# Projects in the research area

**Hybrid bionanosystems based on self-assembled structures, quantum dots, plasmonic and magnetic nanoparticles**

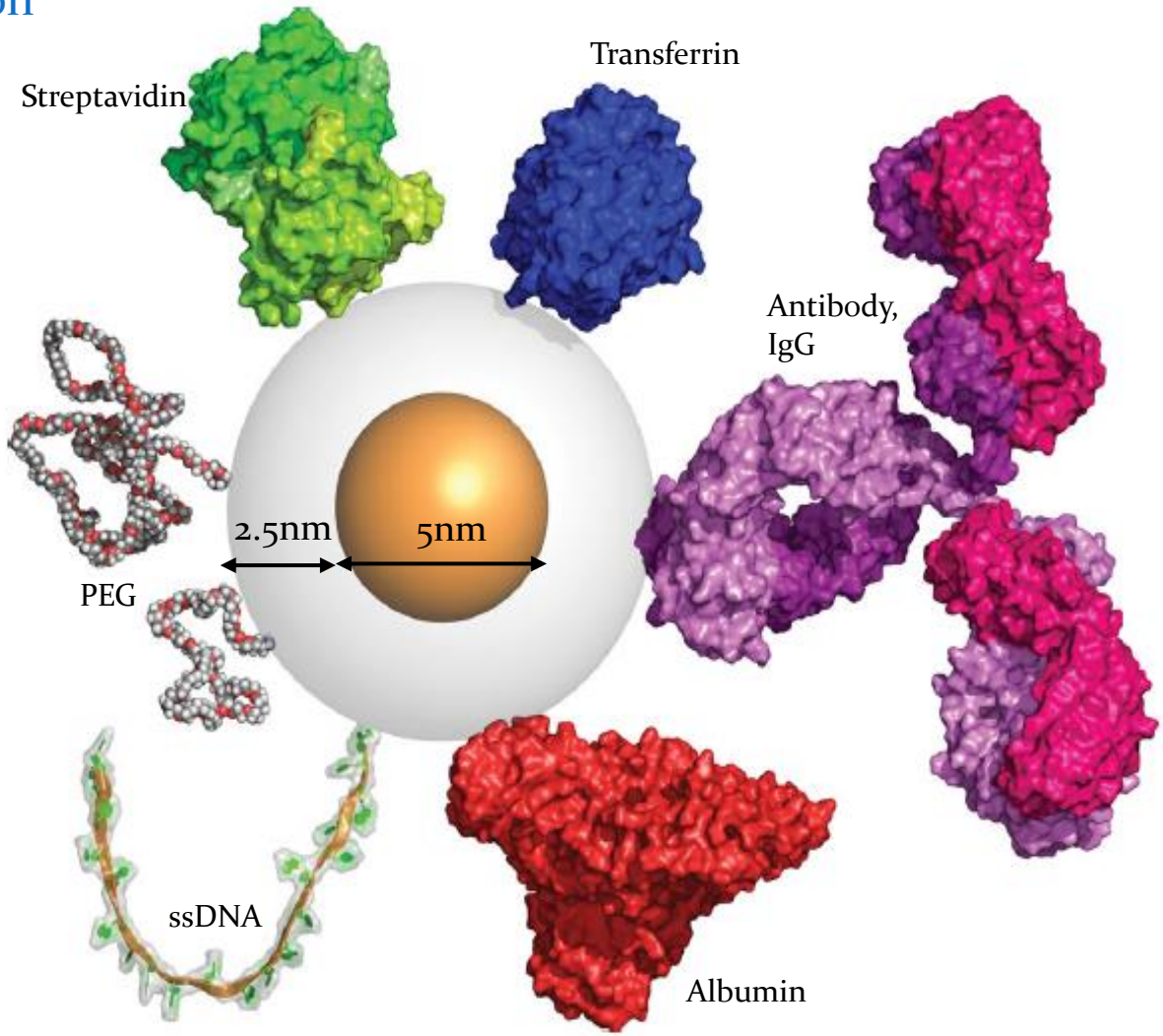
# Strategic Line of Research at CFUM

# What are Bionanosystems ?

## Nanoparticles Biocompatibilization and **Biofunctionalization** Strategies

The strategy for the conjugation of biomolecules to nanoparticles generally falls into four classes:

