

Synthesis of Nanoparticles and Surface Modifications



Synthesis of Quantum Dots

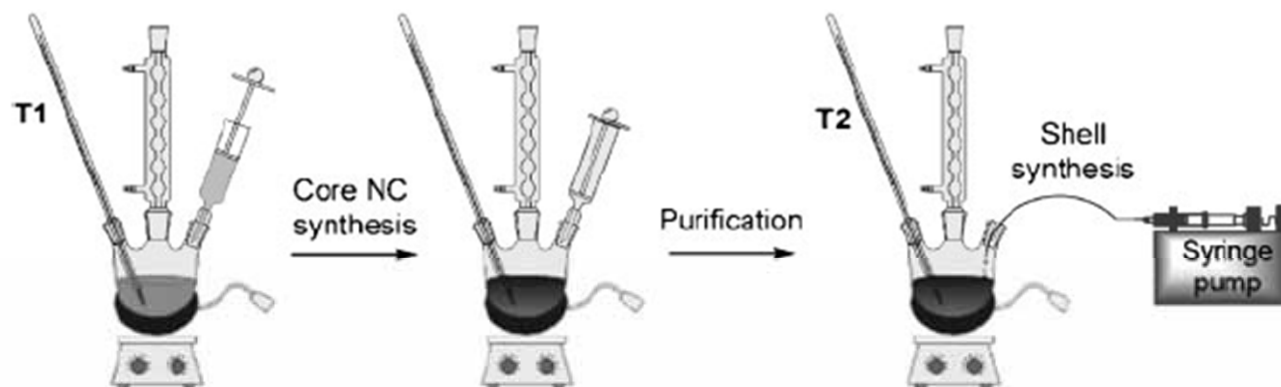
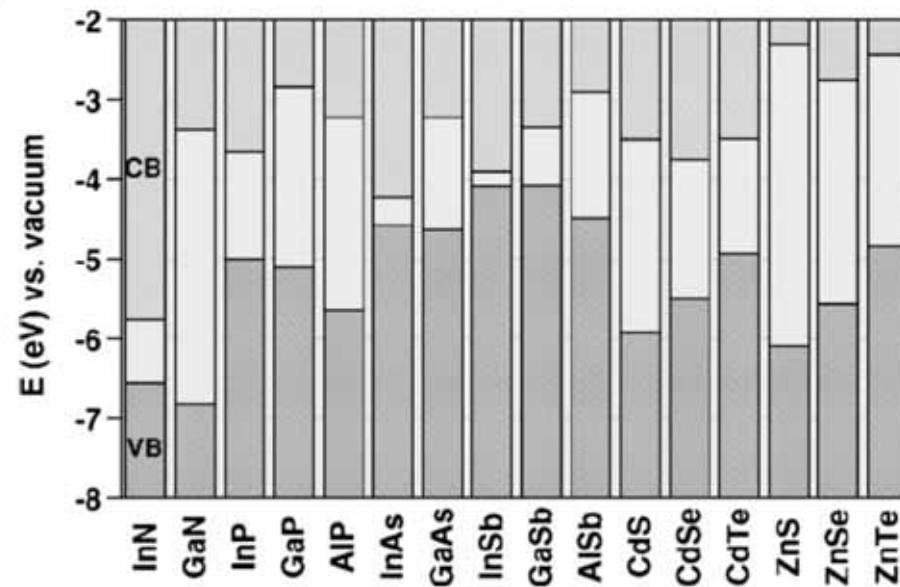


Figure 2. Two-step synthesis of core/shell nanocrystals.





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).

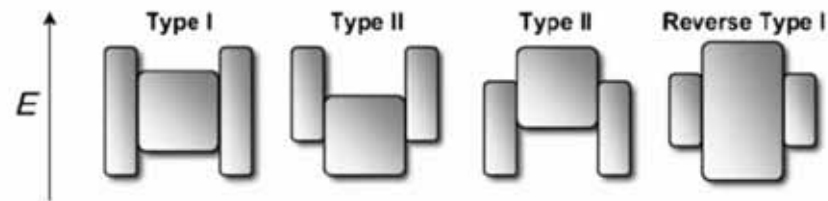


Figure 1. Schematic representation of the energy-level alignment in different core/shell systems realized with semiconductor NCs to date. The upper and lower edges of the rectangles correspond to the positions of the conduction- and valence-band edge of the core (center) and shell materials, respectively.



Successive Ion Layer Adsorption and Reaction

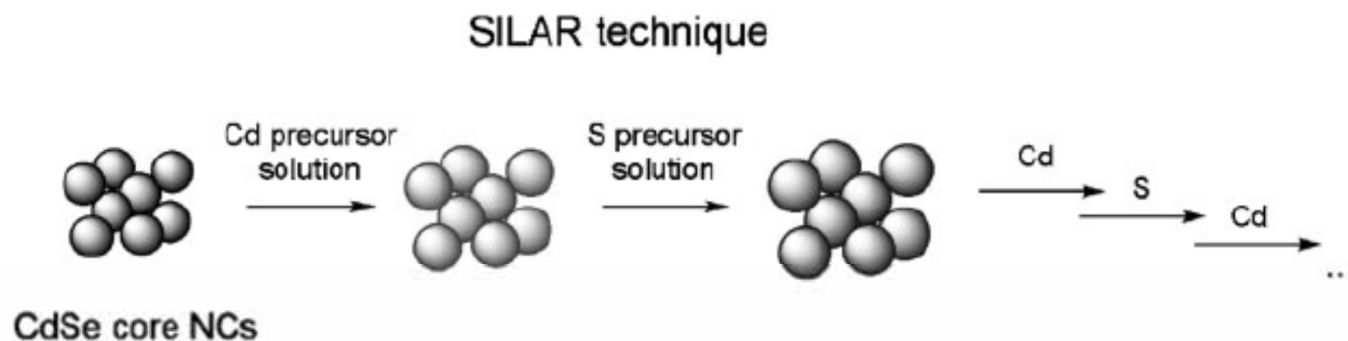


Figure 3. Shell synthesis using the SILAR method, schematically illustrated for the CdSe/CdS core/shell system.



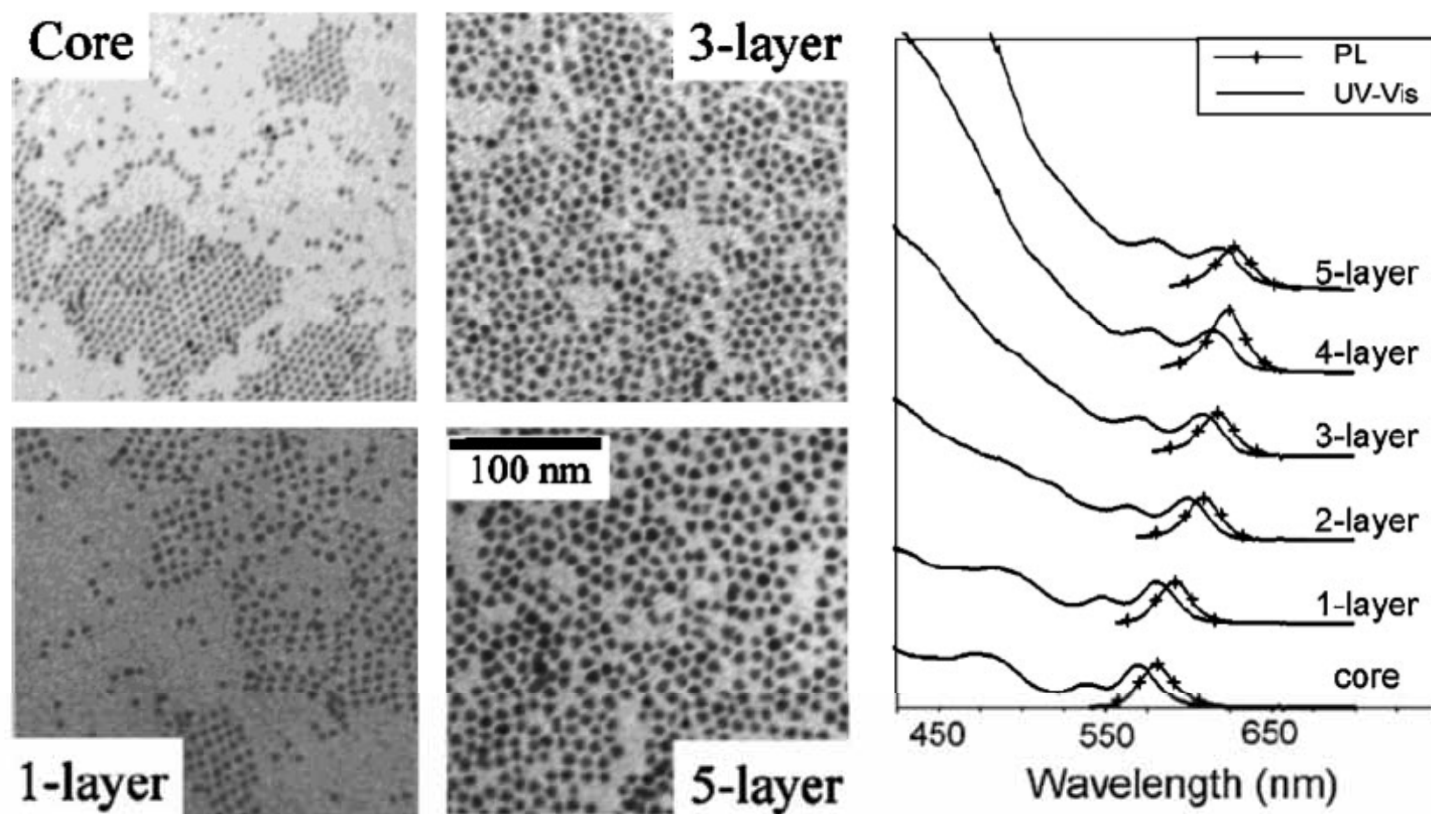


Figure 4. Left panel: TEM images of CdSe NCs depicting the increase in diameter upon growth of several monolayers of a CdS shell by means of the SILAR technique. Right panel: UV/Vis and PL spectra of samples with different shell thicknesses. Reprinted with permission from Reference [25]. Copyright 2001, American Chemical Society.



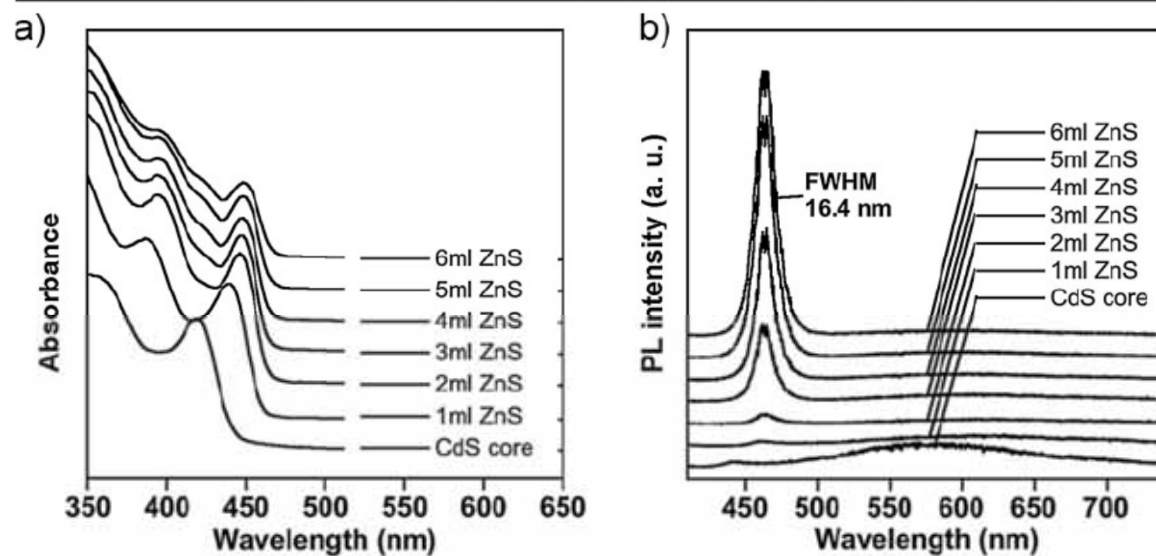
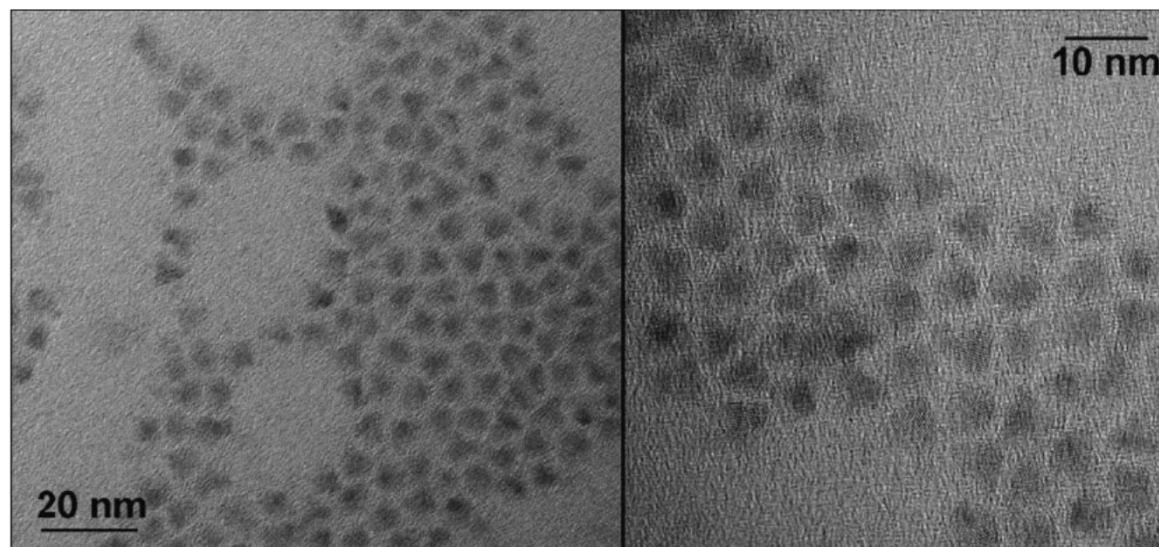


Figure 6. Top: TEM images at different magnifications of CdS/ZnS NCs. [63] Bottom: a) UV/Vis absorption spectra; b) PL spectra recorded during the addition of 6 mL of the ZnS precursor solution corresponding to the growth of a 5-monolayer-thick ZnS shell on 4-nm CdS core NCs.



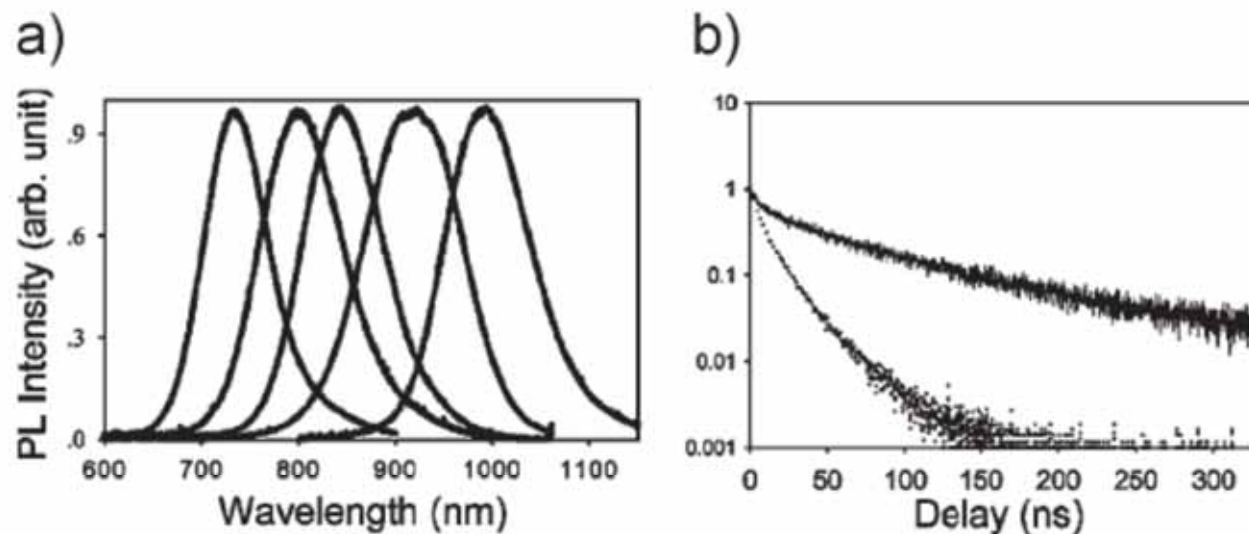


Figure 9. a) Normalized PL spectra of CdTe/CdSe CS NCs having a core/shell radii of 1.6/1.9 nm, 1.6/3.2 nm, 3.2/1.1 nm, 3.2/2.4 nm, 5.6/1.9 nm (from left to right, respectively). b) Normalized PL decays of 3.2/1.1-nm CdTe/CdSe CS NCs and of the corresponding 3.2-nm CdTe core NCs (dotted line). Reprinted with permission from Reference [37]. Copyright 2003, American Chemical Society.





Fig. 1 Suspensions of colloidal CdSe NCs of different sizes (1.7 to 4.5 nm diameter, from left to right) under UV excitation. This iconic image of colloidal nanoscience provides a beautiful visual demonstration of two fundamental nanoscale effects: quantum confinement (size dependent luminescence colours) and large surface to volume ratio (colloidal stability).

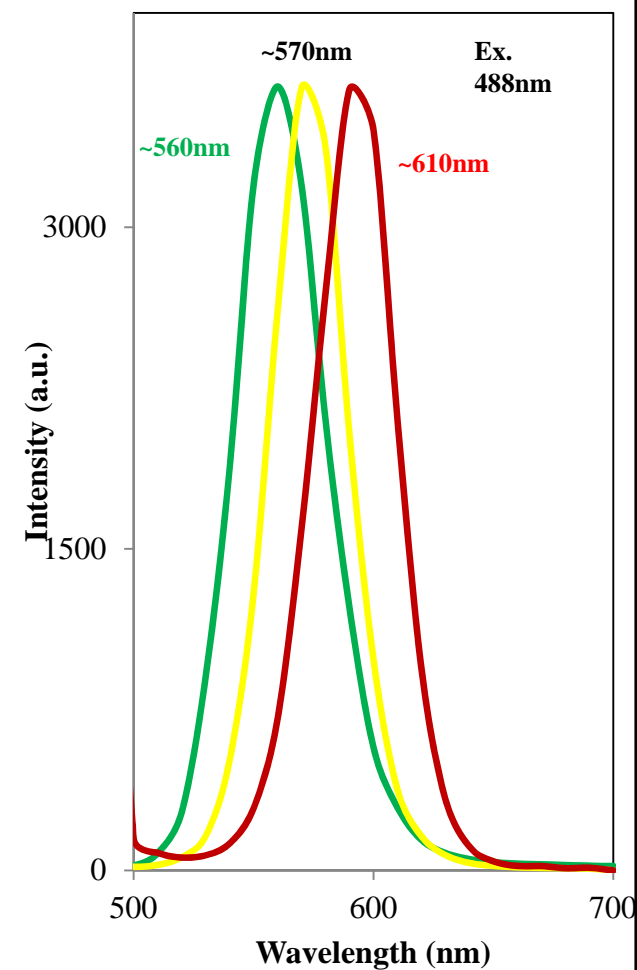
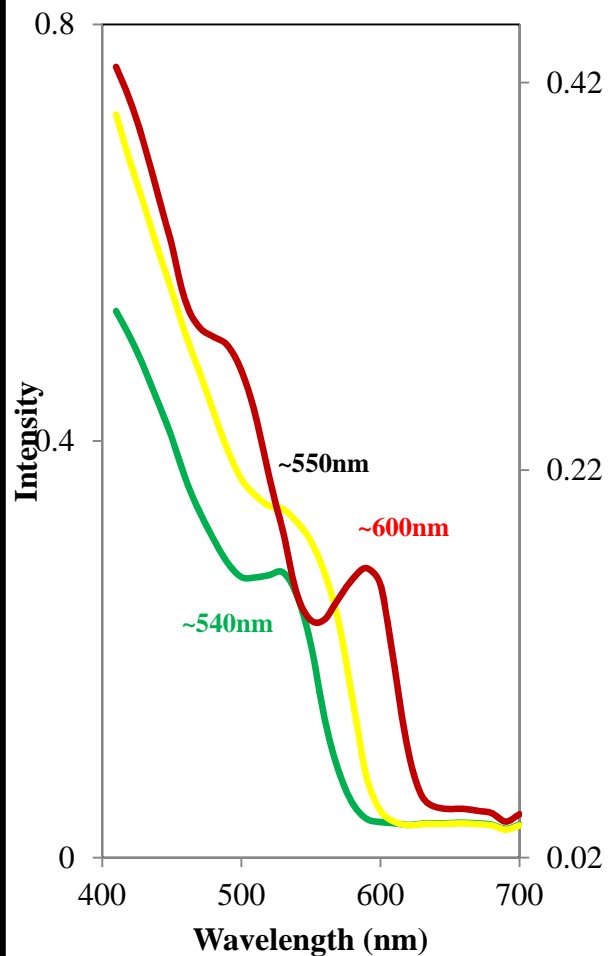
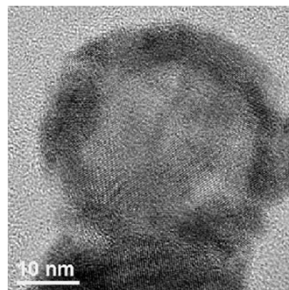


Synthesis of CdSe/ZnS Quantum Dots

20mL (31mg, 0.16 mmol) colloidal solution of CdSe QDs from stock solution (54mg dissolved in 35mL toluene) was placed in a two-neck flask. TOPO (6g) and HAD (6g) were added and then toluene was removed through vacuum, flask refilled with nitrogen. The reaction mixture was heated at 350 °C for two hours. In another flask zinc acetate in 1:3 ratio with respect of CdSe and was dissolved in 4mL of oleic acid stirred at 120 °C for 2 hours obtained a light yellow coloured solution and temperature reduced to 60-70 °C. After cooling to room temperature, TOPSe was mixed with Zn salt solution. And the mixture was injected slowly through syringe in to reaction solution of CdSe-TOPO at 180-200 °C. The stirring was done for another an hour. The similar procedure was followed for work up of reaction as avobe experiment. The final product was re-dispersed in toluene.



