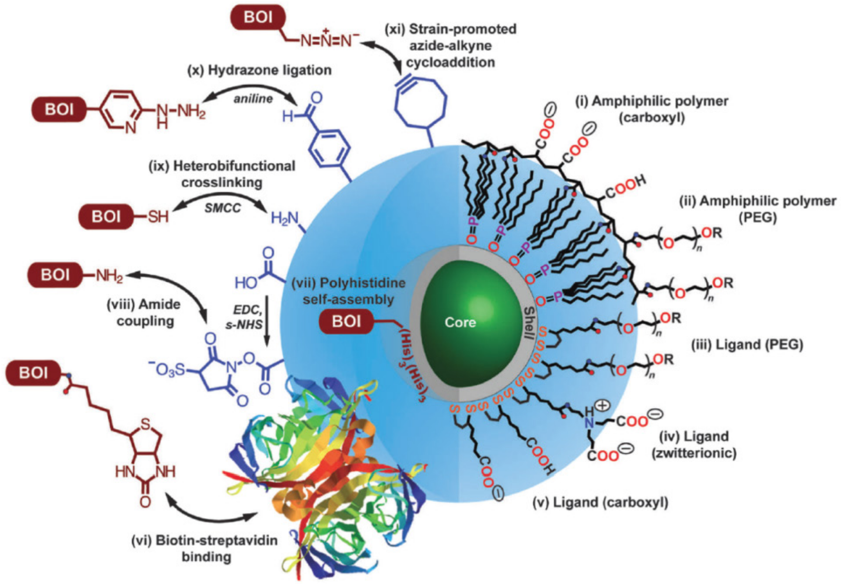
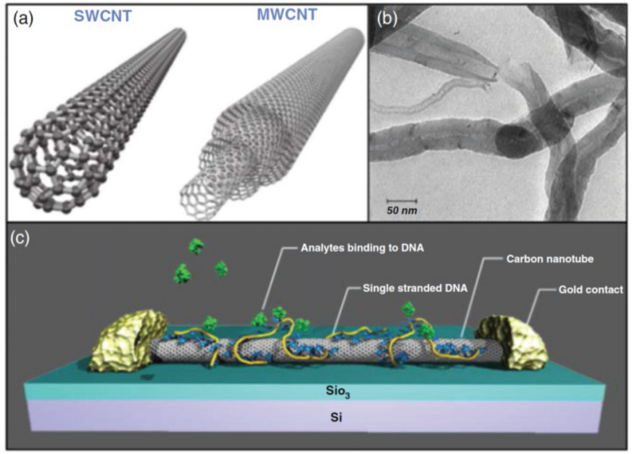
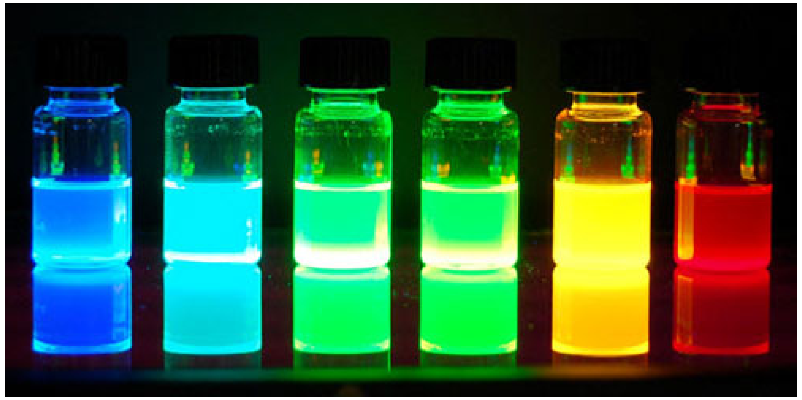
Introduction to BioMEMS & Medical Microdevices

Nanobiosensors – Quantum Dots & Nanoparticles

Prof. Steven S. Saliterman, http://saliterman.umn.edu/



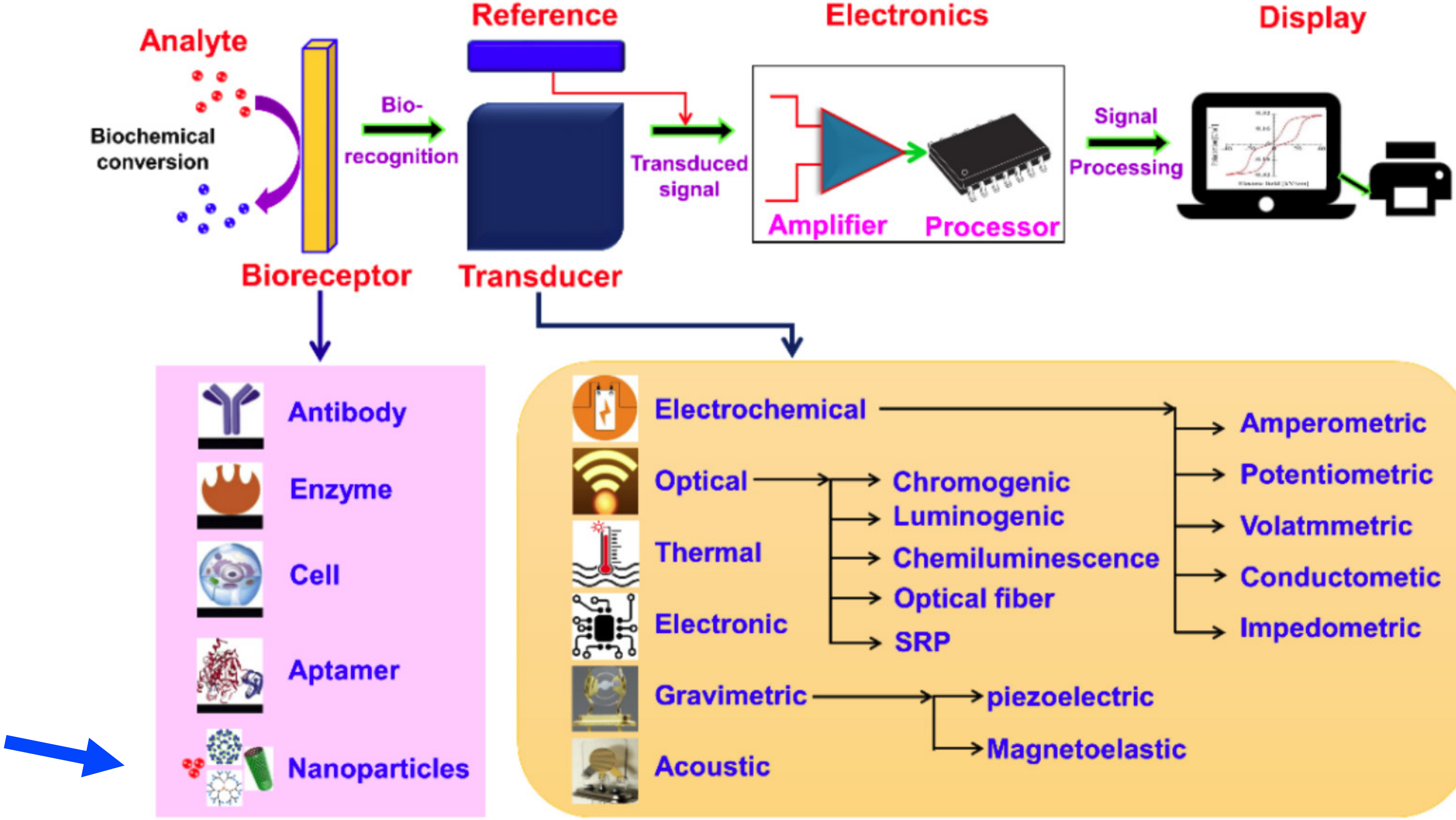




Topics

- Nanoparticle transducers:
  - Quantum dots.
  - Carbon dots.
  - Lanthanide nanoparticles.
  - Gold nanoparticles.
- Label free transducers
  - Nanowires
  - Nanotubes
  - Nanocantilevers
- Appendix:
  - Carbon dots for SNP recognition.
  - Mesoporous membranes.

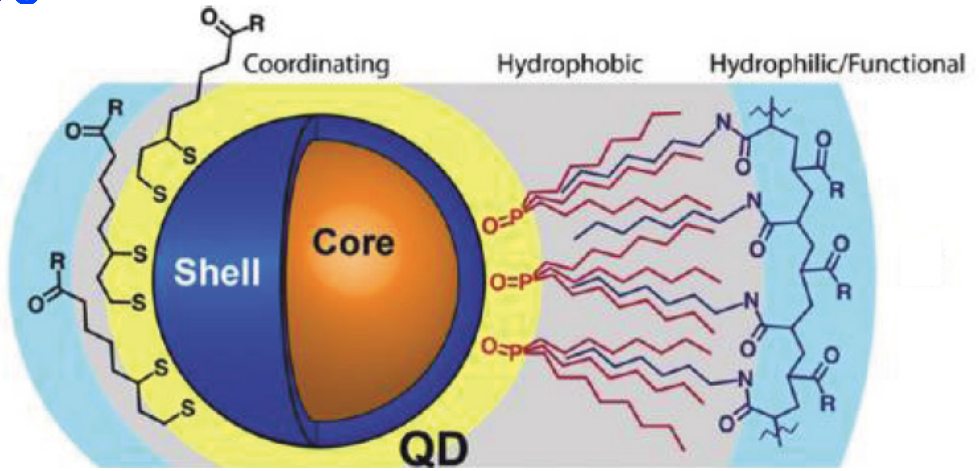
Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).



Naresh V, Lee N. A Review on Biosensors and Recent Development of Nanostructured Materials-Enabled Biosensors. *Sensors*. Feb 2021;21(4)1109. doi:10.3390/s21041109

What are Quantum Dots?

- *Colloidal semiconductor nano-crystals* with diameters in the range of 2-10 nanometers (10-50 atoms).
- These materials can be modified with biological moieties, and properties can be coupled with other molecules and NMs through both *bioconjugation* and *energy transfer (ET)* processes.
- Core, core-shell or core-multi-shell configuration.
- A semiconductor so small that the *size of the crystal* is on the same order as the size of the *Exciton Bohr Radius*.



Hildebrandt N, Spillmann CM, Algar WR, et al. Energy Transfer with Semiconductor Quantum Dot Bioconjugates: A Versatile Platform for Biosensing, Energy Harvesting, and Other Developing Applications. *Chemical Reviews.* 2017;117(2):536-711.

Definition of Exciton Pair & Bohr Radius…

- *Exciton Pair* is defined as an electron and the hole that it leaves behind when it is excited up to the conduction band.
- *Exciton Bohr Radius* is the average distance between the electron in the conduction band and the hole it leaves behind in the valence band.
- Electrons in quantum dots are confined in a small space called a *quantum box*.
- When the radii of the semiconductor nanocrystal is smaller than the Exciton Bohr Radius there is *quantization of the energy levels according to Pauli's exclusion principle*.

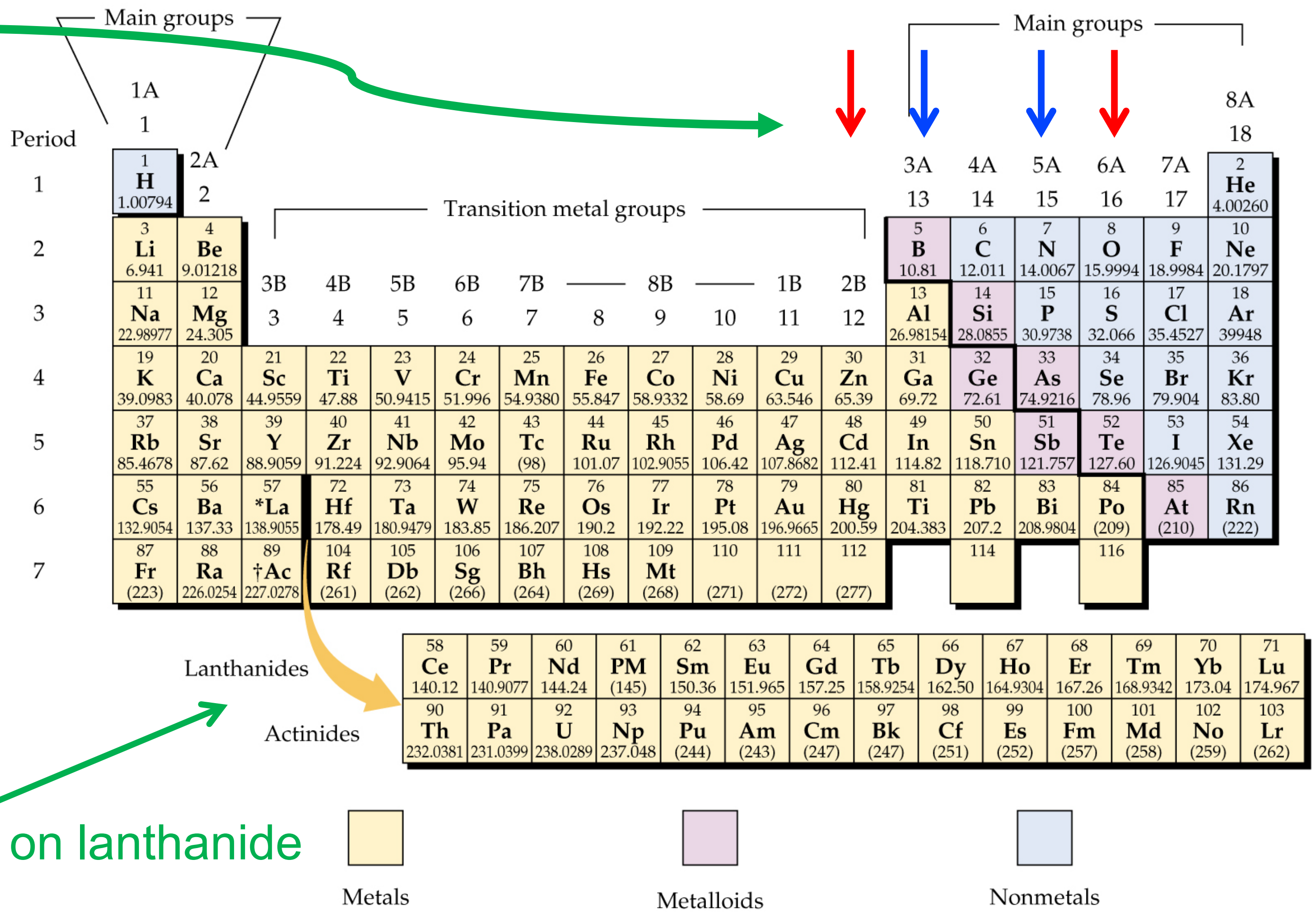
Millipore-Sigma https://www.sigmaaldrich.com/technical-documents/articles/materials-science/nanomaterials/quantum-dots.html

Elements for Quantum Dots…

Inorganic semiconductor crystals composed of members from groups: **2B & 6A** (e.g. **CdTe**, **CdSe**, **ZnS**) or **3A & 5A** (e.g. **InP**) elements.