- ligand-like binding to the surface of the inorganic particle core, commonly by chemisorption of e.g. thiol groups in Au surfaces;
- electrostatic adsorption of positively charged biomolecules to negatively charged nanoparticles or vice versa;
- covalent binding by conjugation chemistry, exploiting functional groups on both particle and biomolecules (e.g. amide bond formation);
- non-covalent, affinity-based receptor-ligand systems (e.g. streptavidin/biotin)




*Phil. Trans. R. Soc. A* 2010 **368**

# What are Bionanosystems ?

- Conjugation of inorganic nanoparticles to biomolecules generates hybrid materials that can be used to let the nanoparticles interact specifically with biological systems.

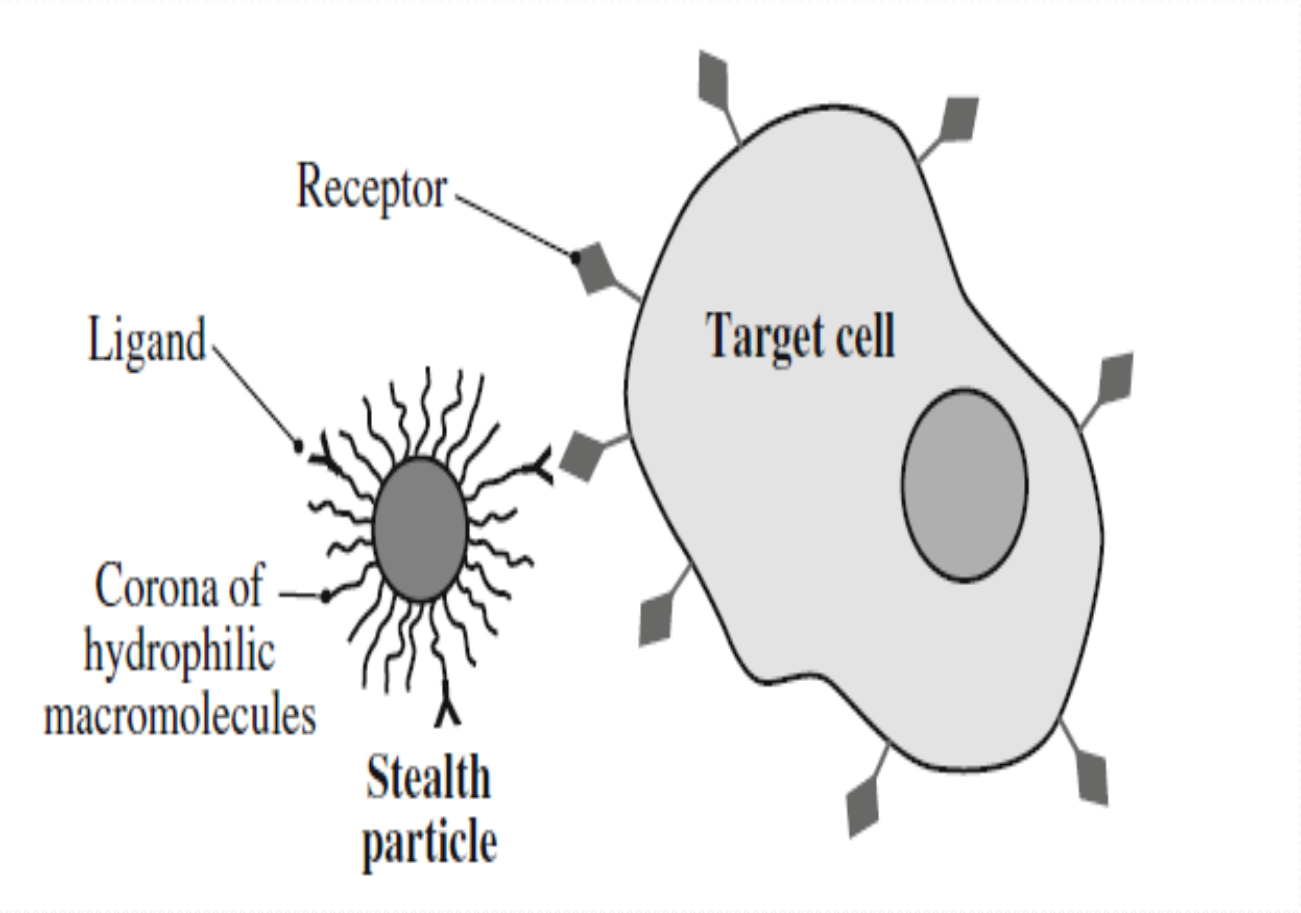
- Nanoparticle–biomolecule conjugates bring together the unique properties and functionality of both materials,