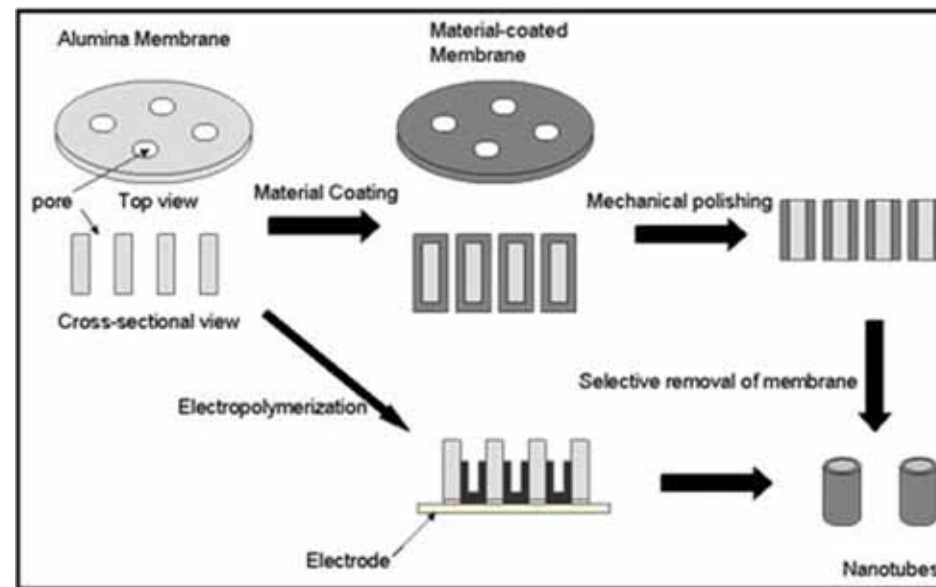
Light emission from CdSe/ZnSe Quantum dots



UV-Visible and PL spectra of CdSe/ZnSe re-dispersed in toluene



Template Synthesis



Porous Materials

- AAO
- MCM-41

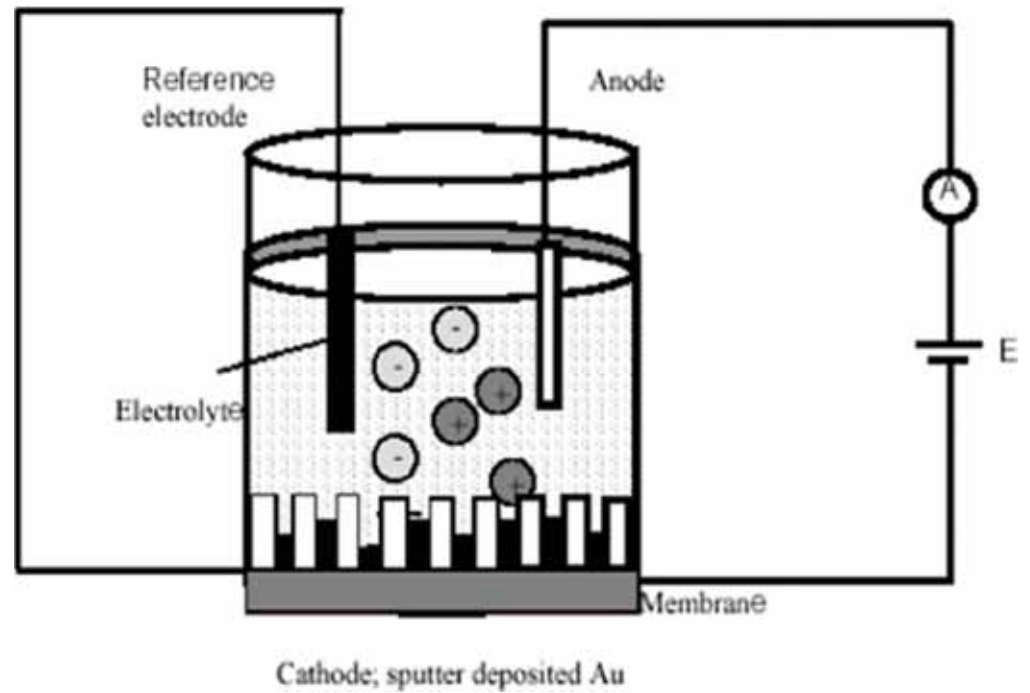
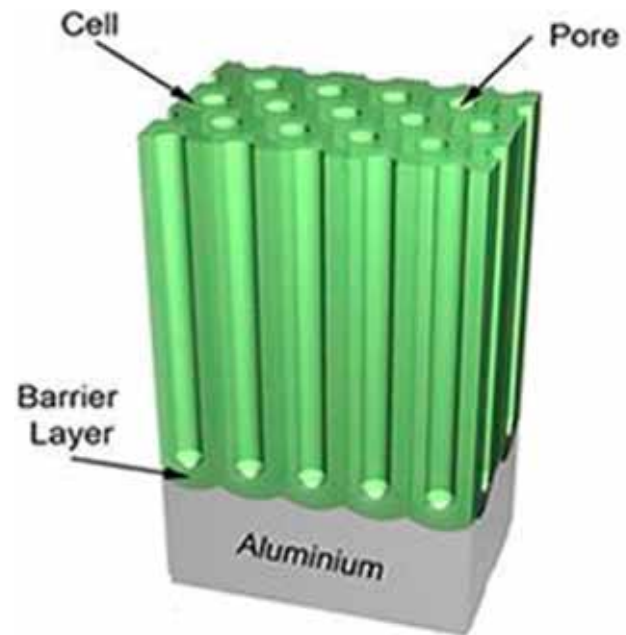
Mobil Crystalline Materials, or MCM-41

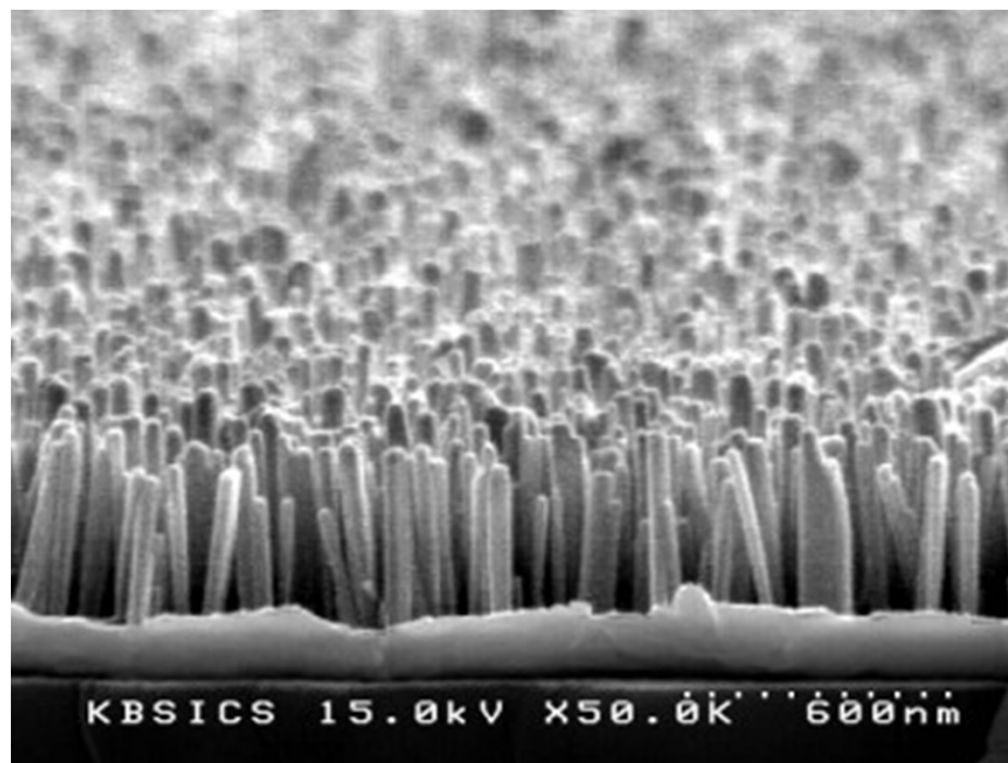
Santa Barbara Amorphous type material, or SBA-15

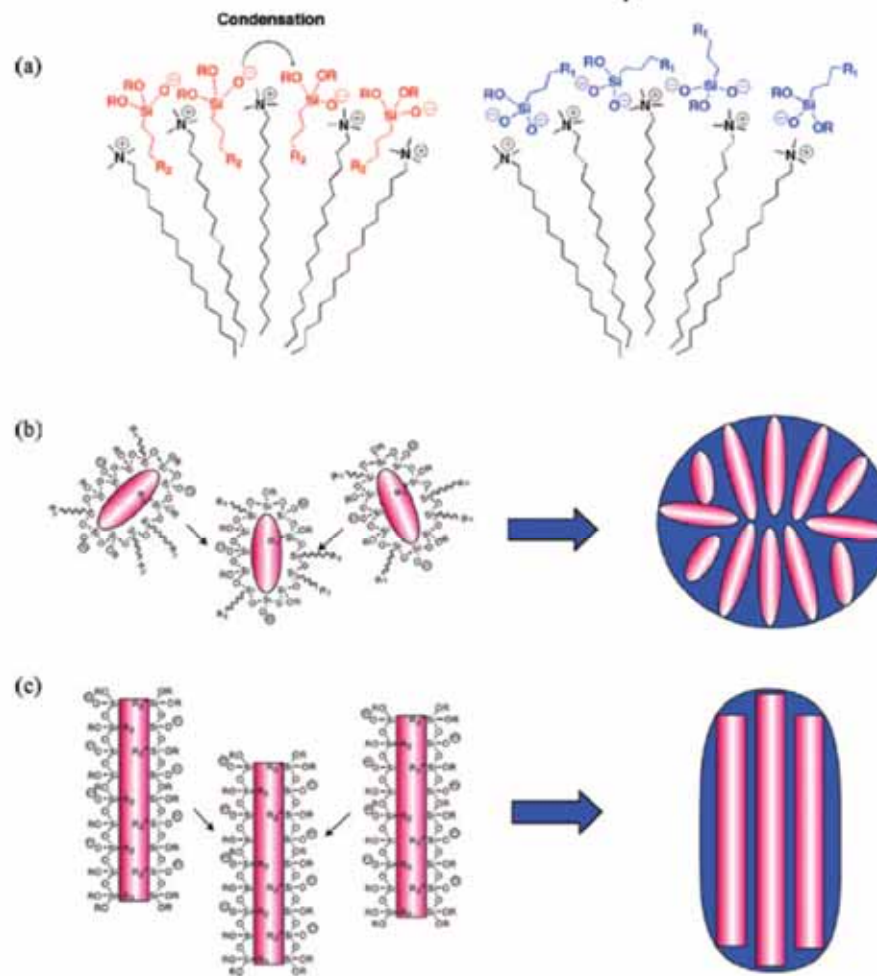
- Micro: $< 2\text{nm}$
- Meso:
- Macro: $> 50\text{nm}$



AAO







^a R, methyl or ethyl groups; R₁, hydrophilic functional groups; R₂, hydrophobic functional groups.



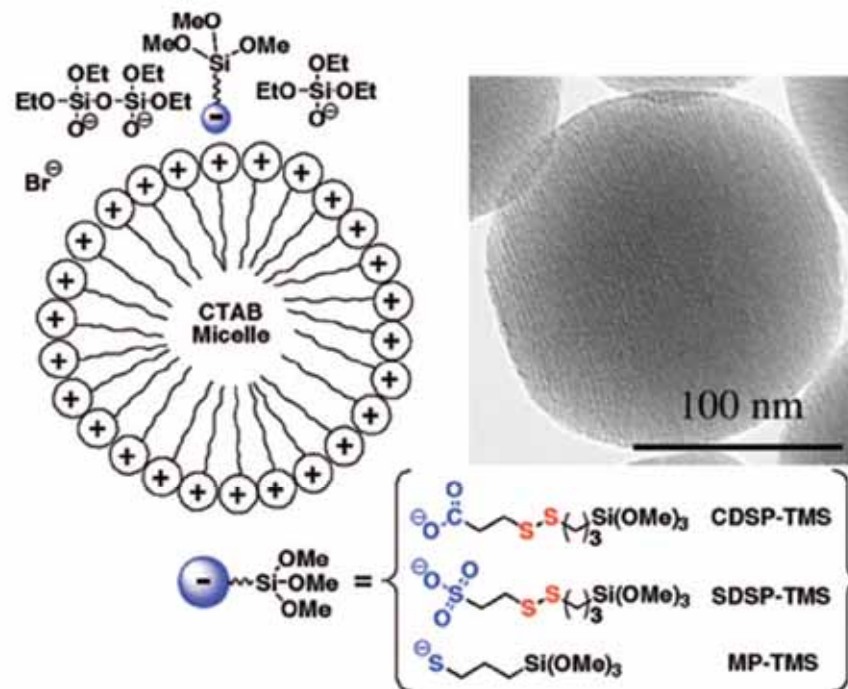


FIGURE 3. Schematic representation of the use of anionic organoalkoxysilanes for controlling the functionalization of the MSN materials. The MCM-41-type mesoporous channels are illustrated by the parallel stripes shown in the transmission electron microscopy (TEM) micrograph of the MSN-SH material. Reproduced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



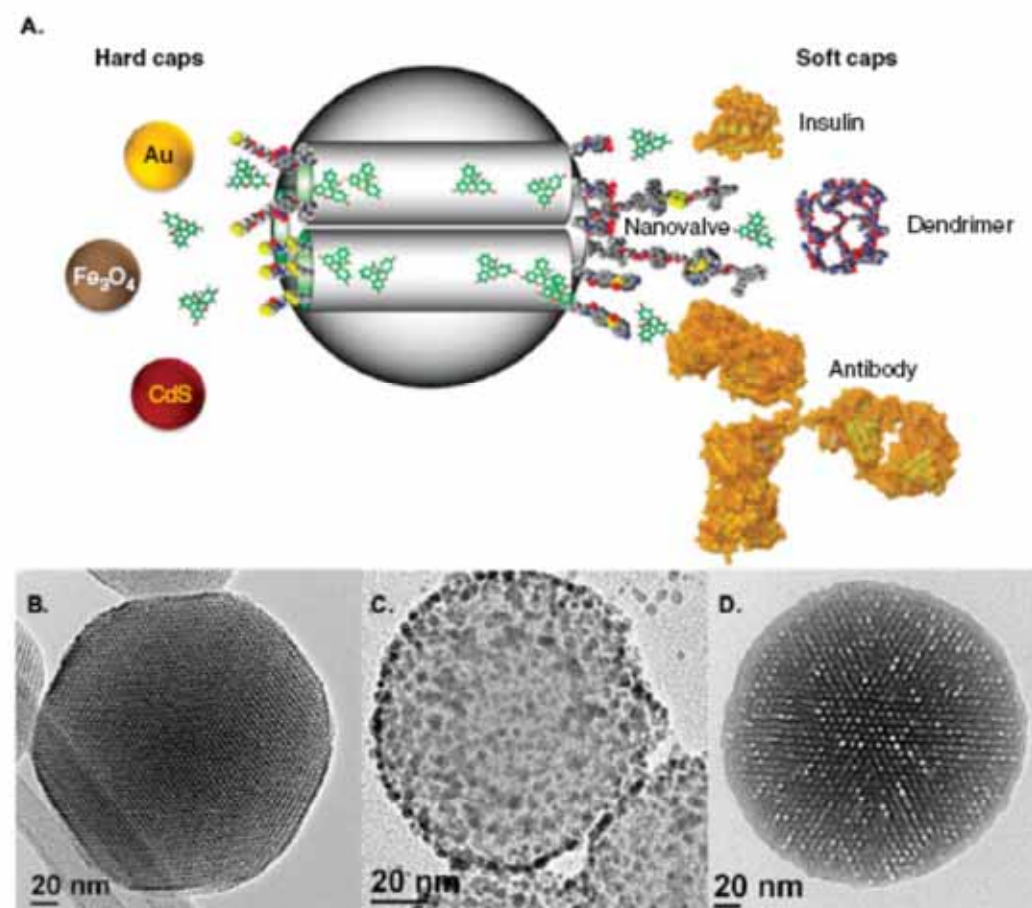


Figure 1. A. Schematic representation of a MSN loaded with drugs and capped with hard caps and soft caps highlighted in this review. Transmission electron microscopy images of (B) a MSN along the axis of the mesopores, (C) capped with hard (Au NP) and (D) with soft (polymer) caps.
MSN: Mesoporous silica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



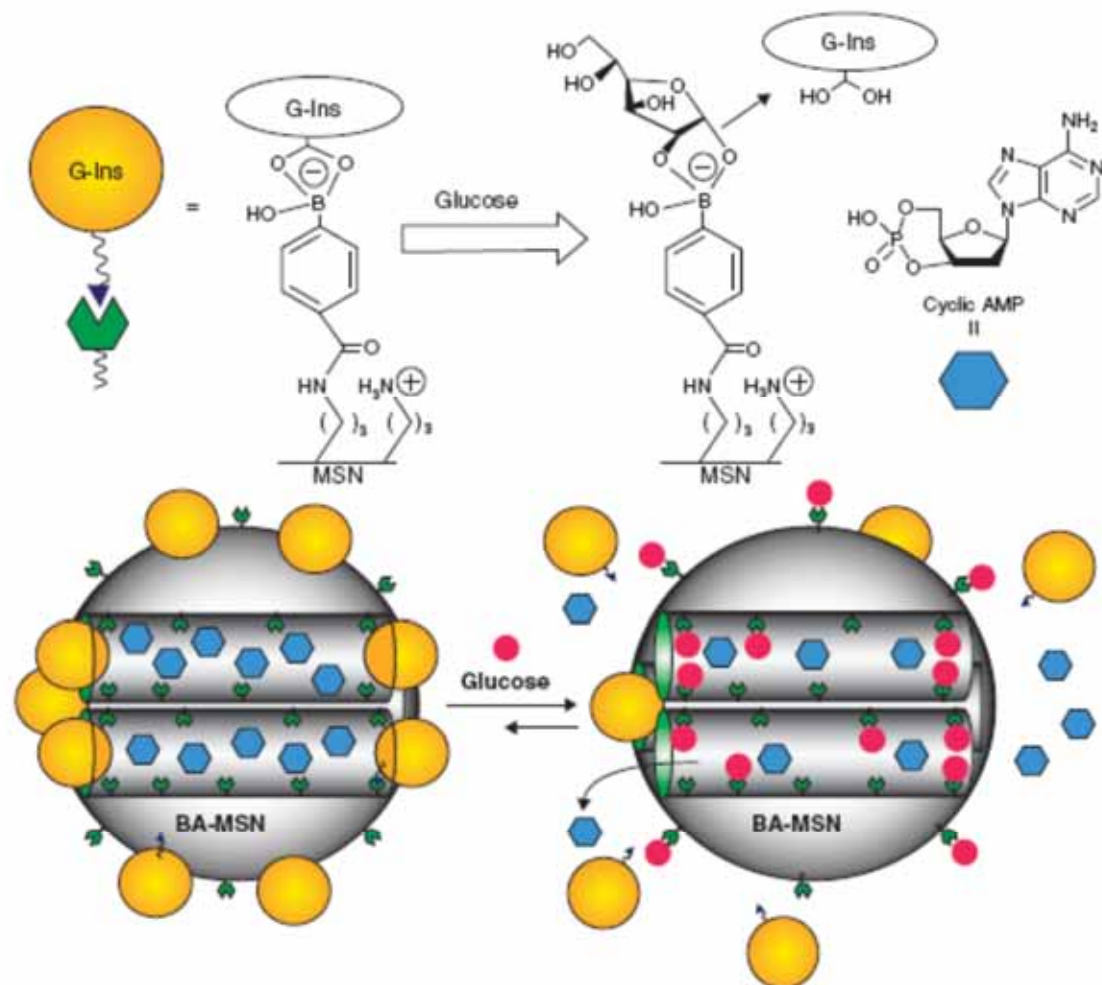


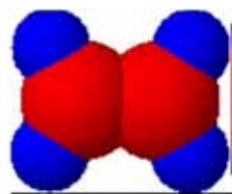
Figure 5. Schematic representation of the glucose-responsive MSN-based double delivery system for controlled release of bioactive G-Ins and cyclic AMP. The controlled release mechanism was achieved by means of the displacement reaction between blood glucose and G-Ins based on reversible boronic acid-diol 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].

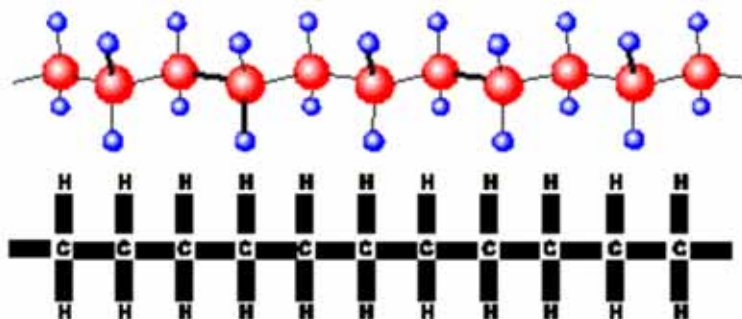
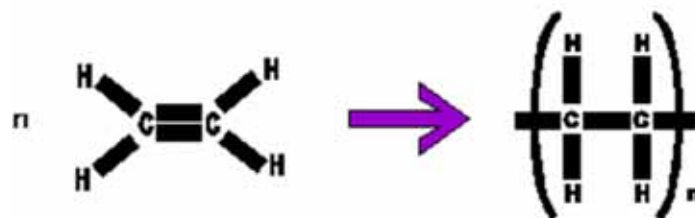
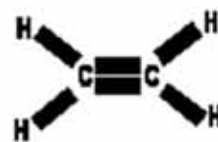
G-Ins: G-insulin; MSN: Mesoporous silica nanoparticle.



Polymer



a monomer ethene

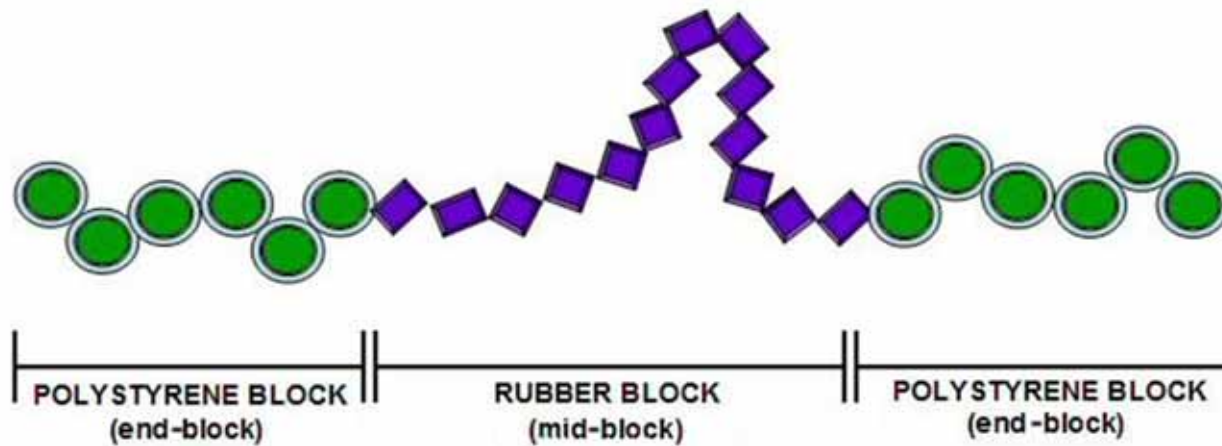


a polymer

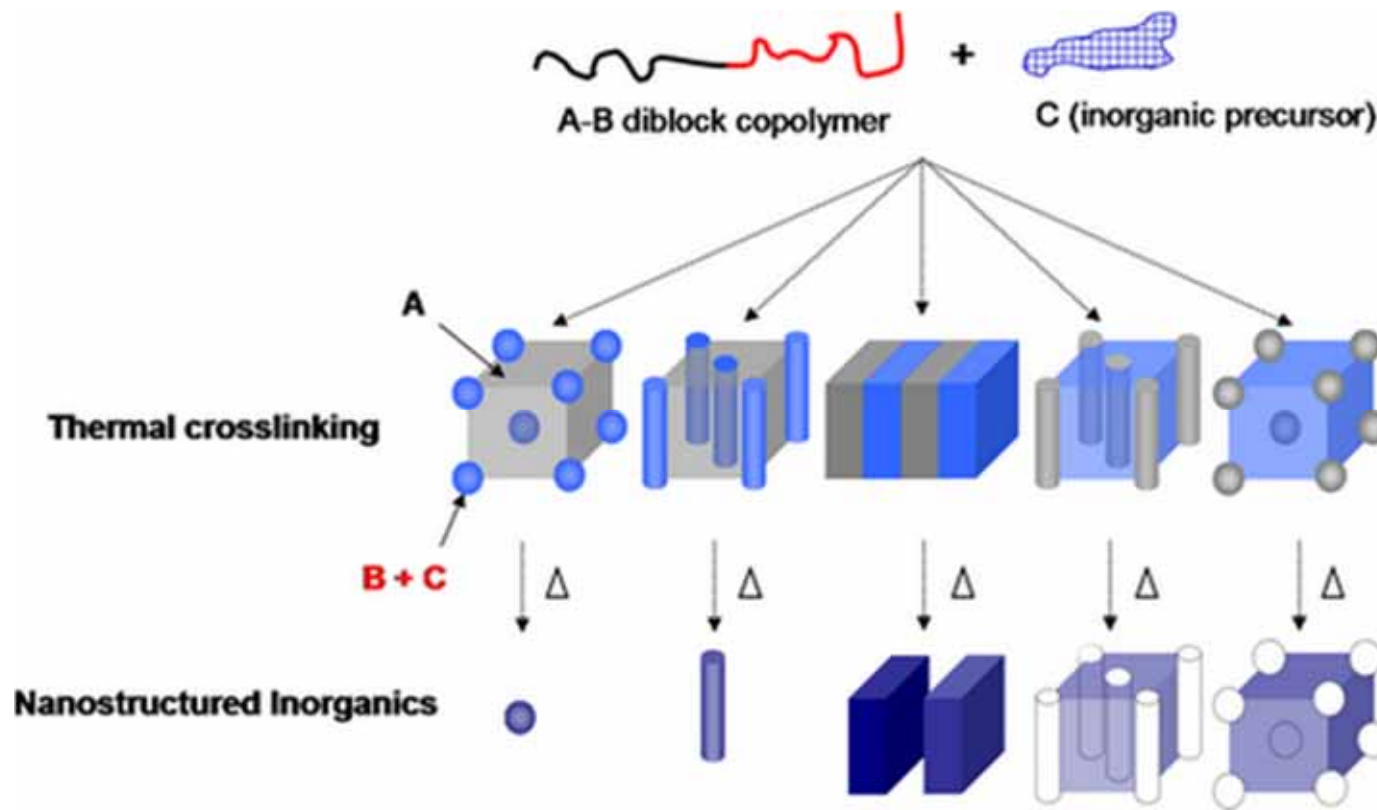
poly(ethene)

