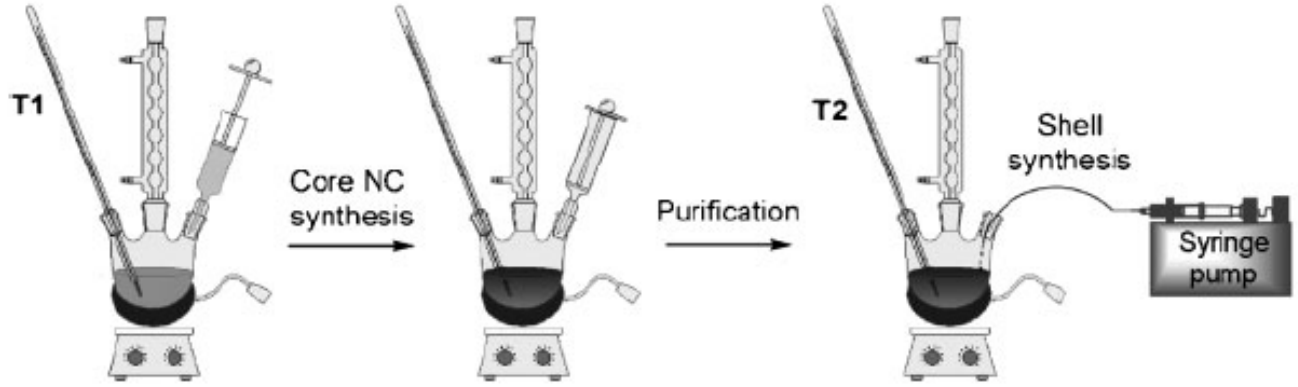
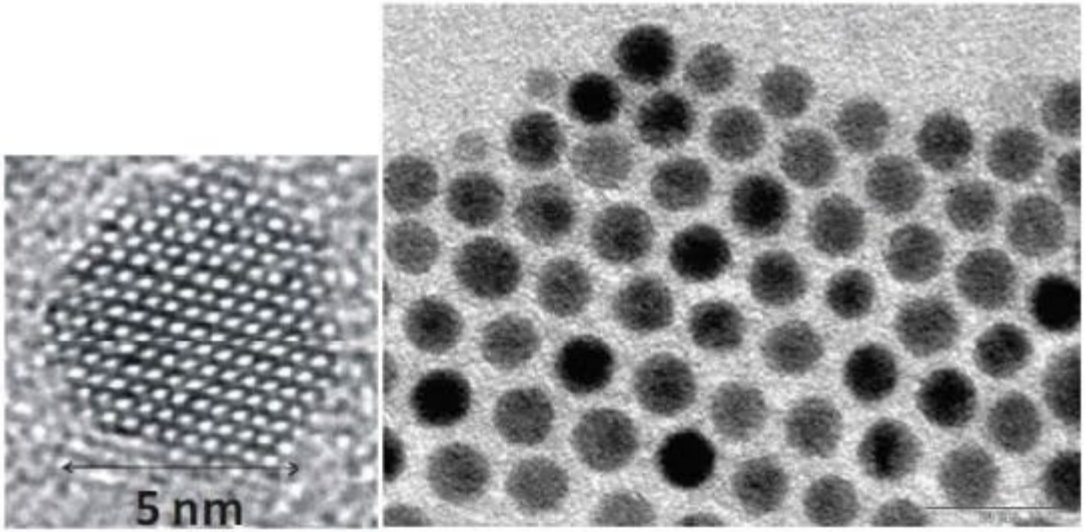


Figure 2. Two–step synthesis of core/shell nanocrystals.

Quantum Dots



Type I Quantum Dots:

Band Alignment: In Type I quantum dots, both the conduction band minimum and the valence band maximum of the shell material lie outside the energy levels of the core material. This means that both electrons and holes are confined within the core material.

Carrier Confinement: Since both charge carriers (electrons and holes) are confined in the same region (the core), they have a higher probability of recombining. This results in strong photoluminescence as the recombination of electrons and holes releases energy in the form of light.

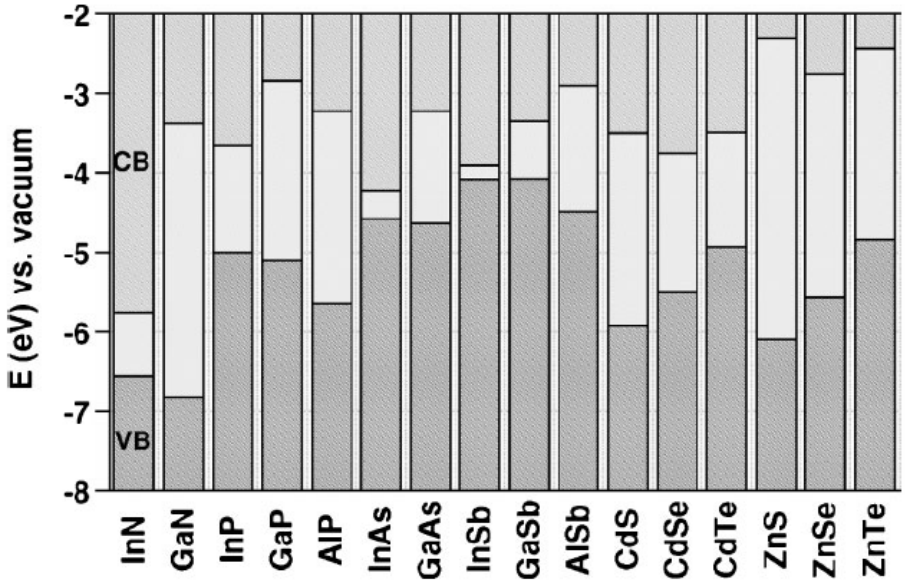
Applications: Due to their efficient confinement of charge carriers and strong luminescence, Type I quantum dots are widely used in applications that require high fluorescence efficiency, such as in bioimaging, light-emitting diodes (LEDs), and quantum dot displays.

Type II Quantum Dots:

Band Alignment: In Type II quantum dots, the conduction band minimum and the valence band maximum are staggered between the core and shell materials. This typically results in the confinement of electrons and holes in different regions; for example, electrons may be confined in the core while holes are localized in the shell, or vice versa.

Carrier Confinement: The spatial separation of charge carriers (electron and hole) reduces their recombination probability, which can lead to longer exciton lifetimes. While this separation can decrease the photoluminescence efficiency, it provides other useful properties, such as tunable emission from the visible to the infrared spectrum.

Applications: The extended carrier lifetimes and tunable emission properties make Type II quantum dots useful for applications in solar energy conversion, where they can help in creating more efficient photovoltaic cells, and in sensors, where their tunable absorption can be exploited for detecting various substances.



Scheme 1. Electronic energy levels of selected III–V and II–VI semiconductors using the valence-band offsets from Reference [12] (VB: valence band, CB: conduction band).

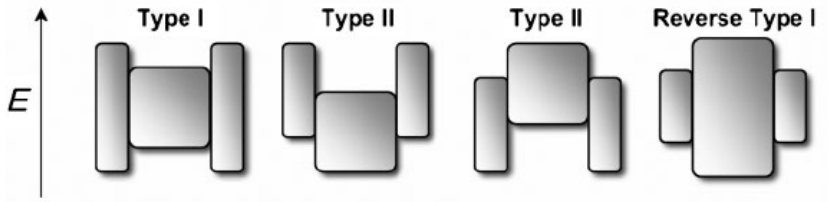
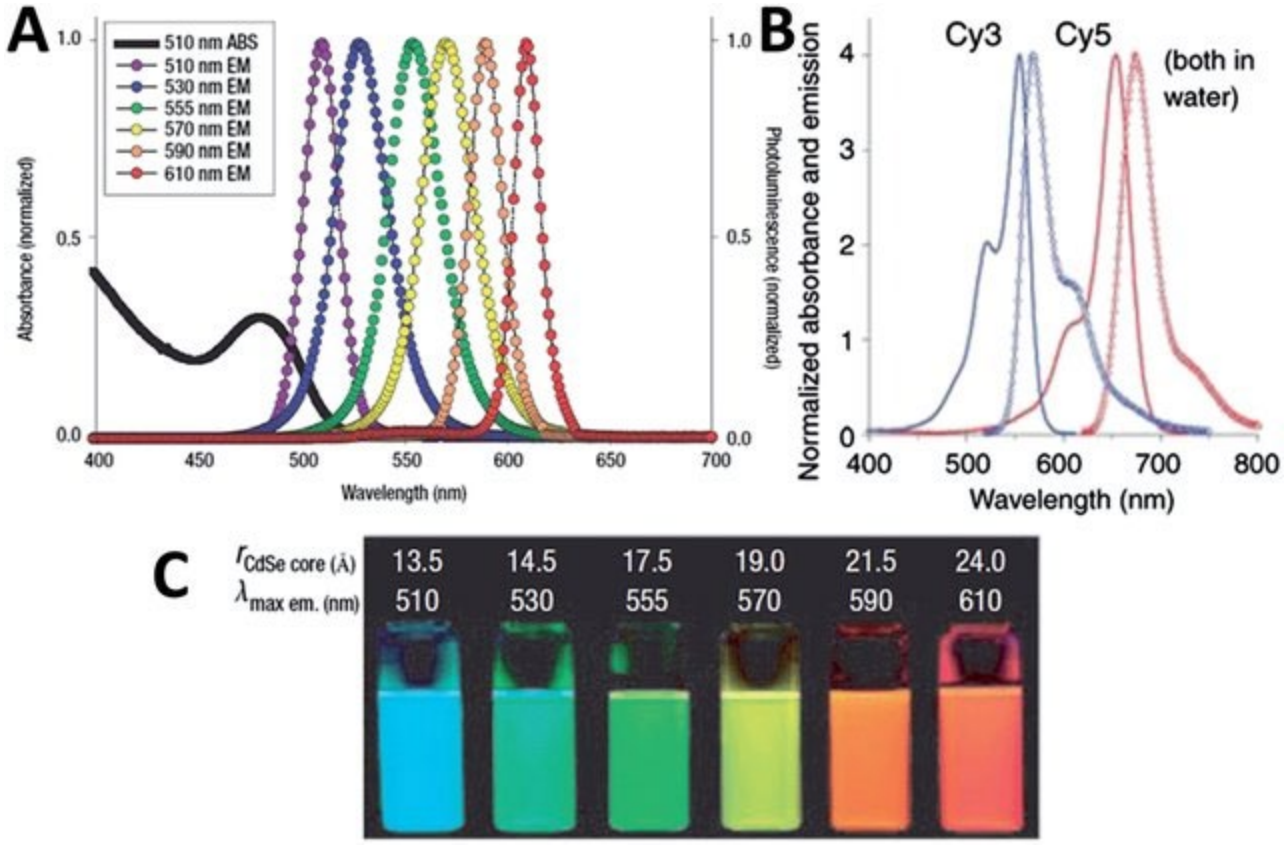


Figure 1. Schematic representation of the energy-level alignment in different core/shell systems realized with semiconductor NCs to date. The upper and lower edges of the rectangles correspond to the positions of the conduction- and valence-band edge of the core (center) and shell materials, respectively.

Optical Properties



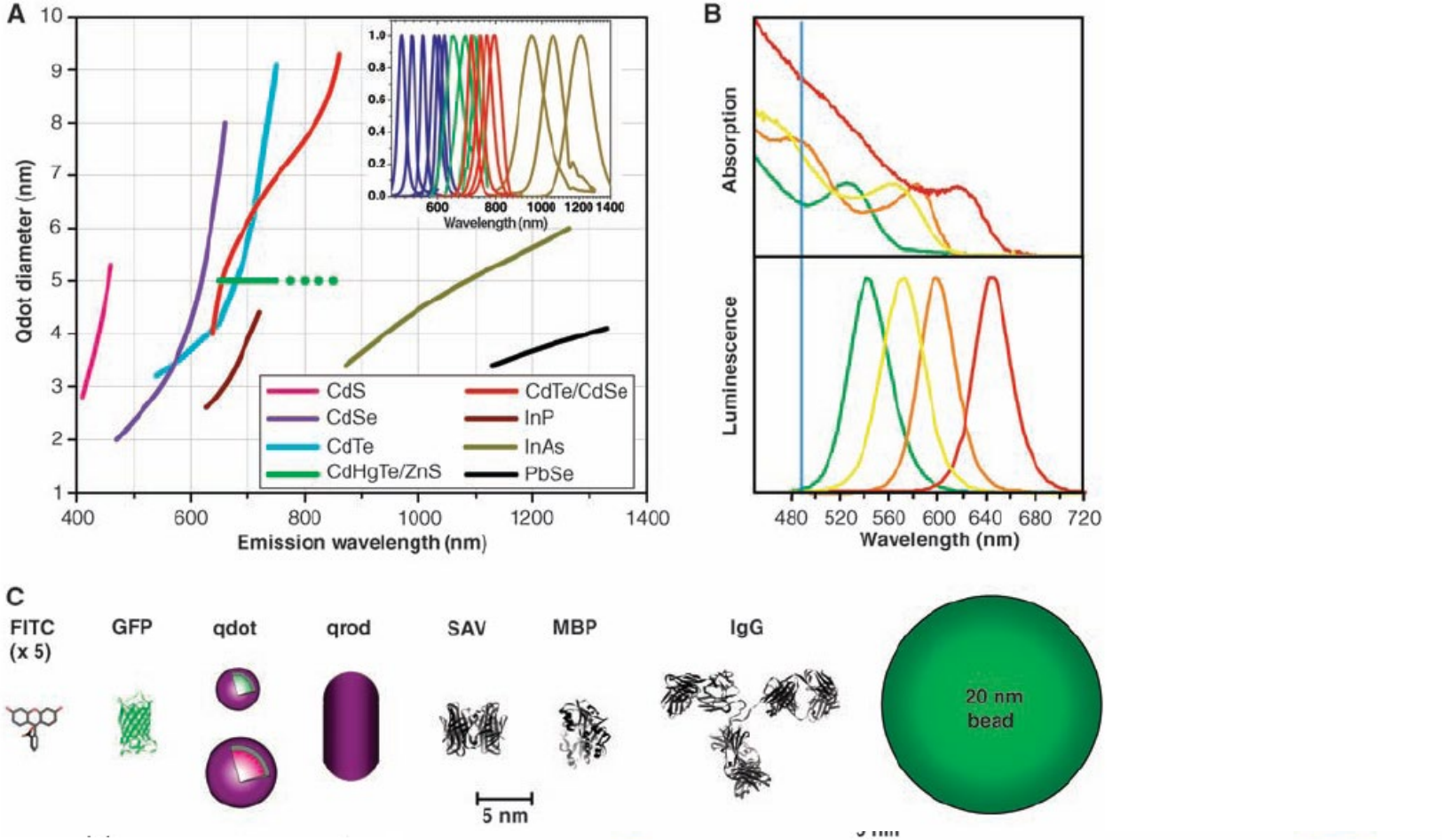
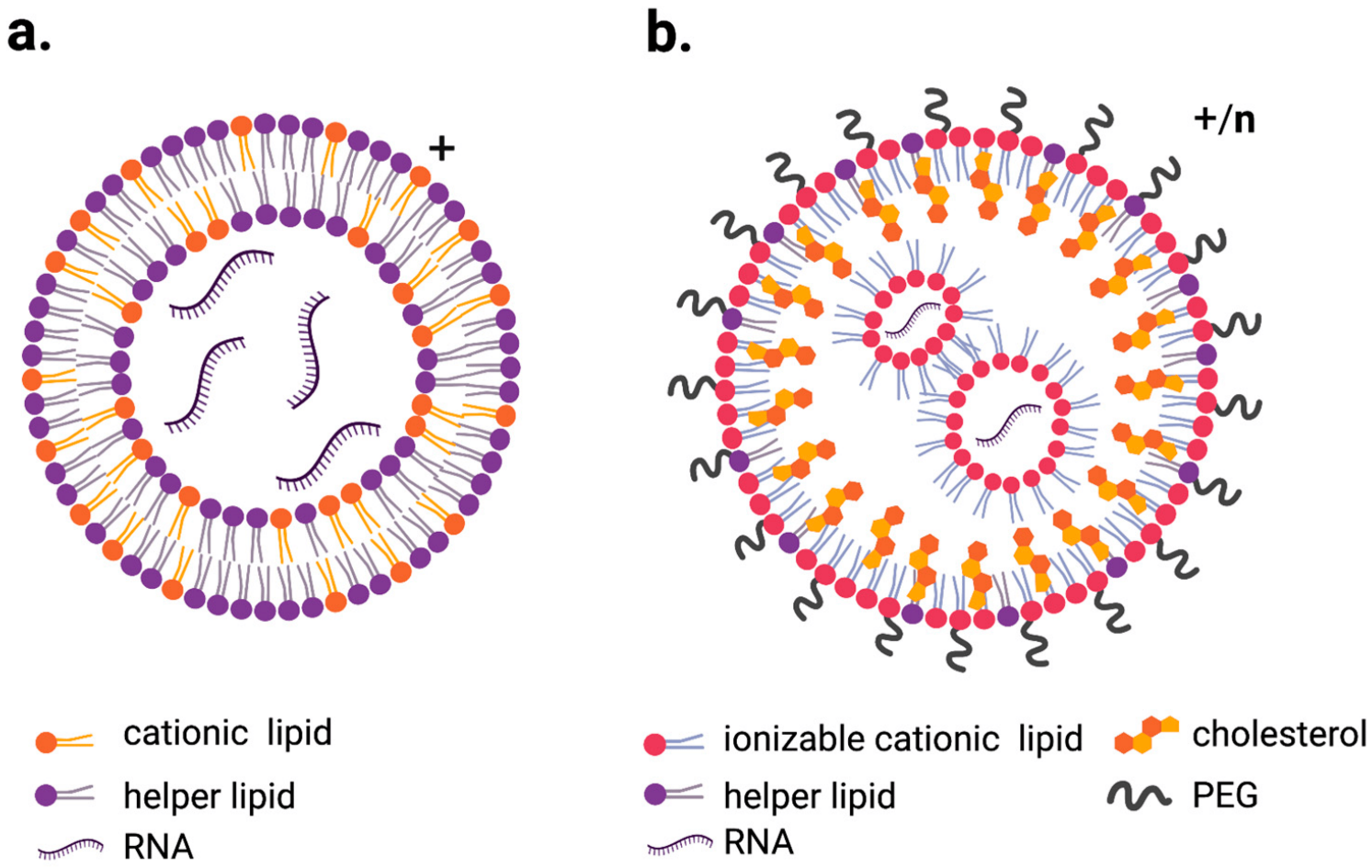