  e.g. fluorescence or magnetic moment of the inorganic particles

  and

  e.g. the ability of biomolecules for highly specific binding by molecular recognition.

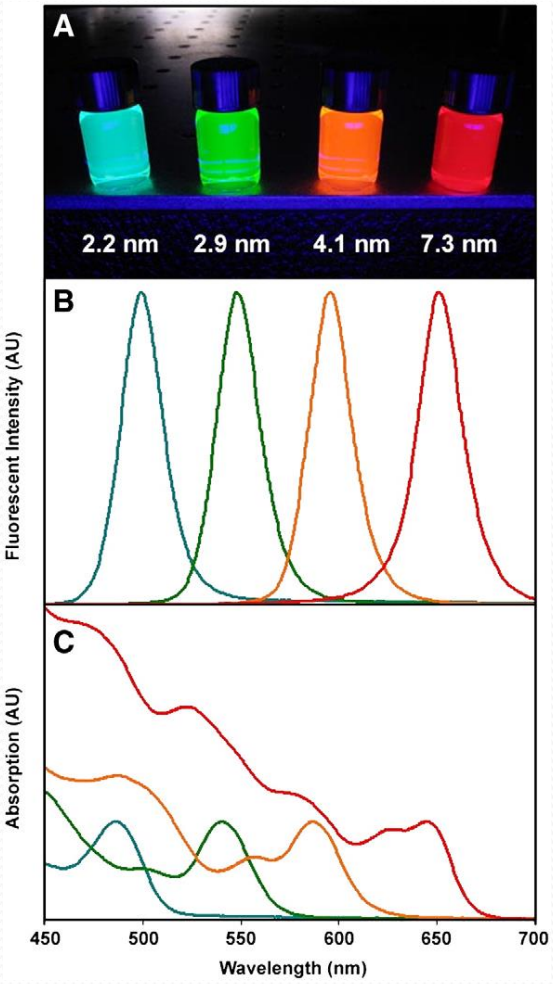
# What are Bionanosystems ?