Diameters from 2 to 10 nm (10-50 atoms).

Cd cadmium
Te tellurium
Se selenium
In indium
P phosphorus
S sulfur
Zn zinc



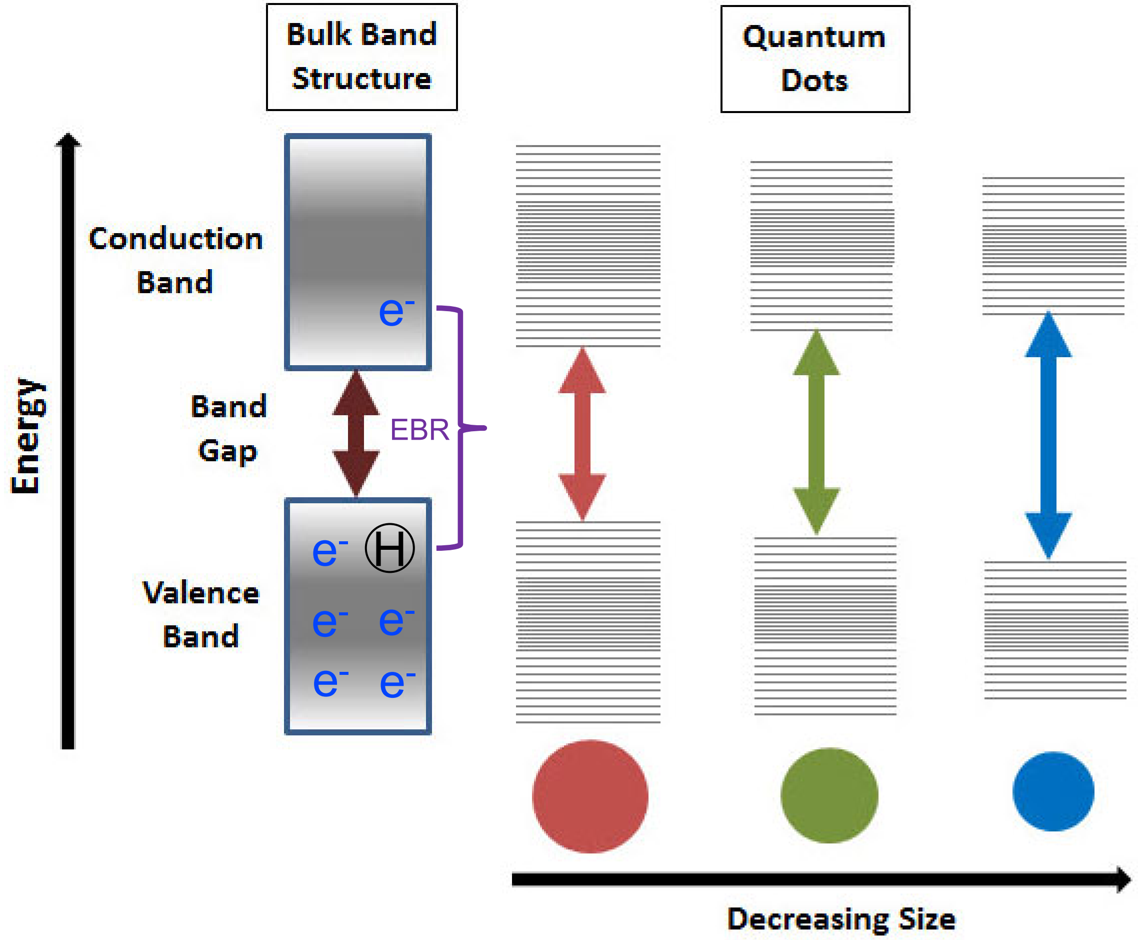
Later discussion on lanthanide nanoparticles.

Image courtesy of Prentice Hall, Inc.

Steven S. Saliterman

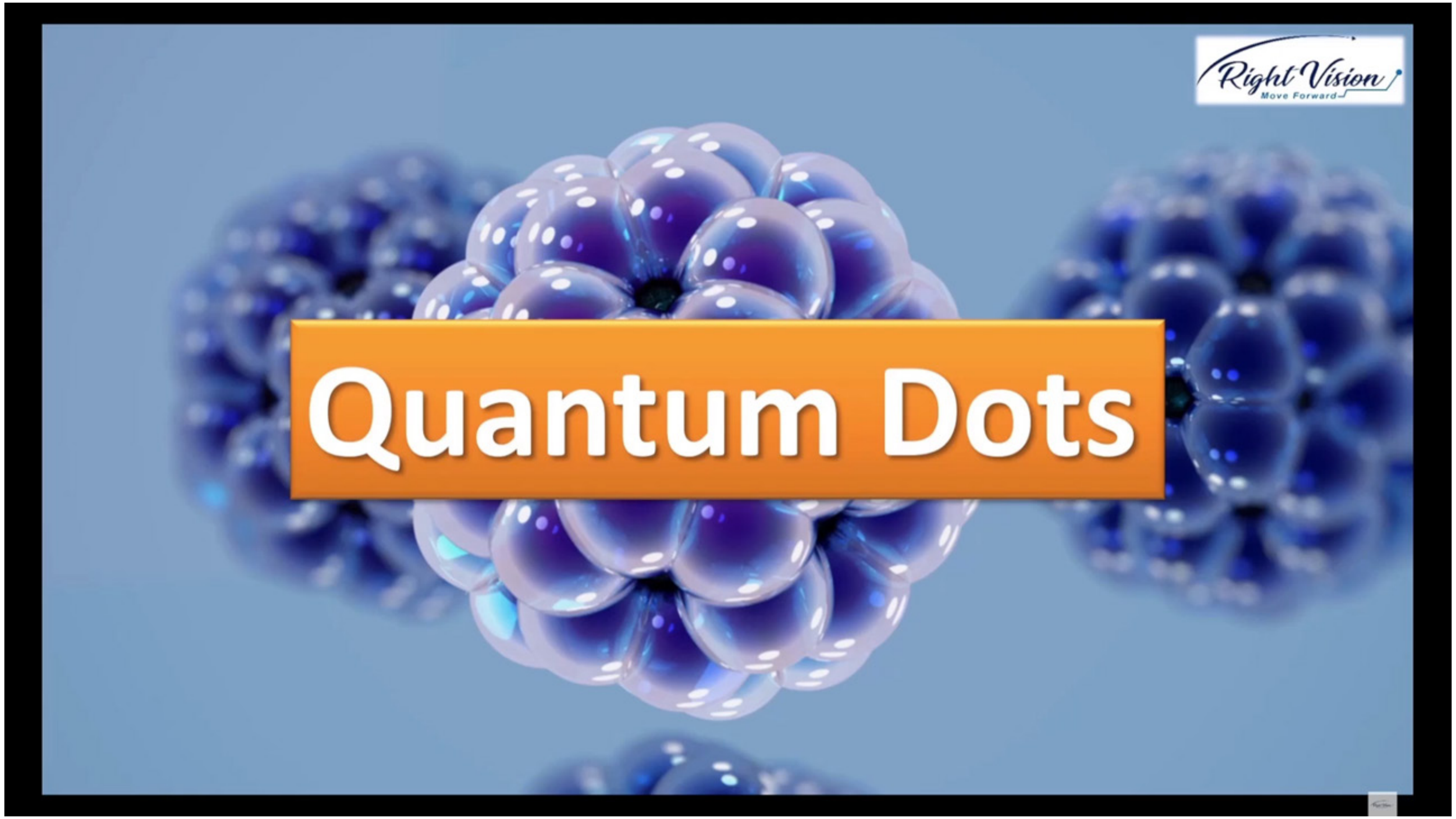
Discrete, Quantized Energy Levels…

- EBR – Exciton Bohr Radius.
- As the size of the crystal decreases, the difference in energy between the highest valence band and the lowest conduction band increases.
- More energy is then needed to excite the dot, and concurrently, more energy is released when the crystal returns to its ground state, resulting in a color shift from red to blue in the emitted light.



Millipore-Sigma https://www.sigmaaldrich.com/technical-documents/articles/materials-science/nanomaterials/quantum-dots.html

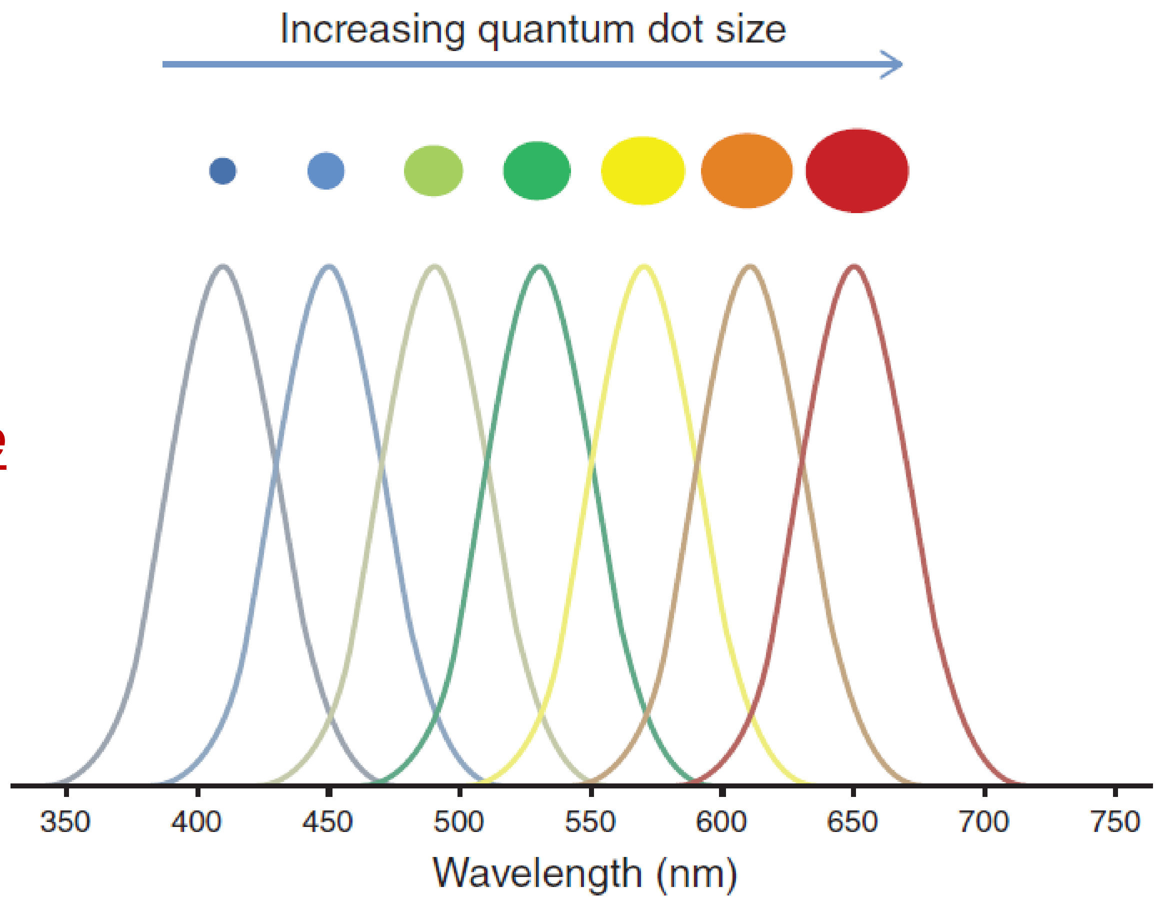
Quantum Dots…



https://youtu.be/0EokkhdppgE

Quantum Confinement…

- For a given material, the color can be tuned continuously across a broad spectral range through *quantum confinement* and control of *nanocrystal size*.
- *Quantum confinement* is the term used to describe changes in electronic properties *as the number of atoms in a crystal becomes small*.
- The onset of quantum confinement coincides with *crystal dimensionality* below the *Exciton Bohr Radius*, which is the preferred electron-hole separation, for a semiconductor material (~5 nm for CdSe).