Fig. 1. (**A**) Emission maxima and sizes of quantum dots of different composition. Quantum dots can be synthesized from various types of semiconductor materials (II-VI: CdS, CdSe, CdTe…; III-V: InP, InAs…; IV-VI: PbSe…) characterized by different bulk band gap energies. The curves represent experimental data from the literature on the dependence of peak emission wavelength on qdot diameter. The range of emission wavelength is 400 to 1350 nm, with size varying from 2 to 9.5 nm (organic passivation/solubilization layer not included). All spectra are typically around 30 to 50 nm (full width at half maximum). Inset: Representative emission spectra for some materials. Data are from (*12*, *18*, *27*, *76*–*82*). Data for CdHgTe/ZnS have been extrapolated to the maximum emission wavelength obtained in our group. (**B**) Absorption (upper curves) and emission (lower curves) spectra of four CdSe/ZnS qdot samples. The blue vertical line indicates the 488-nm line of an argon-ion laser, which can be used to efficiently excite all four types of qdots simultaneously. [Adapted from (*28*)] (**C**) Size comparison of qdots and comparable objects. FITC, fluorescein isothiocyanate; GFP, green fluorescent protein; qdot, green (4 nm, top) and red (6.5 nm, bottom) CdSe/ZnS qdot; qrod, rod-shaped qdot (size from Quantum Dot Corp.'s Web site). Three proteins—streptavidin (SAV), maltose binding protein (MBP), and immunoglobulin G (IgG)—have been used for further functionalization of qdots (see text) and add to the final size of the qdot, in conjunction with the solubilization chemistry (Fig. 2).

Advantages of QDs for Imaging

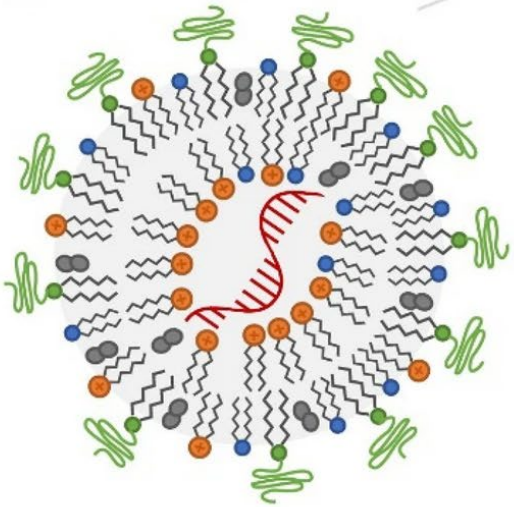
Broad Excitation and Narrow Emission Spectra: Quantum dots can be excited by a wide range of wavelengths but emit light at very specific wavelengths. This narrow emission spectrum allows for the simultaneous use of multiple quantum dot colors for multiplexed imaging, enabling the visualization of several targets within a single sample.
Size- and Composition-Tunable Fluorescence: The emission wavelength of quantum dots can be precisely tuned by changing their size or composition, allowing for the generation of a wide palette of colors from the same material simply by adjusting the quantum dot size. This tunability is advantageous for creating highly multiplexed imaging assays.
High Photostability: Quantum dots are much more resistant to photobleaching than traditional fluorescent dyes and proteins. This property allows for prolonged imaging sessions and repeated exposures, which are essential for long-term studies of dynamic processes in live cells or tissues.
High Quantum Yield: Quantum dots generally have high quantum yields, meaning they are very efficient at converting absorbed light into emitted light. This results in bright signals that can improve the sensitivity and detection limits of bioimaging applications.
Versatility in Functionalization and Bioconjugation: Quantum dots can be functionalized with various biological molecules, such as antibodies, peptides, or nucleic acids, enabling targeted imaging of specific molecules or structures within cells and tissues. This specificity is crucial for studying complex biological processes and for diagnostic purposes.

Lipid Nanoparticles

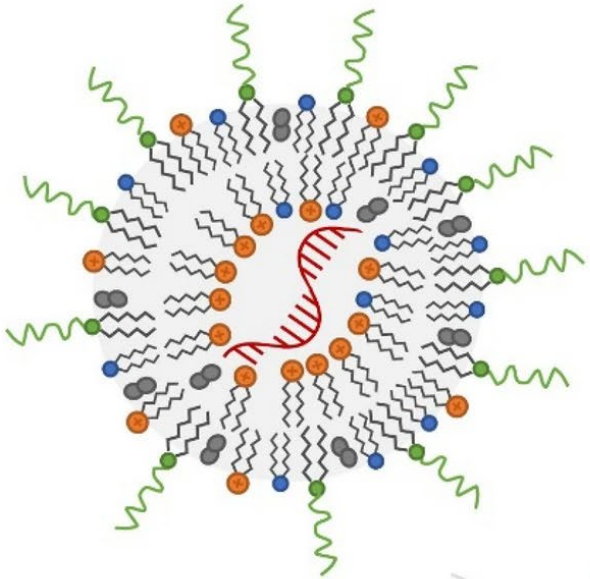


Selection of Lipid Materials: The first step involves selecting appropriate lipid materials. The typical components of LNPs for vaccine delivery include:
Ionizable cationic lipids: Facilitate endosomal escape of the RNA into the cytoplasm.
Phospholipids: Provide structural integrity.
Cholesterol: Stabilizes the lipid bilayer.
Polyethylene glycol (PEG)-lipids: Confer stealth properties to avoid rapid clearance from the body.
Nucleic Acid Encapsulation: The mRNA or other nucleic acid is mixed with the lipid components. The encapsulation is usually achieved through one of the following processes:
Ethanol Dilution Method: Lipids dissolved in ethanol are rapidly mixed with an aqueous solution containing the nucleic acid. This process results in the spontaneous assembly of LNPs encapsulating the mRNA.
Microfluidics: This method involves the controlled mixing of lipid and nucleic acid streams under laminar flow conditions in a microfluidic device. Microfluidics allows for precise control over the nanoparticle size and encapsulation efficiency.
LNP Formation and Size Adjustment: The size of LNPs is crucial for their effectiveness and is typically adjusted to be around 80-100 nanometers.
Sterilization and Quality Control: The LNPs must be sterile for use in vaccines. Sterilization can be achieved by filtration through a sterile filter with a suitable pore size (e.g., 0.22 micrometers).
Formulation: The final LNP formulation is typically prepared in a buffer suitable for injection. The formulation process must ensure that the LNPs are stable and maintain their integrity until they are administered.
Storage: The stability of LNPs is temperature-dependent. They are usually stored at low temperatures (e.g., -80°C) to maintain their structural integrity and functional properties until they are ready to be used.

A



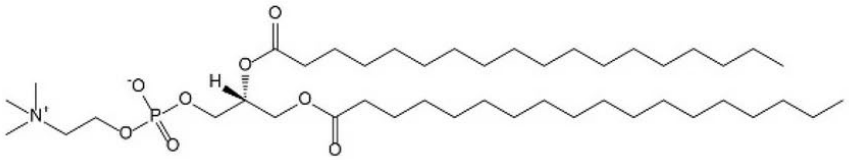
Mushroom



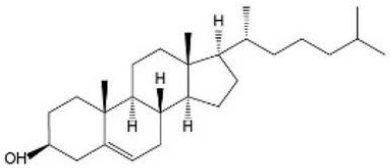
Brush-like

B

DSPC, Phospholipid

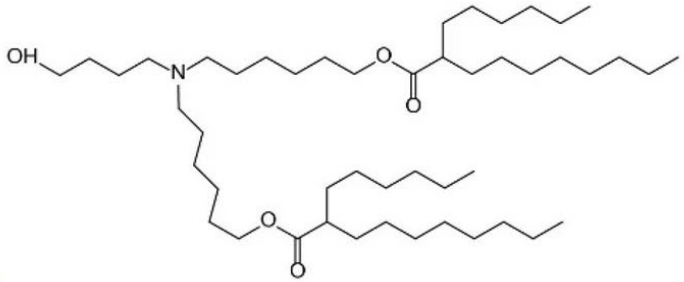


Cholesterol, Sterol Lipid

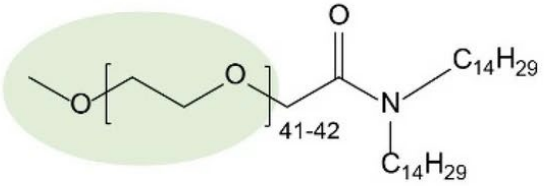


mRNA

ALC-0315, Ionizable Lipid

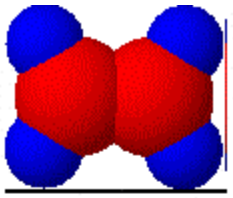


ALC-0159, PEGylated Lipid

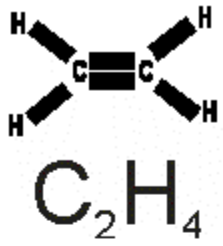


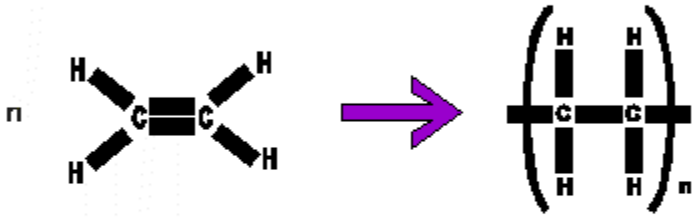
PEG WM=2 kDa, PEG density indext Γ/Γ*=2.5
Particle Diameter=77 nm

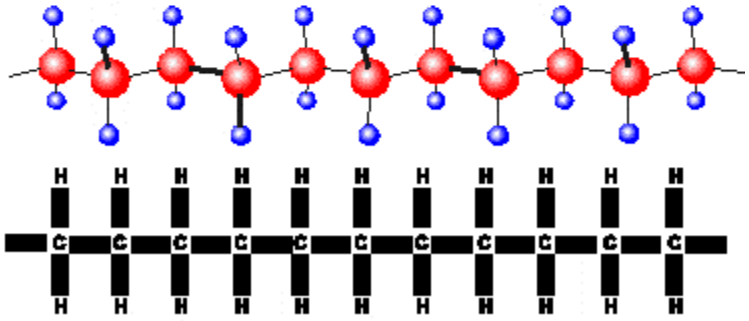
Polymer



a monomer ethene

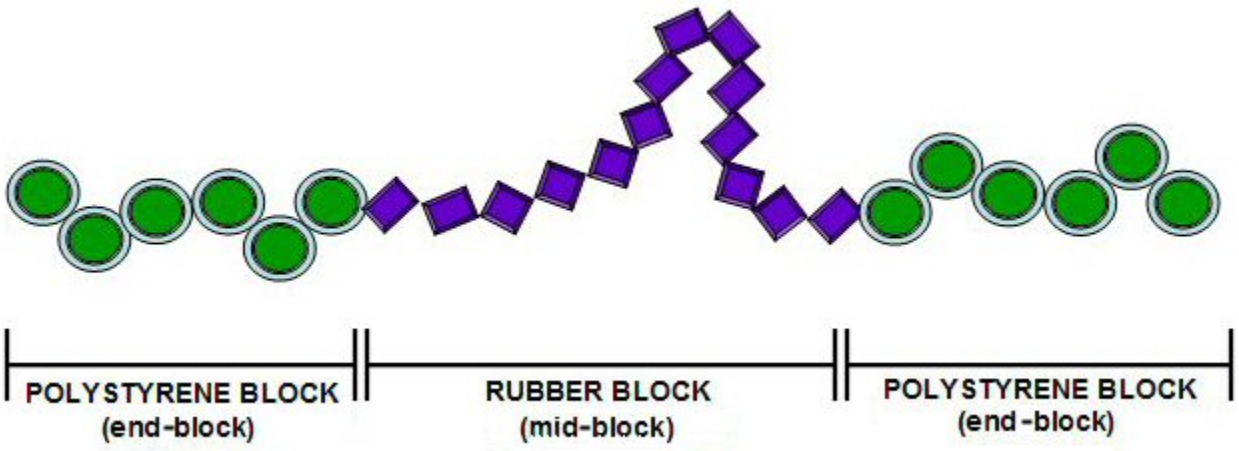




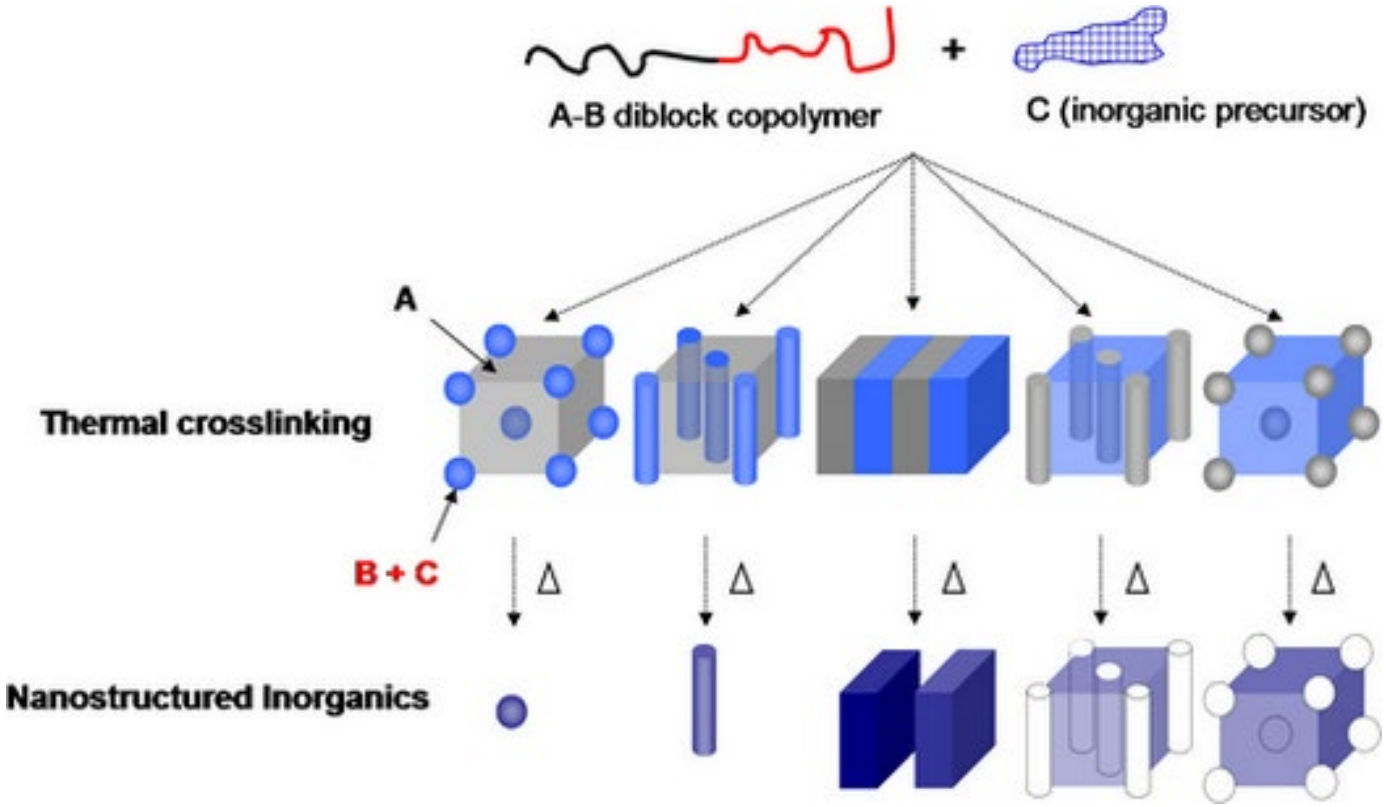


a polymer poly(ethene)