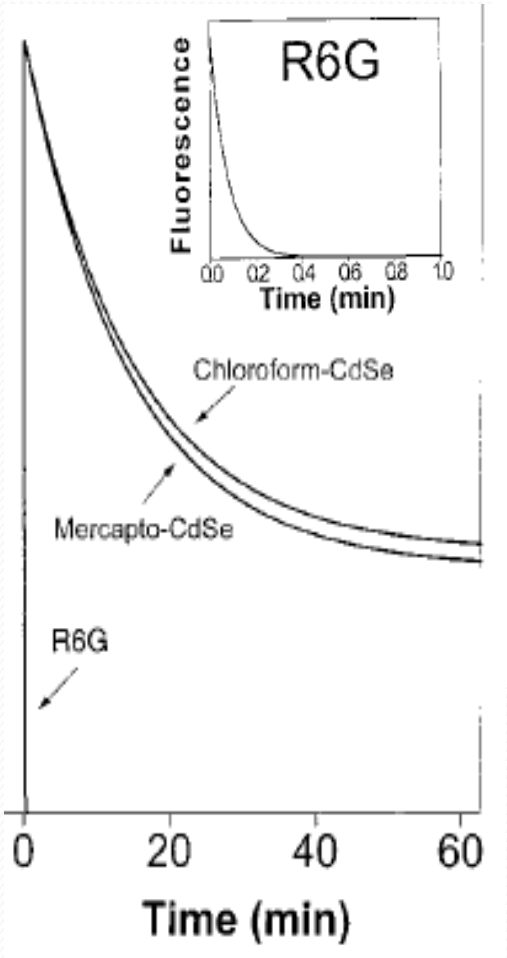

Using molecular recognition to get a nanoparticle to a target cell. The ligand grafted onto the particle surface must be specific to receptors at the surface of the target cell

# Types of Nanosystems

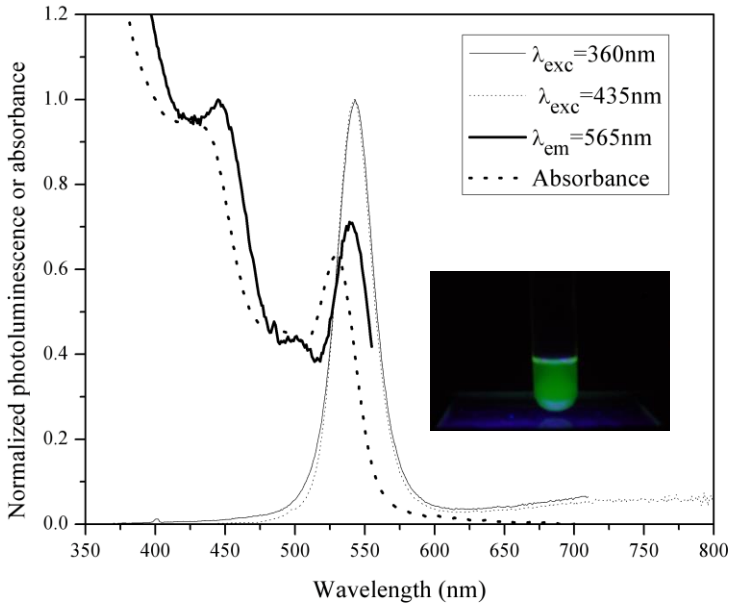
Quantum Dots
(Semiconductor nanocrystals)