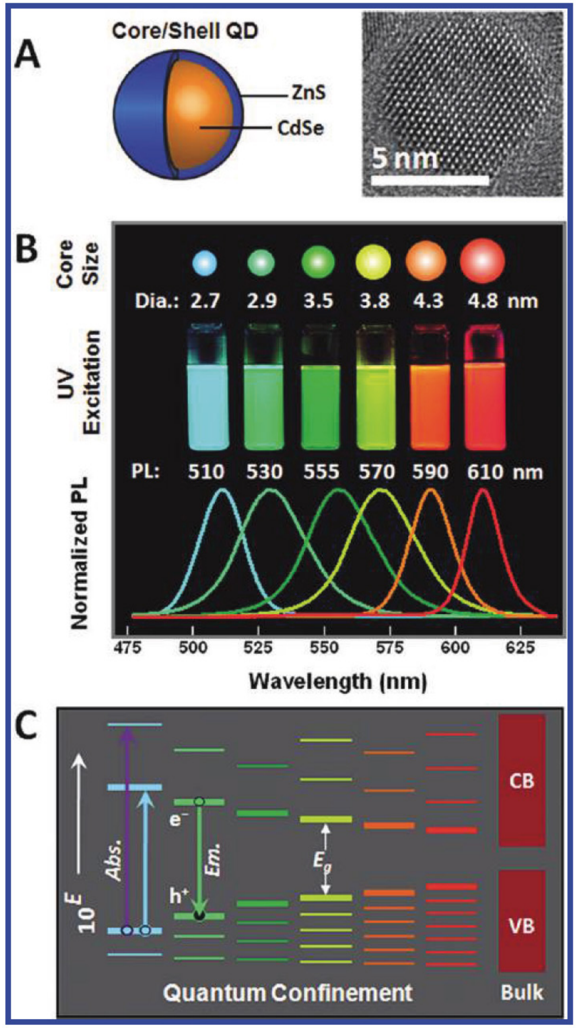
Algar WR, Susumu K, Delehanty JB, Medintz IL. Semiconductor Quantum Dots in Bioanalysis: Crossing the Valley of Death. *Analytical Chemistry.* 2011;83(23):8826-8837.
Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

Efficiency and Brightness…

- Growing shells of another *higher band gap semiconducting material* improves efficiency and brightness.
- Alloyed semiconductor quantum dots allow *tuning* of the optical and electronic properties by merely changing the composition and internal structure *without changing the crystallite size*.

Millipore-Sigma https://www.sigmaaldrich.com/technical-documents/articles/materials-science/nanomaterials/quantum-dots.html

Color & Nanocrystal Size…



a) Structure and TEM image of CdSe/ZnS.

b) PL (photoluminescence) spectra illustrating progressive color changes of CdSe/ZnS with *increasing nanocrystal size.*

c) Qualitative changes in QD energy levels with *increasing nanocrystal size.*

(Band gap energies, E_g, were estimated from PL spectra. Conduction (CB) and valence (VB) bands of bulk CdSe are shown for comparison. The energy scale is expanded as 10^E for clarity.)

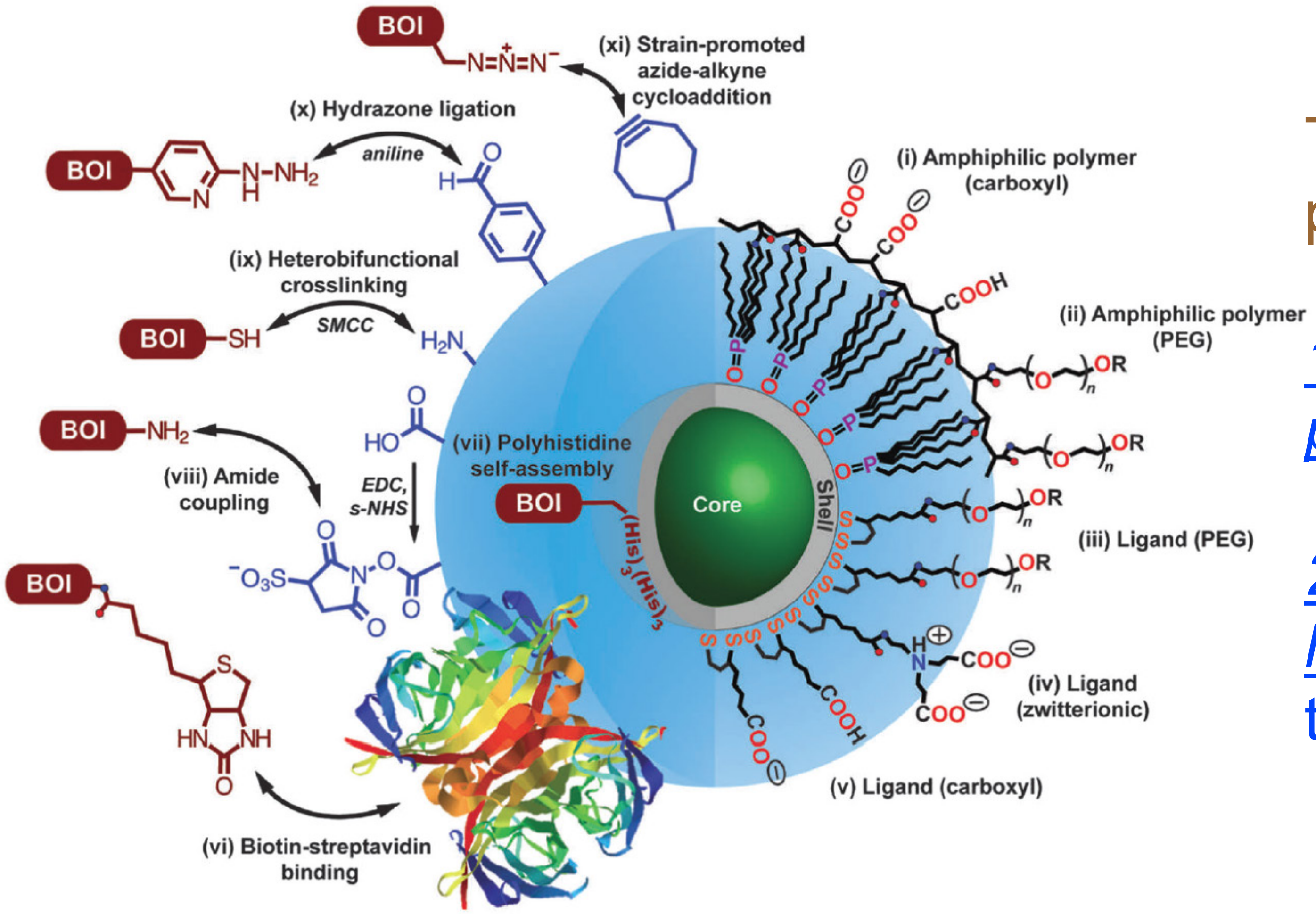
Algar WR, Susumu K, Delehanty JB, Medintz IL. Semiconductor Quantum Dots in Bioanalysis: Crossing the Valley of Death. *Analytical Chemistry.* 2011;83(23):8826-8837.

Use as Biosensors…

- QDs are coated with *organic molecules and macromolecules* to provide aqueous solubility and opportunities for *bioconjugation*.
  - These coatings can be broadly classified as *ligand-based* (e.g., mercaptopropionic acid and dihydrolipoic acid) or *polymer-based* (e.g., polyethylene glycol).
- Multiple QD labels can be excited by a single light source and emit light with *minimal spectral overlapping*.
  - This allows for multi-target assays without the added cost of filtering excitation light.
- QDs offer better spectral properties than traditional fluorescent dues, including *broad excitation spectrum, negligible photobleaching, and a tunable, symmetric and narrow emission spectrum.*

Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

Strategies for Bioconjugation & Surface Coating…



Two surface coating strategies are presented:

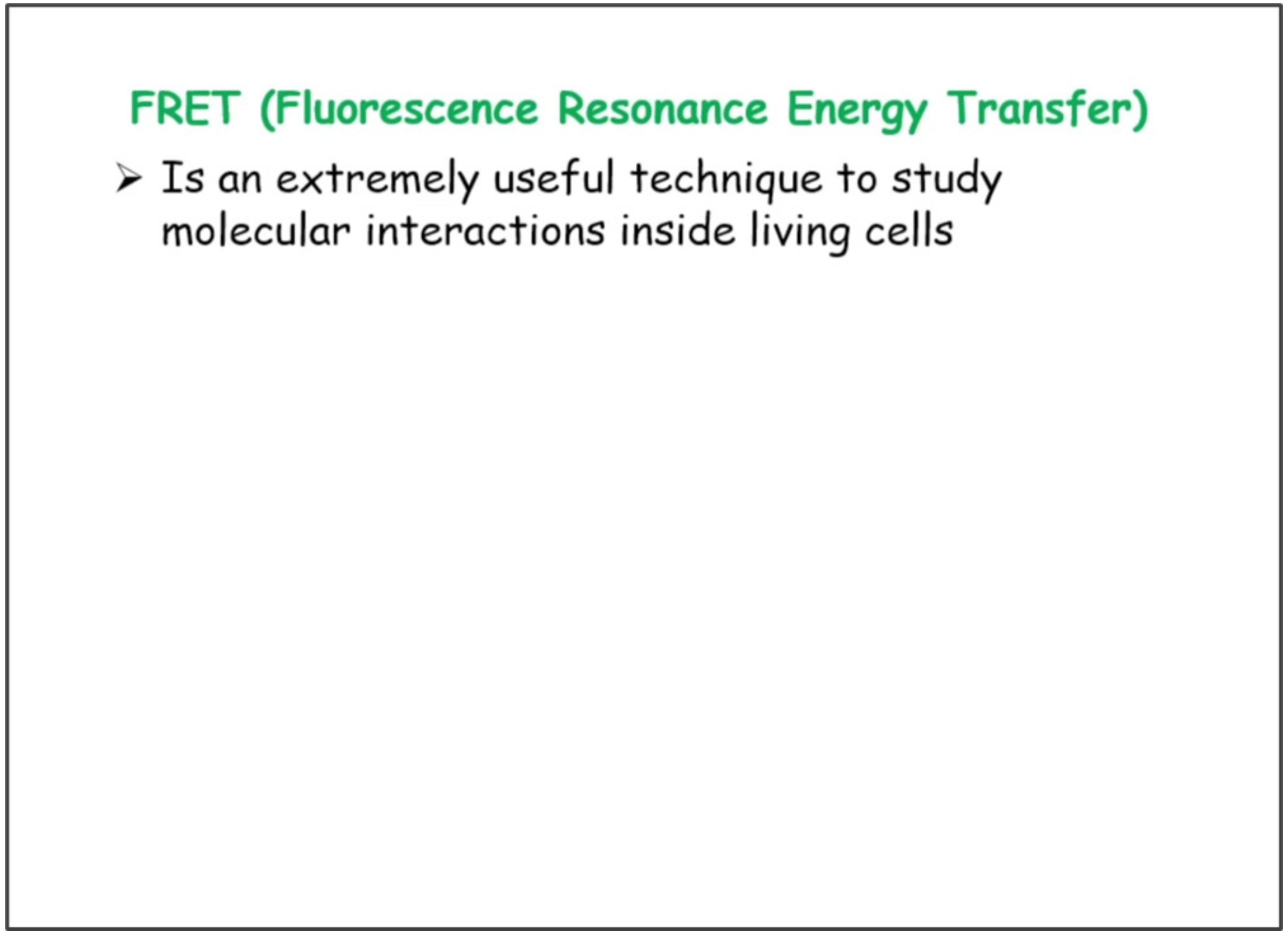
1. encapsulation with amphiphilic polymers (i, ii) and

2. cap exchange with hydrophilic ligands exploiting the thiol-affinity of the ZnS shell of the QD (iii–v).

Petryayeva E, Algar WR, Medintz IL. Quantum Dots in Bioanalysis: A Review of Applications Across Various Platforms for Fluorescence Spectroscopy and Imaging. *Applied Spectroscopy.* 2013;67(3):215-252.