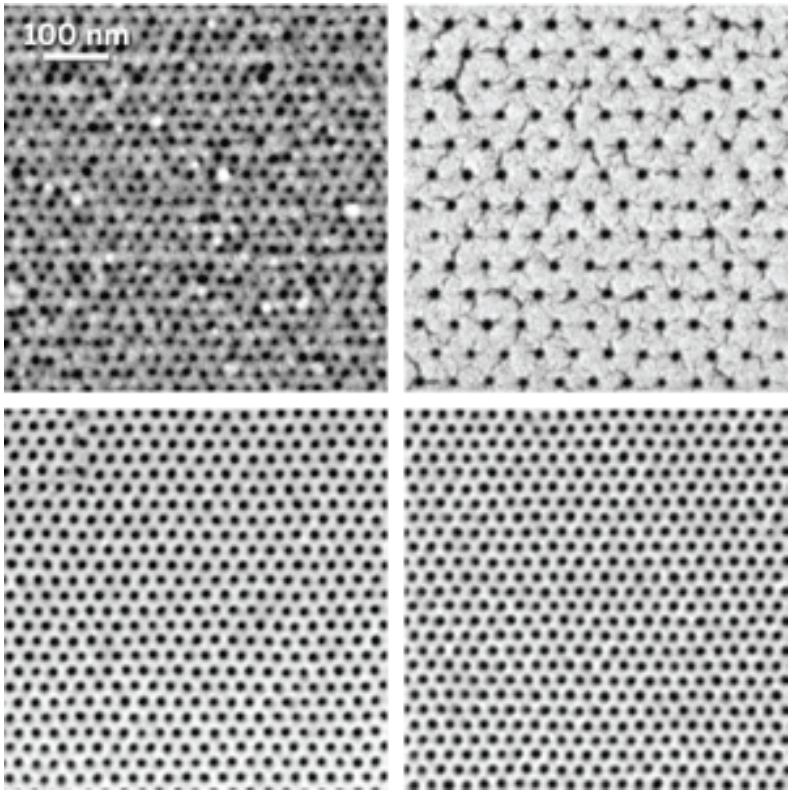
Block copolymer

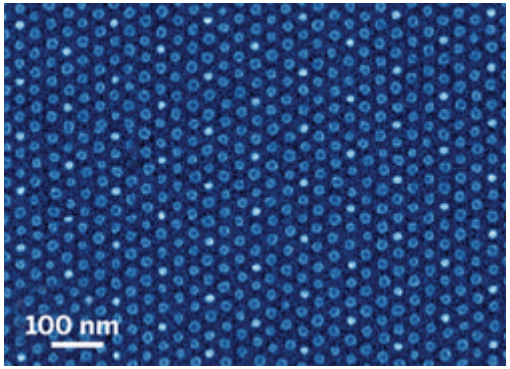


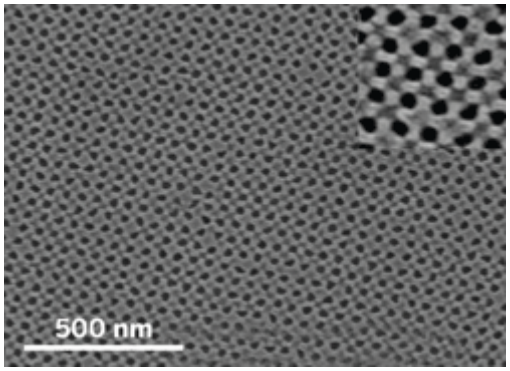
Phase Segregation



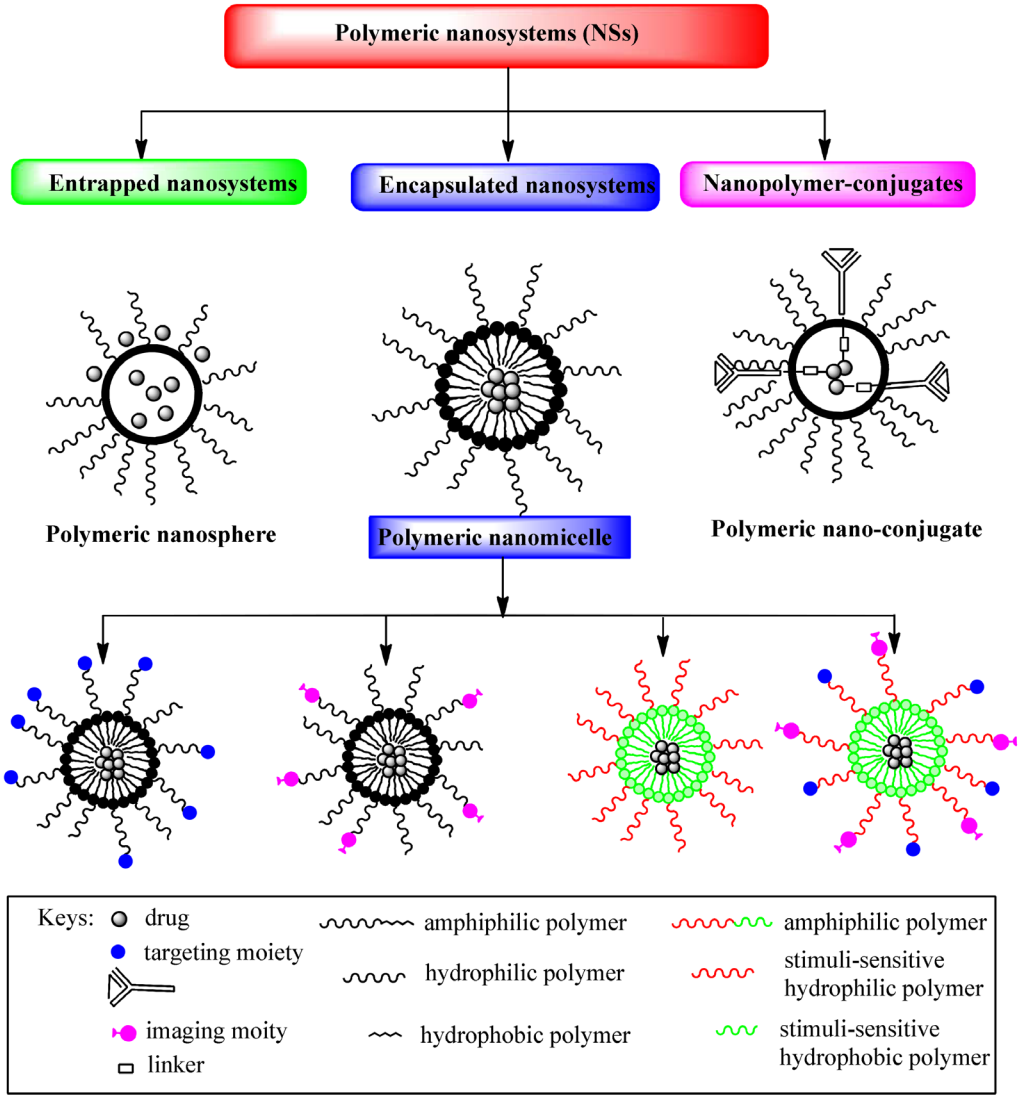
Self-Assembled Block-copolymer



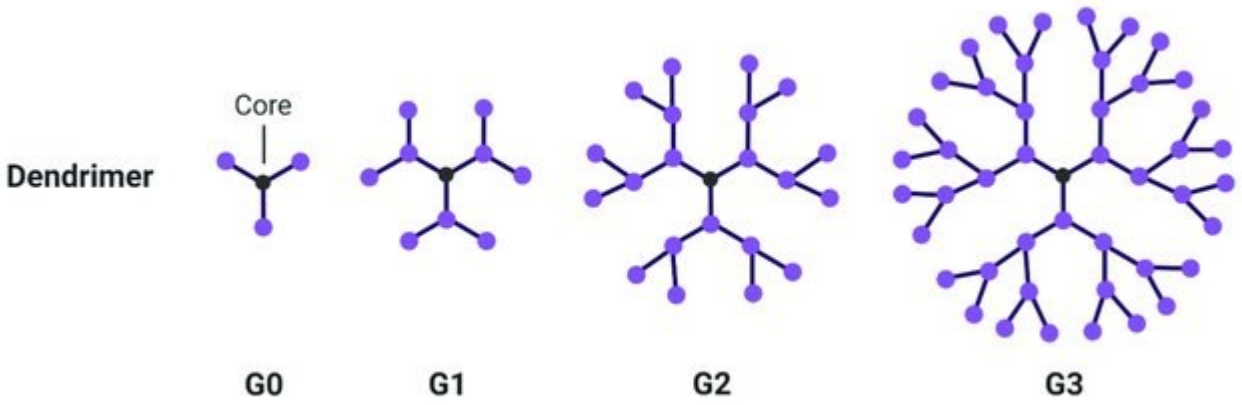




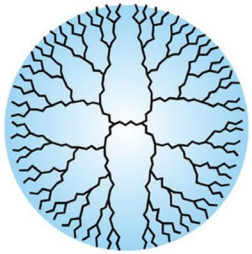
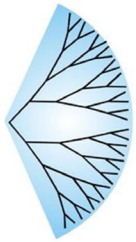
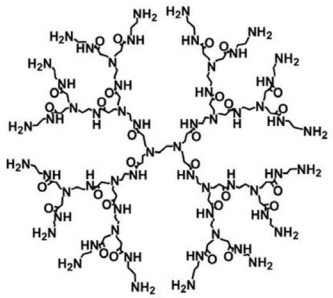
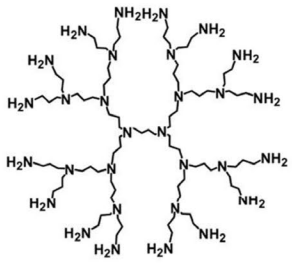
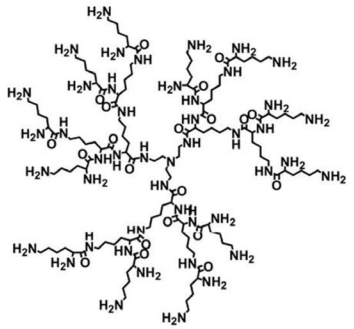
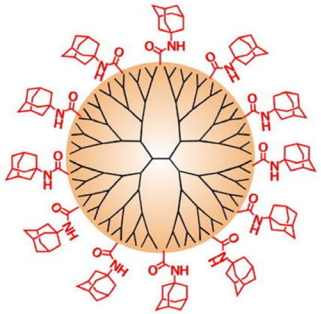
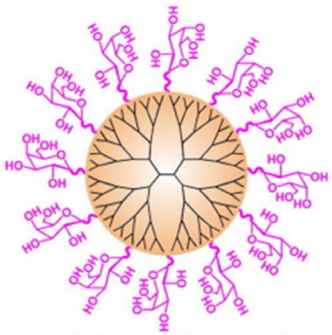
Polymer Nanoparticles



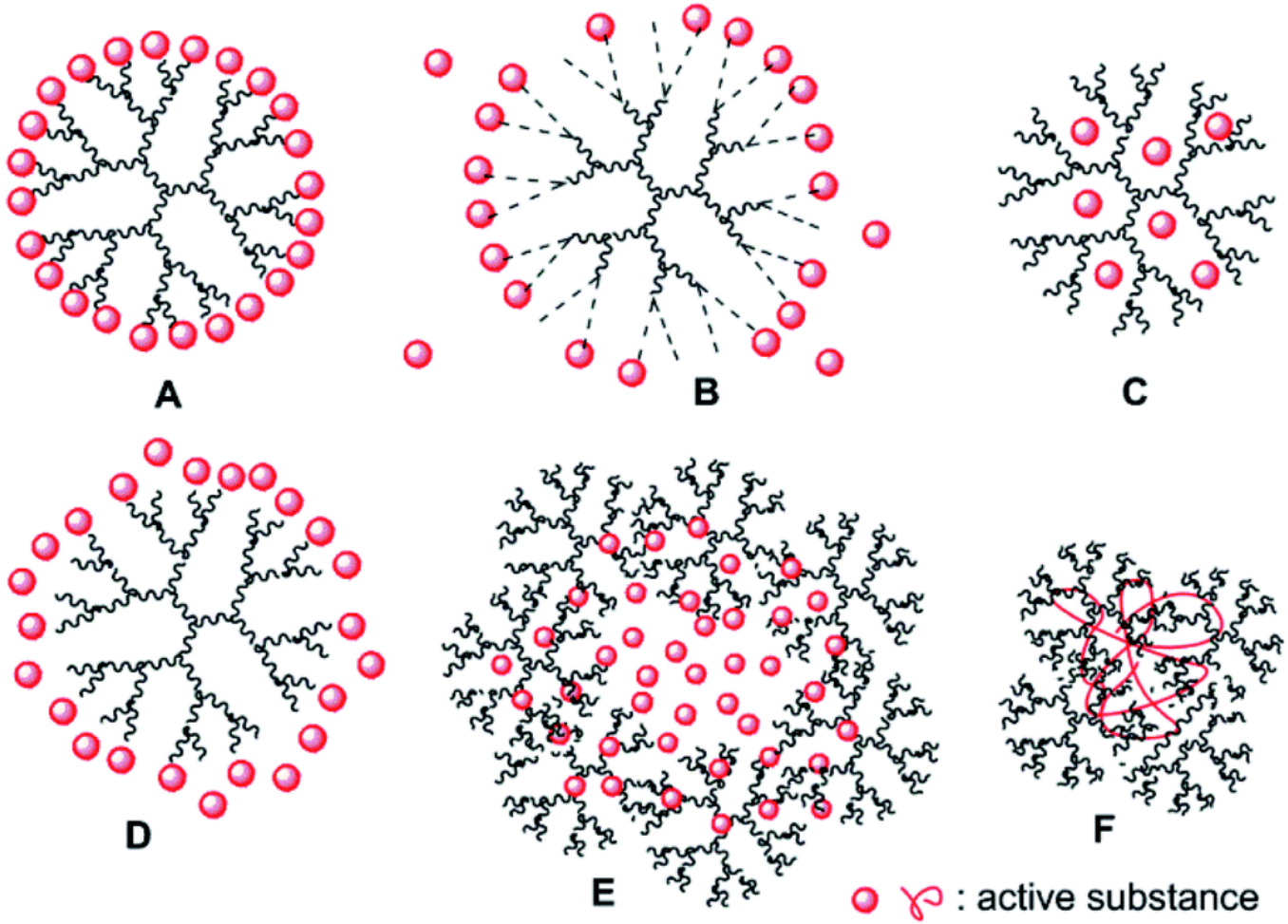
Dendrimer



Dendrimer

Dendrimer generation				
	G3	**G4**	**G5**	**Dendron G5**
Nature of the branches				
	PAMAM	**PPI**	**PLL**	
End-group funciona-lities				
	Hydrophobic moieties	**Biological moieties**		

Dendrimer



Carbon Nanomaterials

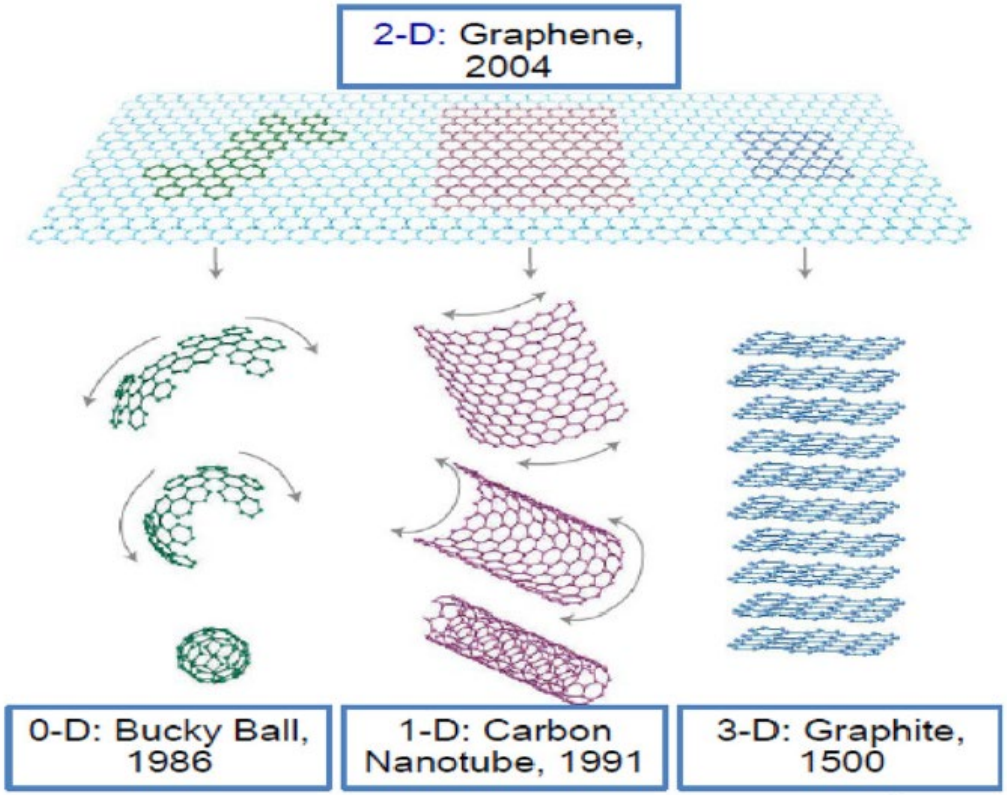


Fig. 1 Mother of all graphene forms. Graphene is a 2D building material for carbon material of all other dimensionalities. It can be wrapped up into 0D buckyballs, rolled into 1D nanotubes or stacked into 3D graphite [23]