**CdSe QDs**



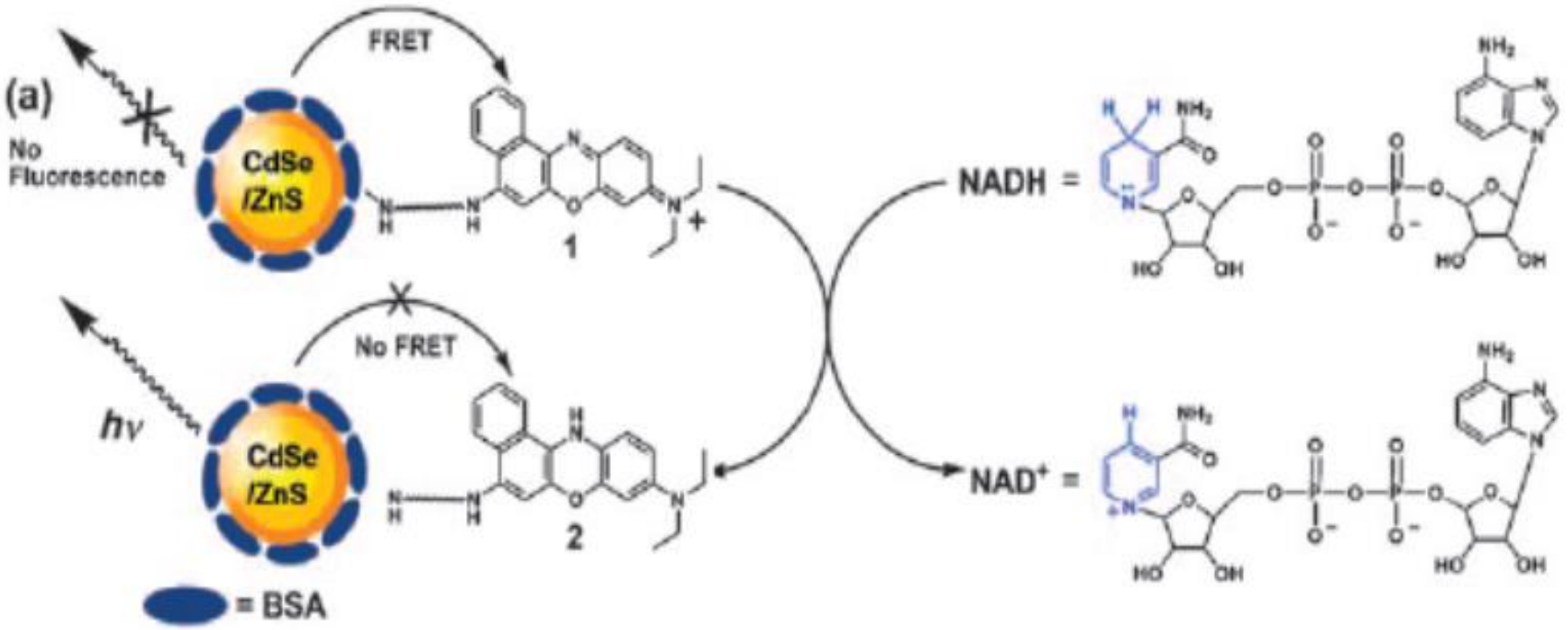

Made @CFUM




Size = 2.7 nm Estimated from an empirical relation proposed by W. William Yu et al.

Chem. Mat. 15 (14), 2854 (2003)

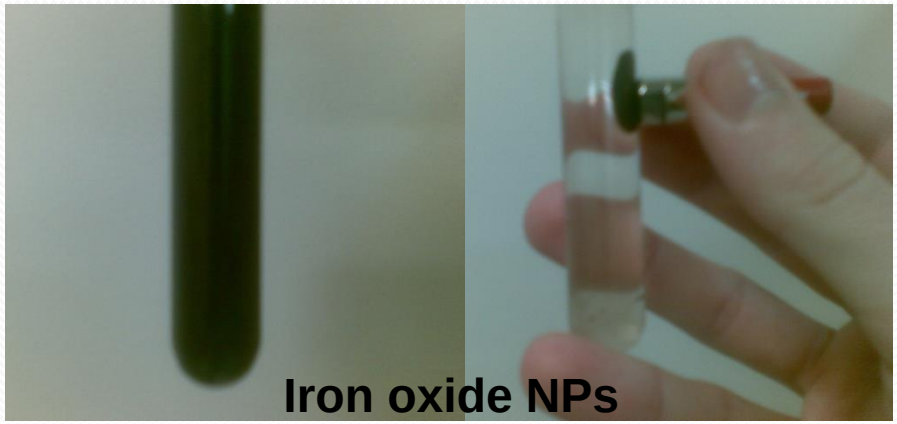
Application (Bio)Sensors



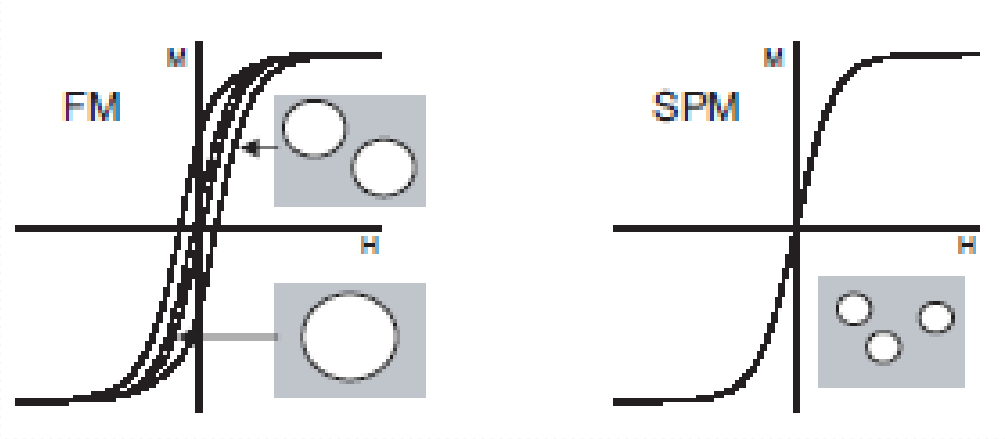

Sensor of NADH (measure of biological activity)