FRET – Fluorescence Resonance Energy Transfer

Movie:

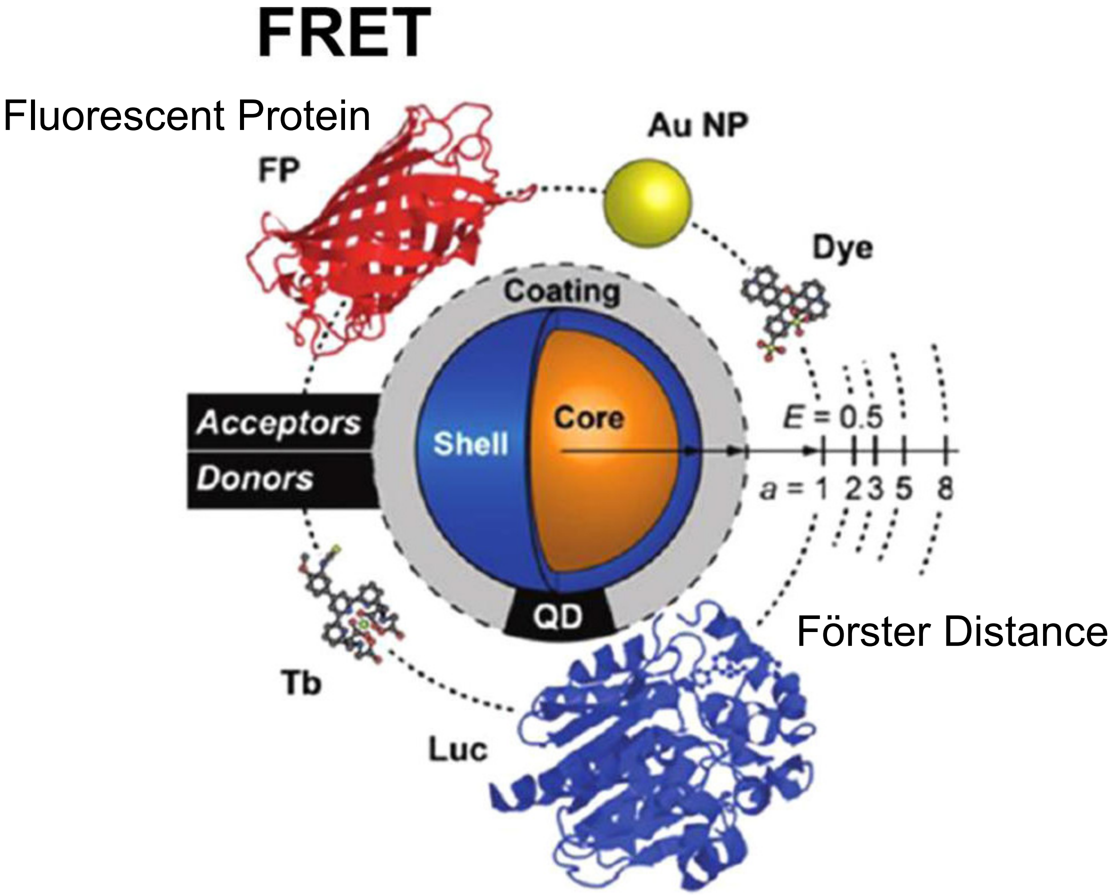


FRET is also called *Förster Resonance Energy Transfer*

https://youtu.be/qwMdtqgdap0

QD Förster Resonance Energy Transfer (FRET)…

- Semiconductor QDs engage in both *Förster resonance energy transfer* (FRET) and *electron/charge transfer* (ET & CT).
- QDs are good FRET *donors* for fluorescent protein (FP), dye, and gold nanoparticle (AuNP) acceptors.
- QDs can function as *acceptors* for long-lifetime terbium (Tb) complexes and bioluminescent luciferase enzyme (Luc) donors.



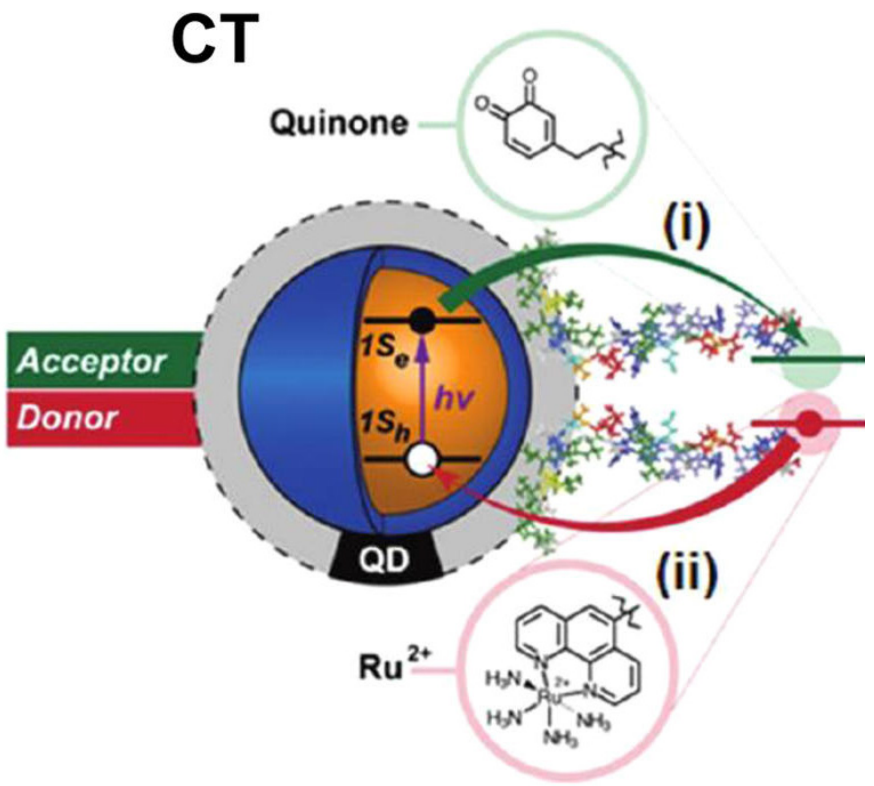
Algar WR, Susumu K, Delehanty JB, Medintz IL. Semiconductor Quantum Dots in Bioanalysis: Crossing the Valley of Death. *Analytical Chemistry.* 2011;83(23):8826-8837.
Hildebrandt N, Spillmann CM, Algar WR, et al. Energy Transfer with Semiconductor Quantum Dot Bioconjugates: A Versatile Platform for Biosensing, Energy Harvesting, and Other Developing Applications. *Chemical Reviews.* 2017;117(2):536-711.

QD Charge Transfer (CT)…

CT quenching is an alternative method of modulating QD photoluminescence:

i. An *electron acceptor* (e.g., quinone) has an unoccupied energy level intermediate in energy to the 1Sh and 1Se band-edge states to which the excited QD transfers an electron,

ii. An *electron donor* (e.g., ruthenium phenanthroline-Ru2+) has an occupied intermediate energy level and transfers an electron to the QD.



Charge transfer inhibits radiative recombination of the exciton.

Algar WR, Susumu K, Delehanty JB, Medintz IL. Semiconductor Quantum Dots in Bioanalysis: Crossing the Valley of Death. *Analytical Chemistry.* 2011;83(23):8826-8837.

Hildebrandt N, Spillmann CM, Algar WR, et al. Energy Transfer with Semiconductor Quantum Dot Bioconjugates: A Versatile Platform for Biosensing, Energy Harvesting, and Other Developing Applications. *Chemical Reviews.* 2017;117(2):536-711.

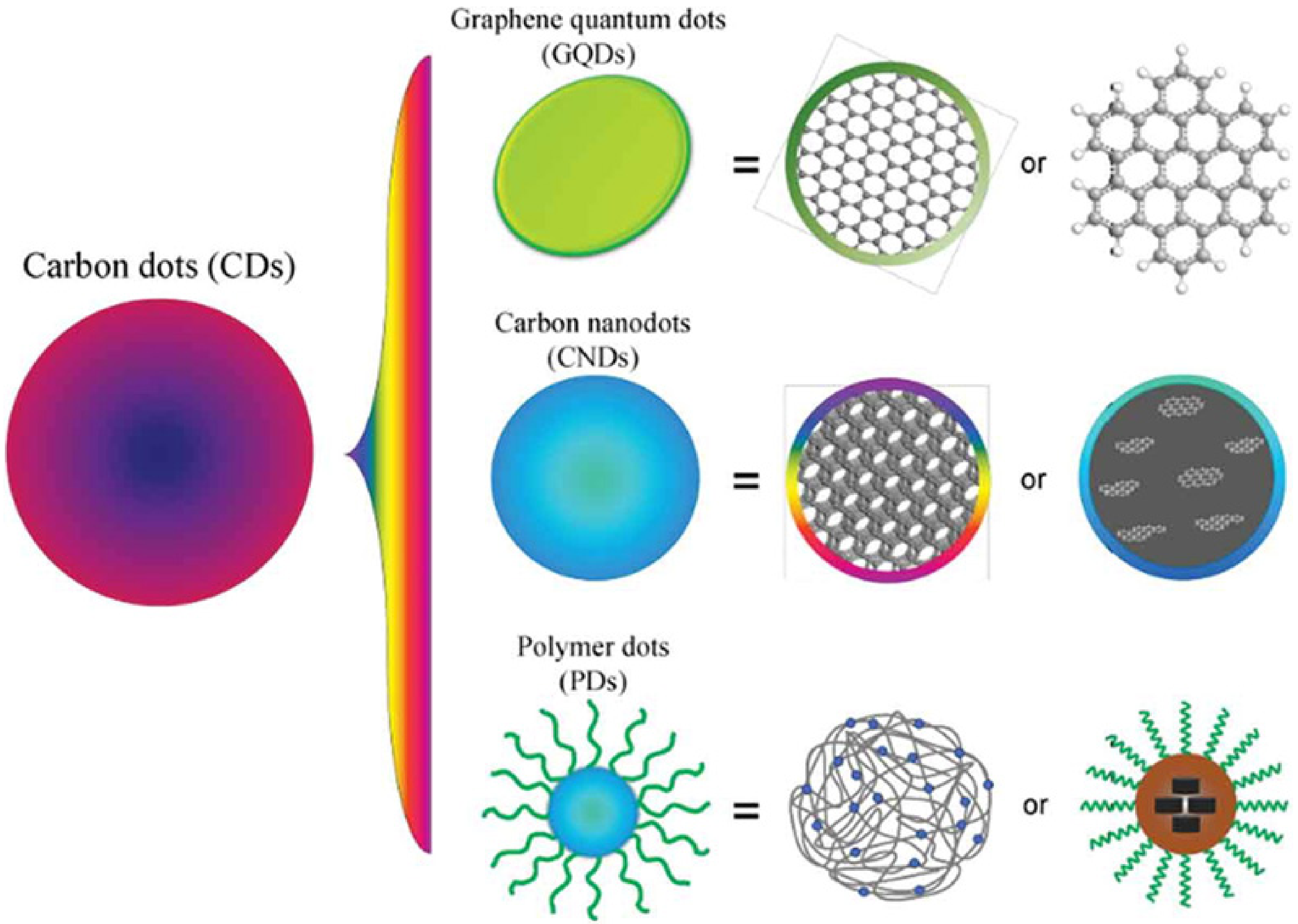
Requirements for ET…

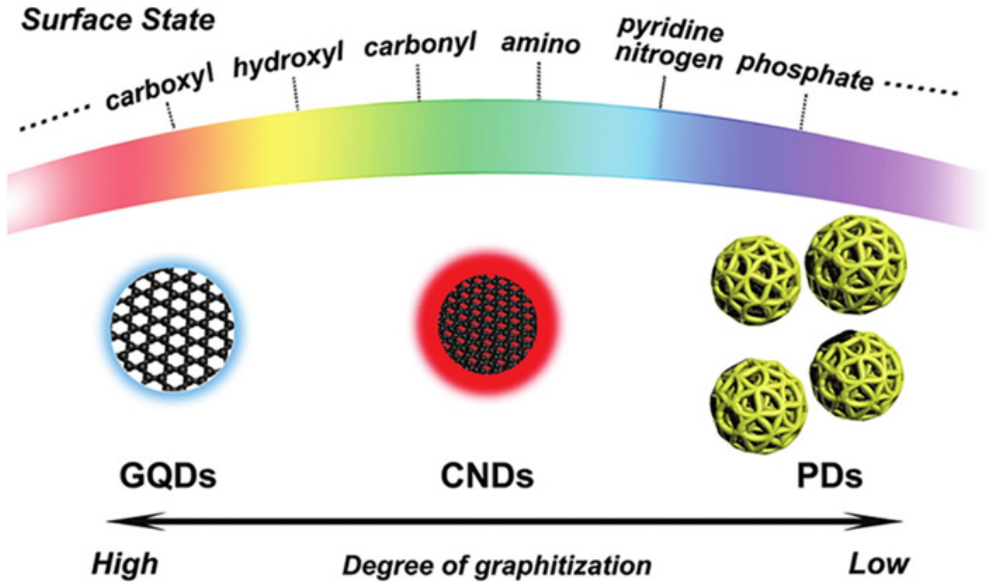
- The ability of QDs to engage in FRET, FRET-based biosensing, and other forms of ET directly depend on:
  - Type and quality of QD material used.
  - Photophysical properties.
  - How the QD was colloidally stabilized in aqueous media and made biocompatible (which, in turn, reflects the choice of surface ligand type utilized).
  - How the QD was modified with it; and how the bioconjugate structure was formed along with its intrinsic physicochemical properties.

Hildebrandt N, Spillmann CM, Algar WR, et al. Energy Transfer with Semiconductor Quantum Dot Bioconjugates: A Versatile Platform for Biosensing, Energy Harvesting, and Other Developing Applications. *Chemical Reviews.* 2017;117(2):536-711.