CNT

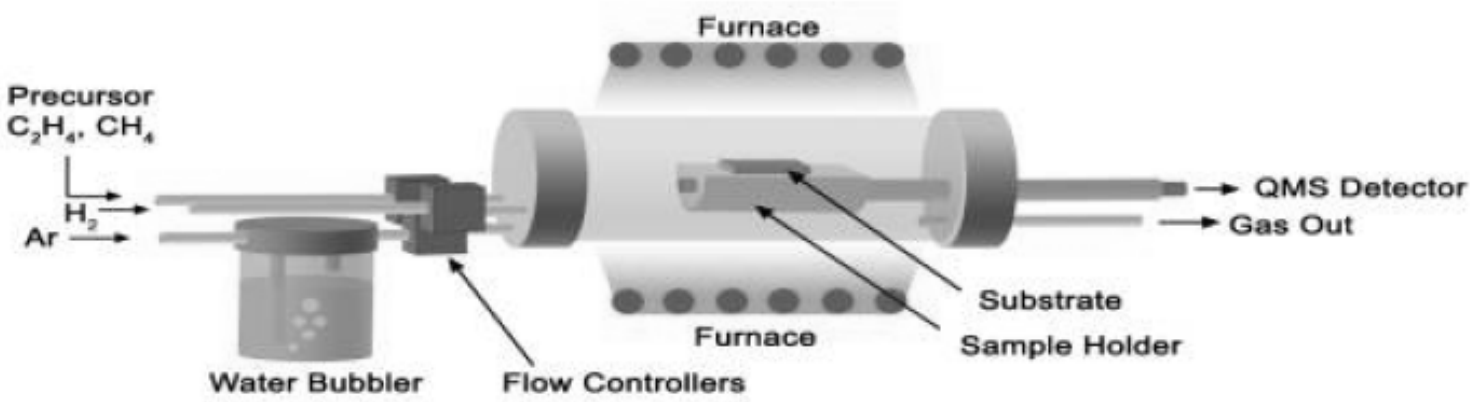
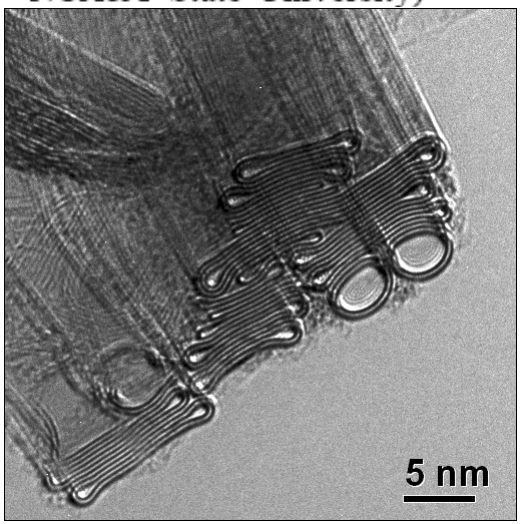
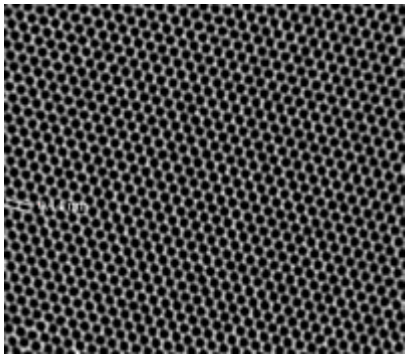


Fig. 1. Schematic of a CVD reactor for carbon nanotube growth. (Sketch by S. Yarmolenko from NCA&T State University)





Graphene

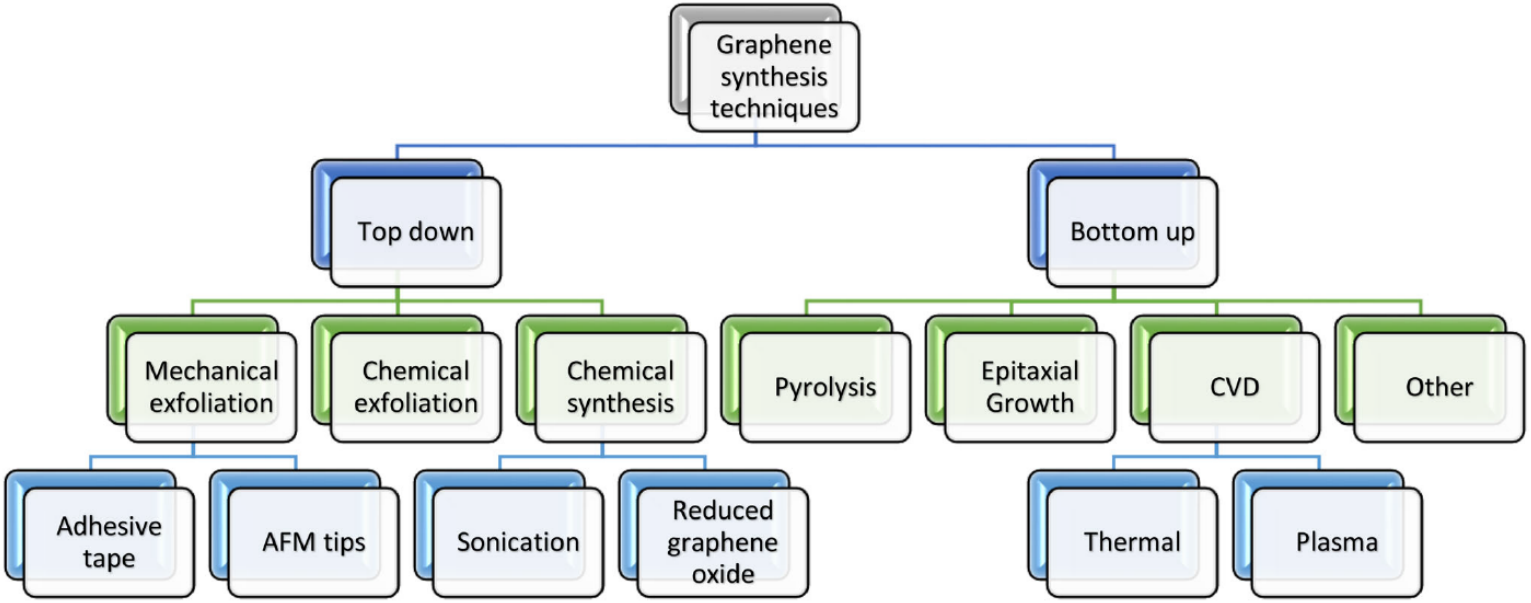
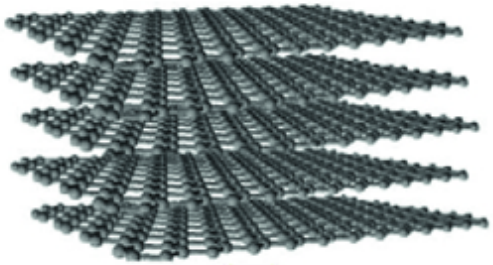
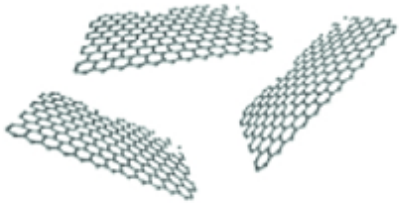


Fig. 2 A process flow chart of Graphene synthesis

Top-down

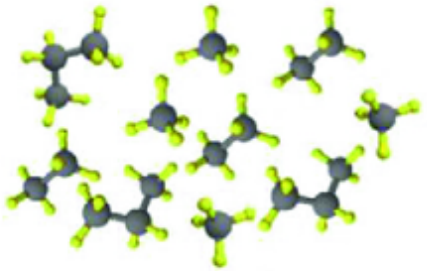
Source: Graphite

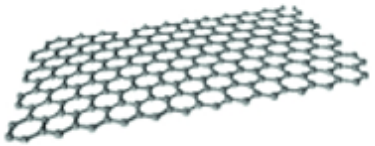


Mechanical exfoliation	Liquid phase and exfoliation	
Scotch tape, AFM tip.	Exfoliation of GIC	Reduction of GO
 **Graphene** **Size: nm~ µm**		
Low cost High quality	Low cost High Productivity Low defect	Low cost High Productivity Easy dispersion

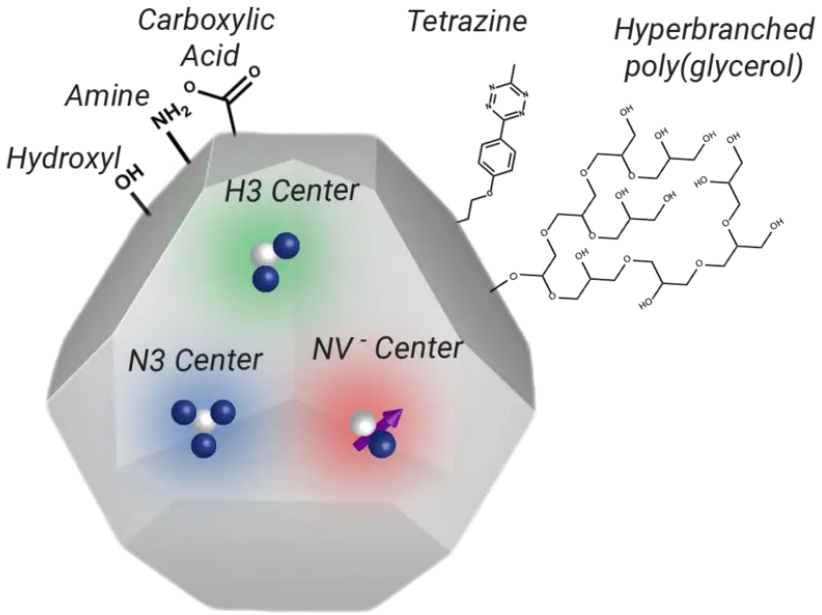
Bottom-up

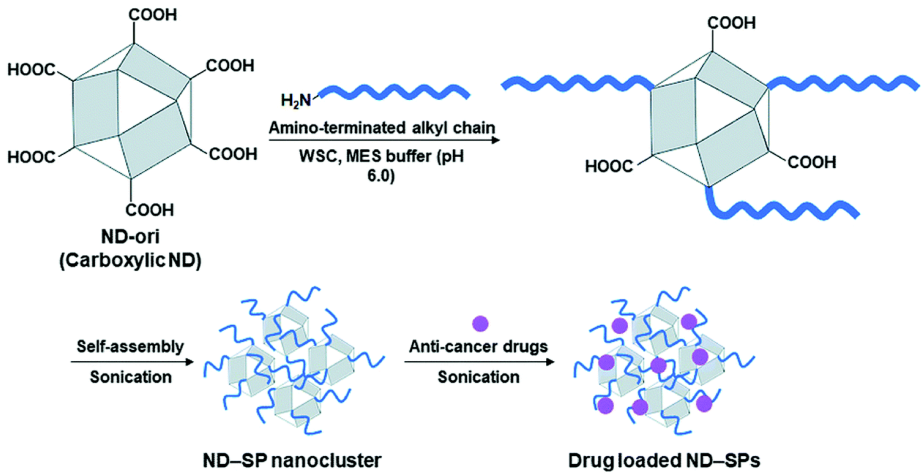
Source: CH_4, C_2H_6, C_3H_8 gas/ SiC



Epitaxial growth	CVD
Annealing of SiC wafer	Dissolving CH4 gas to Ni or Cu/ fast cooling
 **Graphene** **Size: wafer size**	
High transparency High conductivity Flexibility	

Nanodiamond





Mechanism of Fluorescence in Nanodiamonds:

Formation of NV Centers: NV centers are created either naturally during diamond formation or artificially through processes such as ion implantation, electron irradiation, or annealing. These processes introduce nitrogen atoms and vacancies into the diamond lattice, which can then form NV centers upon appropriate annealing conditions.

Excitation: When NV centers in nanodiamonds are excited by light of a certain wavelength (usually in the green spectrum), they absorb energy and transition from their ground state to an excited state.

Photon Emission: The excited NV centers return to their ground state by emitting photons. This emission occurs at characteristic wavelengths in the red to near-infrared spectrum, leading to the observed fluorescence. The wavelength and intensity of the fluorescence can be influenced by the charge state of the NV center and the presence of other defects or impurities in the diamond lattice.

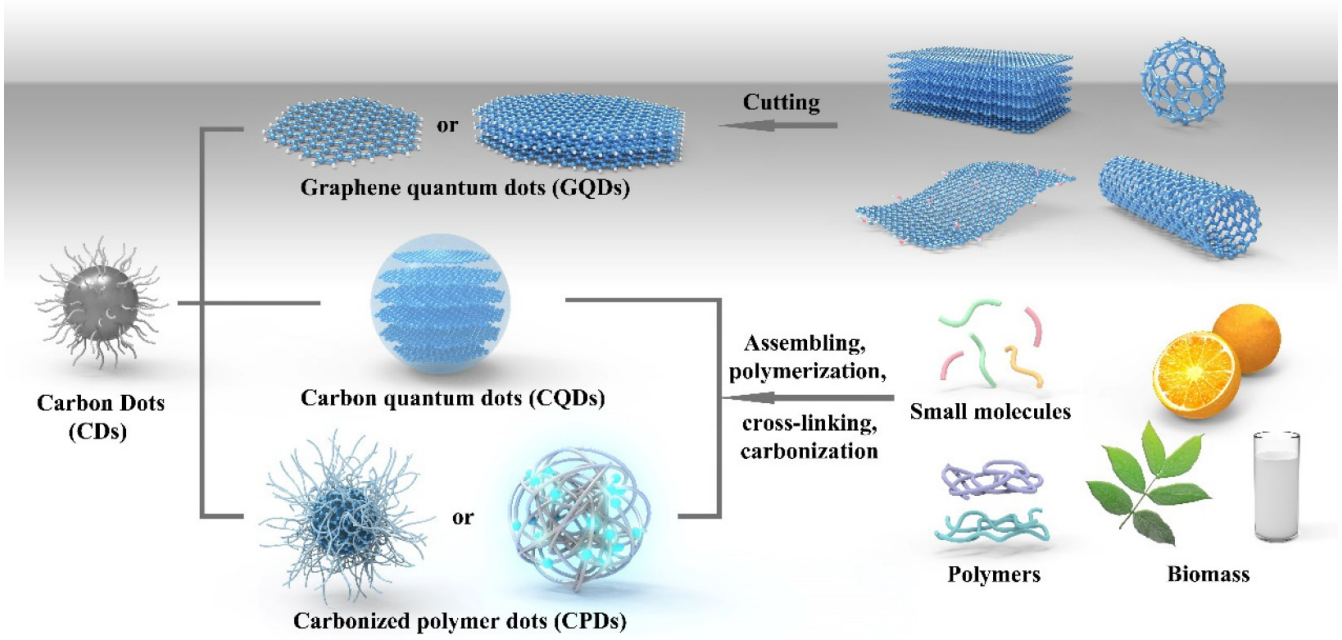
Unique Properties:

Stable Fluorescence: Unlike many organic fluorophores and some other fluorescent materials, NV centers in nanodiamonds are extremely photostable. They do not bleach or blink under standard imaging conditions, making them excellent candidates for long-term imaging and tracking applications in biological systems.

Biocompatibility: Nanodiamonds are generally considered biocompatible, which, combined with their stable fluorescence, makes them suitable for a variety of biomedical applications, including drug delivery tracking, cellular imaging, and biosensing.

Tunable Fluorescence: By controlling the size of the nanodiamonds and the concentration and type of defects (including NV centers), it is possible to tailor their optical properties to some extent.

Carbon Dots



Classification of CDs: including graphene quantum dots (GQDs), carbon quantum dots (CQDs), and carbonized polymer dots (CPDs), and their main preparation approaches.

DOI: (10.1021/acscentsci.0c01306)

Carbon quantum dots (CQDs) are nanometer-sized carbon-based materials that exhibit quantum mechanical properties, including fluorescence.

Characteristics of Carbon Quantum Dots

Size: Carbon quantum dots are typically less than 10 nanometers in diameter.

Composition: They are composed primarily of carbon elements, with some containing heteroatoms like nitrogen, oxygen, or sulfur to modify their electronic and optical properties.

Structure: The structure of CQDs can vary but often includes **graphene-like sp2-hybridized carbon sheets and sp3-hybridized carbon domains**.

Properties

Fluorescence: CQDs exhibit strong fluorescence, which is tunable based on **their size, surface functional groups, and doping elements**. This fluorescence is due to **quantum confinement and edge effects**, where the electronic properties are influenced by the size and structure of the quantum dots.

Photostability: They have high photostability, resisting photobleaching under prolonged illumination.

Biocompatibility: Carbon quantum dots are generally considered to be biocompatible and less toxic than traditional semiconductor quantum dots, making them suitable for biological and medical applications.

Water Solubility: Many CQDs are hydrophilic and easily solubilized in water, facilitating their use in biological environments.