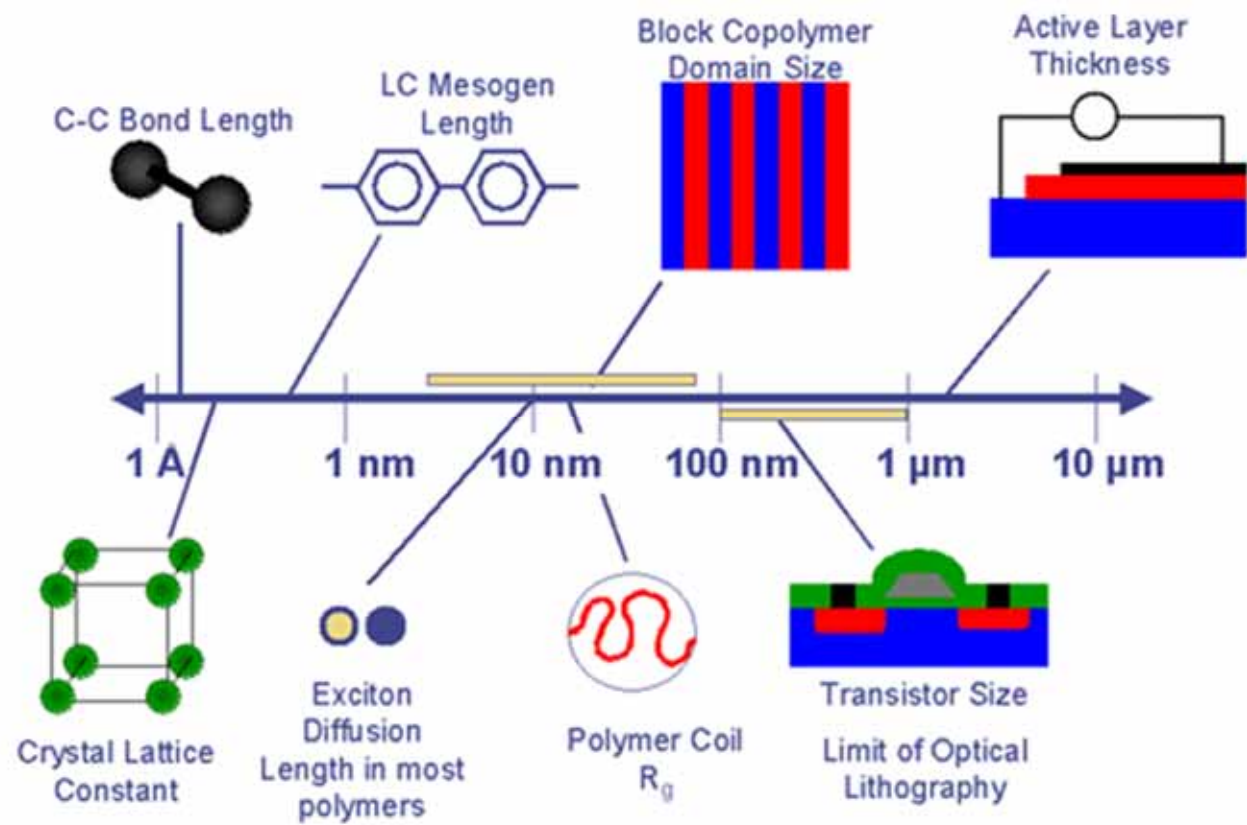


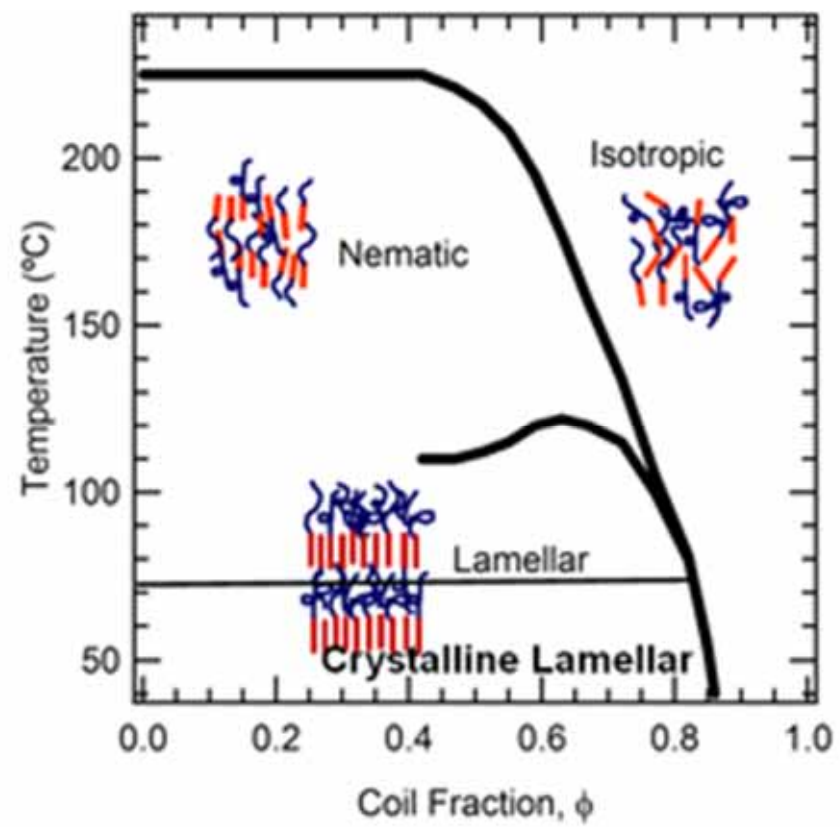
Block copolymer



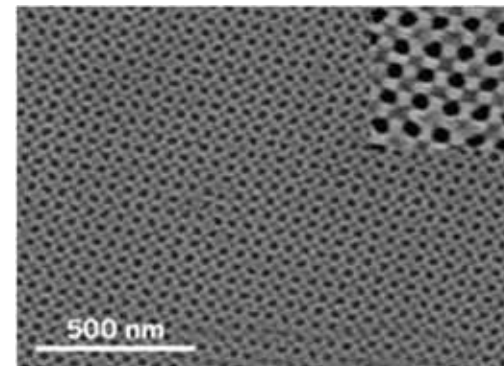
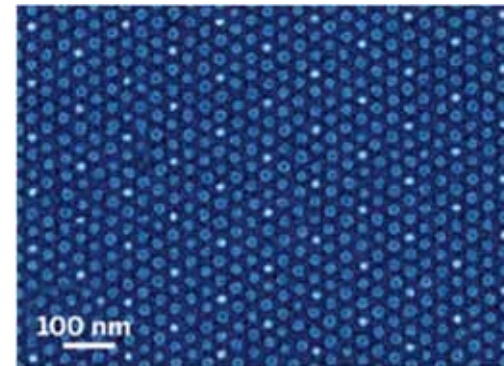
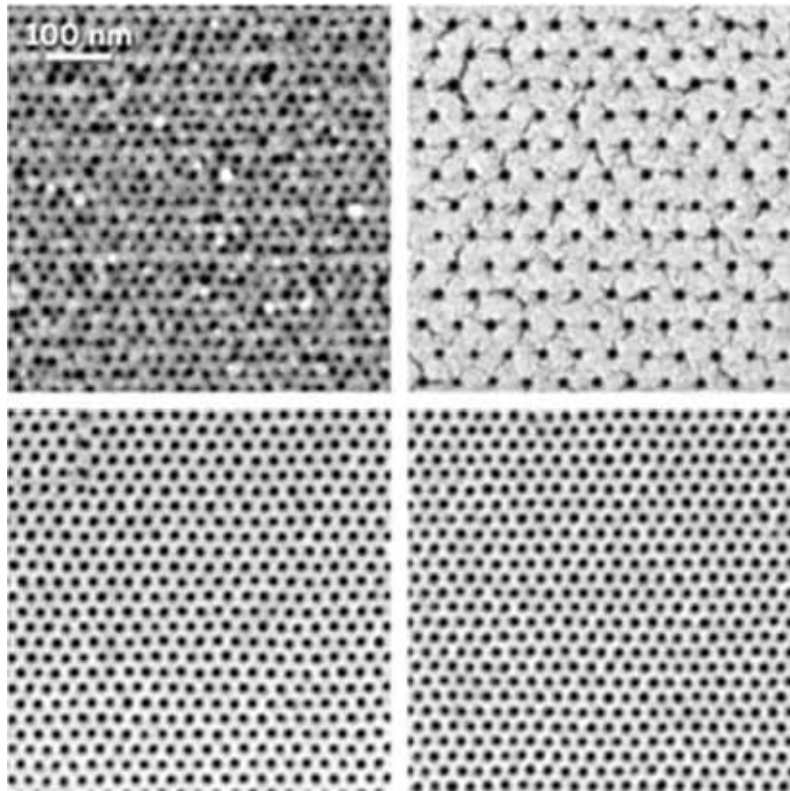
Phase Segregation







Self-Assembled Block-copolymer



CNT

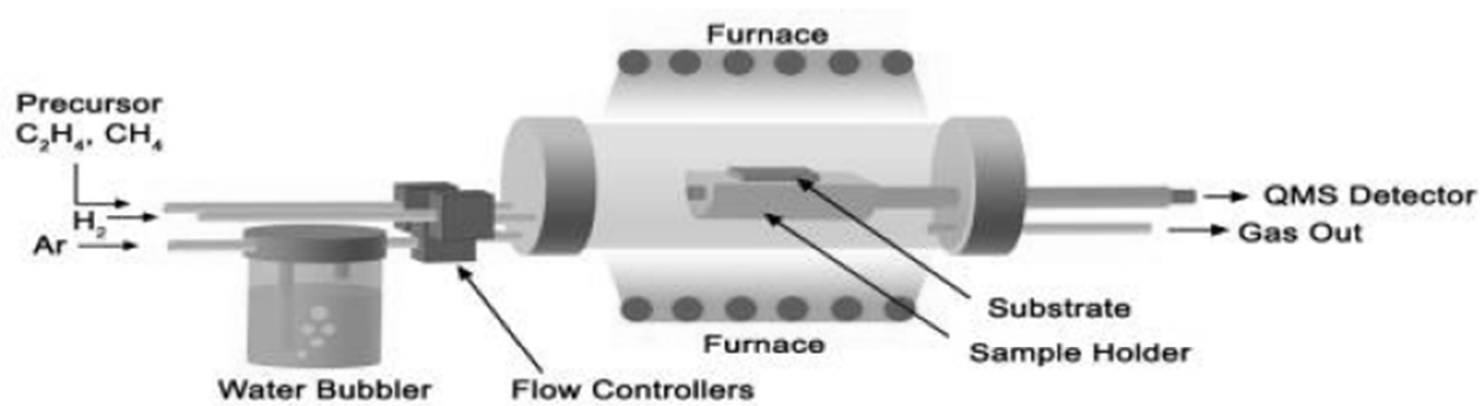
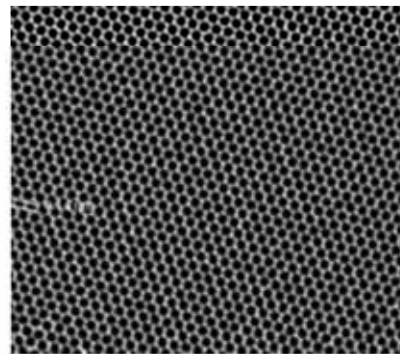
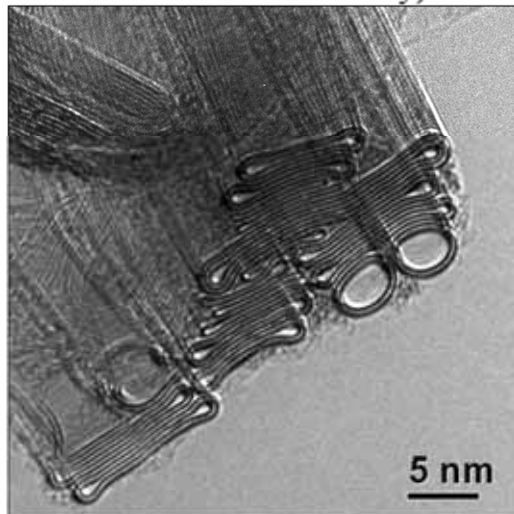


Fig. 1. Schematic of a CVD reactor for carbon nanotube growth. (Sketch by S. Yarmolenko from NCA&T State University)

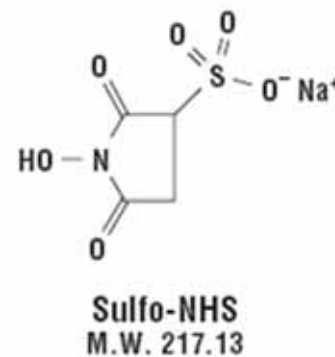
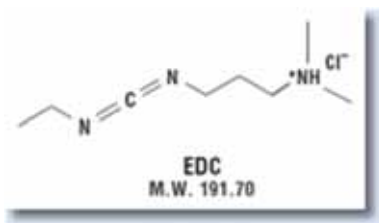
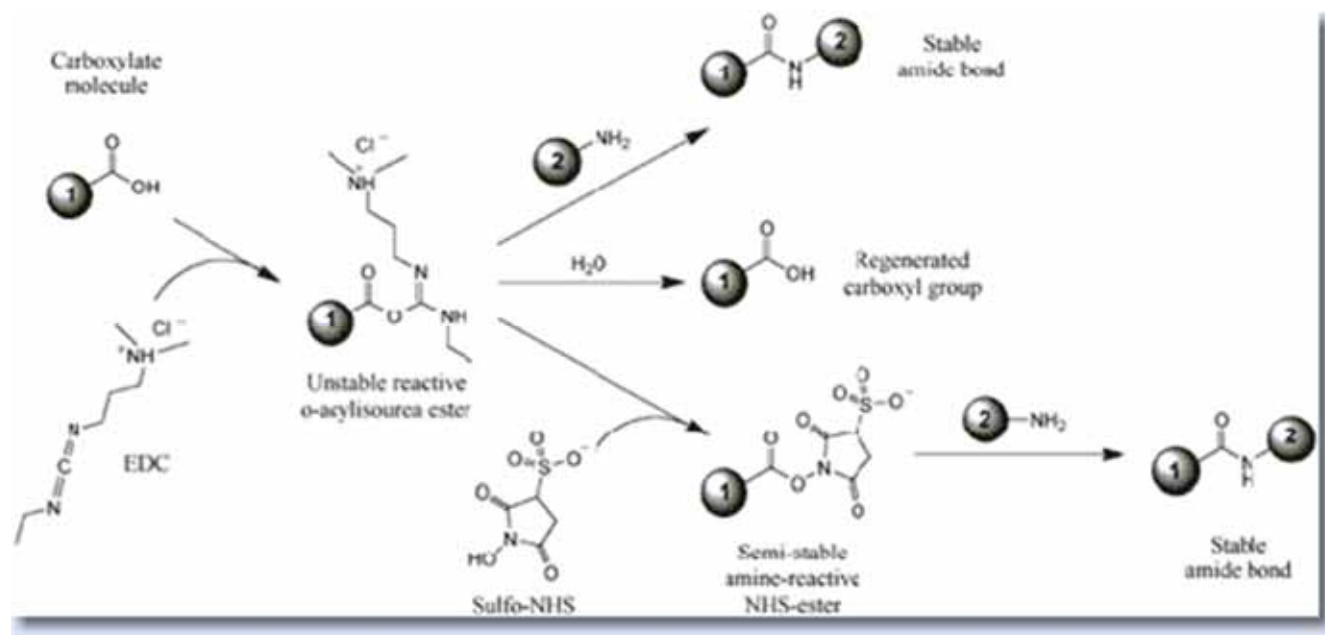


Surface Functionalization

- 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

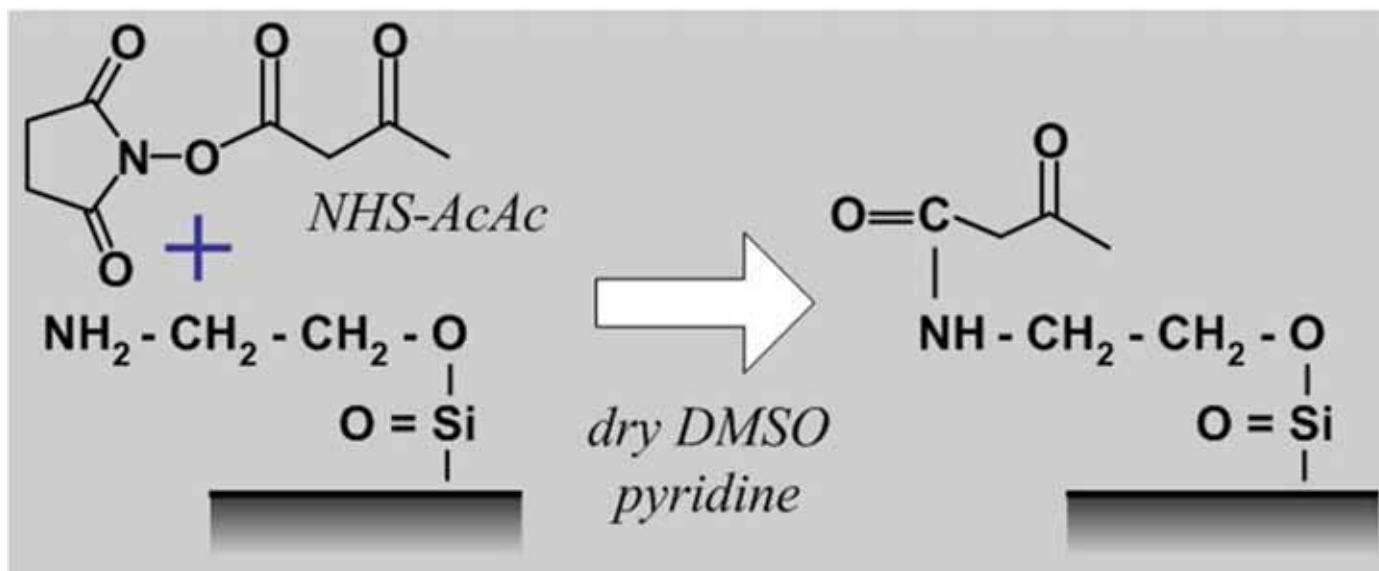


Carboxyl Presenting Surfaces

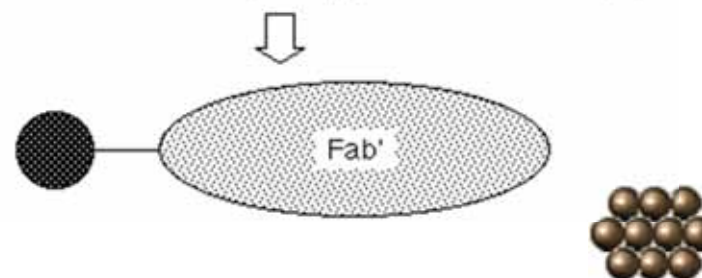
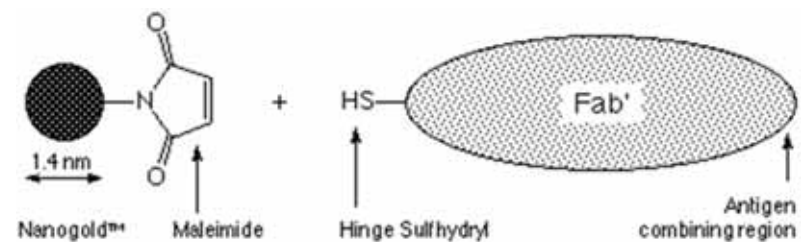
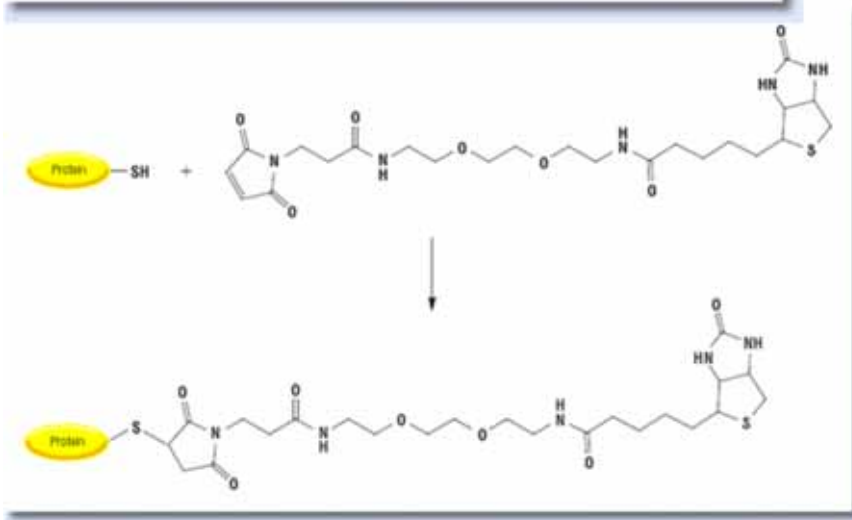
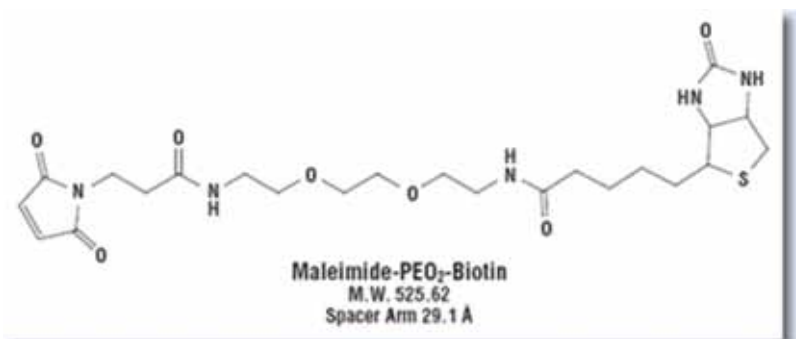
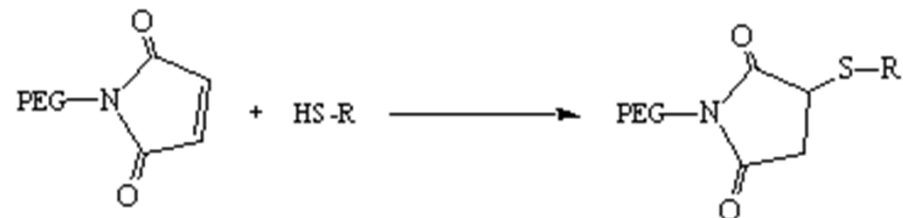


EDC (1-Ethyl-3-[3-dimethylaminopropyl]carbodiimide Hydrochloride)