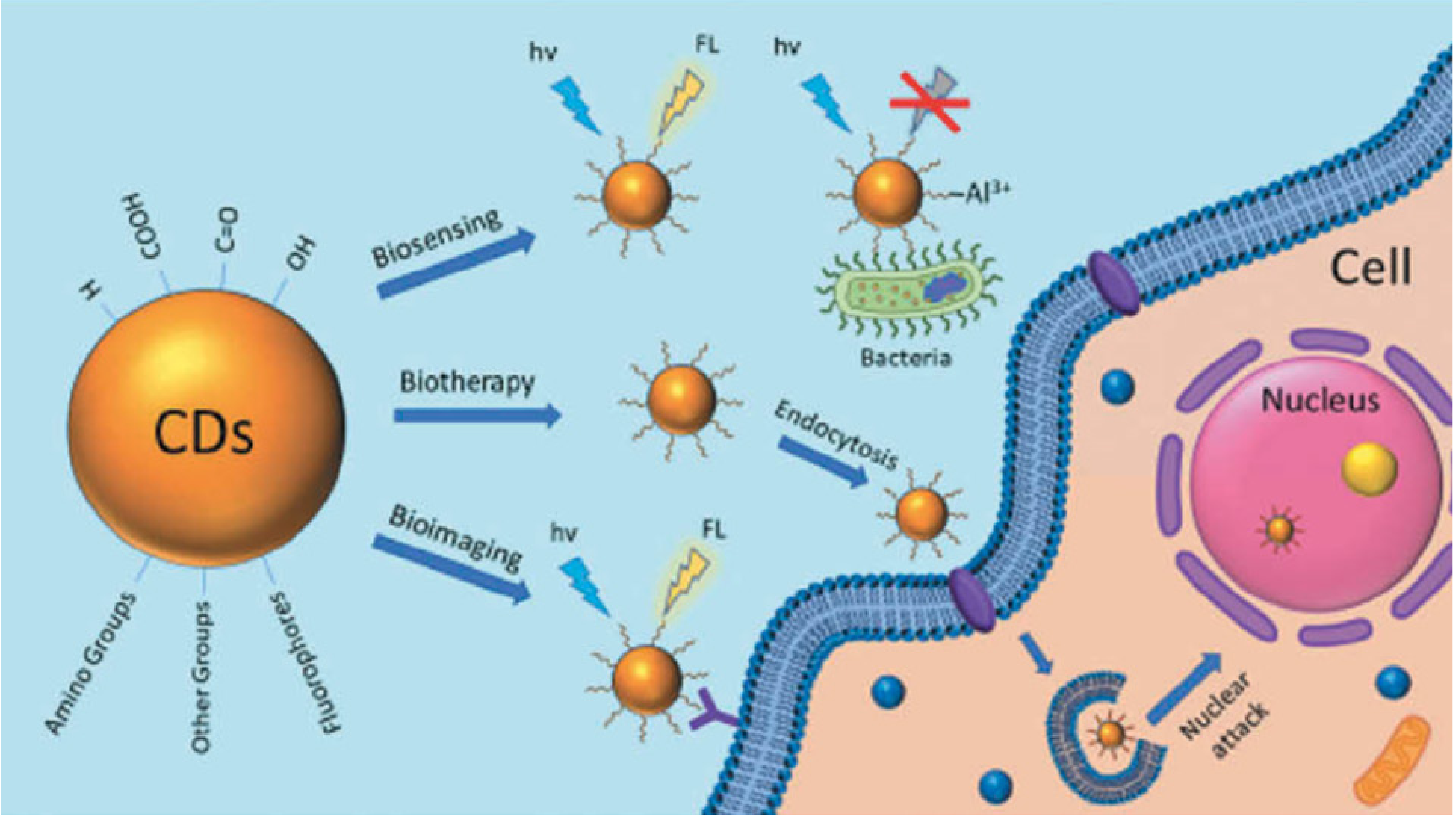
Carbon Quantum Dots

- Carbon dots are small carbon nanoparticles, whereas quantum dots are small semiconductor particles.
- Fluorescent labels for DNA, aptamers, proteins, glucose, phosphate, metal ions, etc.
- Size <10 nm.
- No toxic heavy metals.
- Classified based on the carbon cores – nanodot, graphene quantum dots and polymer dots.



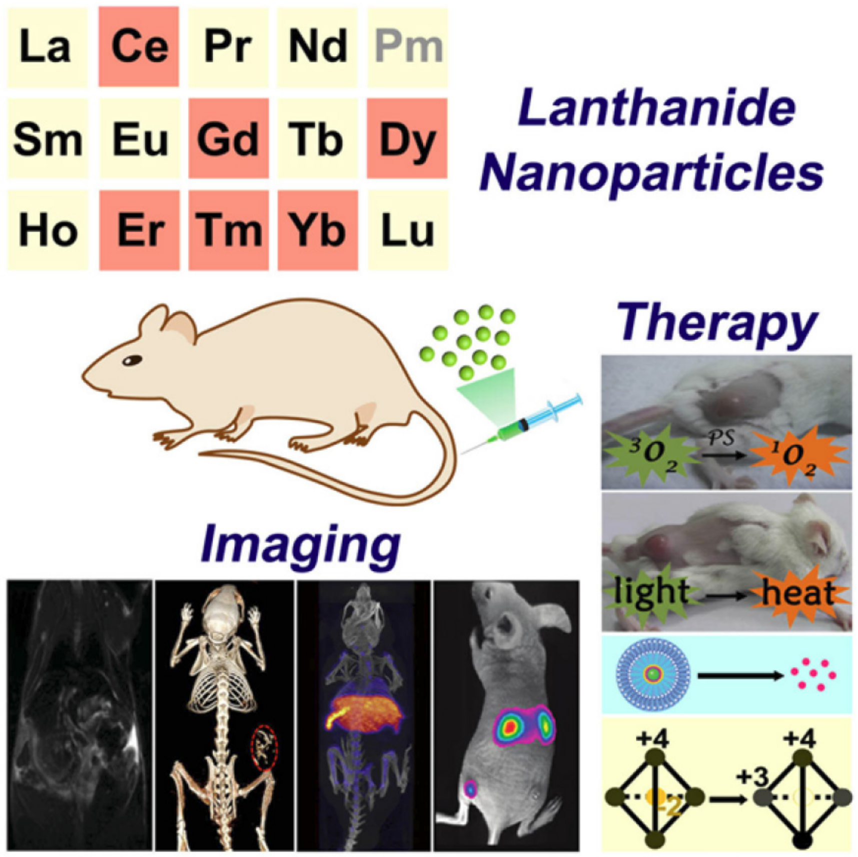


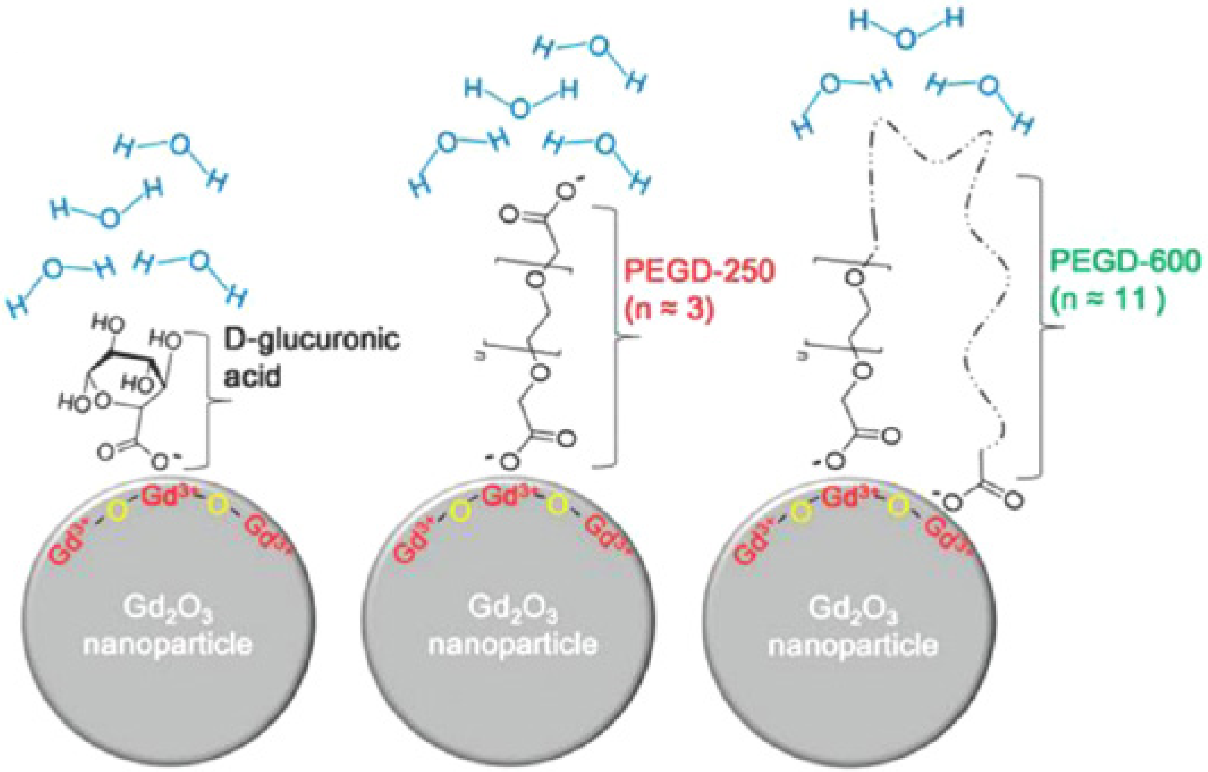
Koutsogiannis P, Thomou E, Stamatis H, Gournis D, Rudolf P. Advances in fluorescent carbon dots for biomedical applications. *Advances in Physics-X*. Jan 2020;5(1)1758592. doi:10.1080/23746149.2020.1758592
.



Koutsogiannis P, Thomou E, Stamatis H, Gournis D, Rudolf P. Advances in fluorescent carbon dots for biomedical applications. *Advances in Physics-X*. Jan 2020;5(1)1758592. doi:10.1080/23746149.2020.1758592
.

Lanthanide Nanoparticles





D-glucuronic acid, PEGD-250, and PEGD-600 on the ultrasmall Gd_2O_3 NPs

Steven S. Saliterman

Dong H, Du SR, Zheng XY, et al. Lanthanide Nanoparticles: From Design toward Bioimaging and Therapy. *Chemical Reviews*. Oct 2015;115(19):10725-10815. doi:10.1021/acs.chemrev.5b00091
.

- Lanthanide luminescent nanoparticles are composed of ions from elements located in the sixth period and IIIB group in the periodic table.
  - The key feature of lanthanide luminescence is that lanthanide ions have *exceedingly long-lived luminescence (μs to ms range), as opposed to conventional dyes that luminesce on the nanosecond scale.*
- *Enhanced sensitivity* of lanthanide materials makes them popular *alternatives to conventional fluorescent dyes* for use in diagnostics.

Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

Lanthanide luminescent nanoparticles.
3B plus lanthanide series.