Reasons for Fluorescence

The fluorescence of carbon quantum dots originates from several mechanisms, including **quantum confinement effects**, **surface states**, and **molecular fluorescence**. The exact mechanism can depend on the synthesis method, surface functionalization, and the presence of doping elements. Quantum confinement plays a significant role in smaller CQDs, where the movement of electrons is restricted to such a degree that it alters the electronic and optical properties of the material. Surface states, related to the functional groups attached to the surface of CQDs, also significantly influence their optical properties. Additionally, the presence of specific dopants can introduce localized energy states in the band gap, further affecting fluorescence.

Applications

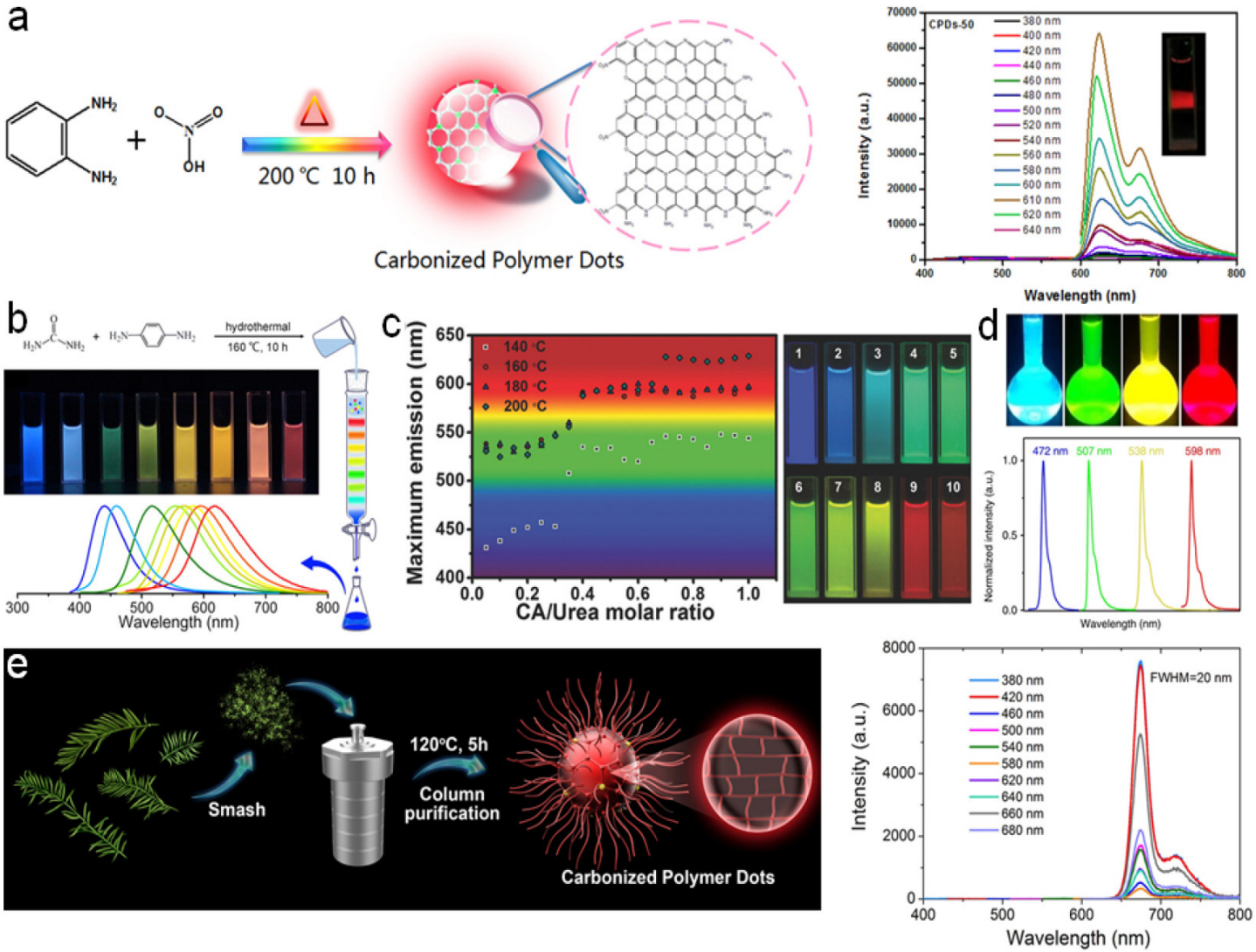
Bioimaging: Their biocompatibility and tunable fluorescence make them excellent candidates for fluorescent labeling and imaging in biological systems.

Sensing: CQDs can be engineered to detect various chemicals and biomolecules, making them useful in environmental monitoring and diagnostics.

Photocatalysis: Their ability to absorb and transfer energy efficiently makes them useful in photocatalytic applications, such as degradation of pollutants and water splitting.

Optoelectronics: CQDs are explored for use in light-emitting diodes (LEDs), solar cells, and other optoelectronic devices due to their electronic and optical properties.

The research and development of carbon quantum dots continue to evolve, revealing new insights into their properties and expanding their range of applications.



Syntheses and optical properties of CDs. Synthesis and PL spectra of (a) red emissive CPDs and (b) multicolor CPDs. Optical properties of (c) multicolor CPDs and (d) CQDs. (e) Synthesis and PL spectra of deep red emissive CPDs.

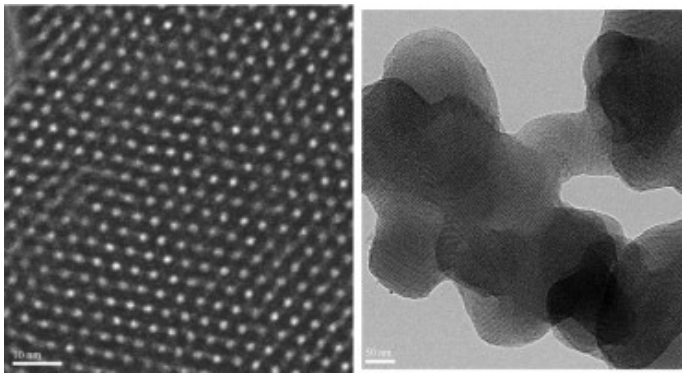
DOI: (10.1021/acscentsci.0c01306)

Porous Materials

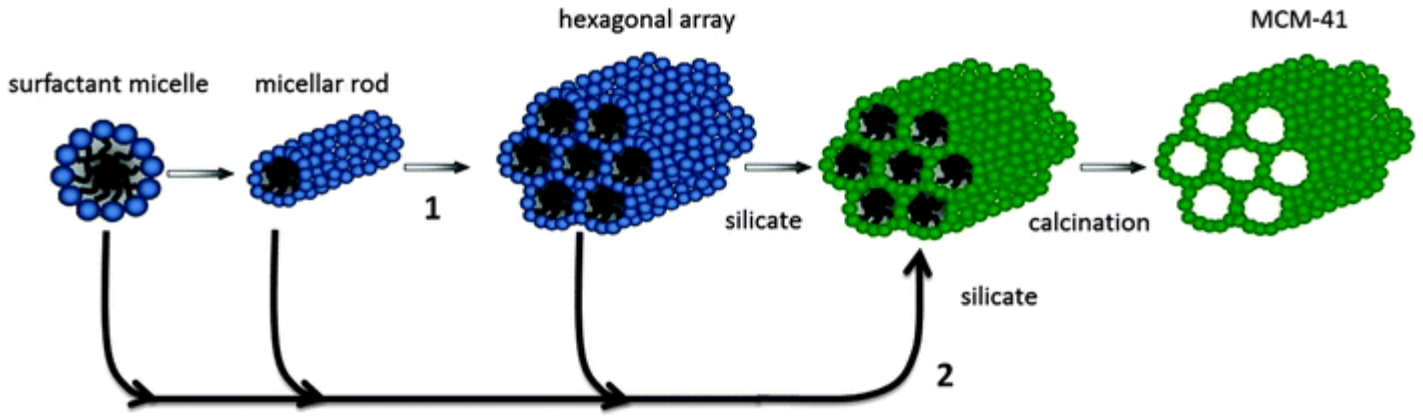
- AAO
- MCM-41

Mobil Crystalline Materials, or MCM-41

Santa Barbara Amorphous type material, or SBA-15



- Micro: < 2nm
- Meso:
- Macro: > 50nm



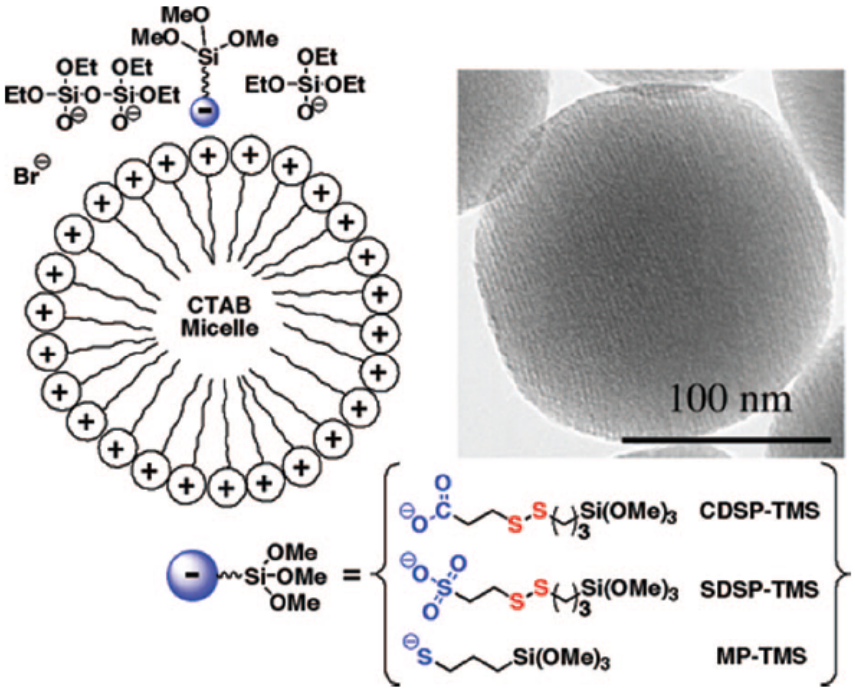


FIGURE 3. Schematic representation of the use of anionic organoalkoxysilanes for controlling the functionalization of the MSN materials. The MCM-41-type mesoporous channels are illustrated by the parallel stripes shown in the transmission electron microscopy (TEM) micrograph of the MSN–SH material. Reproduced with permission from ref 15. Copyright 2005, Royal Society of Chemistry.

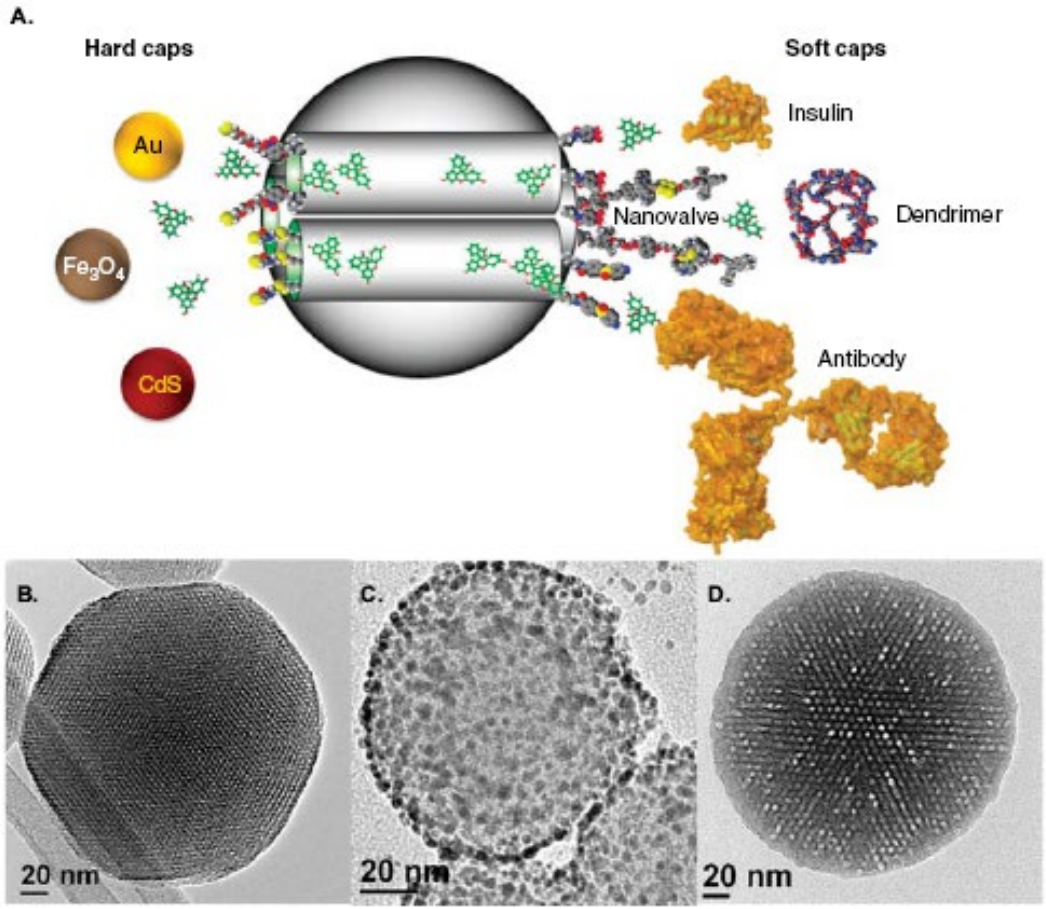


Figure 1. A. Schematic representation of a MSN loaded with drugs and capped with hard caps and soft caps highlighted in this review. Transmission electron microscopy images of (B) a MSN along the axis of the mesopores, (C) capped with hard (Au NP) and (D) with soft (polymer) caps.

MSN: Mesoporous silica nanoparticle.

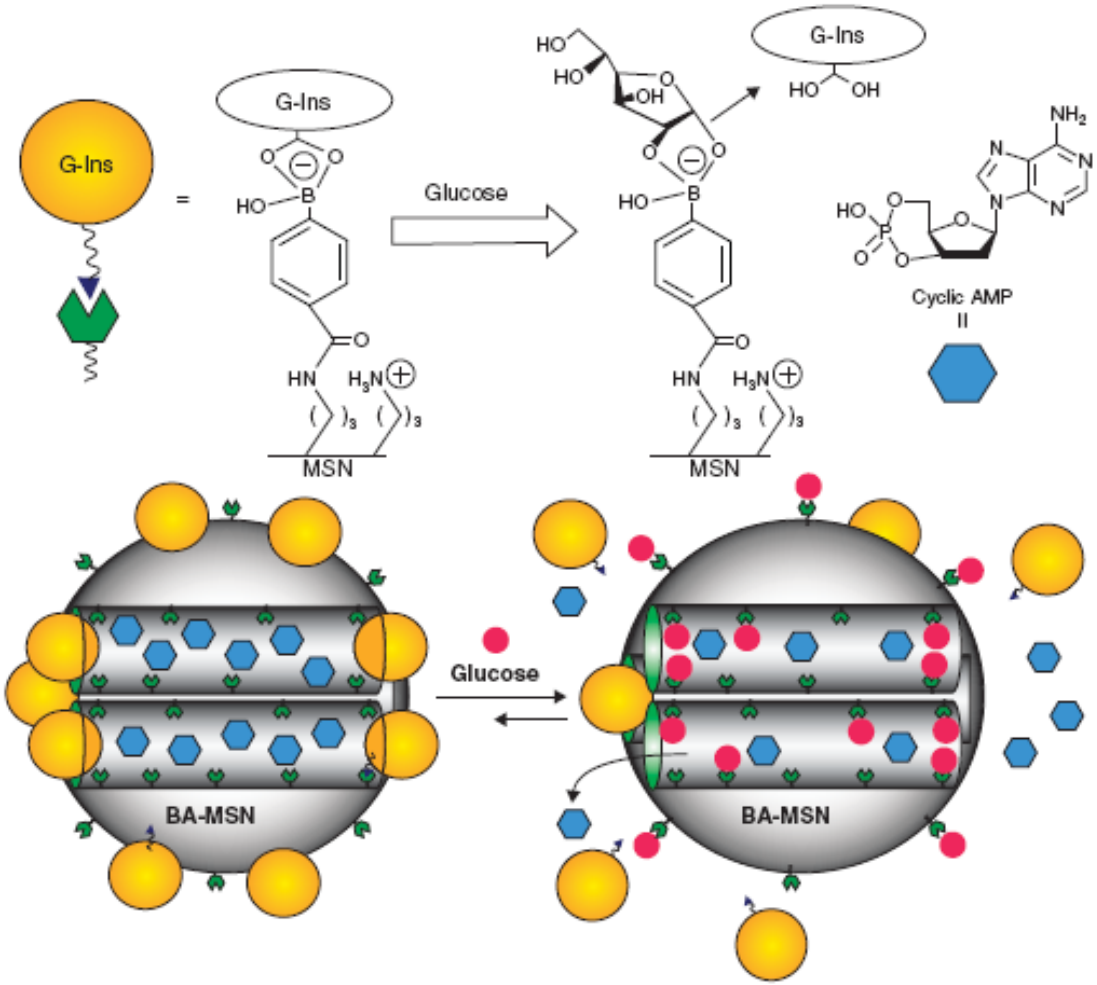
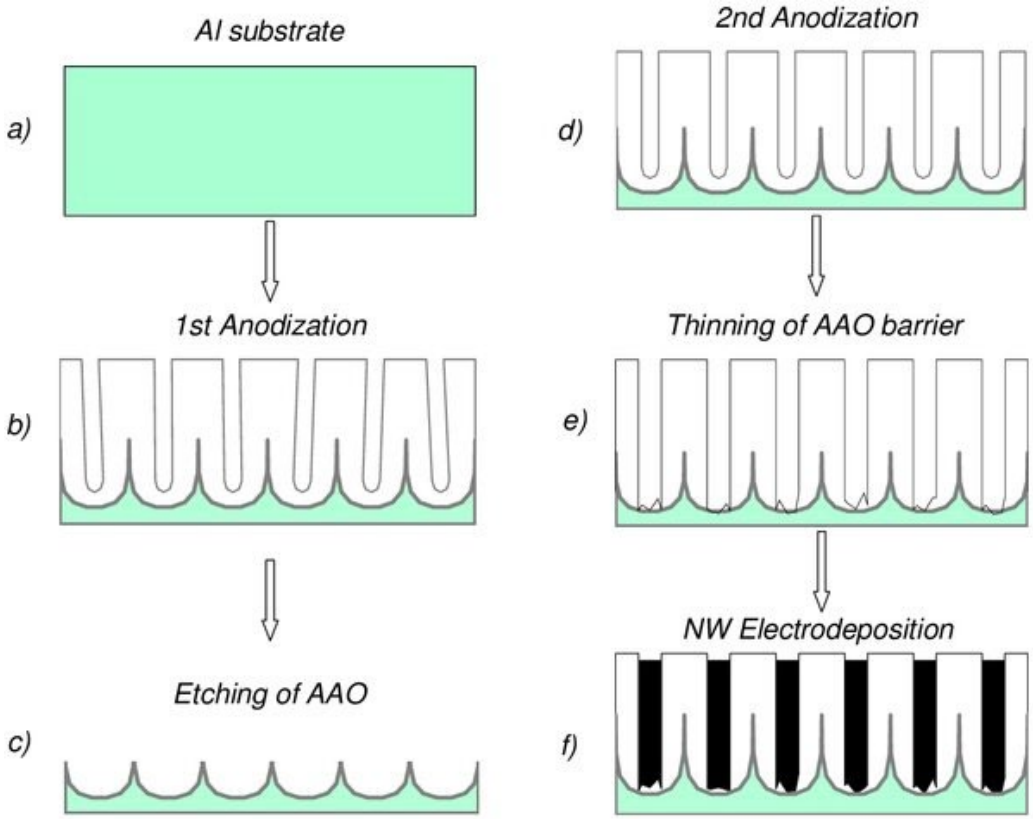