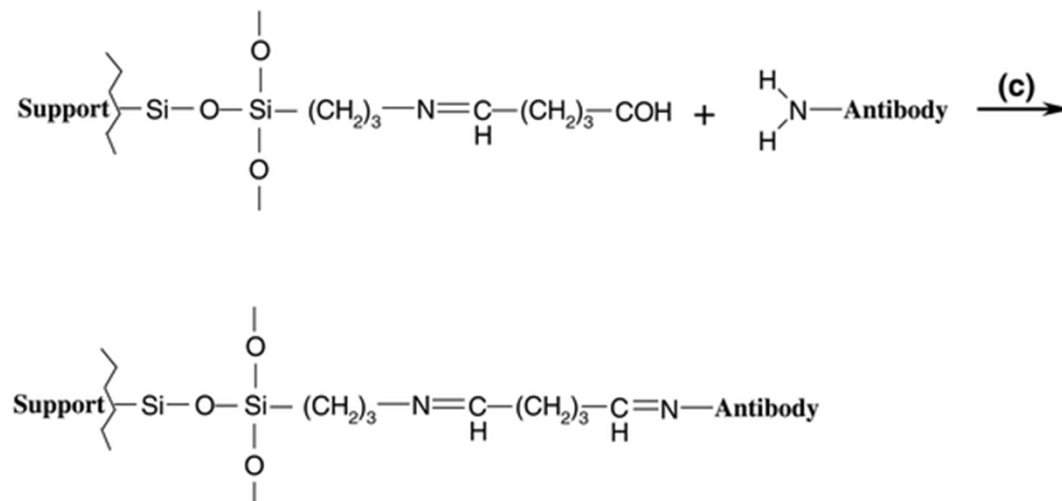
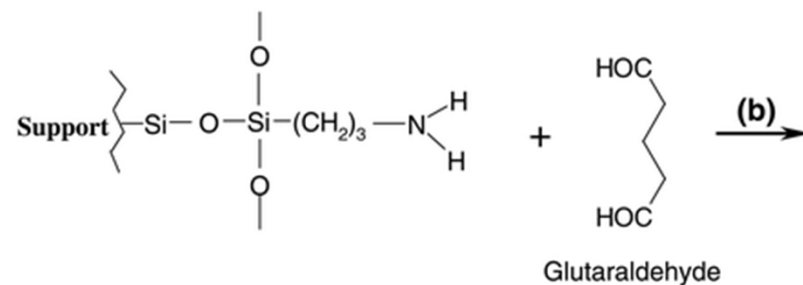
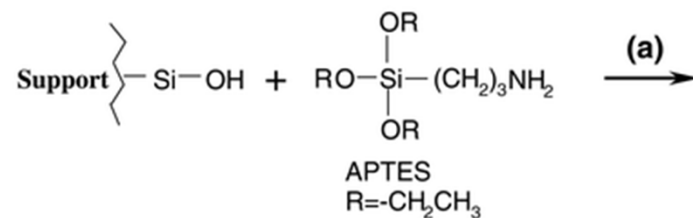
Amine Presenting Surface



Sulfhydryl Labeling



Silica Modification



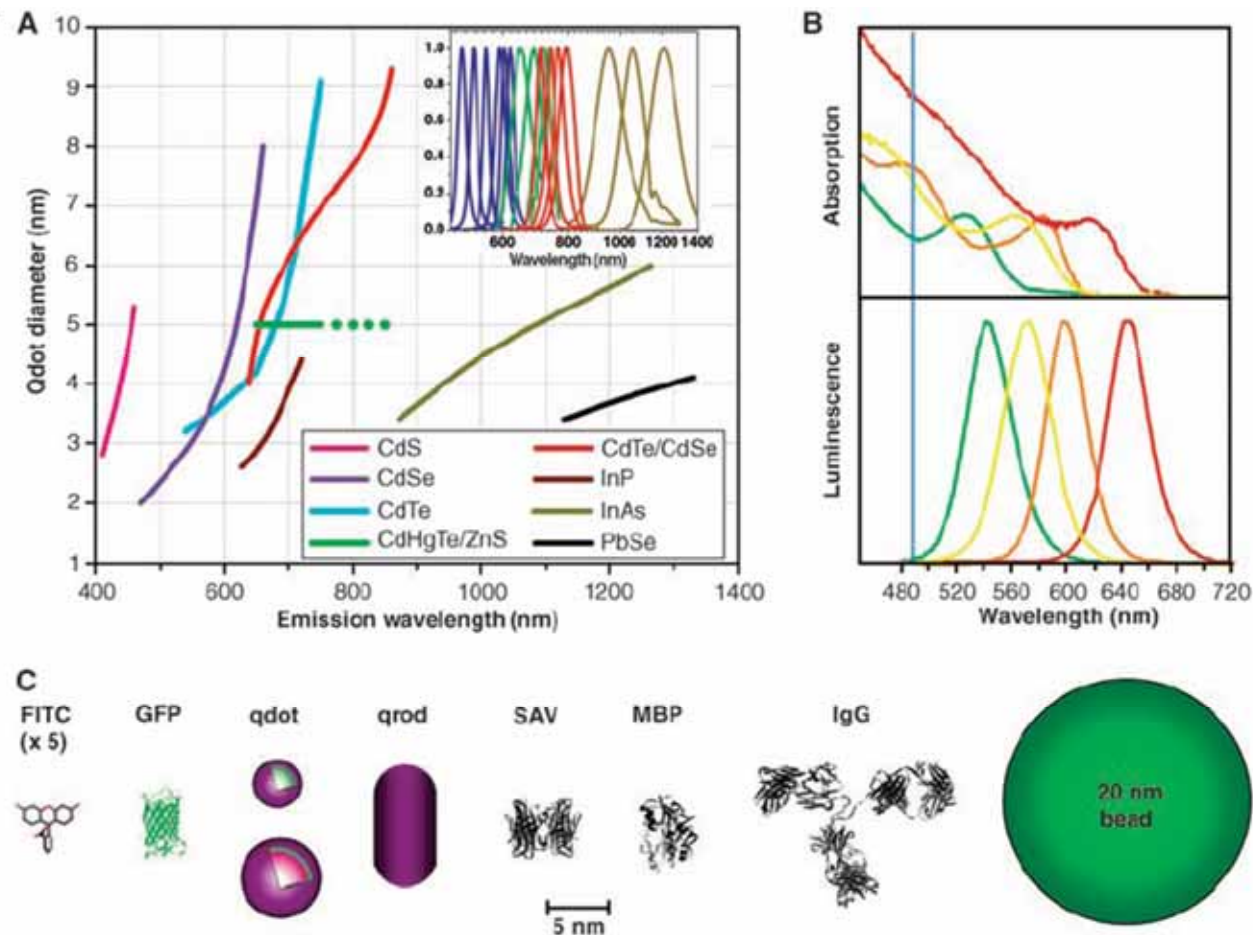
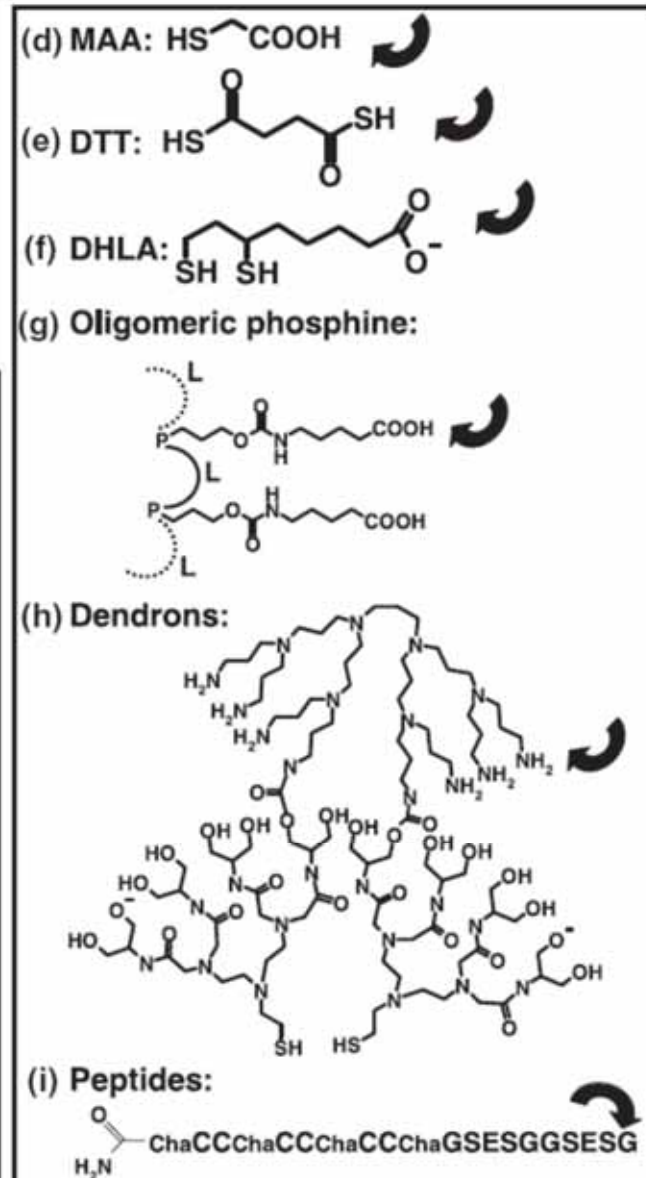
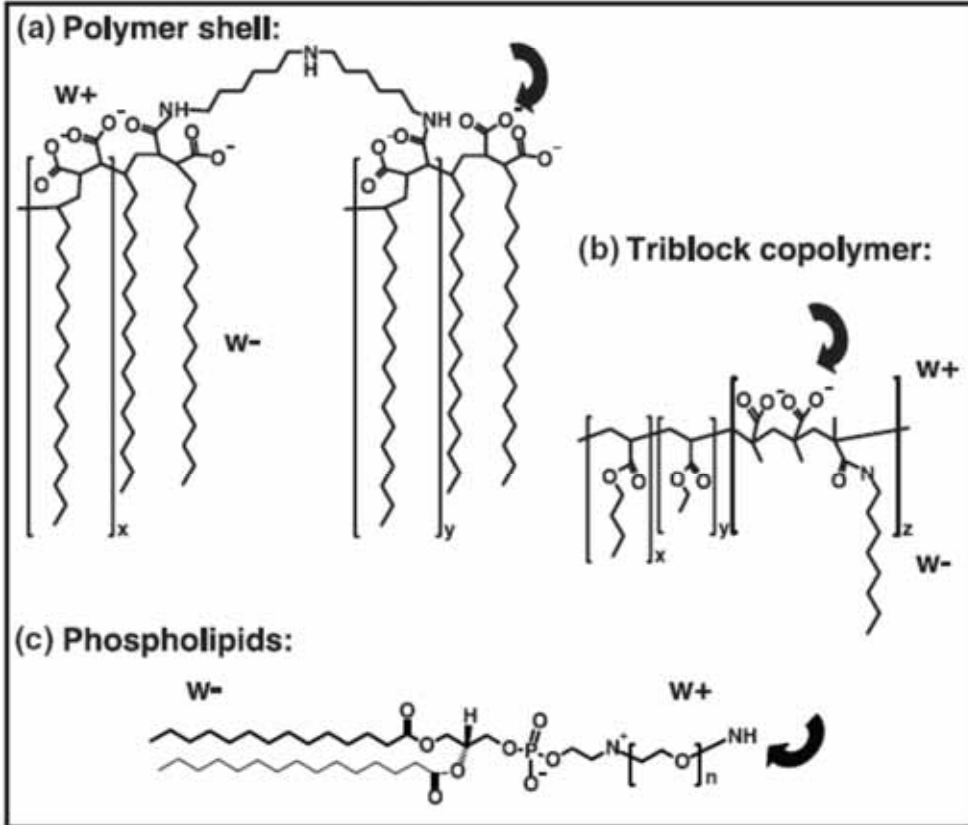
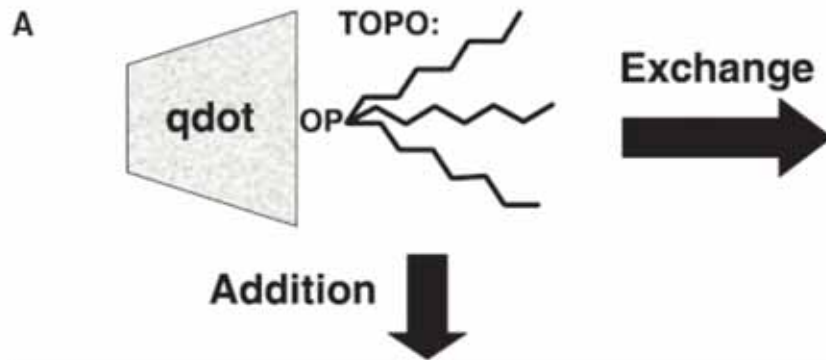
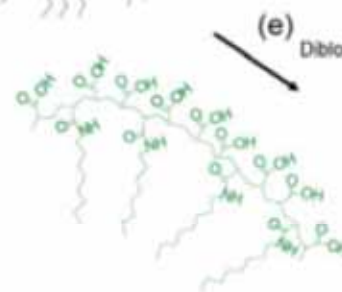
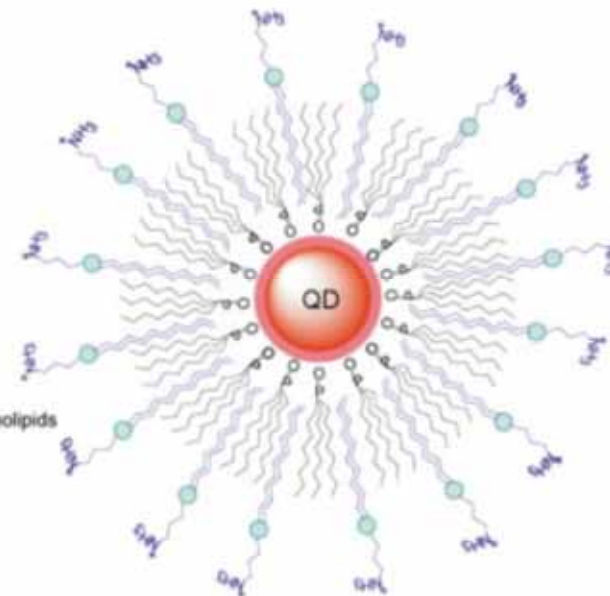
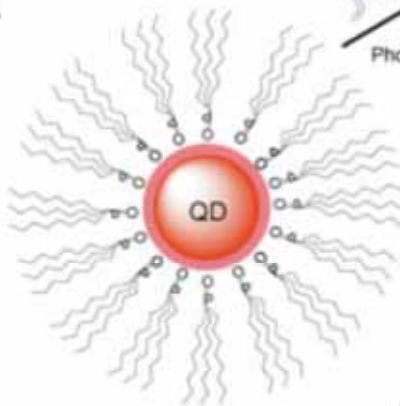
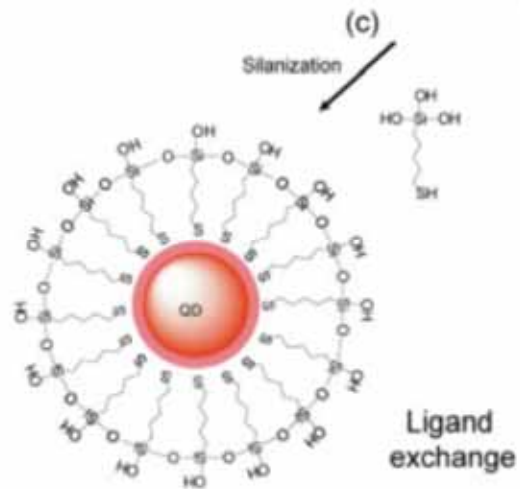
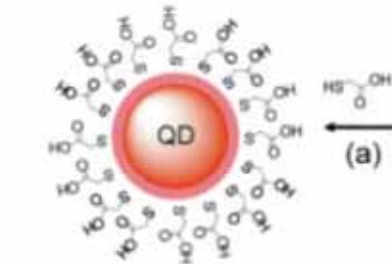
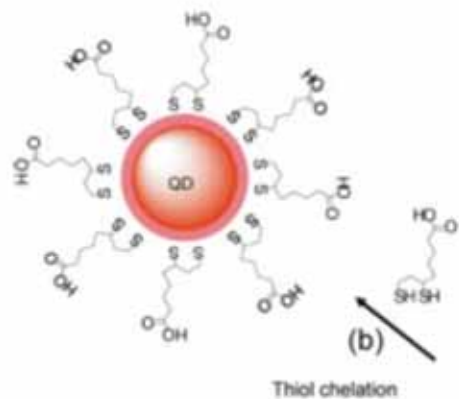


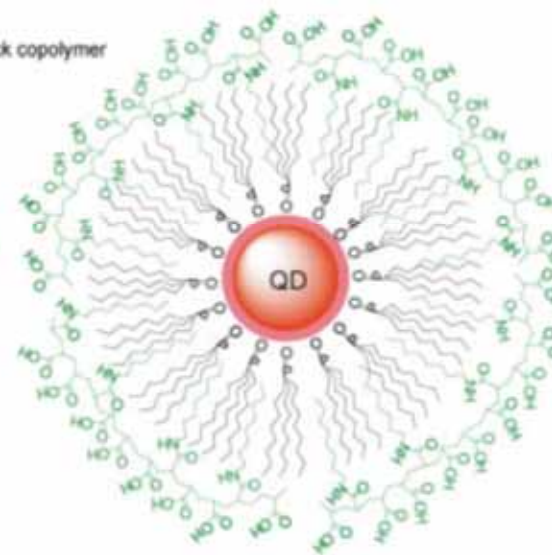
Fig. 1. (A) Emission maxima and sizes of quantum dots of different composition. Quantum dots can be synthesized from various types of semiconductor materials (II-VI: CdS, CdSe, CdTe...; III-V: InP, InAs...; IV-VI: PbSe...) characterized by different bulk band gap energies. The curves represent experimental 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).







Hydrophobic interaction



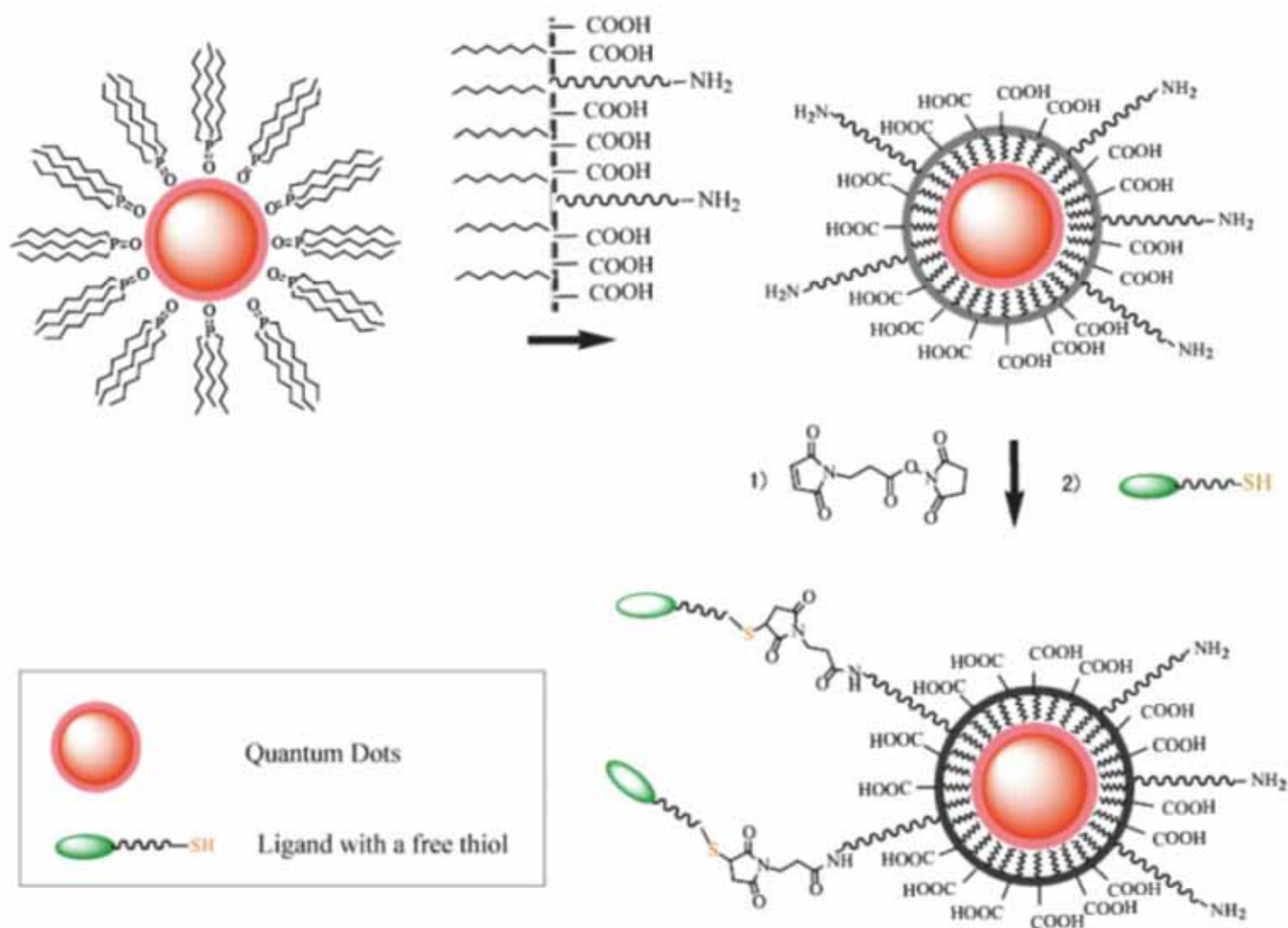
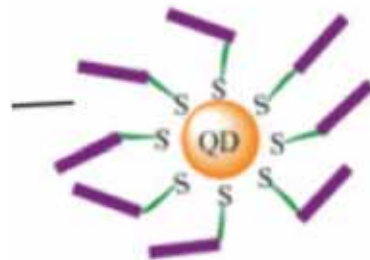


FIGURE 3 Maleimide functionalized QDs for conjugating thiol-containing ligands. TOPO stabilized QDs are coated with a primary amine functionalized tri-block amphiphilic copolymer for producing water-soluble QDs, which facilitate further conjugation to ligands with free thiols through bi-functional cross-linkers.