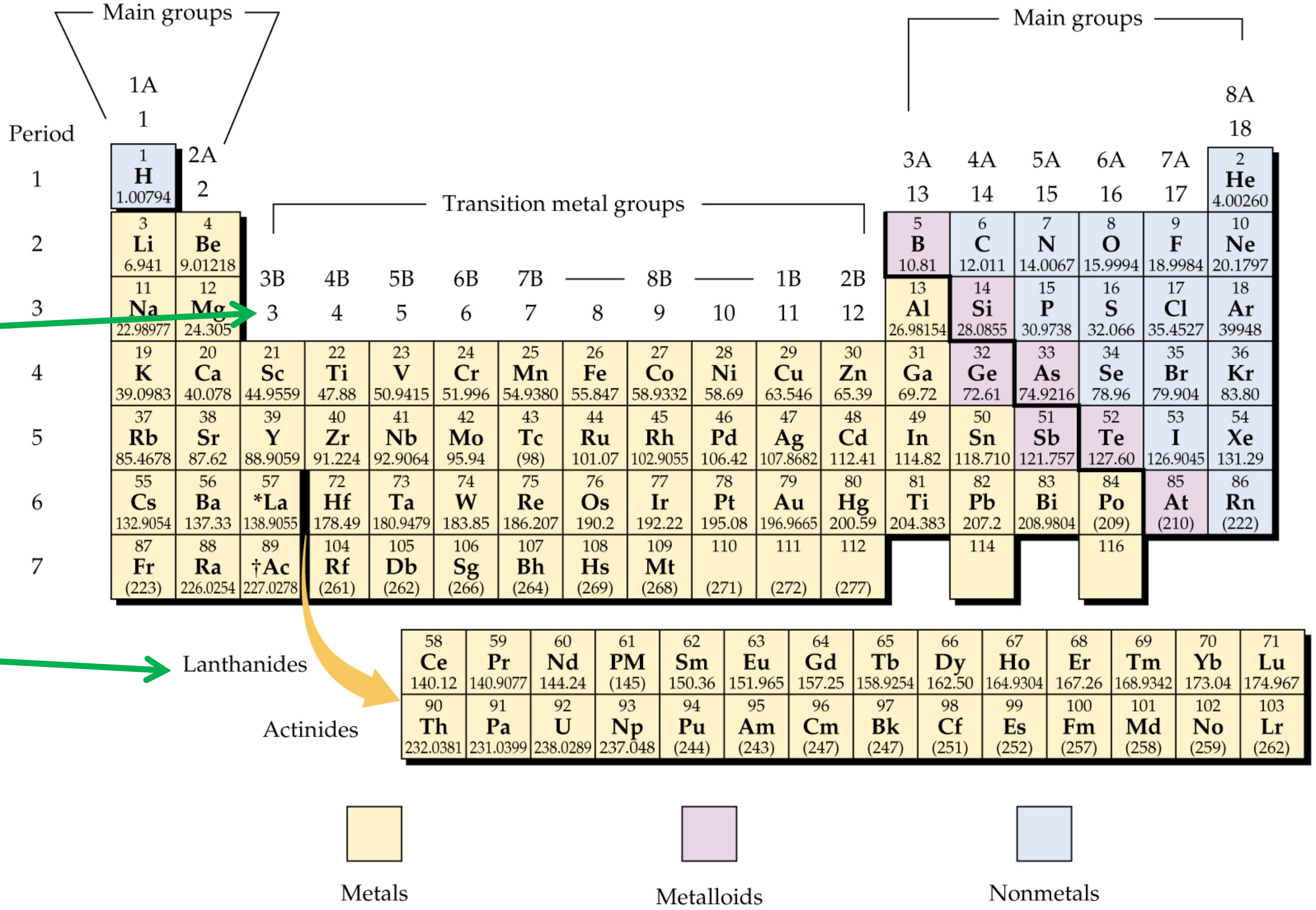


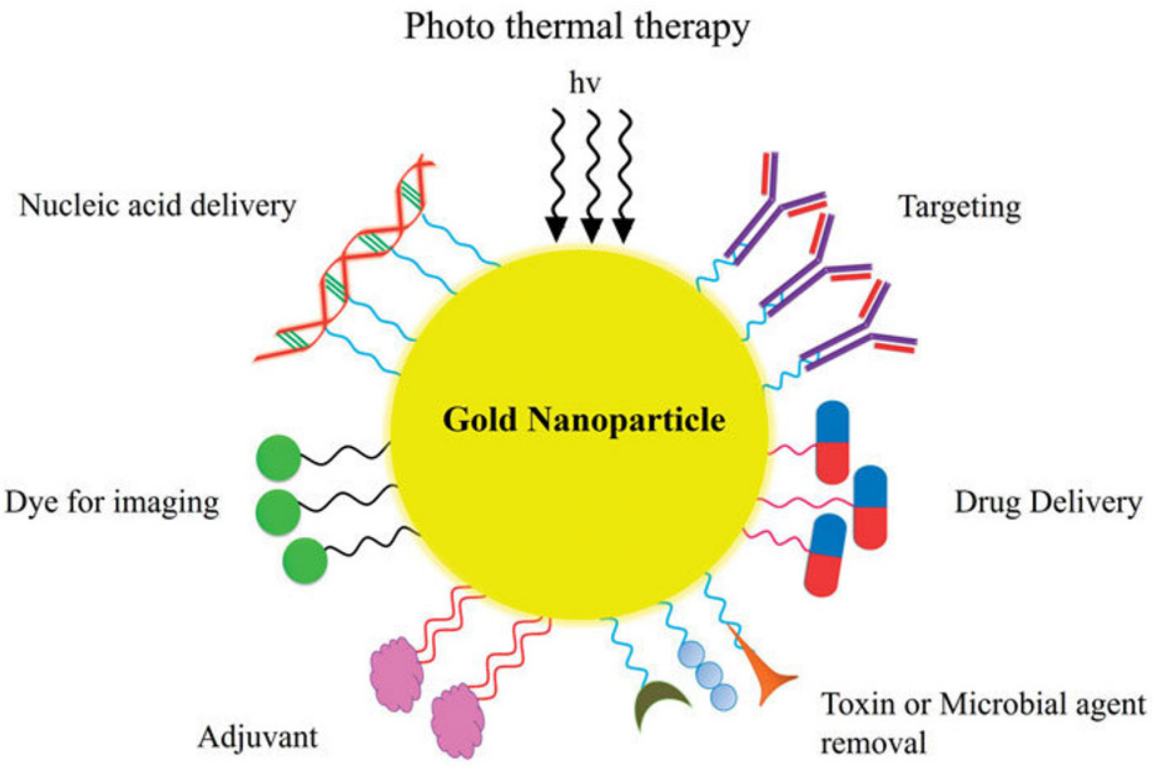
Image courtesy of Prentice Hall, Inc.

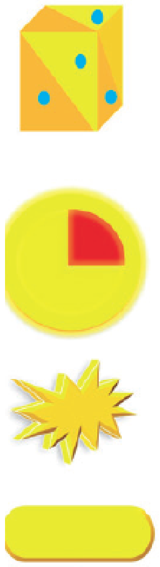
- Coupled with time resolved fluorometery (TRF) gives lanthanide based labels the *unique ability to be probed after the extinction of luminescence from background noise.*
  - This leads to improved ability to resolve analyte signal at lower concentrations where back-ground noise would normally suppress that signal.
- Lanthanide based probes also exhibit excellent *photostability*, *large Stokes shift* (>150 nm), and *sharp-band emissions* (<10 nm full width at half-maximum)

Gold Nanoparticles (Noble Metals)

- Gold nanoparticles (AuNPs) are small gold particles with a diameter of 1 to 100 nm which, once dispersed in water, are also known as *colloidal gold*.
  - *Gold* and *silver* nanoparticles have been studied extensively for use with local surface plasmon resonance (LSPR).
- This appears as an absorption peak in the visible spectra .
- *Nanoclusters* show superior *biocompatibility*.
  - Yet comparable to QDs in terms of their size dependent emissions, strong photoluminescence, and photostability.

Applications…



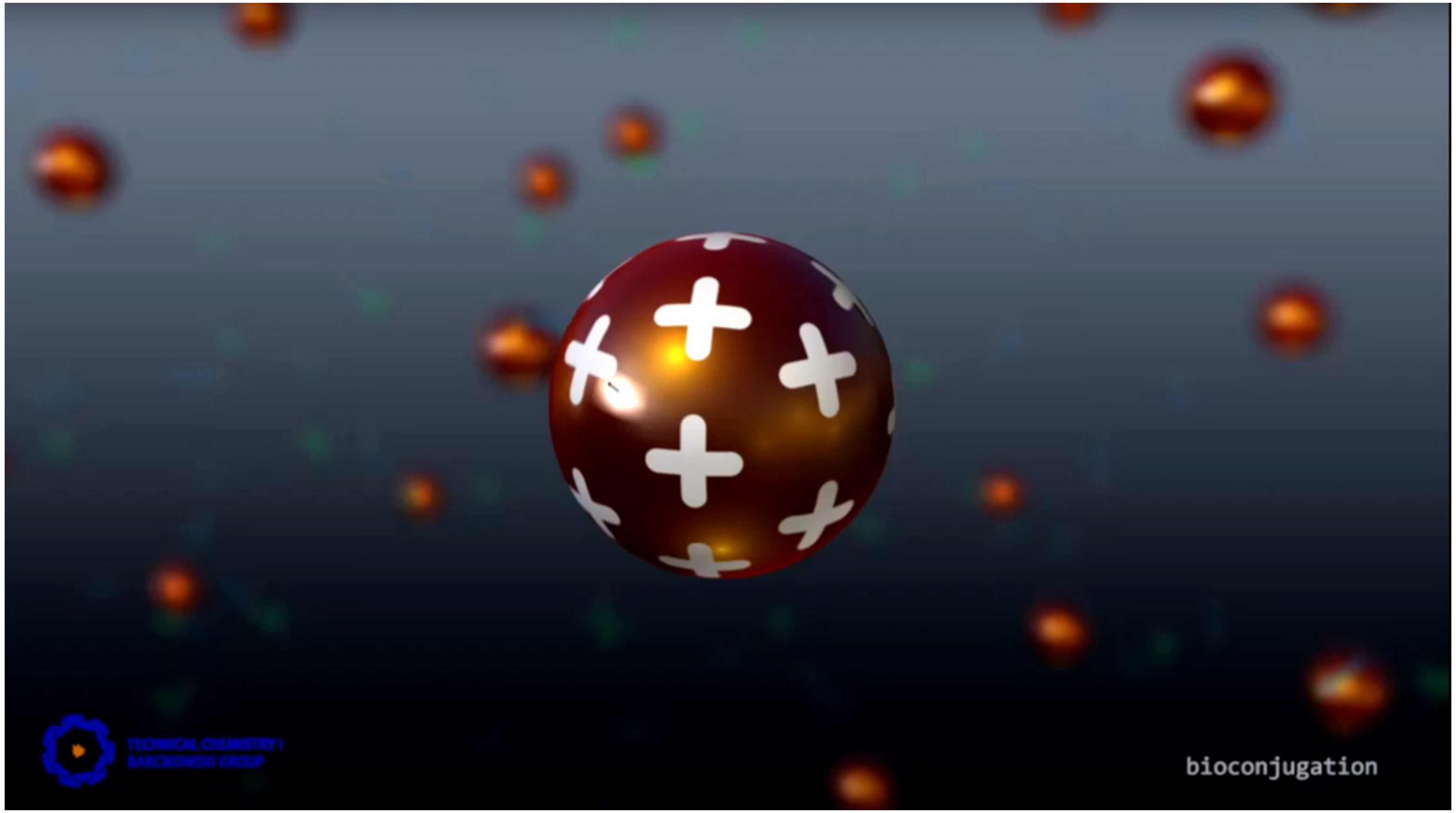


AuNP	Size	Application
Nanocages	40×60nm	Drug loading
Nanoshell	50nm	Toxic drug delivery and Bioimaging
Nanostars	45-120 nm	Bioconjugation
Nanorods	10×40 nm	Immunomagnetic separation and Particle Diffusion

Examples of AuNPs used in phototherapy.

Bagheri S, Yasemi M, Safaie-Qamsari E, et al. Using gold nanoparticles in diagnosis and treatment of melanoma cancer. *Artificial Cells Nanomedicine and Biotechnology*. 2018;46:S462-S471. doi:10.1080/21691401.2018.1430585
.

Gold Nanoparticle Bioconjugation…



https://www.youtube.com/watch?v=-0qfa65hI8M

Features…

- Nobel metal nanoparticles can have a *metal core* consisting of one element, *or* be composed *with a shell* of a different metal (i.e., gold-silver core-shell nanoparticles).
  - These *bimetallic nanoparticles* have the advantage of taking properties from both metals to enhance their optical and electronic properties over monometallic nanoparticles.
- At sizes smaller than 3 nm noble metal nanoparticles are called nanoclusters.
  - Nanoclusters do not display SPR absorption in the visible region, but possess fluorescence emission in the near-infrared to visible region.
  - The *wavelength of emission* can be *tuned* by controlling the size of the cluster, making nanoclusters very useful fluorescent biosensor labels.

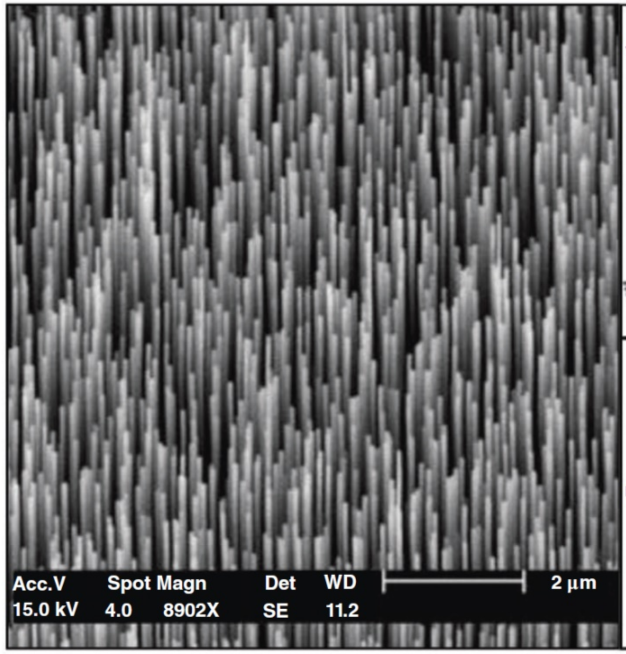
Label-Free Transduction

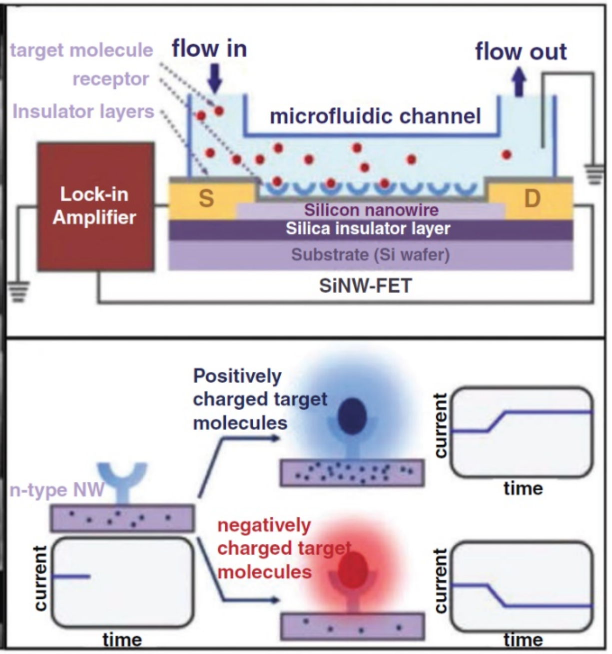
- Nano wires
- Nanotubes
- Nanocantilevers

Nanowires

- Silicon nanowires (SiNWs) are high aspect ratio wires that typically have a diameter of <100 nm, and have been employed recently in highly sensitive microfluidic detection platforms for nucleic acids. Recall FETs:

SEM image of the nitrogen-doped ZnO nanowire array.





SiNW-FET integrated into a microfluidic device for biosensing.

Steven S. Saliterman

Shen, M.-Y., Li, B.-R., & Li, Y.-K. (2014). Silicon nanowire field-effect-transistor based biosensors: From sensitive to ultra-sensitive. Biosensors and Bioelectronics, 60, 101–111. https://doi.org/10.1016/j.bios.2014.03.057.