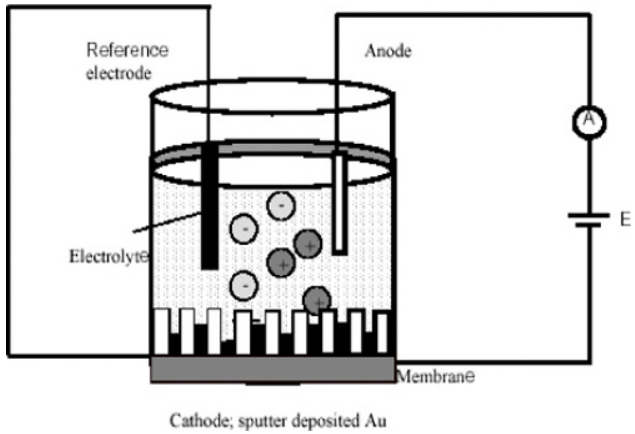
Figure 5. Schematic representation of the glucose-responsive MSN-based double delivery system for controlled release of bioactive G-Ins and cyclic AMP. The controlled release mechanism was achieved by means of the displacement reaction between blood glucose and G-Ins based on reversible boronic acid-diol complexation. High glucose concentration triggers the G-Ins uncapping and the release of cyclic AMP sequentially to diminish the higher than normal level of blood glucose.

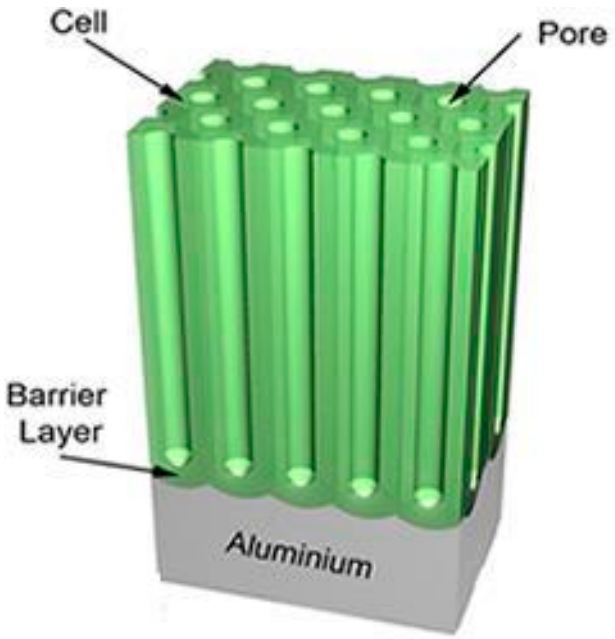
Reproduced with permission from [19].

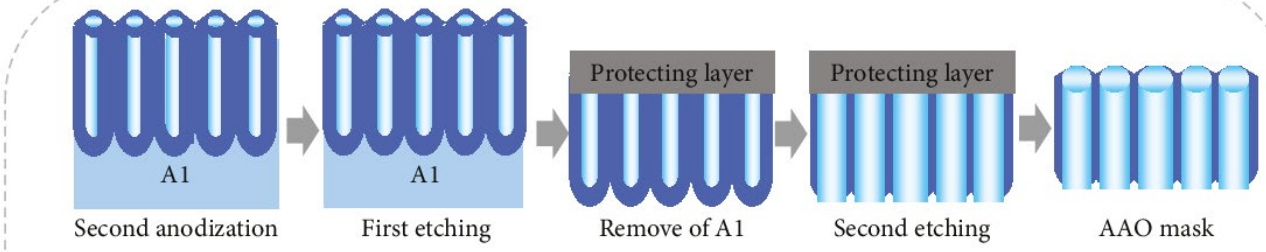
G-Ins: G-insulin; MSN: Mesoporous silica nanoparticle.

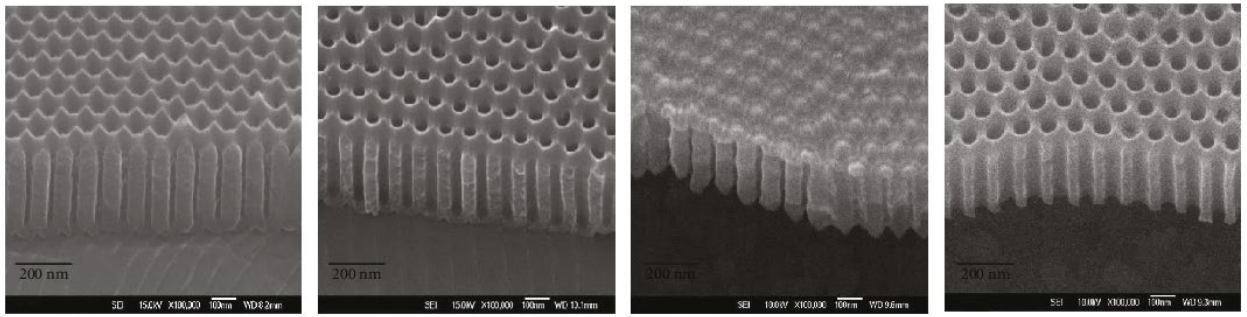
AAO


Al substrate
a)
1st Anodization
b)
Etching of AAO
c)
2nd Anodization
d)
Thinning of AAO barrier
e)
NW Electrodeposition
f)

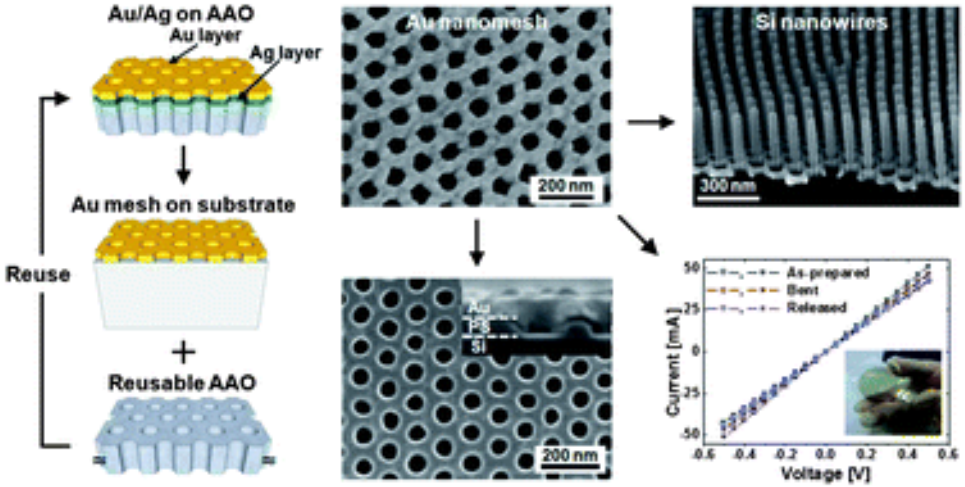

Reference electrode
Anode
A
E
Electrolyte
Membrane
Cathode; sputter deposited Au

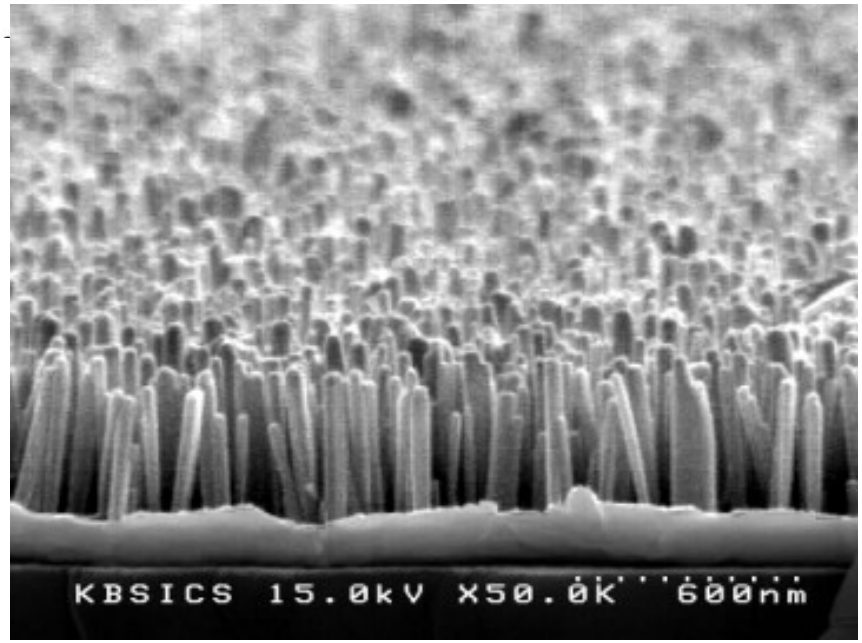

Cell
Pore
Barrier Layer
Aluminium


A1
A1
Protecting layer
Protecting layer
Second anodization
First etching
Remove of A1
Second etching
AAO mask


200 nm
200 nm
200 nm
200 nm

(a) (b) (c) (d)


Au/Ag on AAO
Au layer
Ag layer
Au mesh on substrate
Reuse
Reusable AAO
Au nanomesh
200 nm
Si nanowires
200 nm
Au
PS
Si
200 nm
As-prepared
Bent
Released
Current [mA]
Voltage [V]

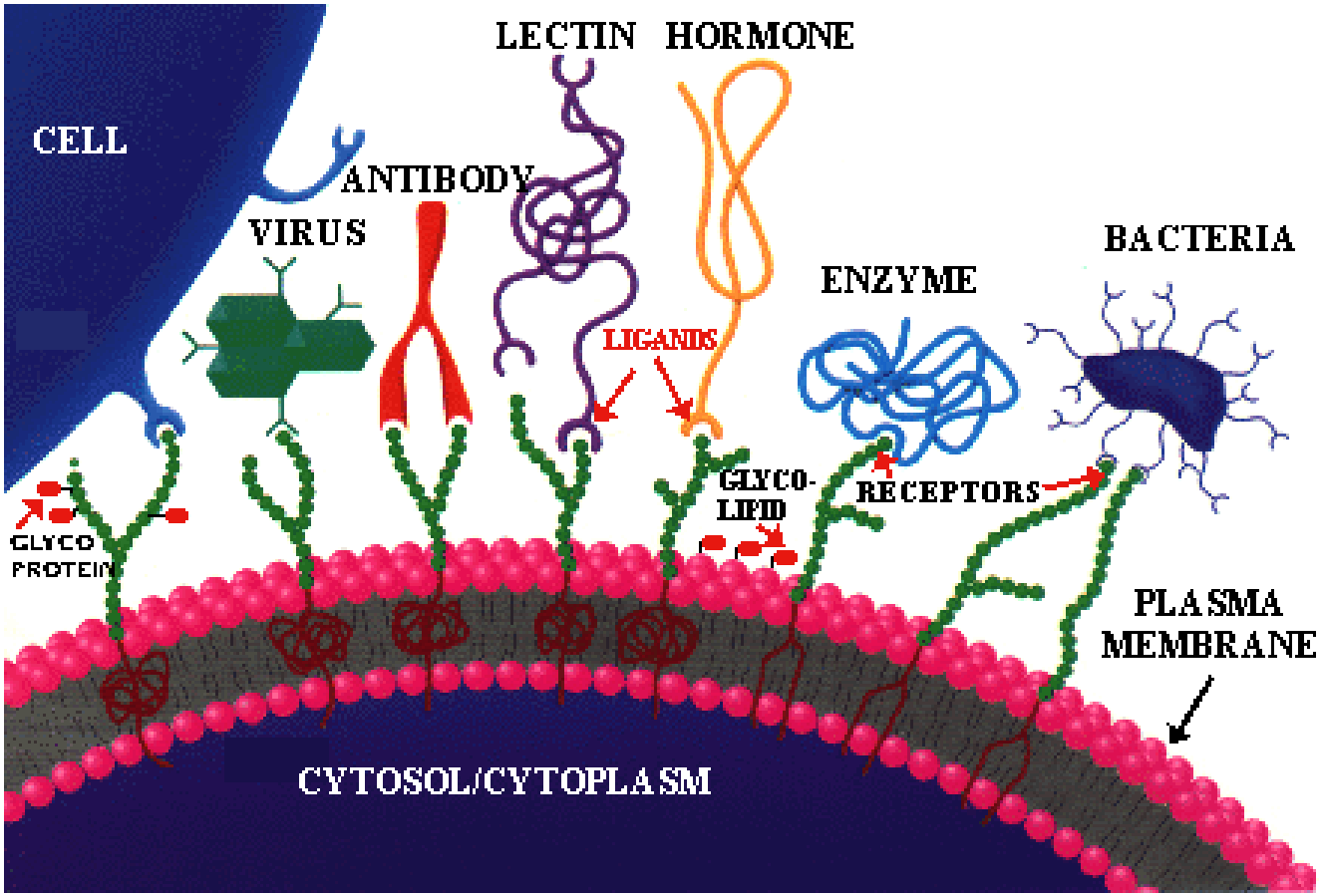

KBSICS 15.0kV X50.0K 600nm

Surface Functionalization

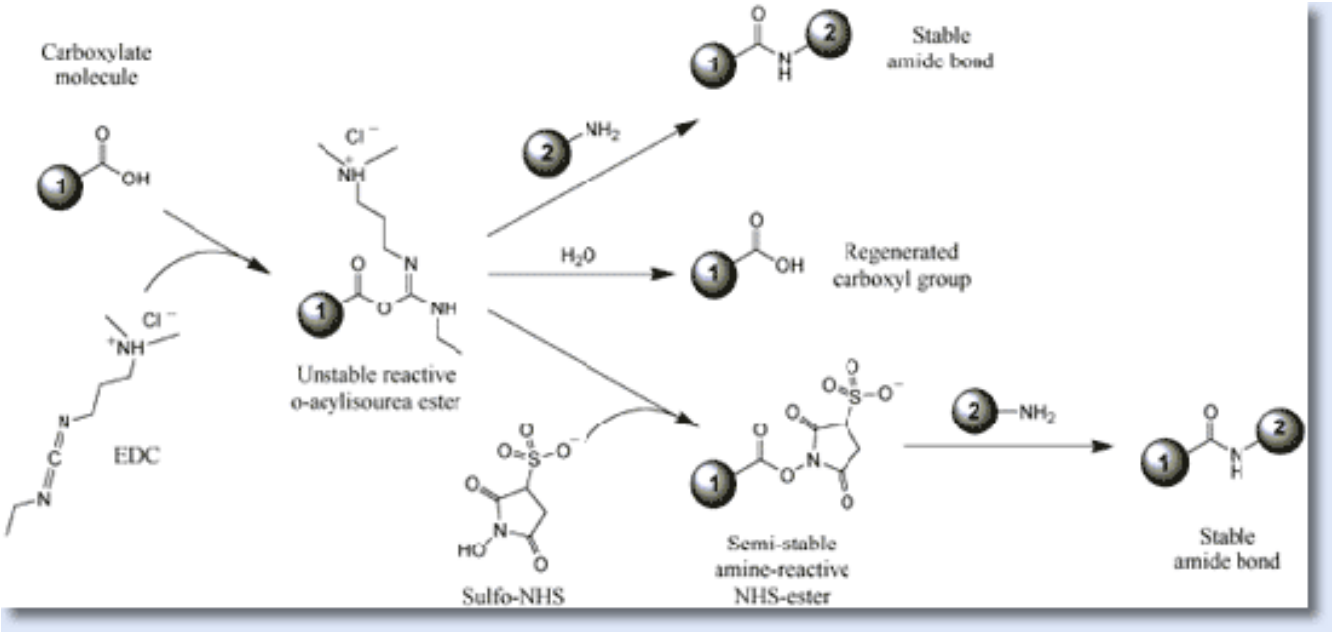
- Recognition
  - Molecular Recognition
    - Protein
    - DNA
    - Saccharide
- Reporting/Detection
  - Dye
  - Quantum dots
  - SPR
  - SERS/LSPR
- Separation
  - Gel/Chromatography
  - Magnetic