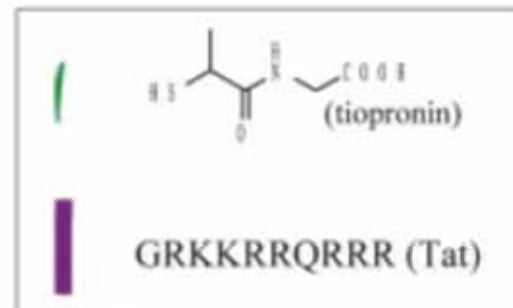




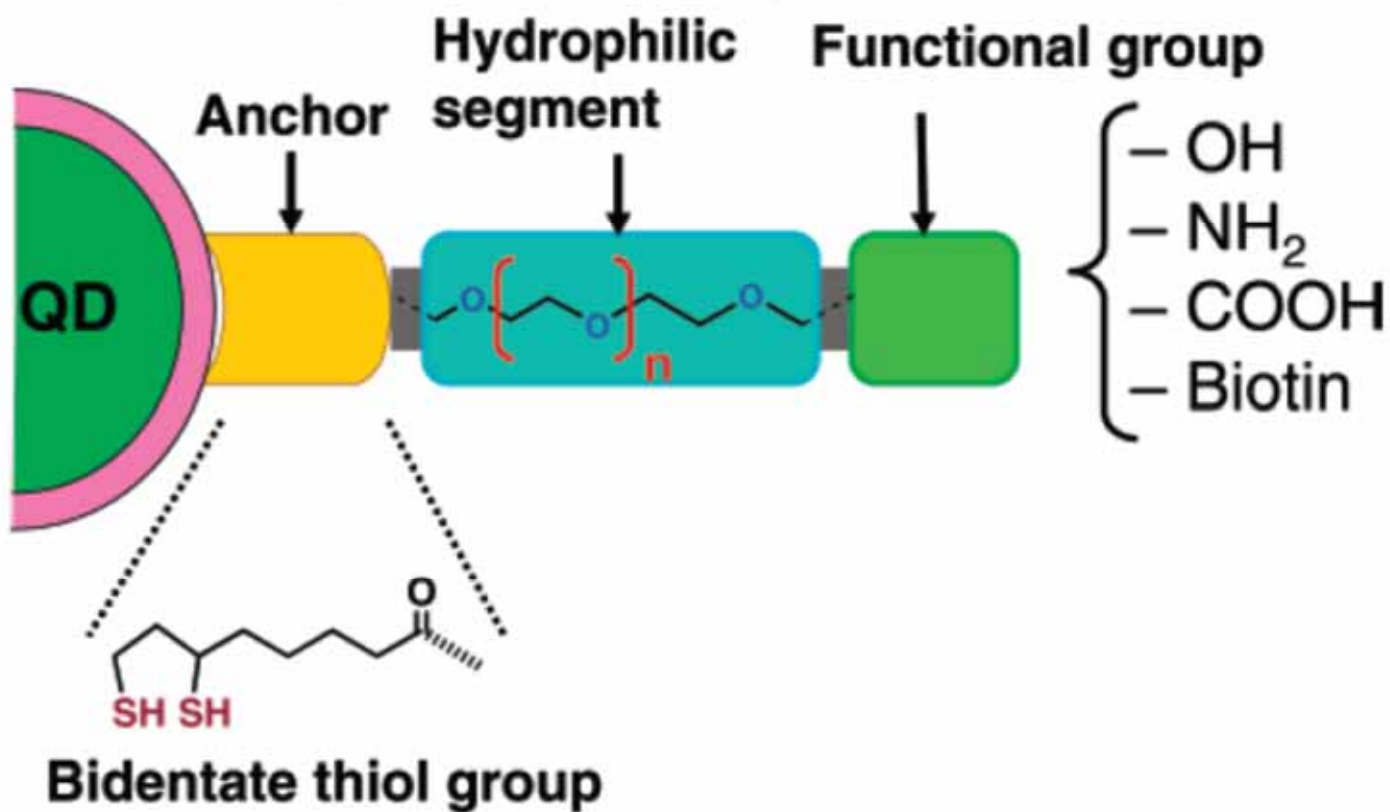
Cells incubated with tiopronin coated QDs



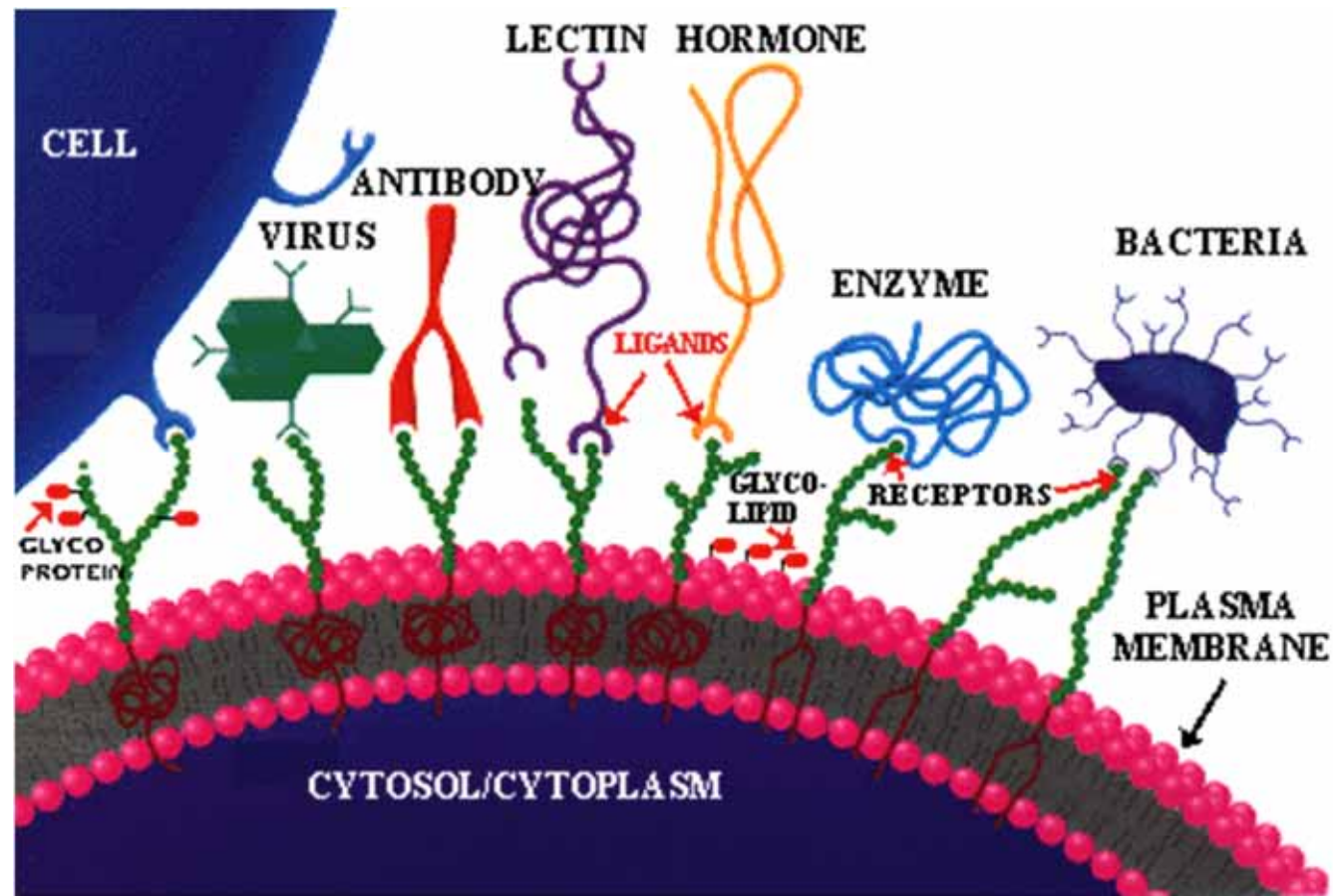
Cells incubated with Tat functionalized QDs



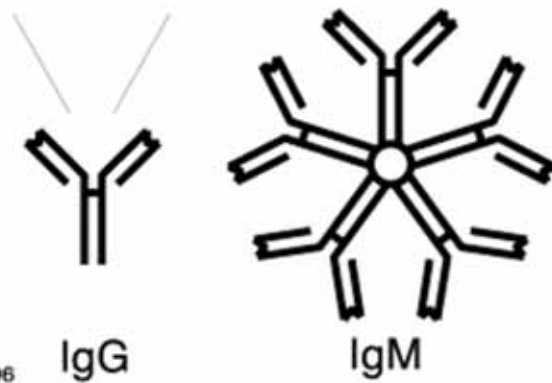
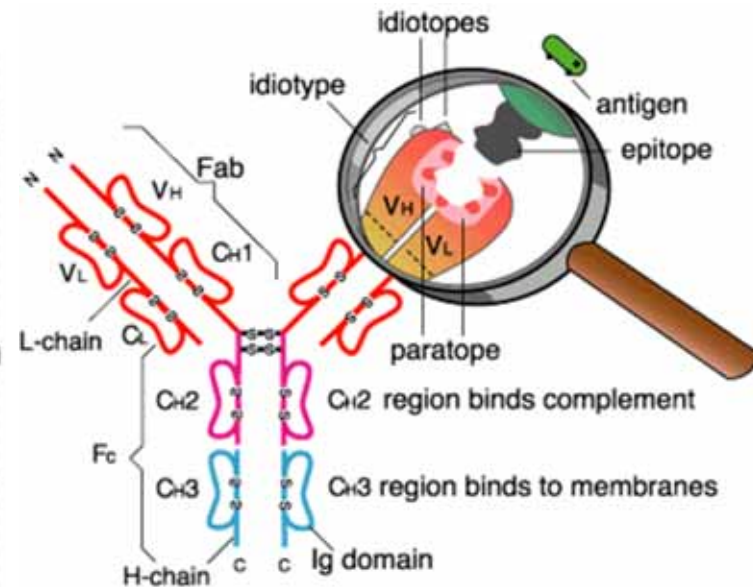
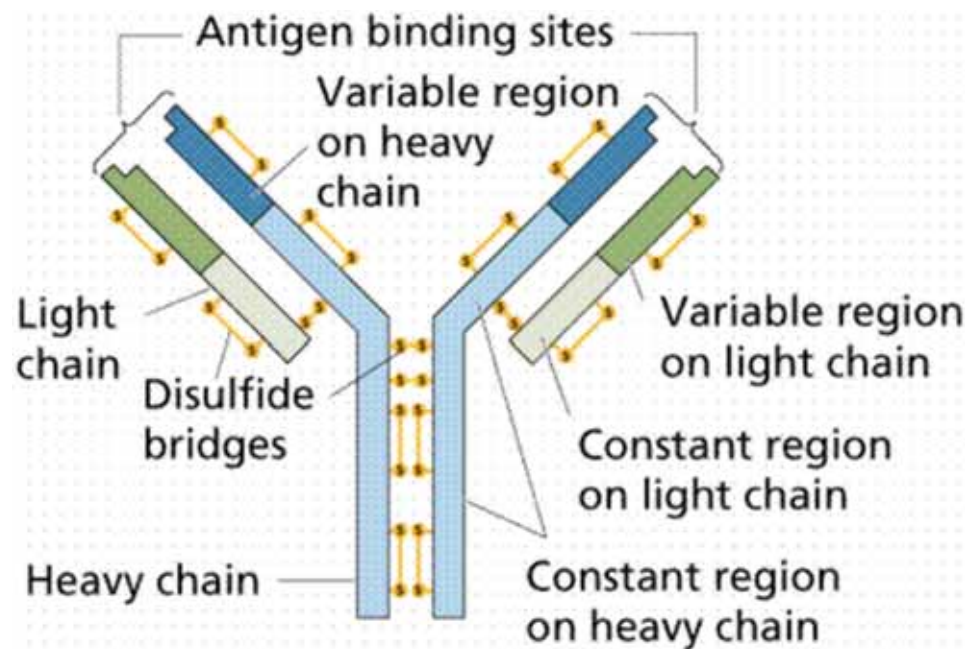
Scheme 1. Modular Design of Hydrophilic Ligands with Terminal Functional Groups Used in This Study



Molecular Recognition



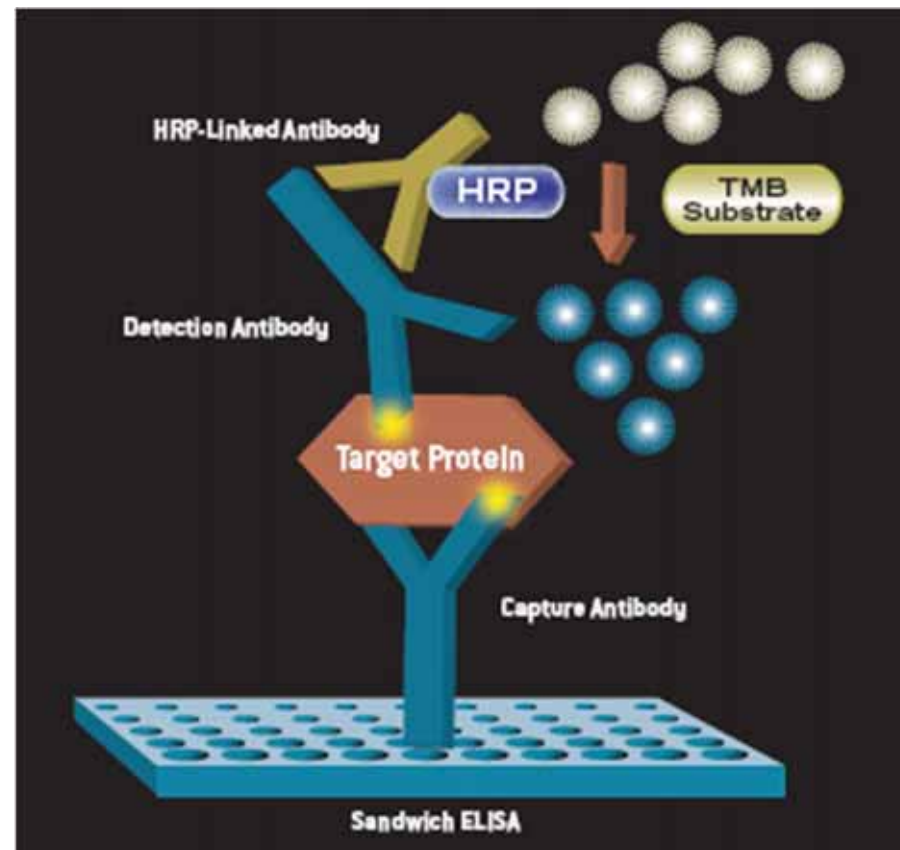
Antibody and Antigen



Bendzen 1996



Enzyme-Linked ImmunoSorbent Assay (ELISA)

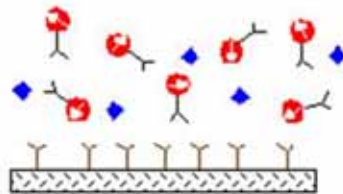


Labeling
BSA/PEG

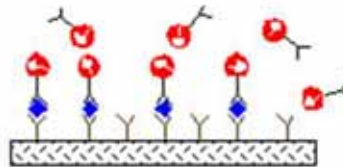


Microarray

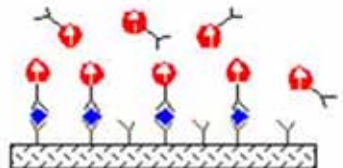
◆ Biomolecules of interest Y Capture antibody ▨ Solid support ● Magnetically labeled antibody



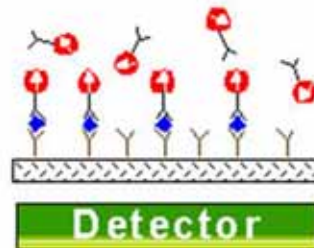
Add biomolecules of interest and magnetically labeled detect antibodies to well coated with capture antibody.



Immobilized immune complexes form on solid support.



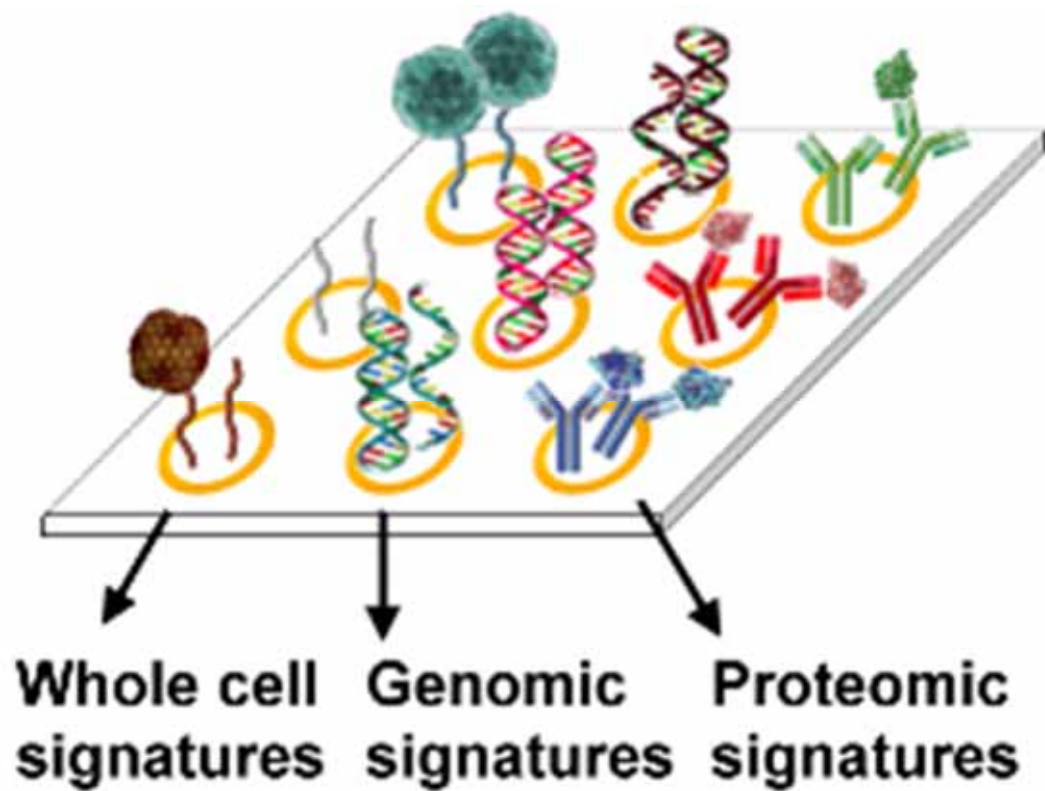
Apply external magnetic field, magnetic dipoles align.



Remove field, measure net magnetization due to bound antibody labels. Unbound labels randomize quickly and contribute no net signal.



Microarray



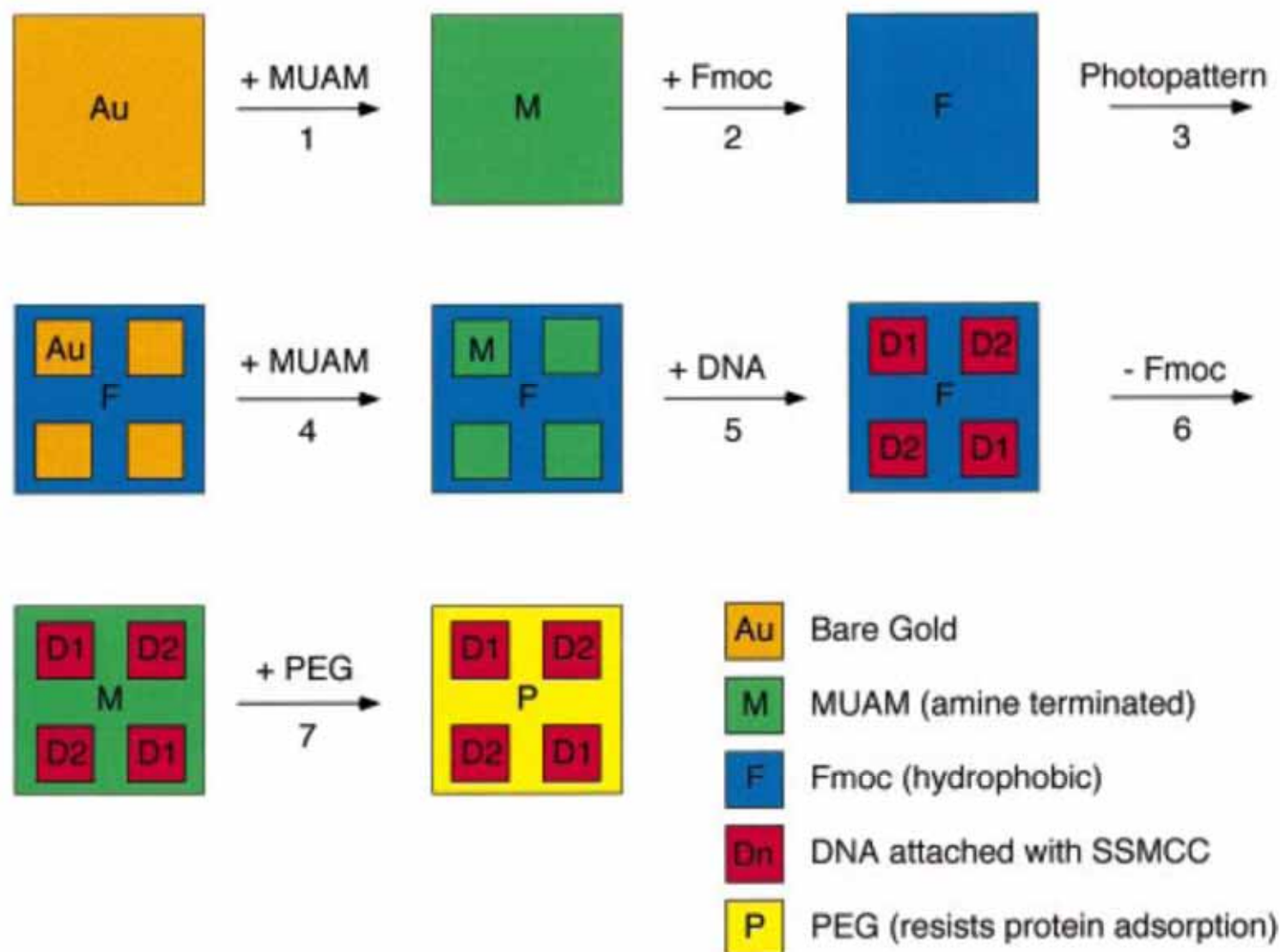


Figure 1. Fabrication scheme for the construction of multi-element DNA arrays. A clean gold surface is reacted with the amine-terminated alkanethiol MUAM, and subsequently reacted with Fmoc-NHS to create a hydrophobic surface. This surface is then exposed to UV radiation through a quartz mask and rinsed with solvent to remove the MUAM+Fmoc from specific areas of the surface, leaving bare gold pads. These bare gold areas on the sample surface are filled in with MUAM, resulting in an array of MUAM pads surrounded by a hydrophobic Fmoc background. Solutions of DNA are then delivered by pipet onto the specific array locations and are covalently bound to the surface via the bifunctional linker SSMCC. In the final two steps, the Fmoc-terminal groups on the array background are removed and replaced by PEG groups which prohibit the nonspecific binding of analyte proteins to the background.



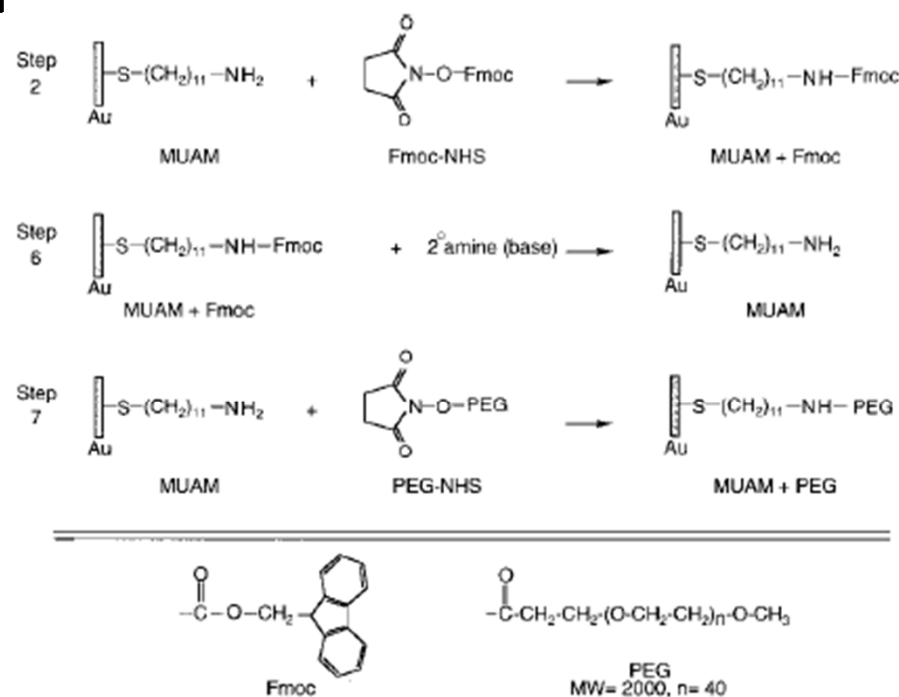


Figure 2. Surface reaction scheme showing the steps involved in the reversible modification of the array background. (Step 2) The starting amine-terminated alkanethiol surface (MUAM) is reacted with the Fmoc-NHS protecting group to form a carbamate linkage thus creating a hydrophobic Fmoc-terminated surface. (Step 6) After DNA immobilization (see Figure 3), the hydrophobic Fmoc group is removed from the surface with a basic secondary amine, resulting in the return of the original MUAM surface. (Step 7) In the final array fabrication step, the deprotected MUAM is reacted with PEG-NHS to form an amide bond that covalently attaches PEG to the array surface.