Attachment Options…

1. Electrostatic Absorption
   - Employs electrostatic attraction to absorb ionic species onto oppositely charged absorbents and has been successfully applied for capturing DNA with negatively charged oligo probes linked to an amine-terminated layer on the nanowire.
2. Covalent Bonding
   - Silane chemistry is used to introduce amino terminal groups on the SiNW surface that react with aldehyde, carboxylic acid, and epoxy groups present on proteins and other biomolecules

Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

Features…

- Charged biomolecules bind to the surface of the nanowire and alter its electric field.
- Quantum confinement is possible with diameters less 2.2 nm.
- A single binding event may cause sufficient charge leading to *depletion or accumulation* of carriers throughout a much larger percentage of the conducting channel cross-section.
- *Dopants or addition of Au or Ag nanoparticles increases sensitivity.*

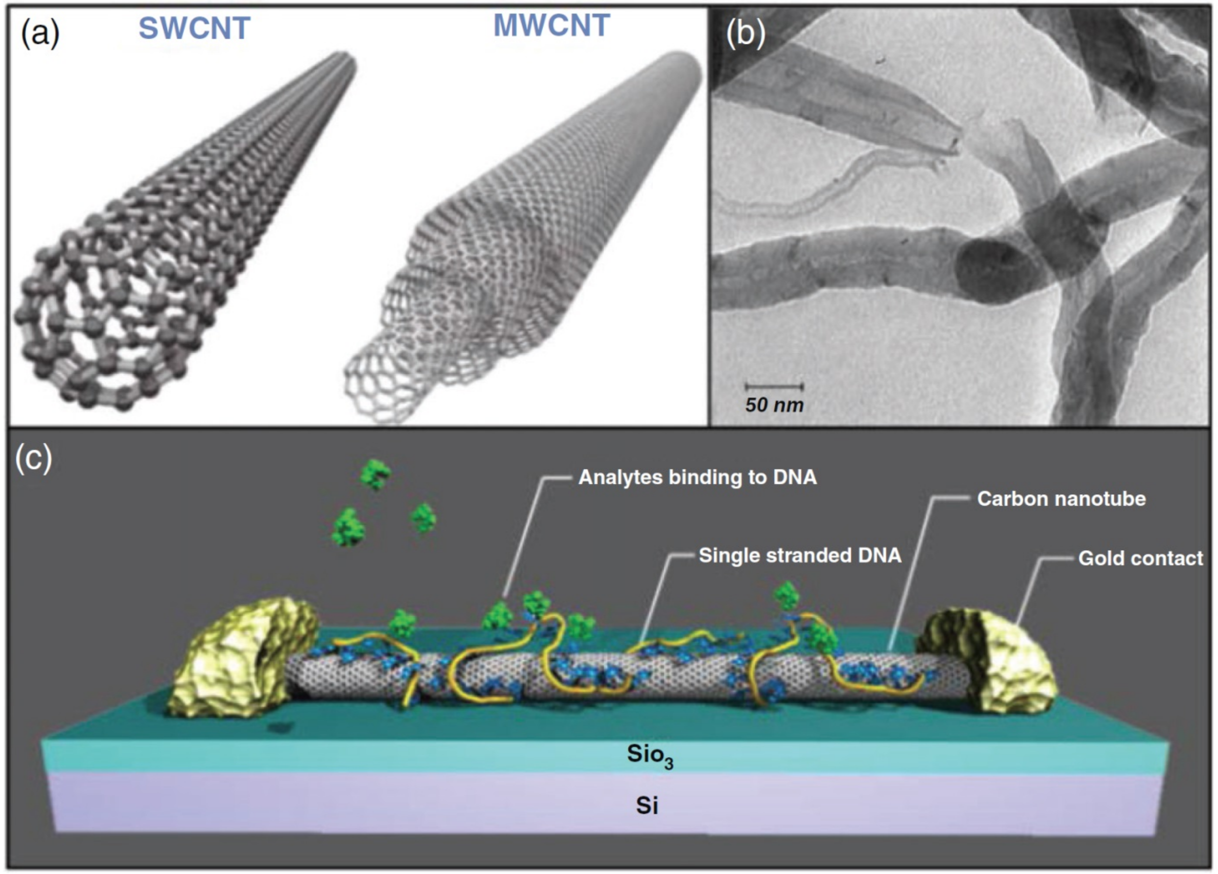
Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

Nanotubes

Hollow cylindrical tubes made up of carbon atoms.

a) Single-walled carbon nanotube (SWCNT) and multiwalled carbon nanotube (MWCNT).
b) TEM images of MWCNTs.
c) A graphic of a DNA functionalized CNT field effect transistor.

Dimensions from 1-100 nm x centimeters



a) Gajewiczet et al. (2012).; b) Abbasi, Zebarjad, Baghban, and Youssefi (2015); c) Johnson (2017).

Features…

- High aspect ratio, high conductivity, high mechanical strength, and biocompatibility make them excellent electrode materials for use in biosensors.
- SWCNTS can act as either semi-conducting, or metallic in nature depending on the chirality of the structure, while MWCNTS will exhibit metallic behavior if only a single layer within is metallic.
- *Fabricated by three techniques: laser ablation, electric arc discharge, and chemical vapor deposition.*

Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

- The most common functionalization strategy is to treat the CNTs with *acids to expose oxides* on the surface.
  - These carboxylates can be linked to the amino groups on nucleotides or proteins using a carbodimide procedure.
    - This reduces van der Waals interactions, improving dispensability and solubility.
    - Also leads to decreased electron transport critical to biosensor sensitivity.
- Often integrated into FETs and used as electrochemical sensors for DNA, proteins, cells, and other pathogen biomarkers.

Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

Nanocantilevers

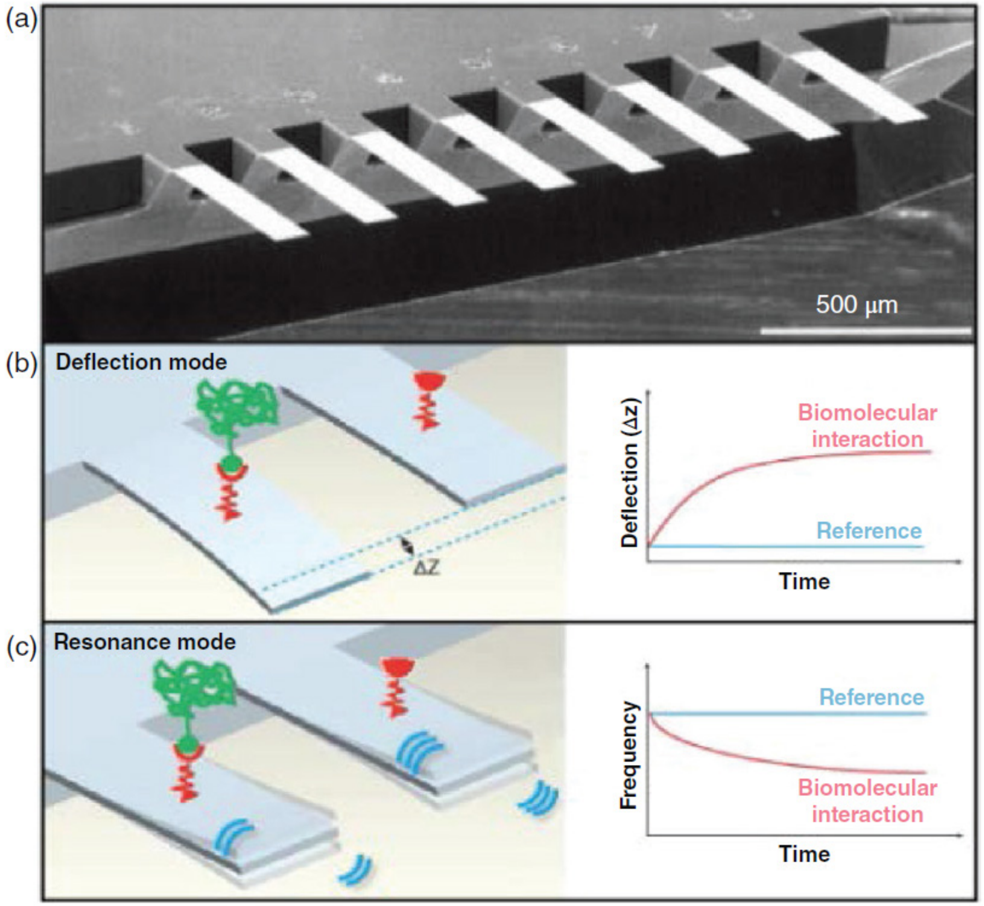
Nanocantilevers are flexible beams typically constructed of silicon, silicon nitride, or quartz that are clamped on one side.

a) Cantilever array based artificial nose .

Two modes of cantilever-based biomolecule detection:

b) Deflection mode.

c) Resonance mode.



a) Baller, M. K., Lang, H. P., Fritz, J., Gerber, C., Gimzewsk, J. K., Drechsler, U., … Guntherodt, H. J. (2000). A cantilever array-based artificial nose. Ultramicroscopy, 82(1–4), 1–9. https://doi.org/10.1016/S0304-3991(99)00123-0
b, c) Hwang, K. S., Lee, S. M., Kim, S. K., Lee, J. H., & Kim, T. S. (2009). Micro- and nanocantilever devices and systems for biomolecule detection. Annual Review of Analytical Chemistry, 2,77–98. https://doi.org/10.1146/annurev-anchem-060908-155232.

Features…

- Beams are functionalized with biorecognition elements to absorb target analytes if they are present in sample.
  - The analyte adds mass to the beam which affects the beams conformational or *resonant* properties.
- Nanoscale dimensions results in better sensitivity and increased surface-to-volume ratio which enhances the target capture efficiency.

Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

Types of Cantilevers…

- Static Devices
  - An analyte binds to the beam causing surface stress that deflects the beam up or down proportional to the amount of target. Detectable by reflected laser light or piezoelectrically.
  - Able to operate in a variety of buffers.
- Dynamic Excitation Devices
  - the cantilever is *actuated* and the added mass of captured target will produce a shift in the cantilever's resonant frequency.
  - Lower limits of detection compared to static.
  - Aqueous buffers dampen the signal.

Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

Summary

- Nanoparticle transducers:
  - Quantum dots.
  - Carbon dots.
  - Lanthanide nanoparticles.
  - Gold nanoparticles.
- Label free transducers
  - Nanowires
  - Nanotubes
  - Nanocantilevers
- Appendix:
  - Carbon dots for SNP recognition.
  - Mesoporous membranes.

Further Reading…

CHEMICAL REVIEWS

ACS AuthorChoice

Review

pubs.acs.org/CR

Energy Transfer with Semiconductor Quantum Dot Bioconjugates: A Versatile Platform for Biosensing, Energy Harvesting, and Other Developing Applications

Niko Hildebrandt,[§,○] Christopher M. Spillmann,[†,○] W. Russ Algar,[‖,○] Thomas Pons,[⊥] Michael H. Stewart,[‡] Eunkeu Oh,[‡,#] Kimihiro Susumu,[‡,#] Sebastian A. Díaz,[†,▽] James B. Delehanty,[†] and Igor L. Medintz[*,†]

[†]Center for Bio/Molecular Science and Engineering, Code 6900, and [‡]Optical Sciences Division, Code 5600, U.S. Naval Research Laboratory, Washington, DC 20375, United States

[§]NanoBioPhotonics Institut d'Electronique Fondamentale (I2BC), Université Paris-Saclay, Université Paris-Sud, CNRS, 91400 Orsay, France

[‖]Department of Chemistry, University of British Columbia, Vancouver, BC V6T 1Z1, Canada

[⊥]LPEM; ESPCI Paris, PSL Research University; CNRS; Sorbonne Universités, UPMC, F-75005 Paris, France

[#]Sotera Defense Solutions, Inc., Columbia, Maryland 21046, United States

[▽]American Society for Engineering Education, Washington, DC 20036, United States

CHEMICAL REVIEWS

Review

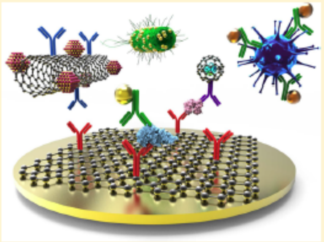
pubs.acs.org/CR

Nanoparticle-Based Immunochemical Biosensors and Assays: Recent Advances and Challenges

Zdeněk Farka,[†] Tomáš Juřík,[†,‡] David Kovář,[†] Libuše Trnková,[§] and Petr Skládal[*,†,‡]

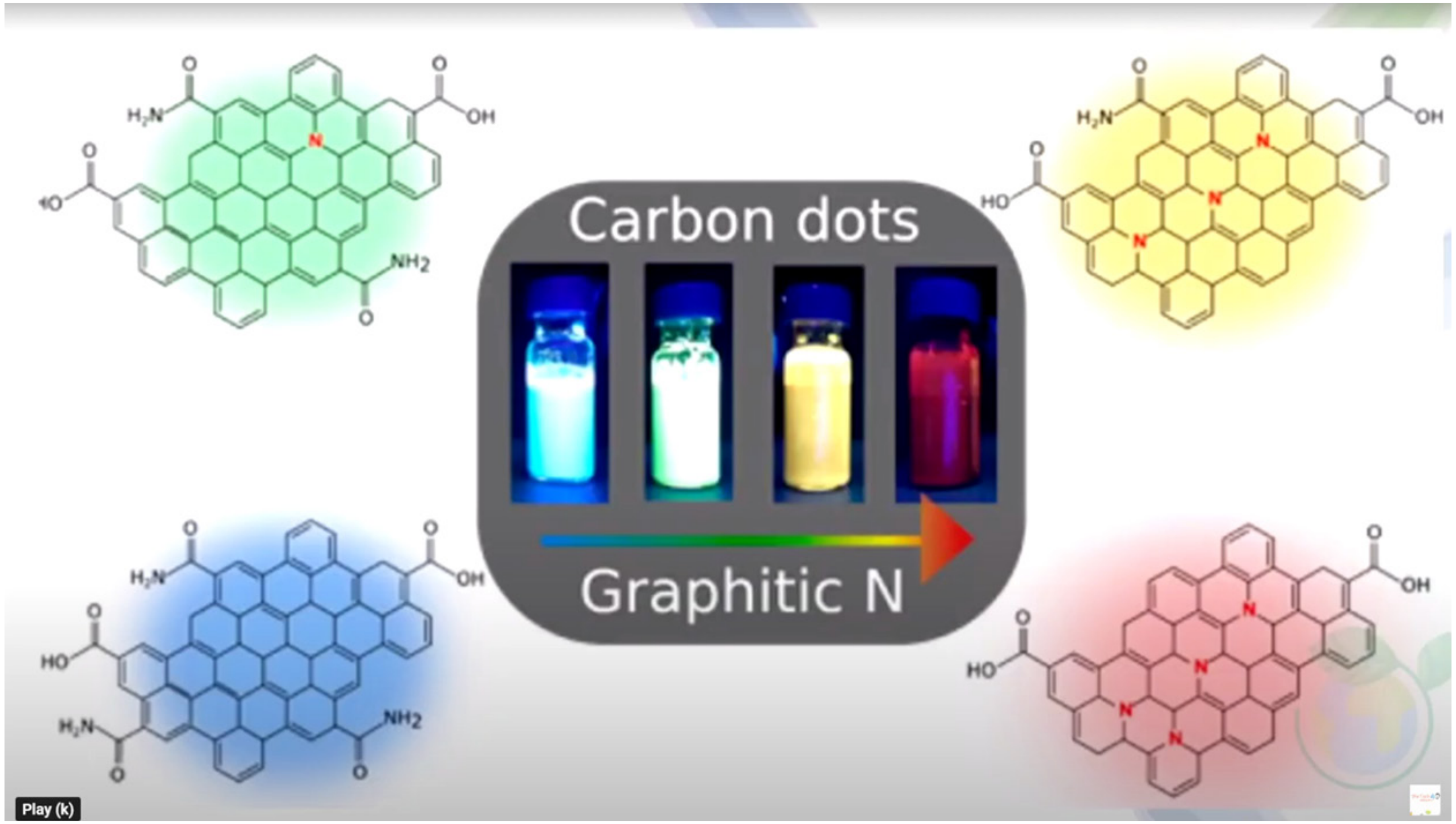
[†]Central European Institute of Technology (CEITEC), [‡]Department of Biochemistry, Faculty of Science, and [§]Department of Chemistry, Faculty of Science, Masaryk University, Kamenice 5, 625 00 Brno, Czech Republic