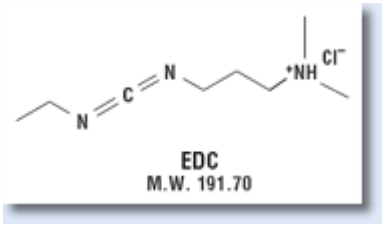
- Surfaces
  - Gold and silver
  - Silicon oxide (glass)
  - Quantum dots
  - Polymer

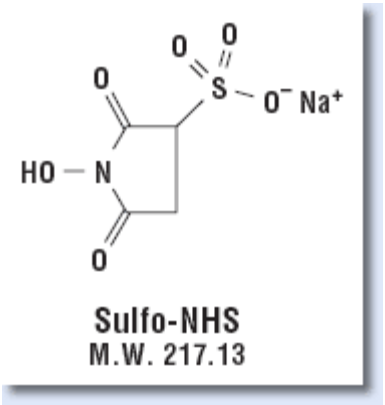
Molecular Recognition



Carboxyl Presenting Surfaces

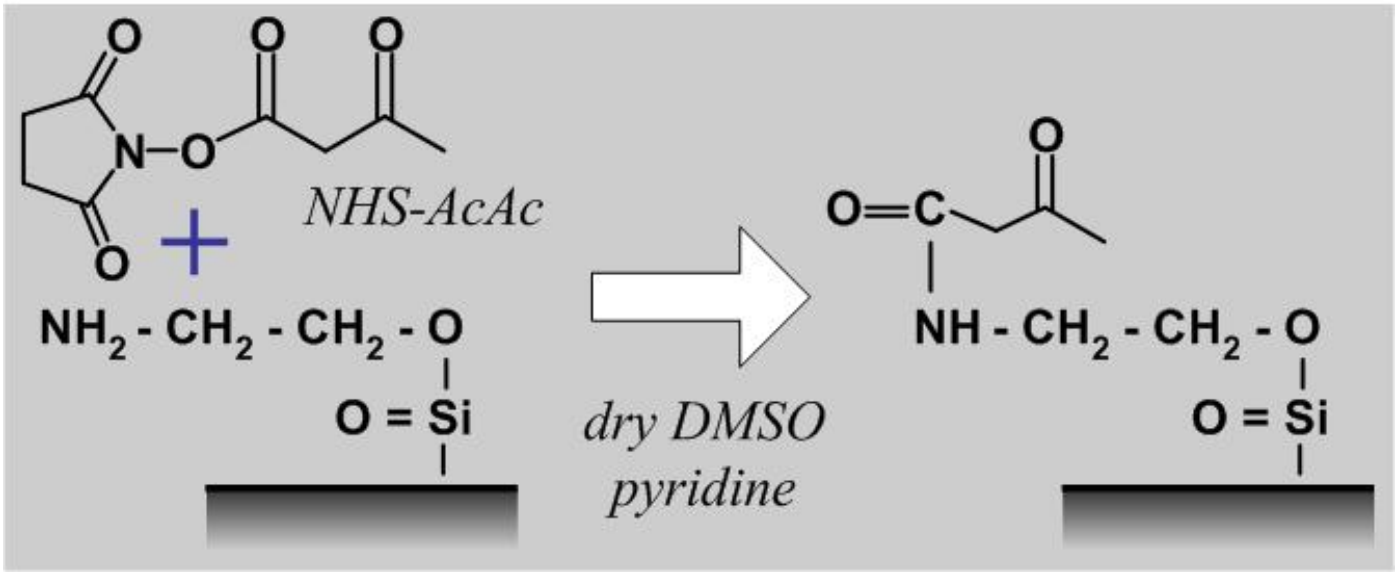




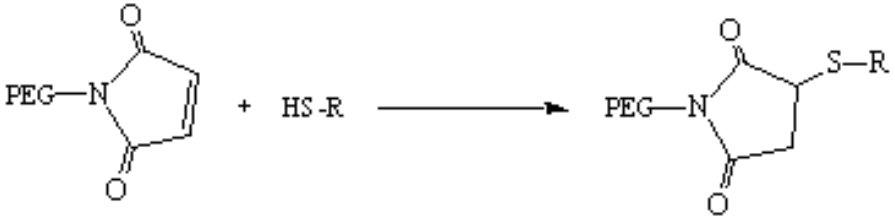


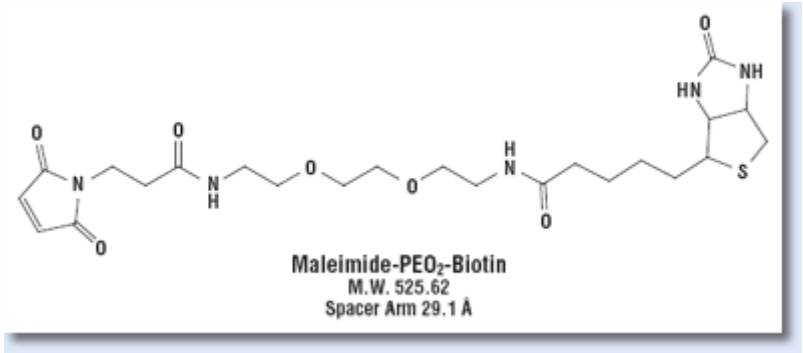
EDC (1-Ethyl-3-[3-dimethylaminopropyl]carbodiimide Hydrochloride)

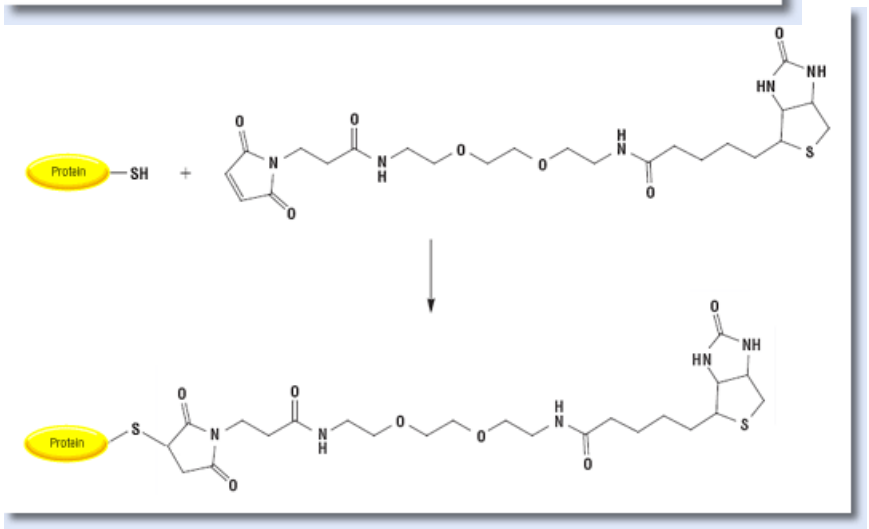
Amine Presenting Surface

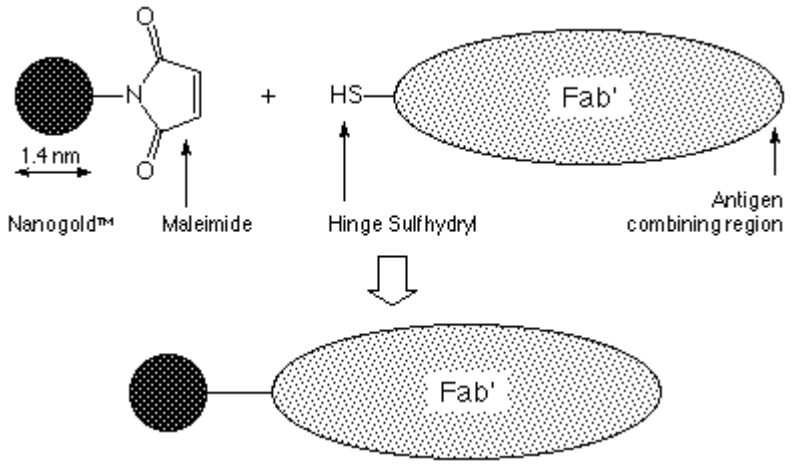


Sulfhydryl Labeling

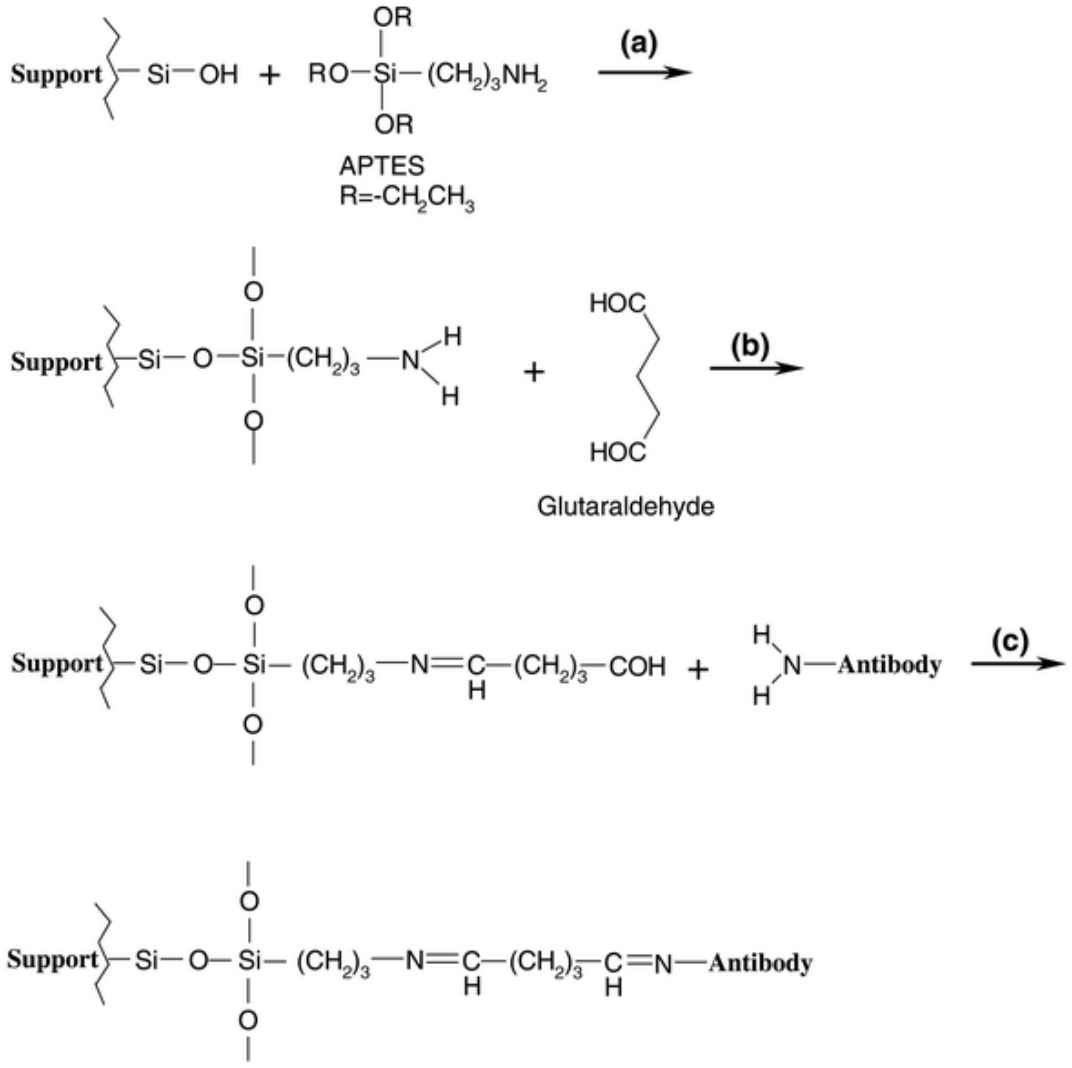




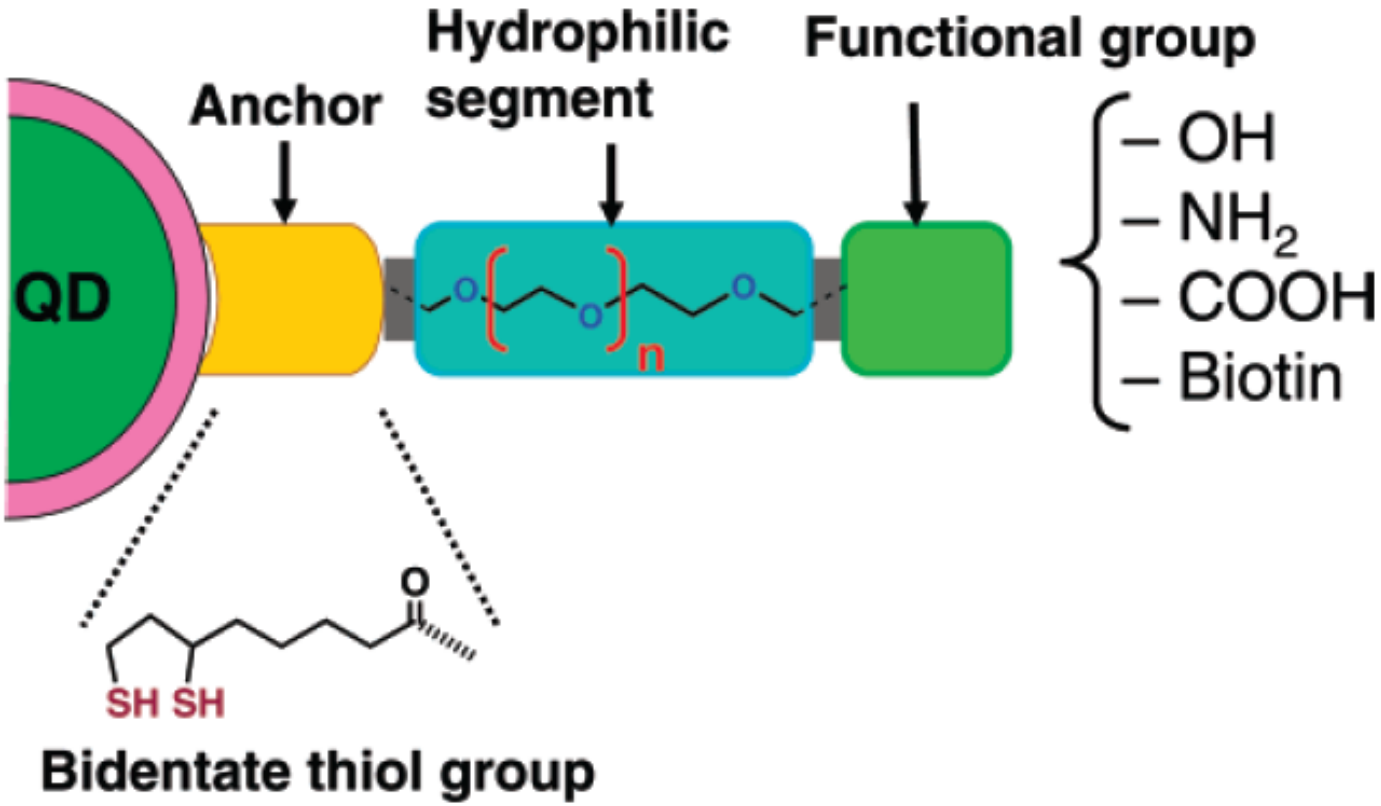




Silica Modification



Scheme 1. Modular Design of Hydrophilic Ligands with Terminal Functional Groups Used in This Study