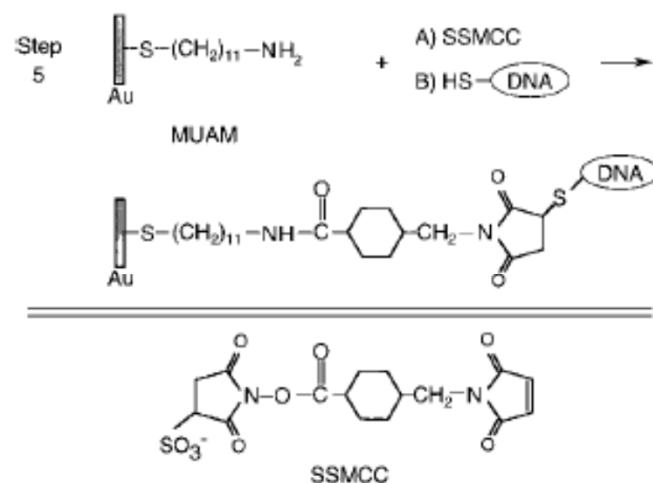
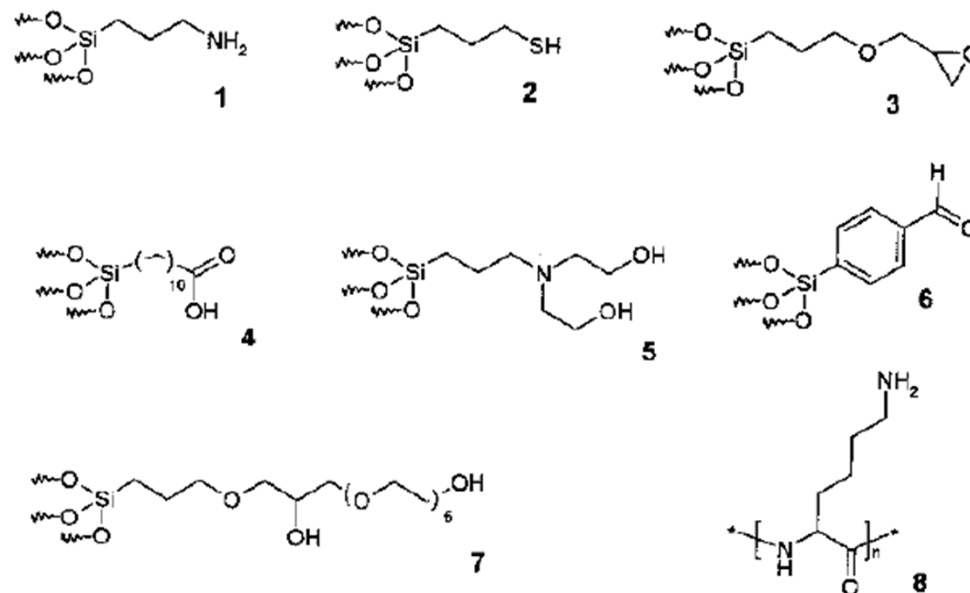
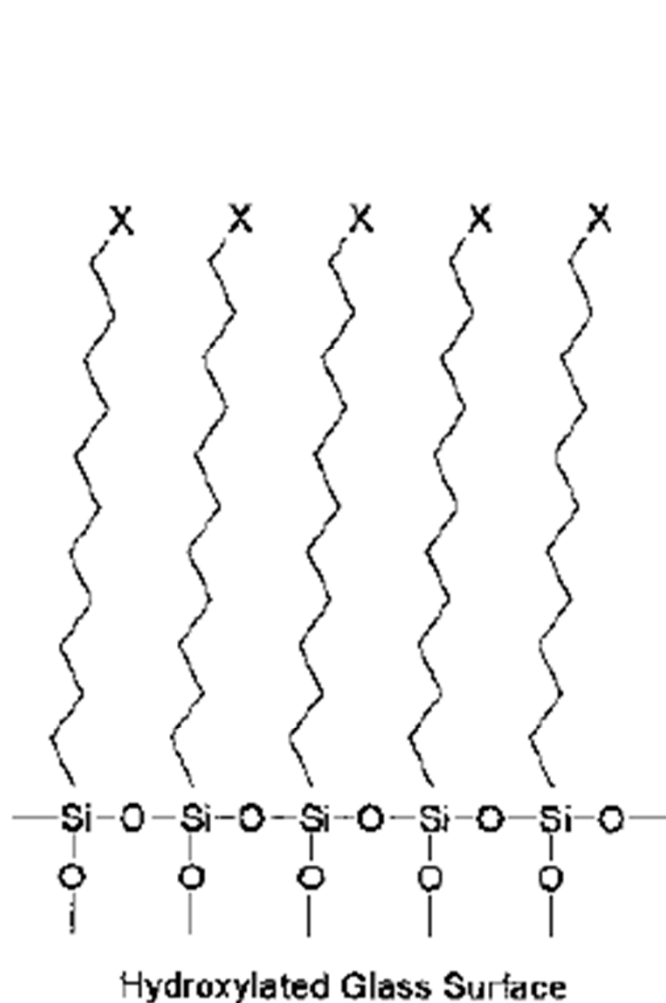


Figure 3. Surface reaction scheme showing the immobilization of thiol-terminated DNA to the array surface. In Step 5 of the DNA array fabrication, the heterobifunctional linker SSMCC is used to attach 5'-thiol modified oligonucleotide sequences to reactive pads of MUAM. This linker contains an NHSS ester functionality (reactive toward amines) and a maleimide functionality (reactive toward thiols). The surface is first exposed to a solution of the linker, whereby the NHSS ester end of the molecule reacts with the MUAM surface. Excess linker is rinsed away and the array surface is then spotted with 5'-thiol-modified DNA that reacts with the maleimide groups forming a covalent bond to the surface monolayer.



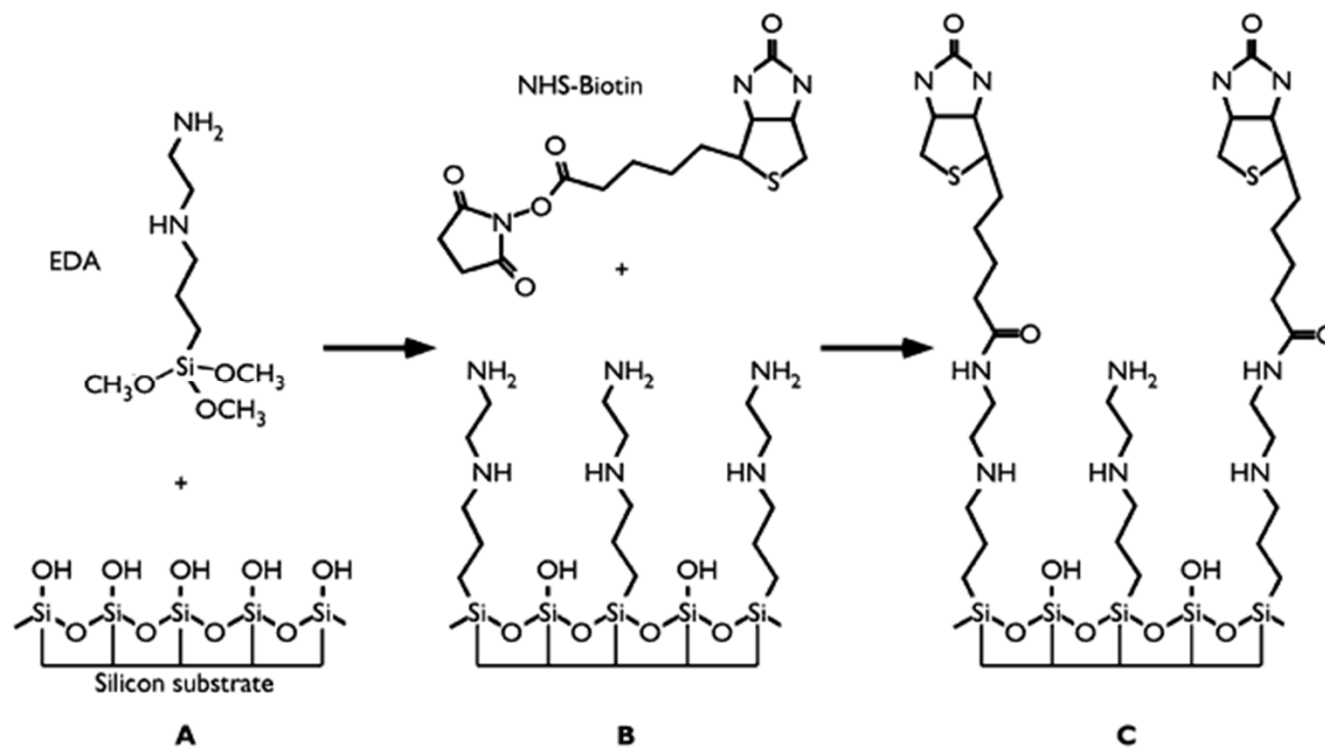
Glass Surface Modification



Scheme 2.2 Reagents for derivatization of glass surfaces. 1 APTES = aminopropyltriethoxysilane; 2 MPTS = 3-mercaptopropyltrimethoxysilane; 3 GPTS = glycidoxypropyltrimethoxysilane; 4 TETU = triethoxysilane undecanoic acid;

5 HE-APTS = bis(hydroxyethyl)aminopropyltriethoxysilane; 6 4-trimethoxysilylbenzaldehyde; 7 GPTS/HEG = glycidoxypropyltrimethoxysilane-hexaethylene glycol; 8 poly(lysine).

Scheme 2.1 2D schematic description of a polysiloxane monolayer on a glass surface (X = terminal functional)



Biotin-Streptavidin

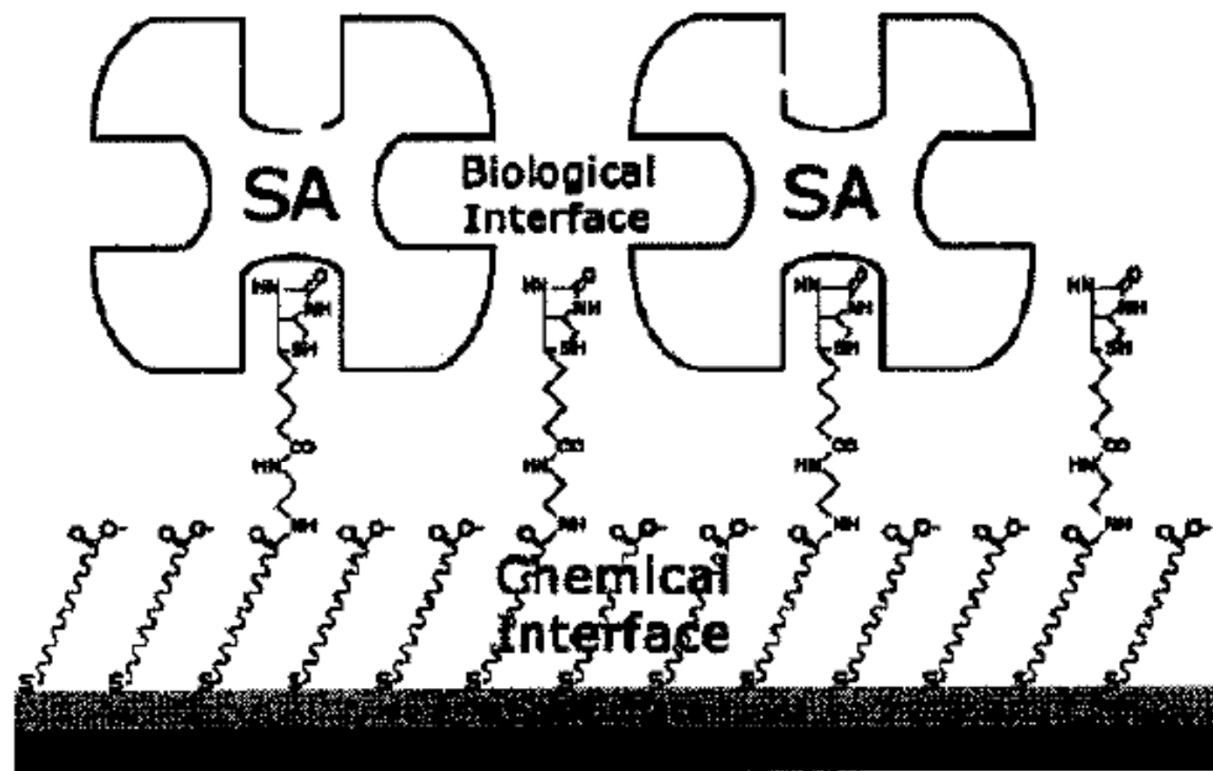
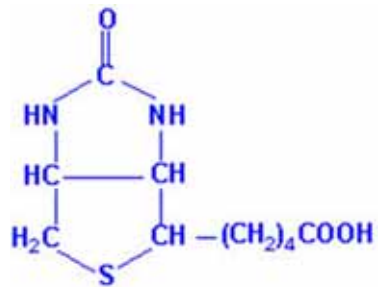


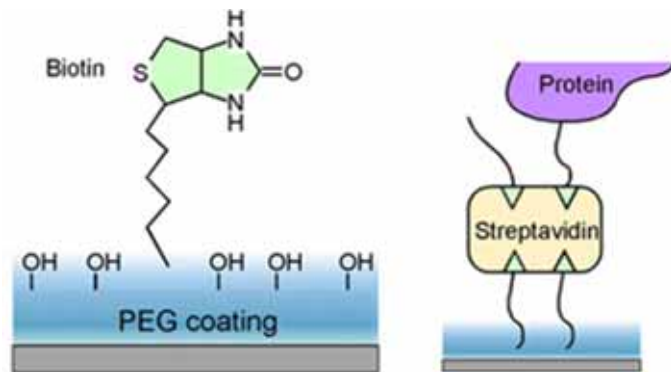
Figure 2.3 Schematic representation of a streptavidin sensor surface assembled on a reaction-controlled biotinylated SAM [28].

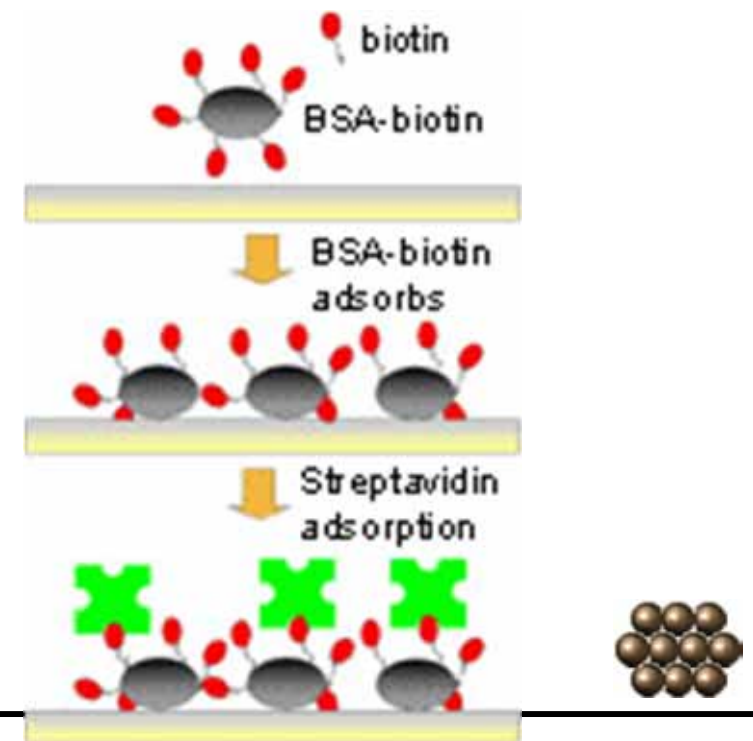
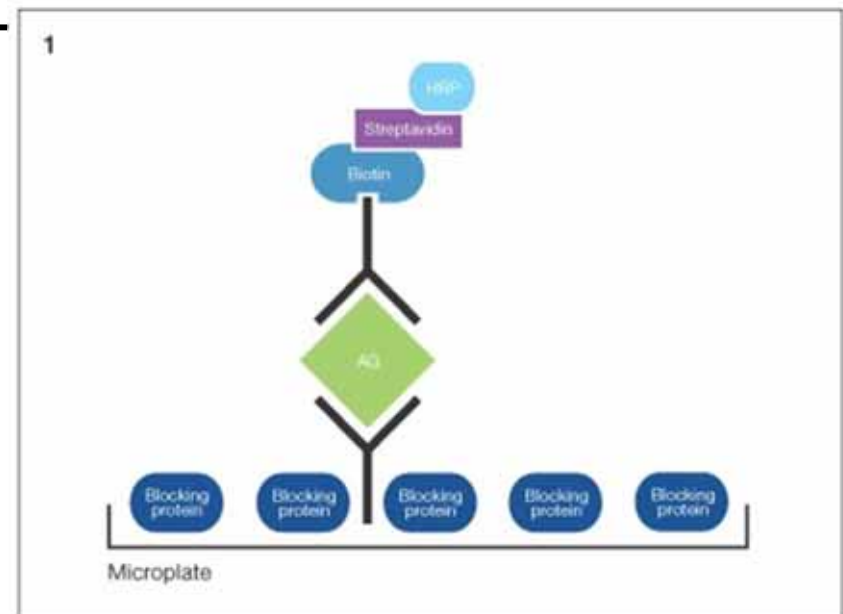
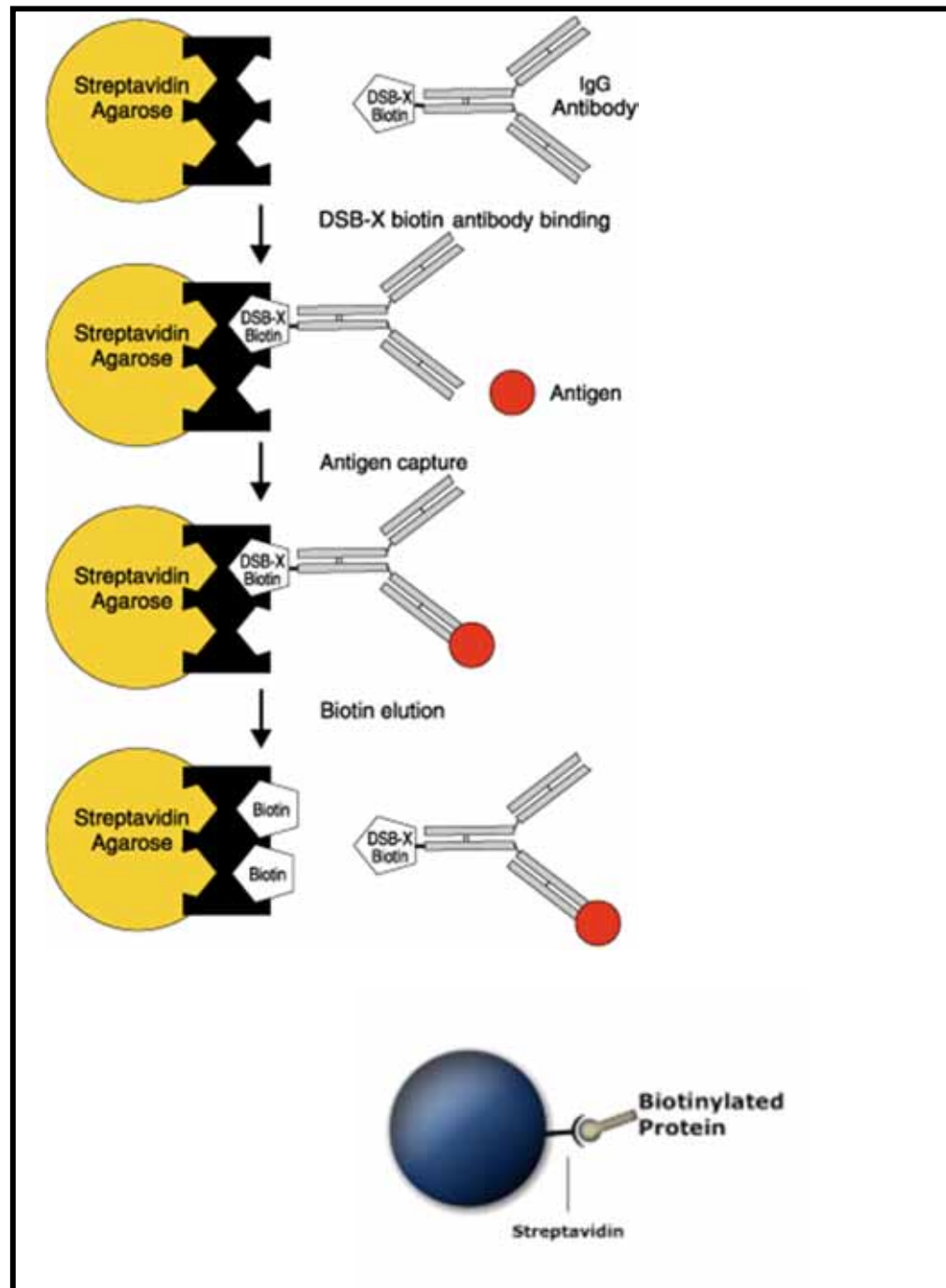


Biotin

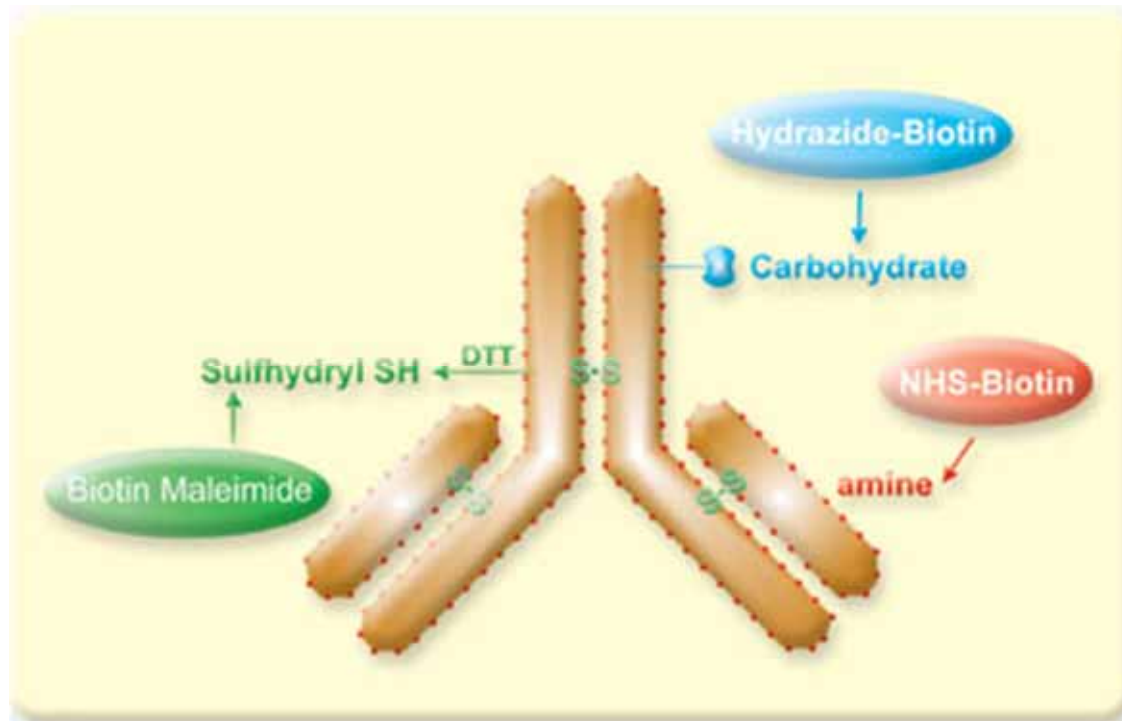


Avidin has a very strong affinity for biotin with a K_D (dissociation constant) of approximately 10^{-15} M^{-1}