ABSTRACT: We review the progress achieved during the recent five years in immunochemical biosensors (immunosensors) combined with nanoparticles for enhanced sensitivity. The initial part introduces antibodies as classic recognition elements. The optical sensing part describes fluorescent, luminescent, and surface plasmon resonance systems. Amperometry, voltammetry, and impedance spectroscopy represent electrochemical transducer methods; electrochemiluminescence with photoelectric conversion constitutes a widely utilized combined method. The transducing options function together with suitable nanoparticles: metallic and metal oxides, including magnetic ones, carbon-based nanotubes, graphene variants, luminescent carbon dots, nanocrystals as quantum dots, and photon up-converting particles. These sources merged together provide extreme variability of existing nanoimmunosensing options. Finally, applications in clinical analysis (markers, tumor cells, and pharmaceuticals) and in the detection of pathogenic microorganisms, toxic agents, and pesticides in the environmental field and food products are summarized.



Farka, Z. et al., Nanoparticle-based immunochemical biosensors and assays: Recent advances and challenges. Chemical Reviews, 2017;117(15) 9973-10042.

Carbon Dot Video



Steven S. Saliterman

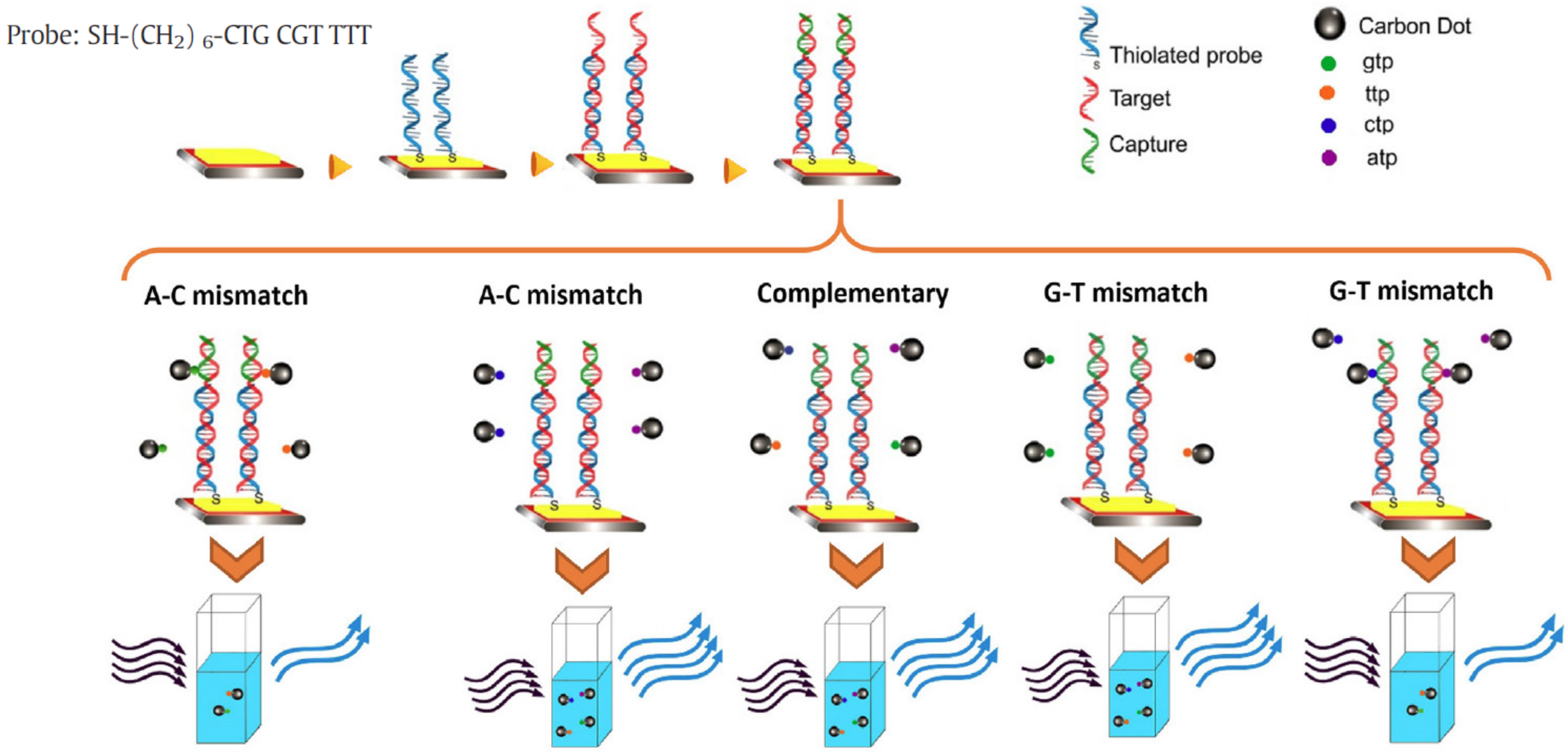
https://www.youtube.com/watch?v=VJQiEzqAF9g

Carbon Dots for SNP Recognition

- Single nucleotide polymorphism are variation in a single DNA base pair, occurring one in 500-1000 base pairs.
- Eight possible SNPs: A-C, A-A, A-G, C-C, C-T, T-T, T-G, and G-G.
- Many pathogenic and genetic diseases such as cystic fibrosis, Alzheimer's, sickle cell anemia and certain cancers are caused by these point mutations.
- Traditionally *organic fluorescent dyes* are used as fluorescent probes for the determination of nucleic acids. QDs offer better properties as previously noted.
- In contrast, *CDs* have the desired advantages of low toxicity, environmental friendliness, and low cost.

Motaghi H, Mehrgardi MA. Spectrofluorometric genotyping of single nucleotide polymorphisms using carbon dots as fluorophores. *Spectrochimica Acta Part a-Molecular and Biomolecular Spectroscopy.* 2019;206:154-159.

- Fluorescence assay for genotyping of different SNPs by employing the CDs that have been linked to adenosine, cytidine, guanosine, and thymidine mononucleotides probe using phosphoramidite chemistry through CDs surface amine groups.
- In the present method, the DNA probe was immobilized on the surface of the gold compact recordable disk. The monobase functionalized carbon dots (MB-CDs)were accumulated on the disk surface via hybridization of monobases with mismatch sites.
- After binding of MB-CDs to target DNA, the decreases in the fluorescence intensities of residual CDs were followed.

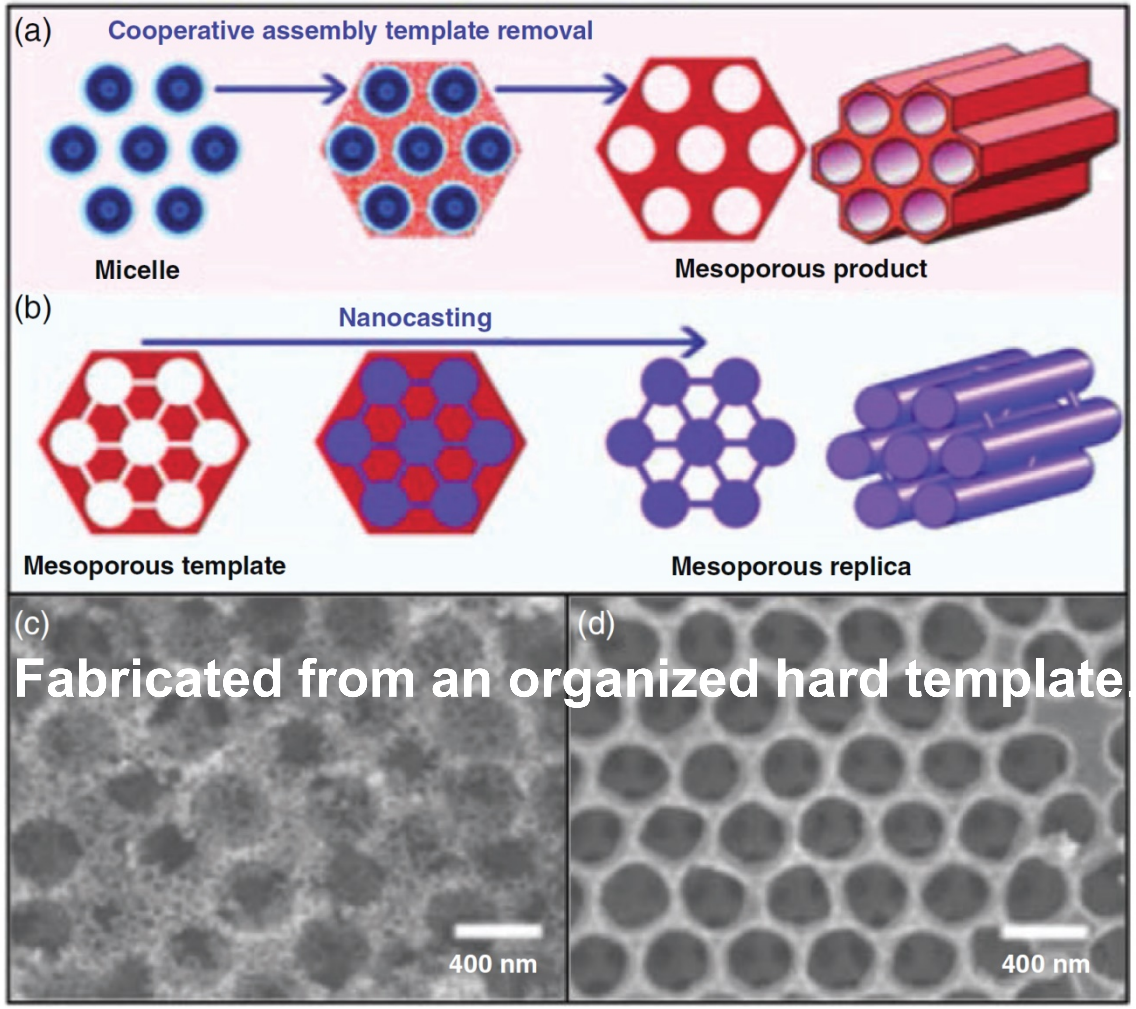


Scheme 1. Schematic illustration of Spectrofluorometric Genotyping of various SNPs.

Motaghi H, Mehrgardi MA. Spectrofluorometric genotyping of single nucleotide polymorphisms using carbon dots as fluorophores. *Spectrochimica Acta Part a-Molecular and Biomolecular Spectroscopy.* 2019;206:154-159.

Mesoporous Membranes

- Pore morphologies: microporous (<2 nm), <u>mesoporous (2–50 nm)</u>, and macroporous (>50 nm).
- Pores can be cylindrical, conical, slit-like, or irregular in shape, and be arranged in well-ordered pores with vertical alignment, or in a random network of tortuous pores.
- Rapid and sensitive free transduction system.
- Quantum effects from nano-sized framework.



Sposito AJ, Kurdekar A, Zhao JQ, Hewlett I. Application of nanotechnology in biosensors for enhancing pathogen detection. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology.* 2018;10(5).

- Non-oxide materials are generally fabricated using a templating processing where either of two templates are used: supramolecular aggregates of amphiphilic species (soft templating), or preformed mesoporous solid structures (hard templating)
  - In soft templating the mesopore morphology is driven by the thermodynamics of the surfactant-inorganic precursor interaction. Electrostatic and steric interactions also play a role in pore morphology, while temperature, ionic strength, pH, and concentration control the long range pore organization.
  - In hard templating a mesoporous sacrificial mold is first constructed as a template for a replica mold.

- Optical and electrochemical biosensing.
- For silicate based membranes, silane chemistry is commonly used .
- Glutaraldehyde, a crosslinker that links amine groups, has also been used for linking both antibodies and DNA to polymer and aluminum based membranes.
- Pore diameters can be fabricated to specific target dimensions such that when target is captured in the channel via biorecognition there is a significant reduction in ionic mobility within the channel due to steric effects.
- DNA translocation time through nanopores is another parameter that can be used to identify specific nucleotides passing through the sensor.