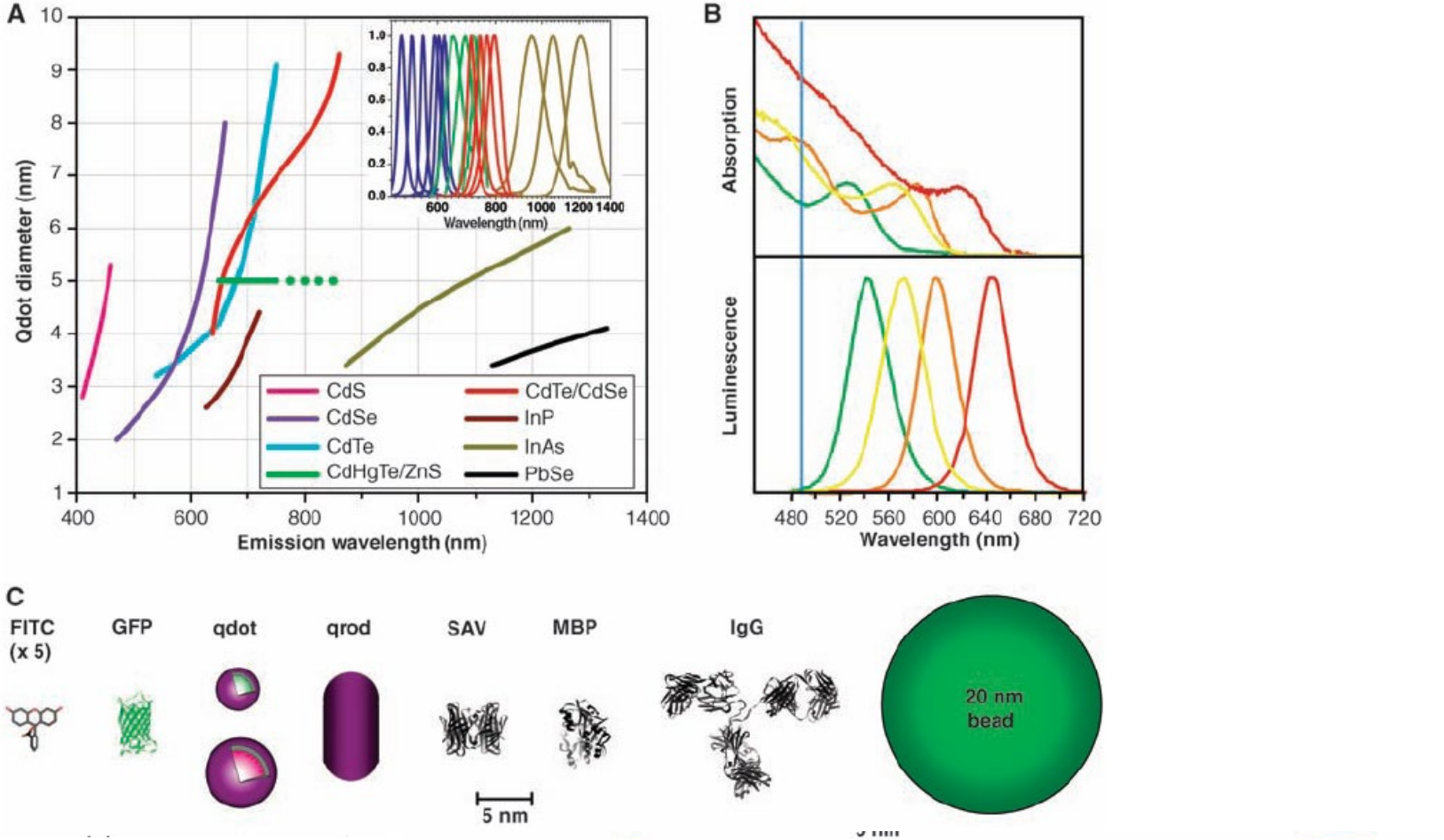
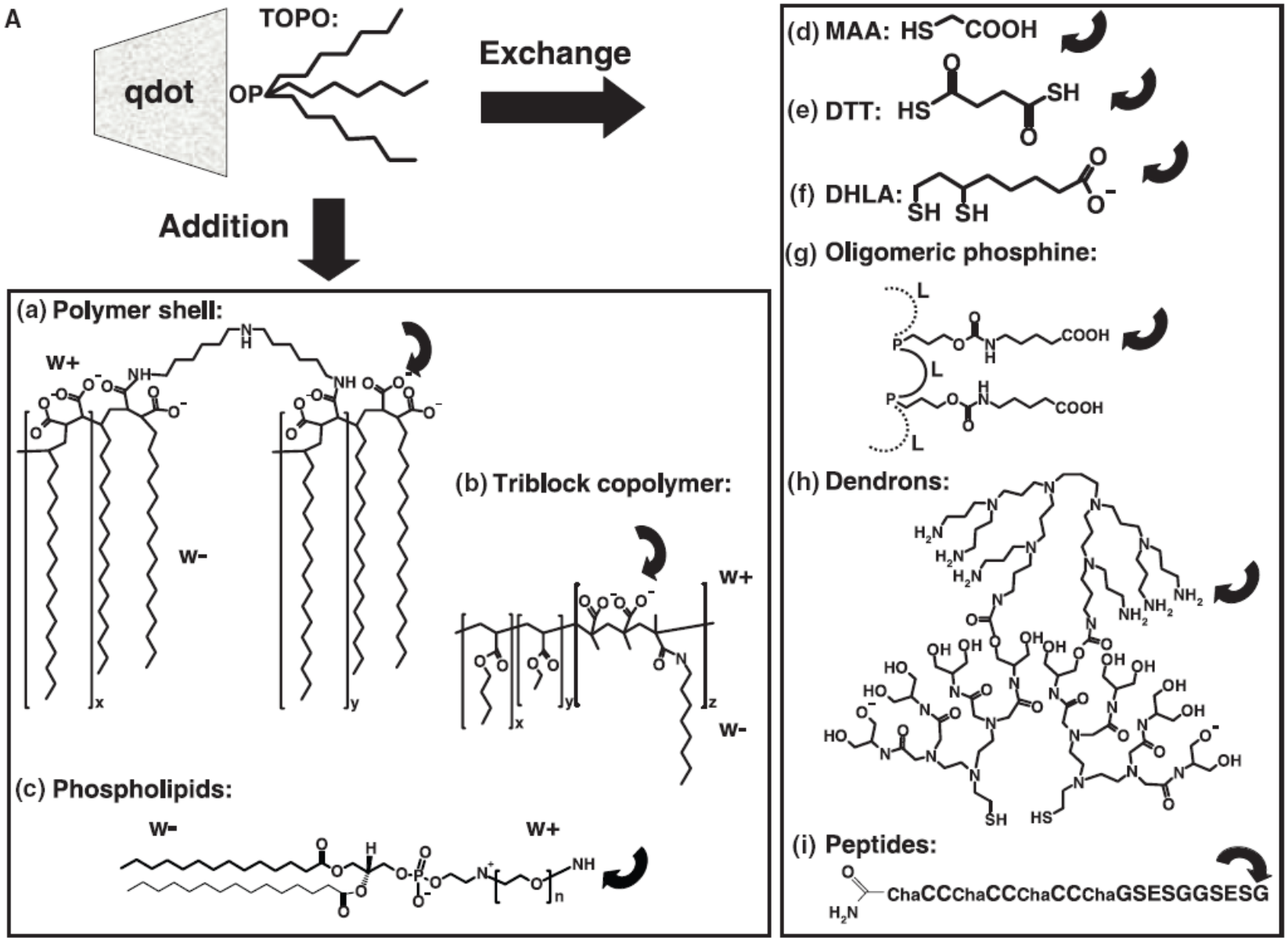
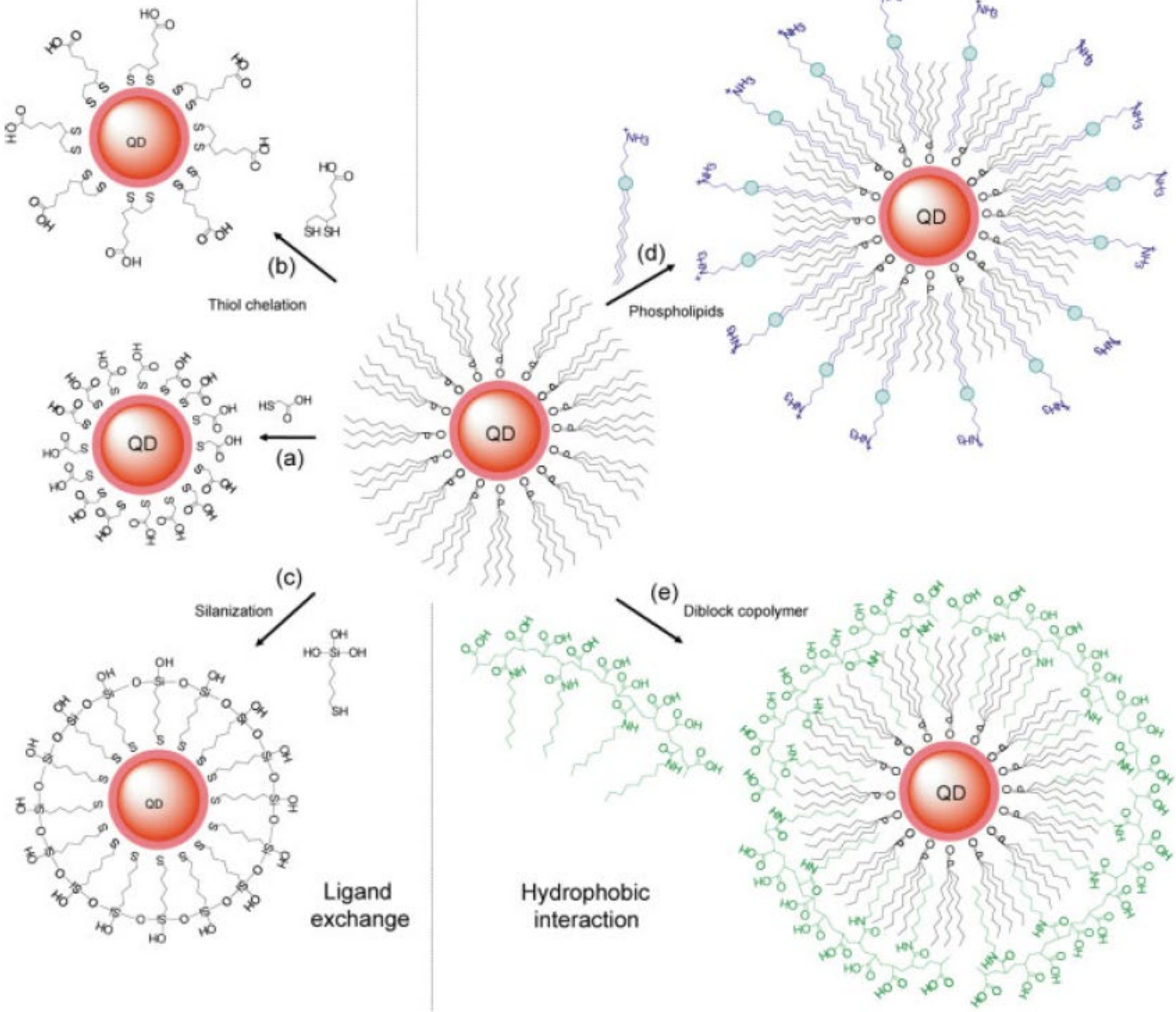


Fig. 1. (**A**) Emission maxima and sizes of quantum dots of different composition. Quantum dots can be synthesized from various types of semiconductor materials (II-VI: CdS, CdSe, CdTe…; III-V: InP, InAs…; IV-VI: PbSe…) characterized by different bulk band gap energies. The curves represent experimental data from the literature on the dependence of peak emission wavelength on qdot diameter. The range of emission wavelength is 400 to 1350 nm, with size varying from 2 to 9.5 nm (organic passivation/solubilization layer not included). All spectra are typically around 30 to 50 nm (full width at half maximum). Inset: Representative emission spectra for some materials. Data are from (*12*, *18*, *27*, *76*–*82*). Data for CdHgTe/ZnS have been extrapolated to the maximum emission wavelength obtained in our group. (**B**) Absorption (upper curves) and emission (lower curves) spectra of four CdSe/ZnS qdot samples. The blue vertical line indicates the 488-nm line of an argon-ion laser, which can be used to efficiently excite all four types of qdots simultaneously. [Adapted from (*28*)] (**C**) Size comparison of qdots and comparable objects. FITC, fluorescein isothiocyanate; GFP, green fluorescent protein; qdot, green (4 nm, top) and red (6.5 nm, bottom) CdSe/ZnS qdot; qrod, rod-shaped qdot (size from Quantum Dot Corp.'s Web site). Three proteins—streptavidin (SAV), maltose binding protein (MBP), and immunoglobulin G (IgG)—have been used for further functionalization of qdots (see text) and add to the final size of the qdot, in conjunction with the solubilization chemistry (Fig. 2).


A
qdot
TOPO:
OP
Exchange
Addition
(a) Polymer shell:
W+
W-
(b) Triblock copolymer:
W+
W-
(c) Phospholipids:
W-
W+
(d) MAA: HS COOH
(e) DTT: HS SH
(f) DHLA: SH SH
(g) Oligomeric phosphine:
L
COOH
(h) Dendrons:
(i) Peptides:
ChaCCChaCCChaCCChaGSESGGSESG


QD
(a)
(b)
Thiol chelation
(c)
Silanization
(d)
Phospholipids
(e)
Diblock copolymer
Ligand exchange
Hydrophobic interaction

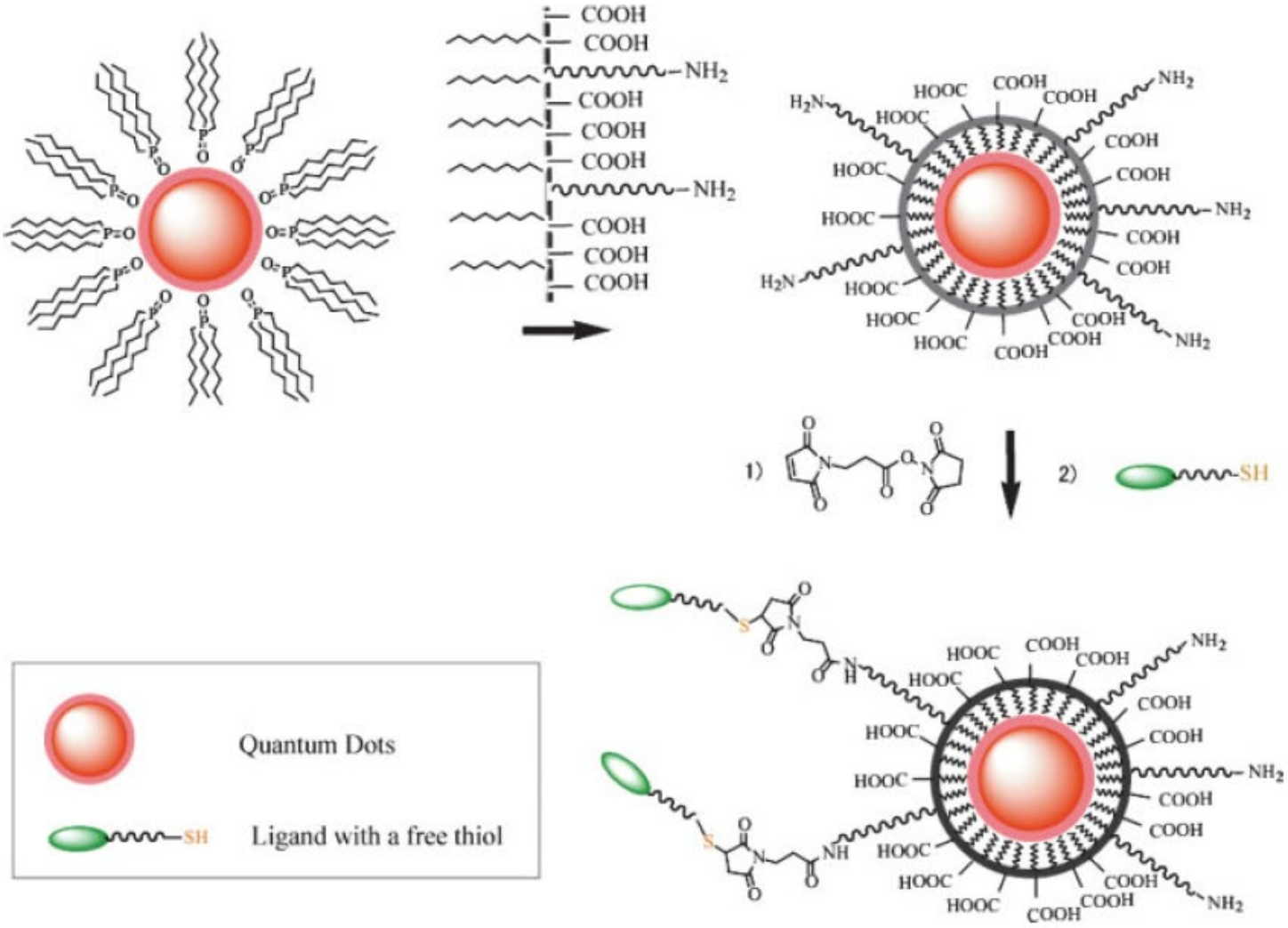


FIGURE 3 Maleimide functionalized QDs for conjugating thiol-containing ligands. TOPO stabilized QDs are coated with a primary amine functionalized tri-block amphiphilic copolymer for producing water-soluble QDs, which facilitate further conjugation to ligands with free thiols through bi-functional cross-linkers.