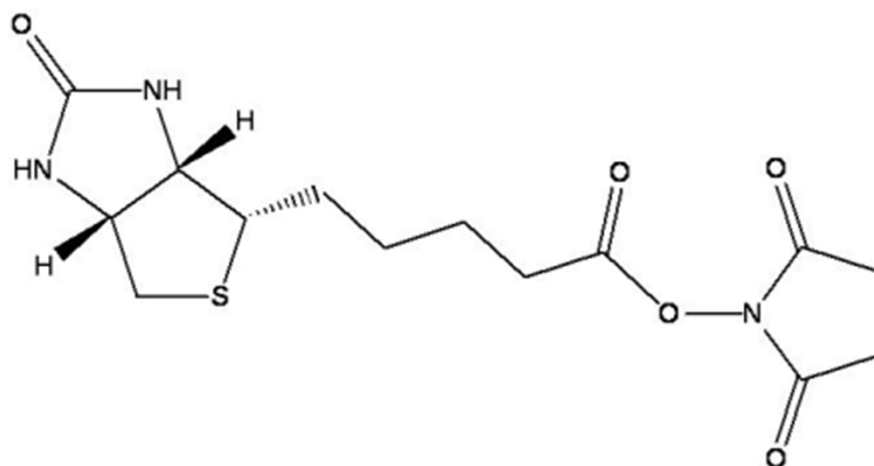




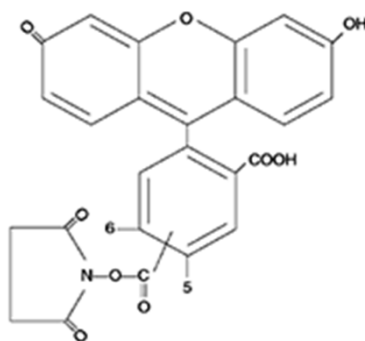
Protein Labeling



Amine Reactive Labeling



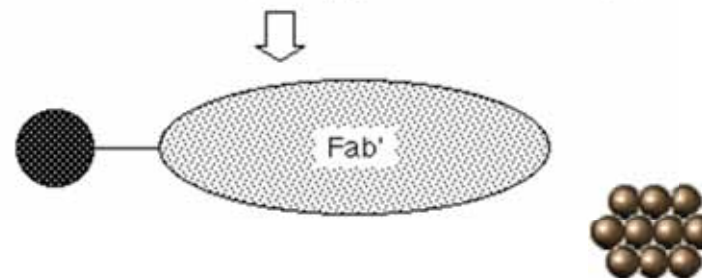
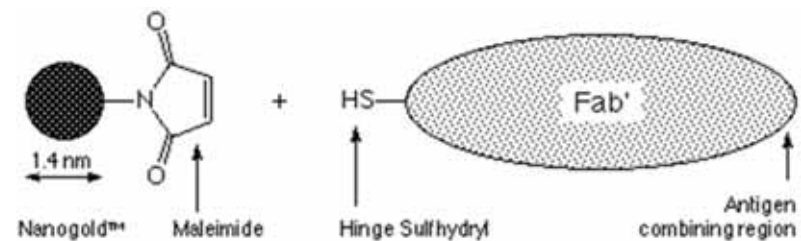
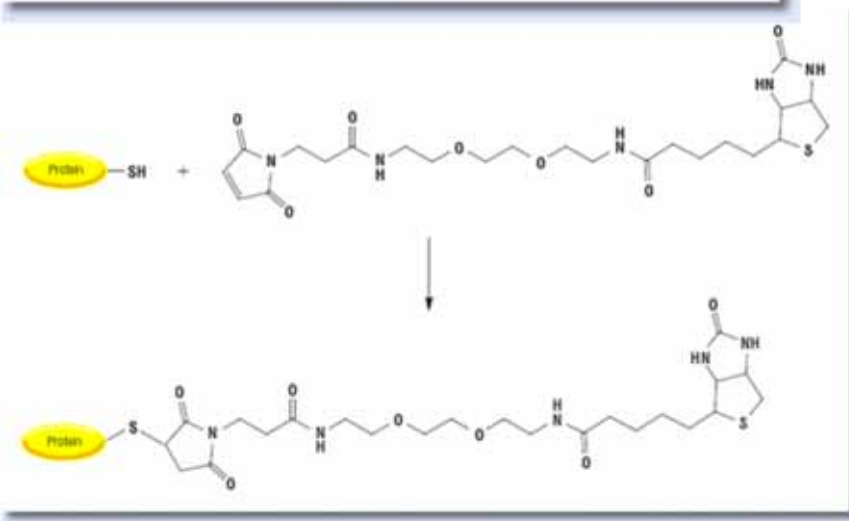
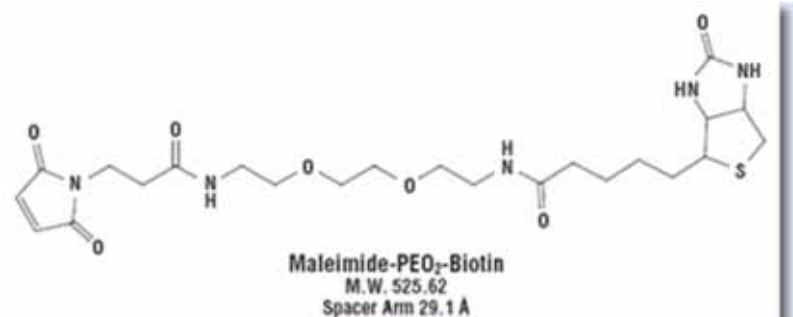
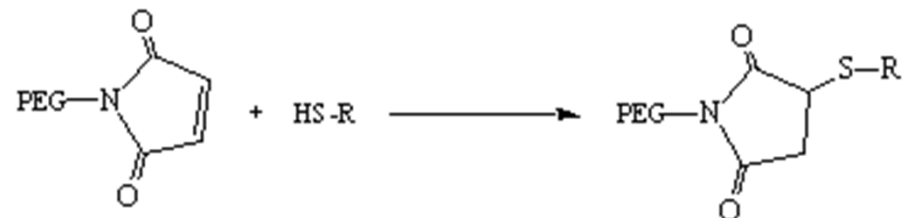
NHS ester

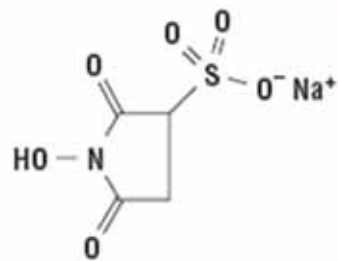


NHS-Fluorescein
MW 473.4

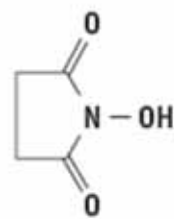


Sulfhydryl Labeling

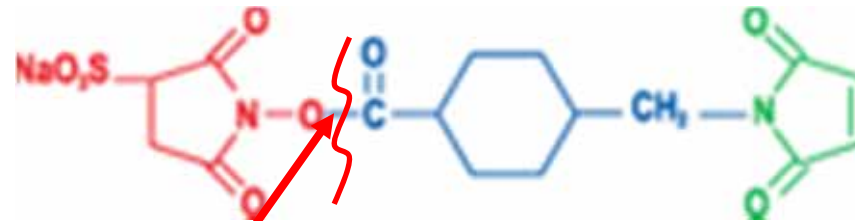




Sulfo-NHS
M.W. 217.13



NHS
M.W. 115.09

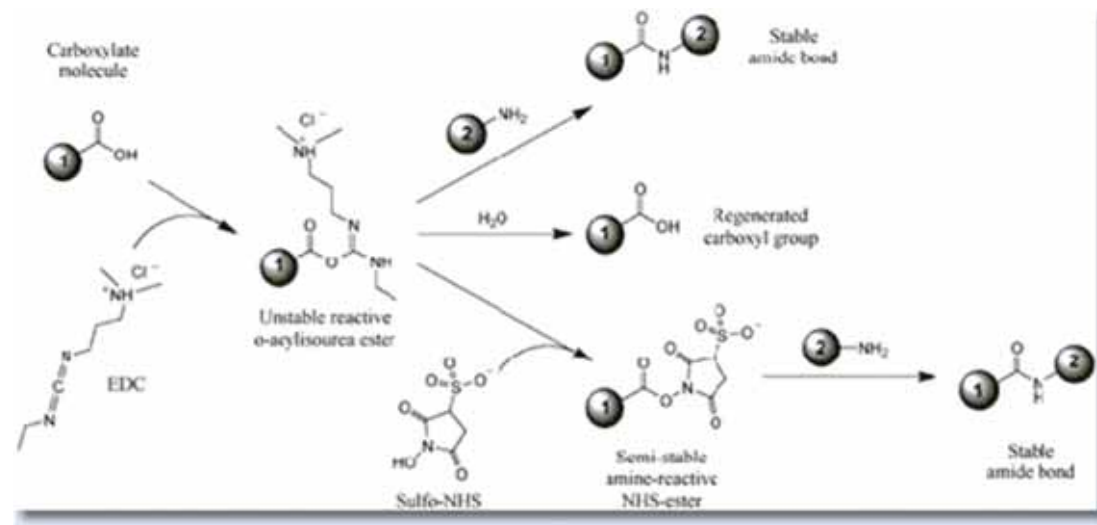
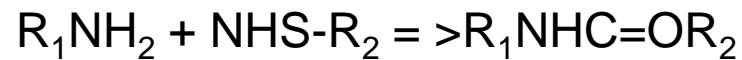


SulfoSuccinimidyl-4-(N-Maleimidomethyl)Cyclohexane-1-Carboxylate
SSMCC

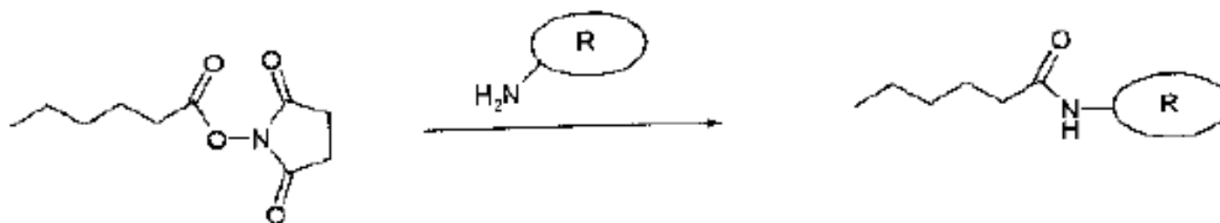
The most popular NH_2 - and SH - crosslinker

N-hydroxysuccinimide

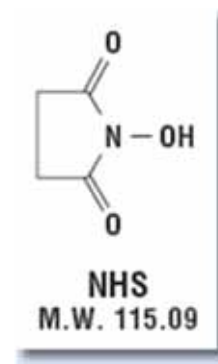
$\text{NH}_2 \Rightarrow$ amide



N-hydroxysuccinimide (NHS)



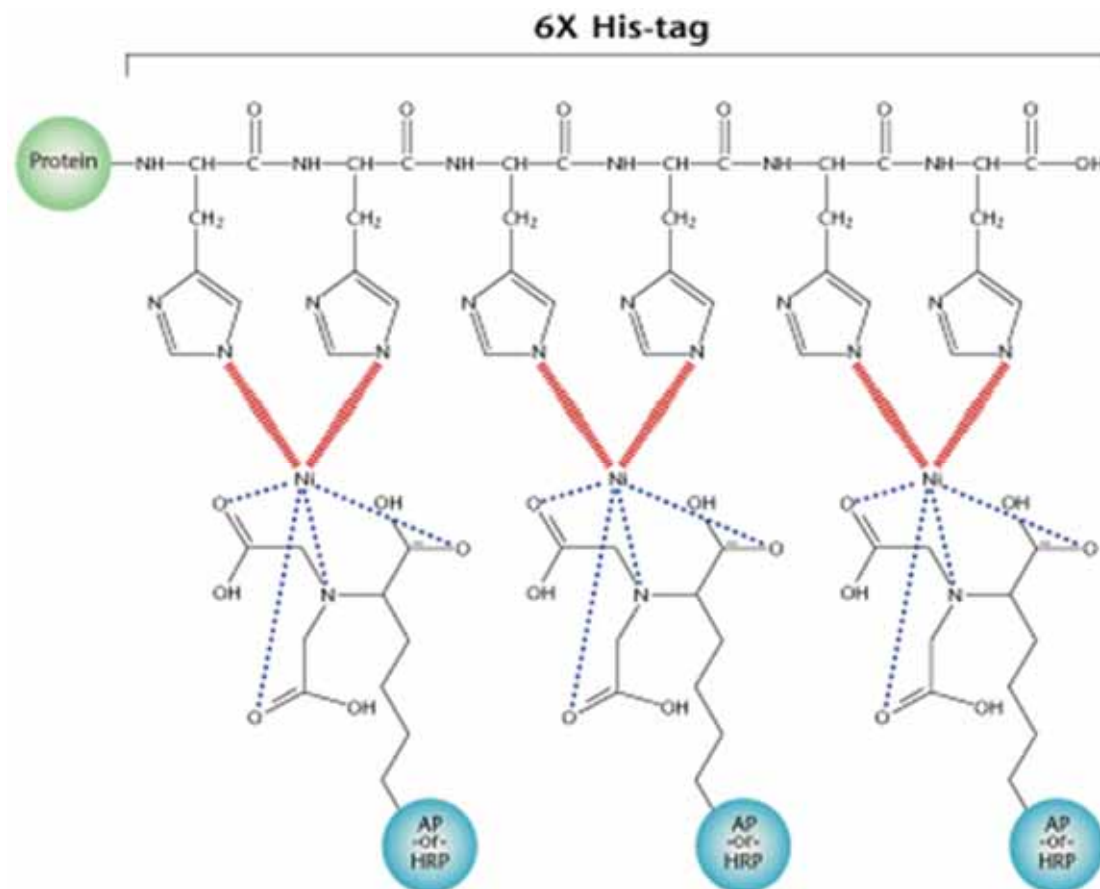
Scheme 2.6 Surface coupling reaction of NHS-esters with the amino residues of the side-chains of polypeptides (lysine units). R, protein.



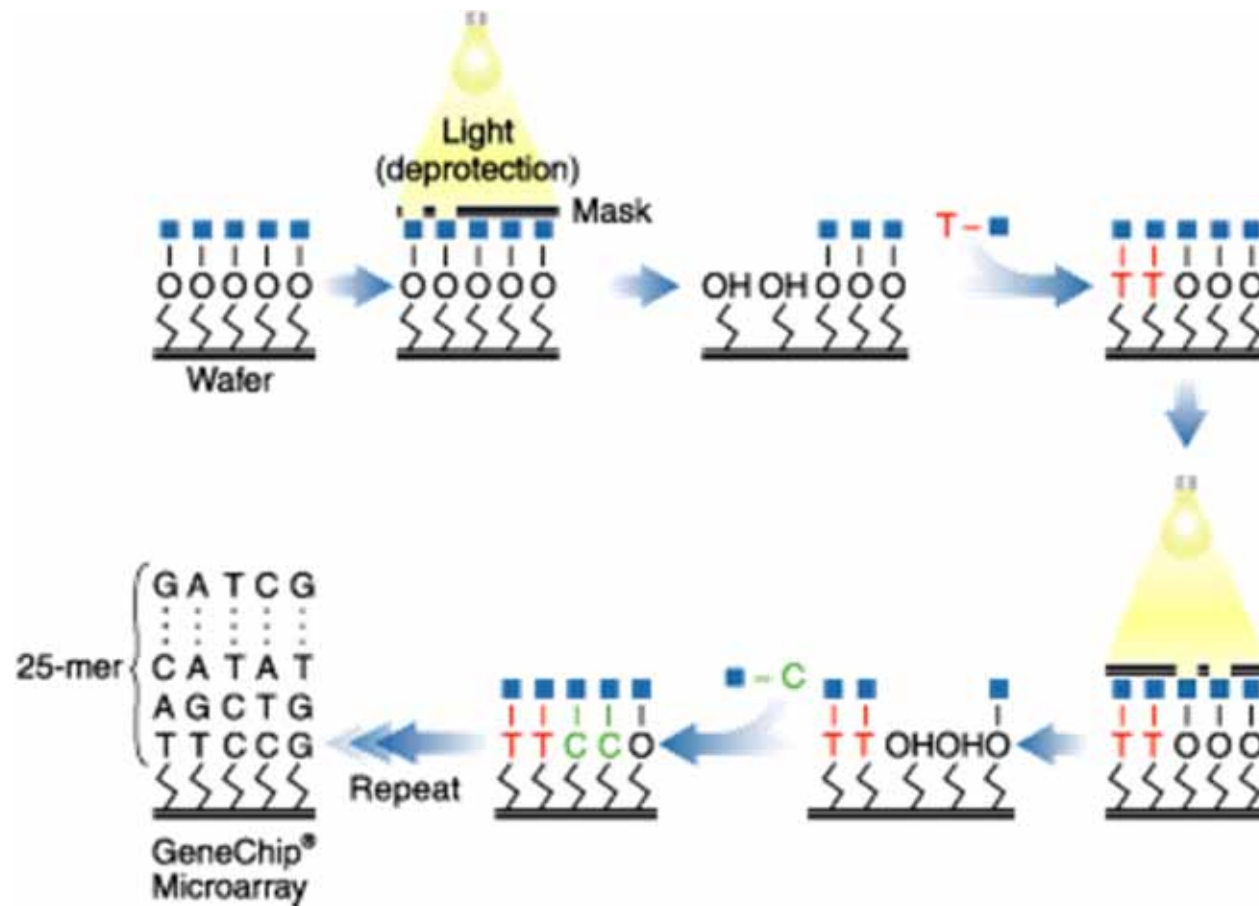
N-hydroxysuccinimide



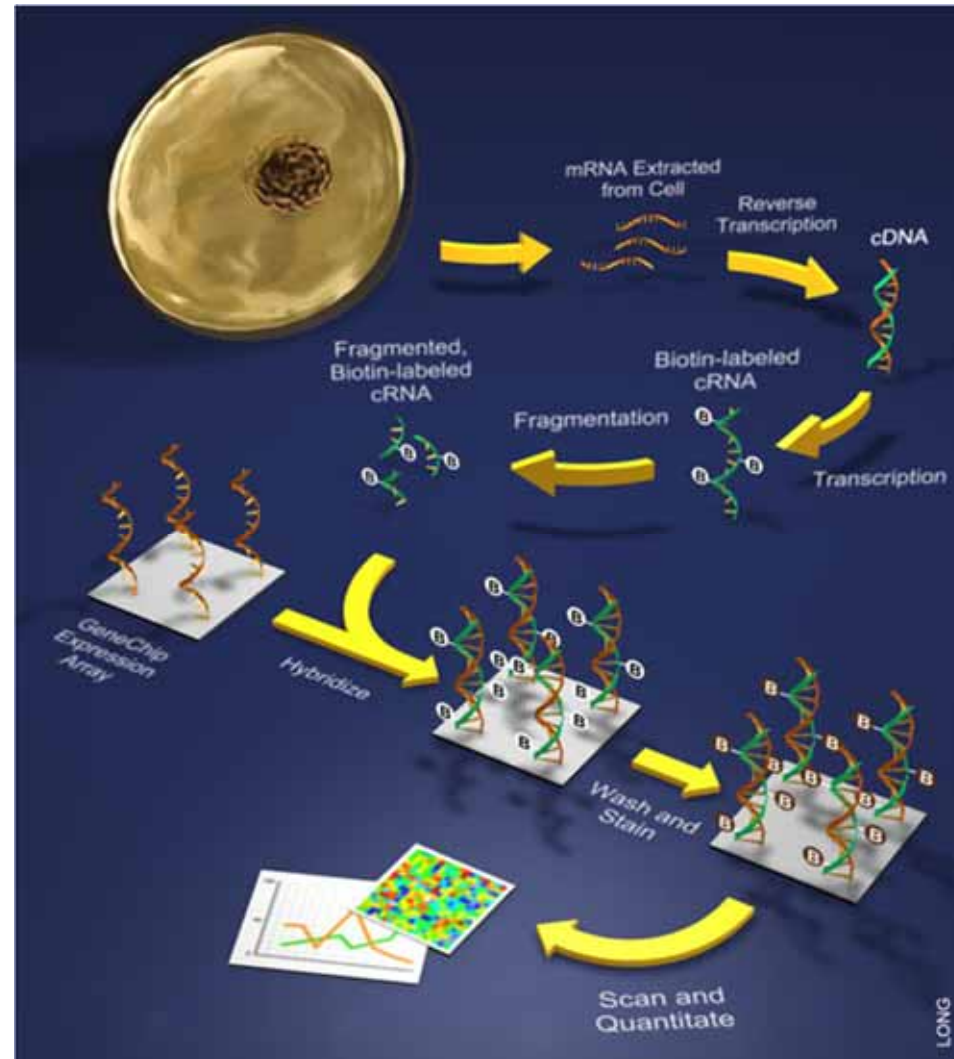
His Tag



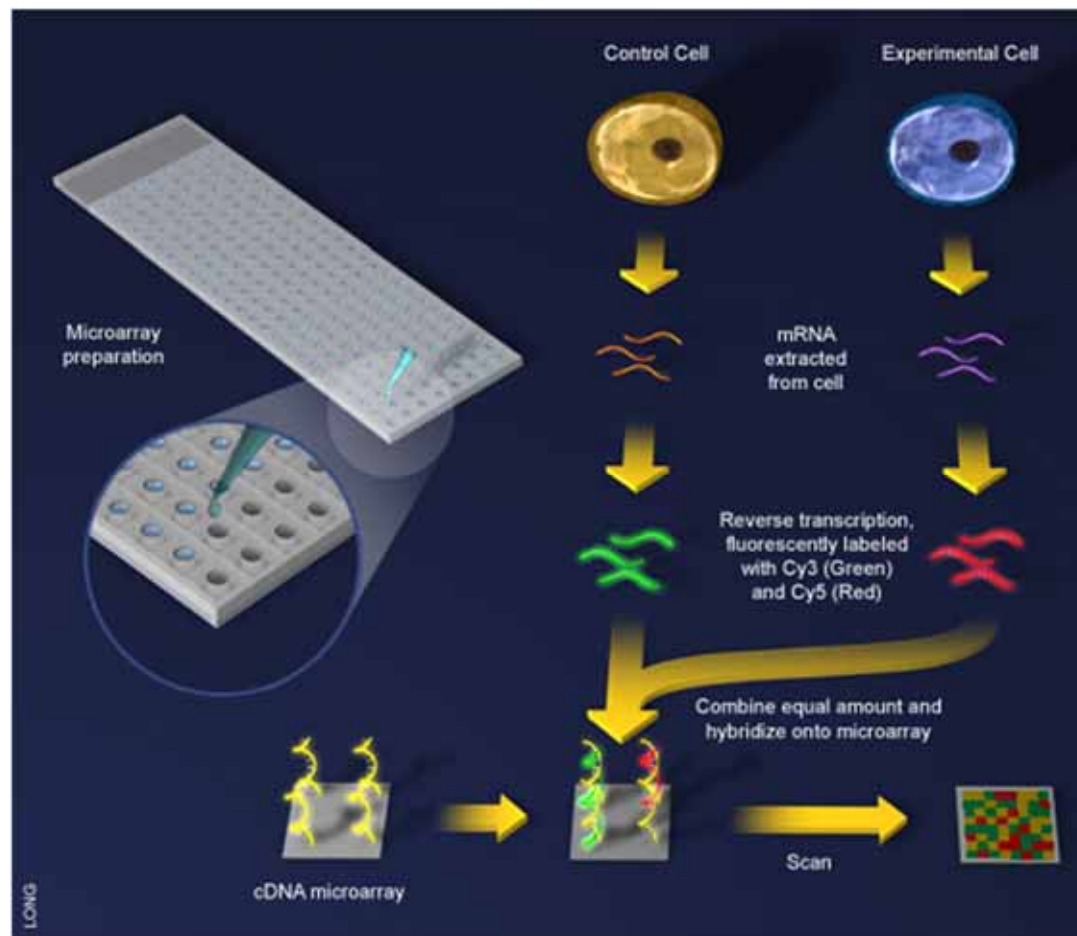
GeneChip



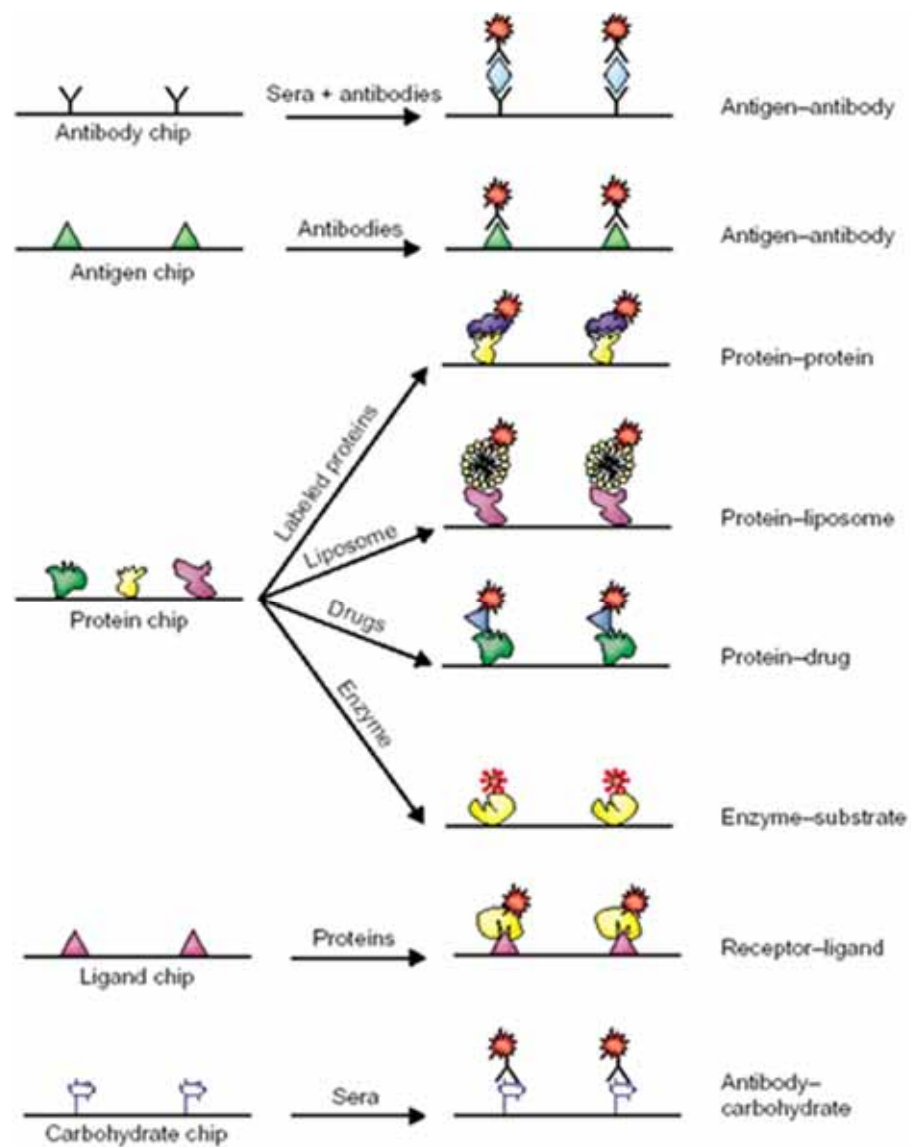
Scheme



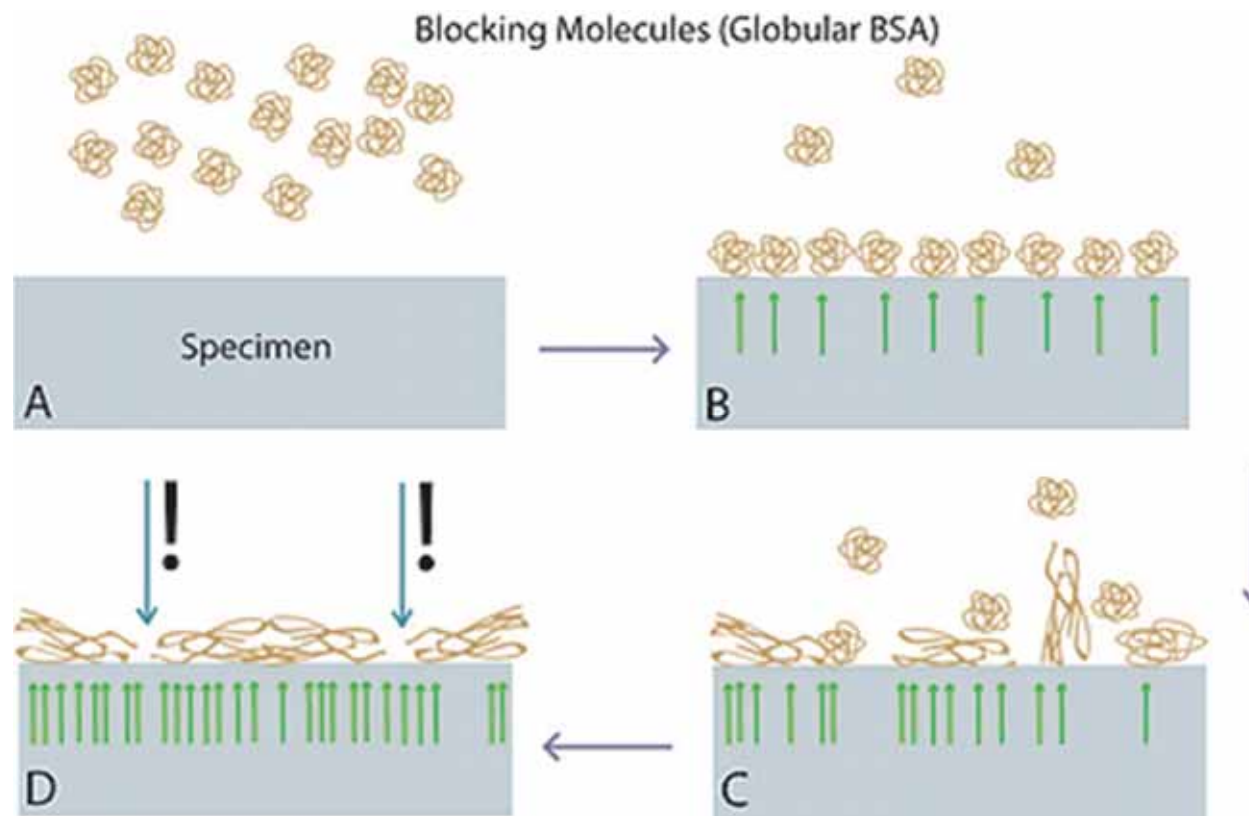
cDNA Microarray



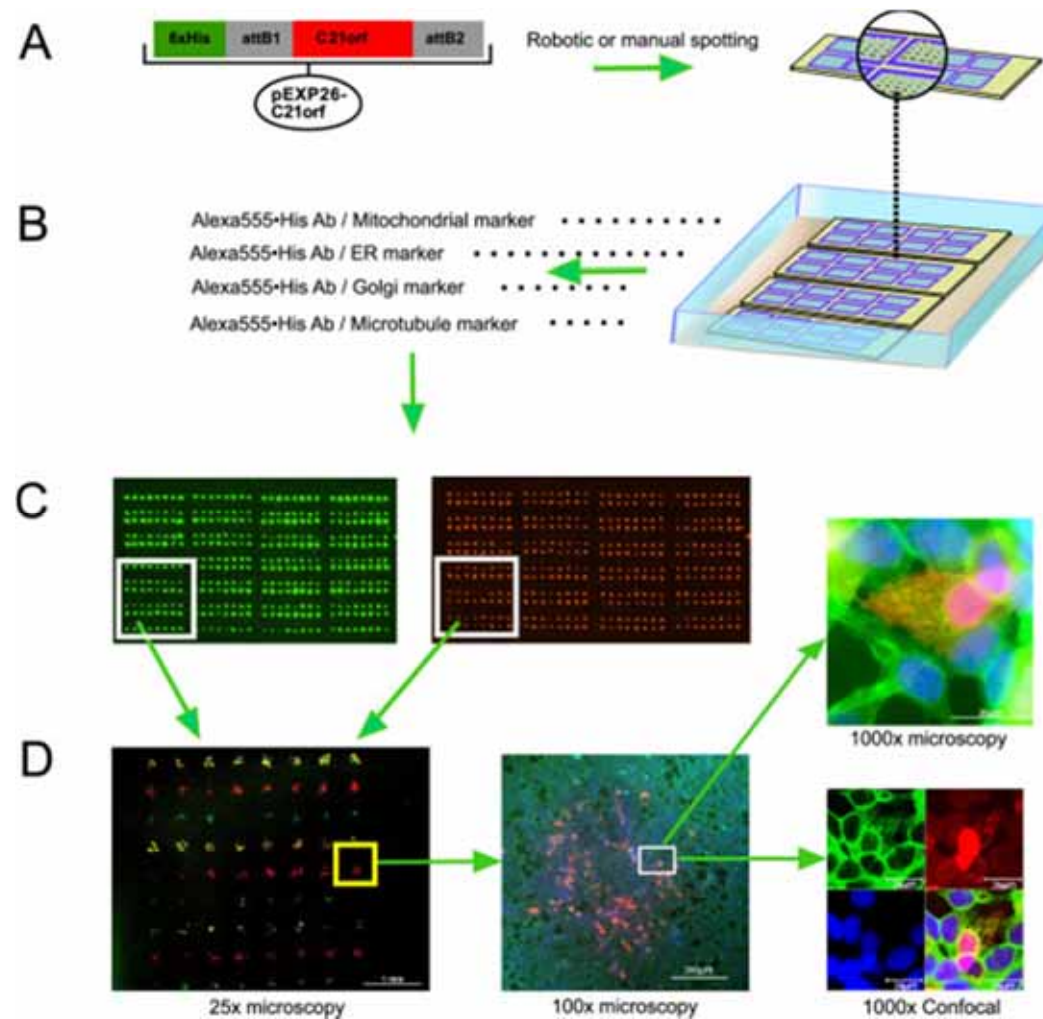
Protein Array



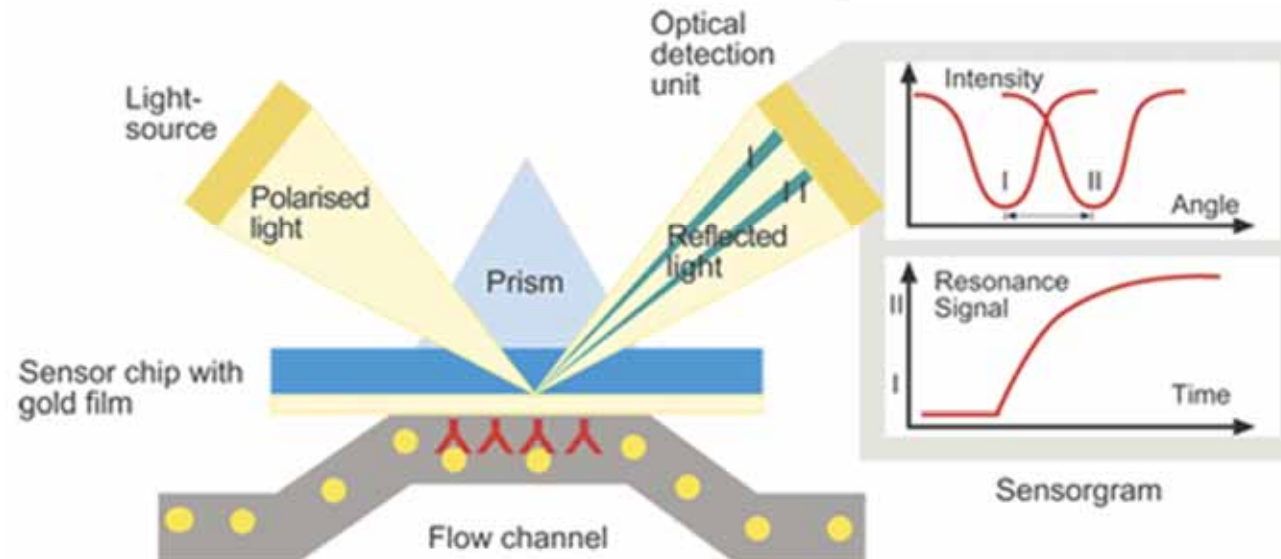
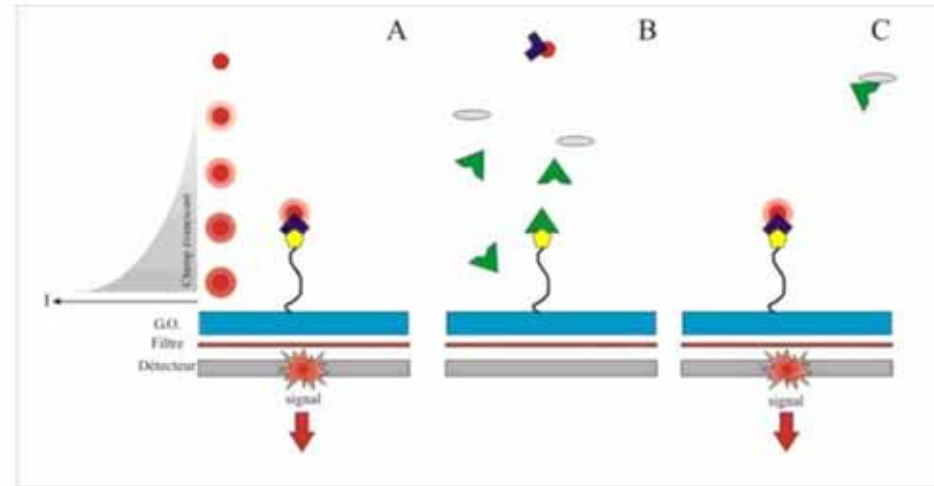
BSA Blocking



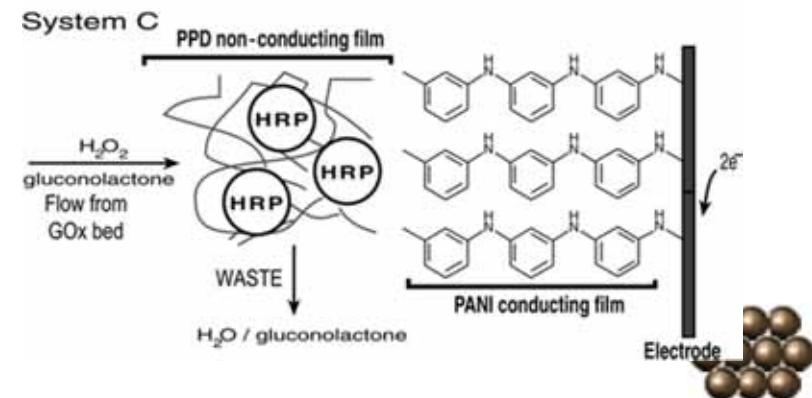
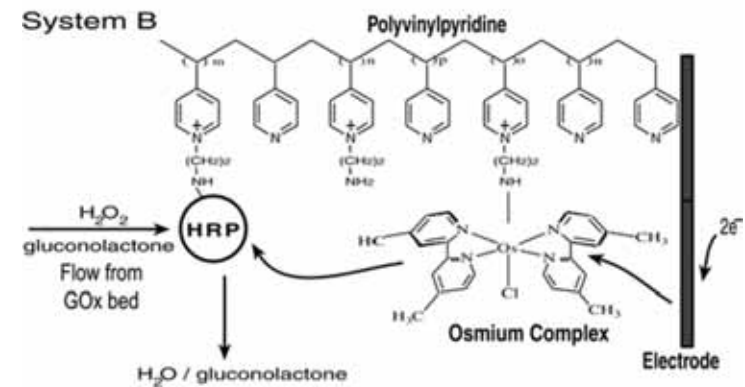
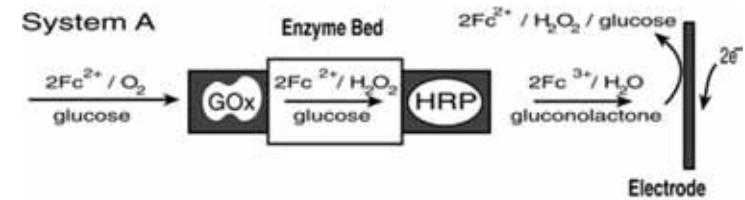
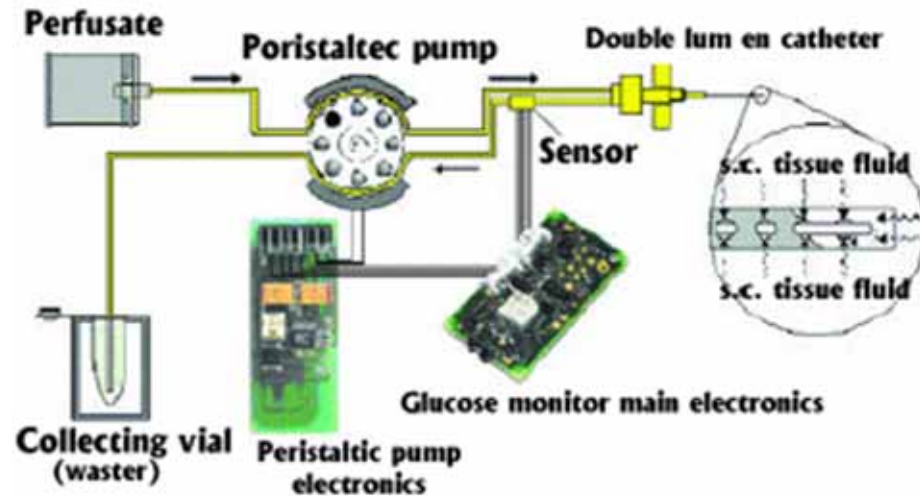
Cell Array



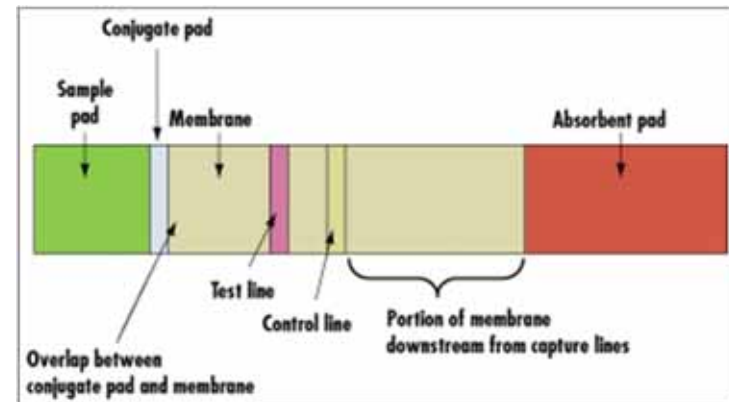
Surface Plasmon Resonance (SPR)



Glucose Sensor



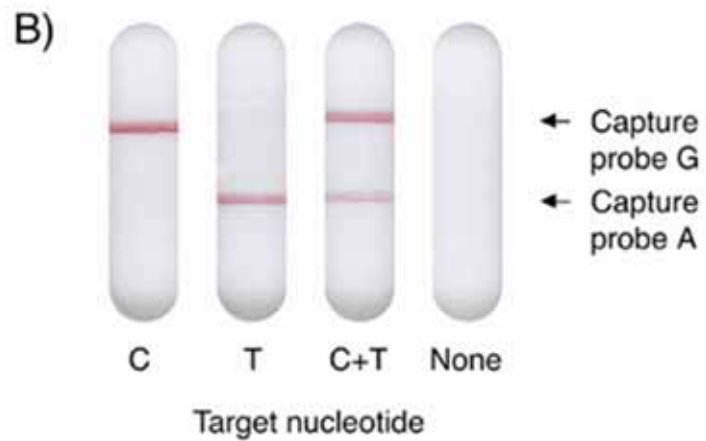
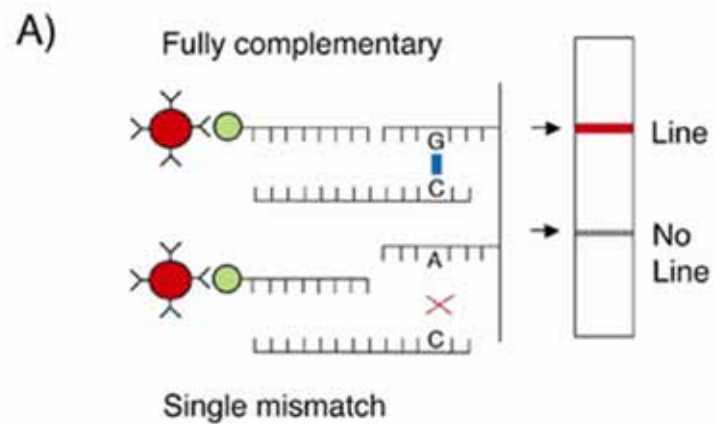
hCG immunoassay



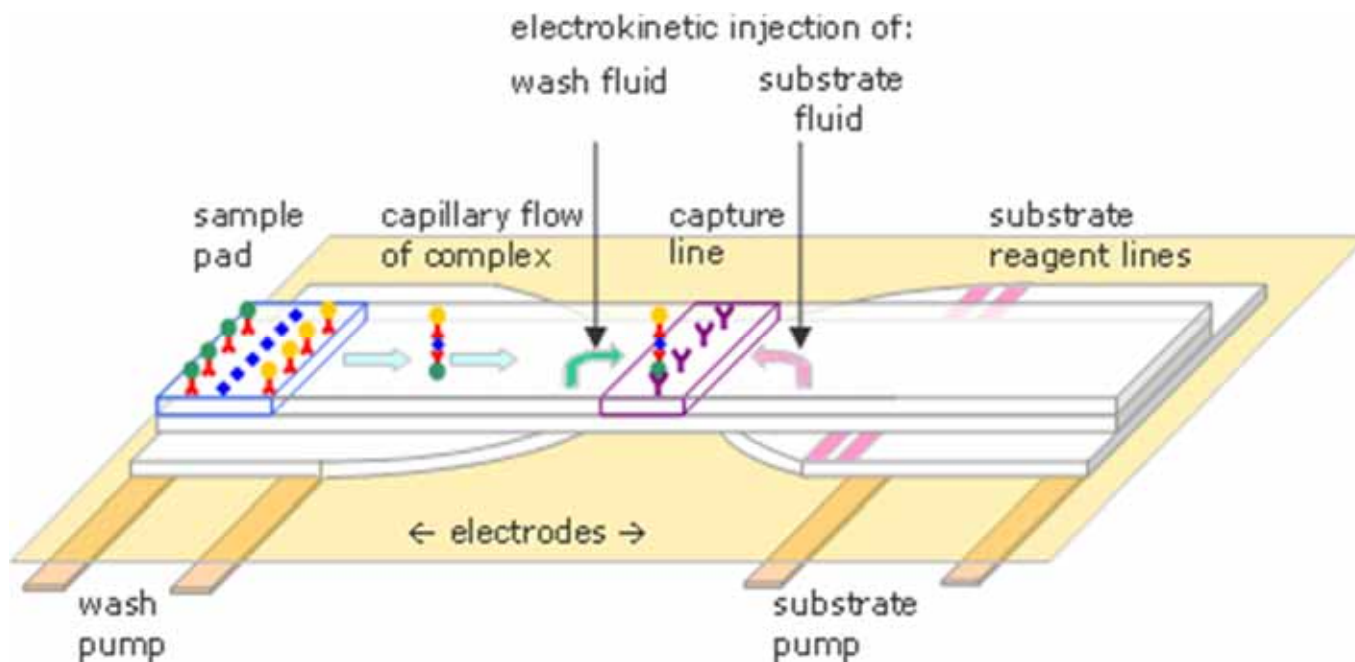
human chorionic gonadotropin (hCG)



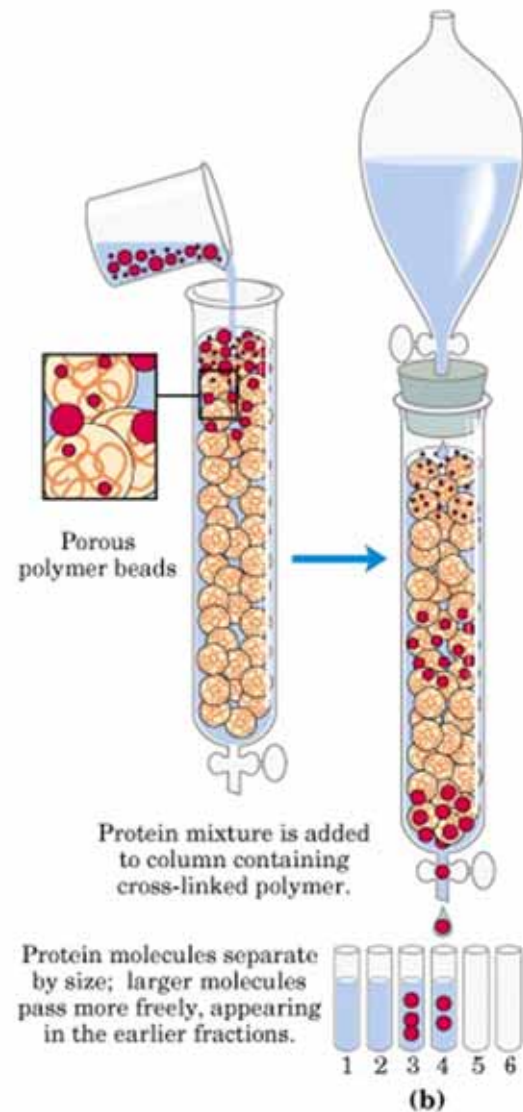
Nucleotide Sensor



Microfluidic Immunoassay

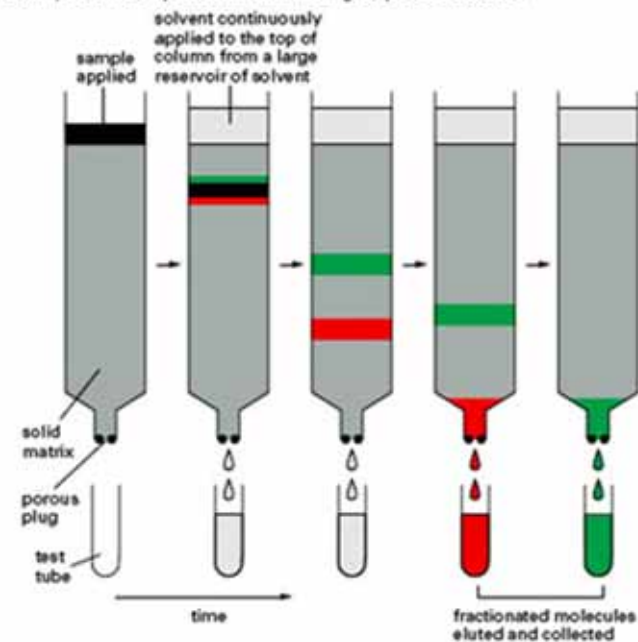


Chromatography



COLUMN CHROMATOGRAPHY

Proteins are often fractionated by **column chromatography**. A mixture of proteins in solution is applied to the top of a cylindrical column filled with a permeable solid matrix immersed in solvent. A large amount of solvent is then pumped through the column. Because different proteins are retarded to different extents by their interaction with the matrix, they can be collected separately as they flow out from the bottom. According to the choice of matrix, proteins can be separated according to their charge, hydrophobicity, size, or ability to bind to particular chemical groups (see *below*).



Reverse Phase