Angew. Chem. Int. Ed. 2008, 47, 1 – 6

# Magnetic Nanoparticles



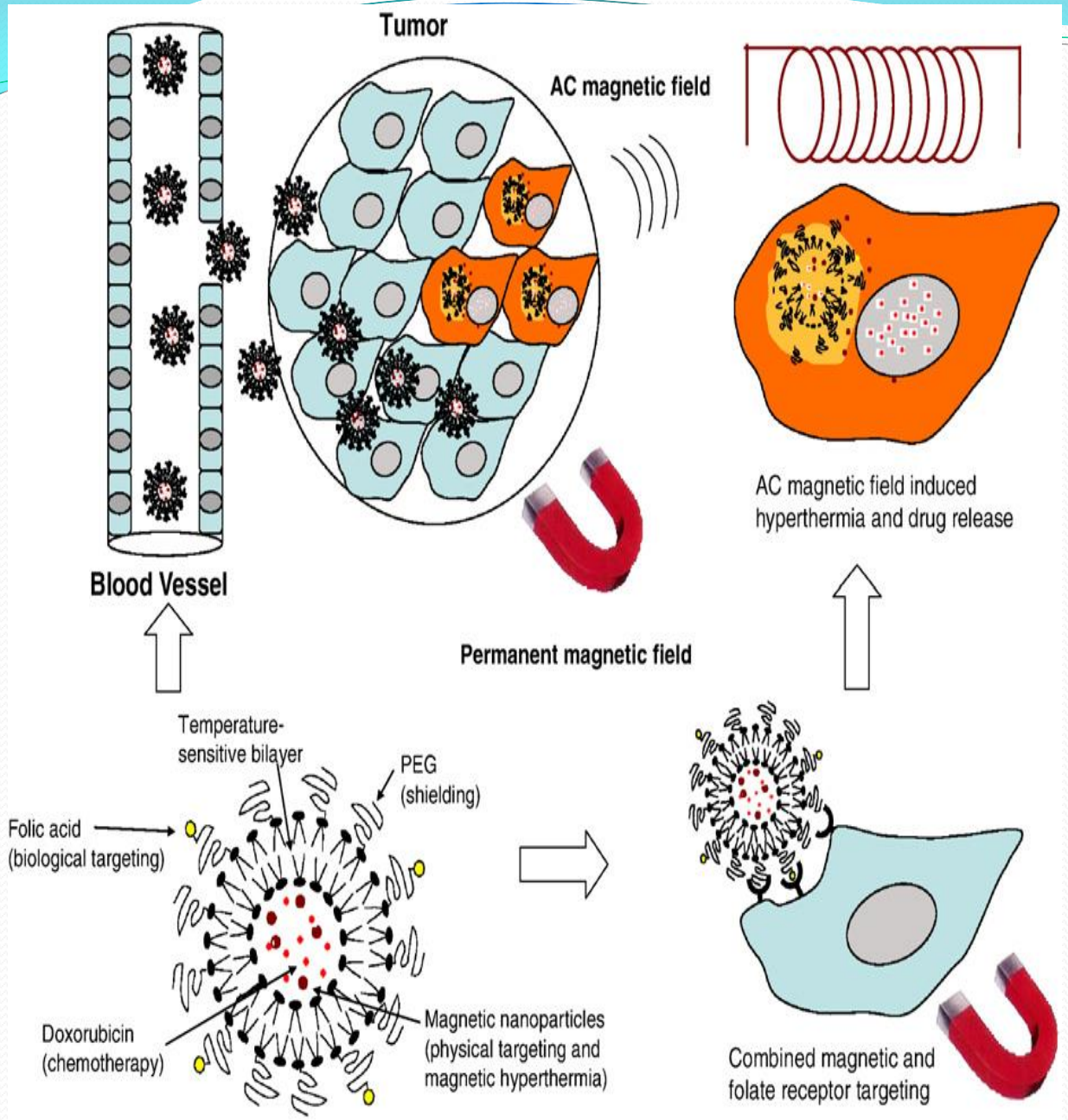

Made @CFUM




No remanescent magnetization

J. Phys. D: Appl. Phys. **36** (2003) R167–R181

# Application : Targeted drug delivery and hyperthermia using magnetoliposomes




Multifunctional drug carrier:

folate receptor targeted temperature sensitive magnetoliposome containing doxorubicin,

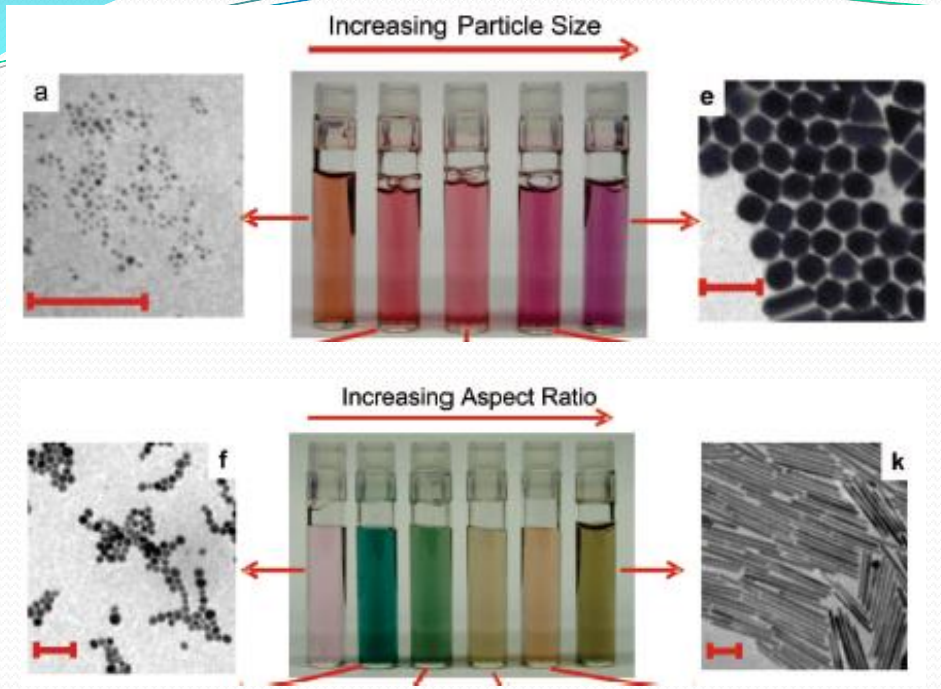
which can be targeted:

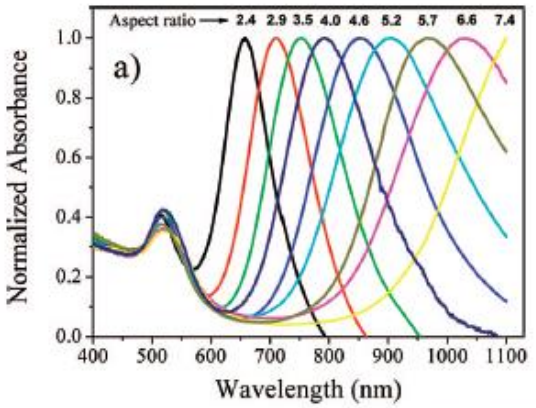
- physically by magnetic field
- biologically by folic acid to tumor cells.

Drug release will be triggered by hyperthermia upon local application of an AC magnetic field on the tumor tissue.

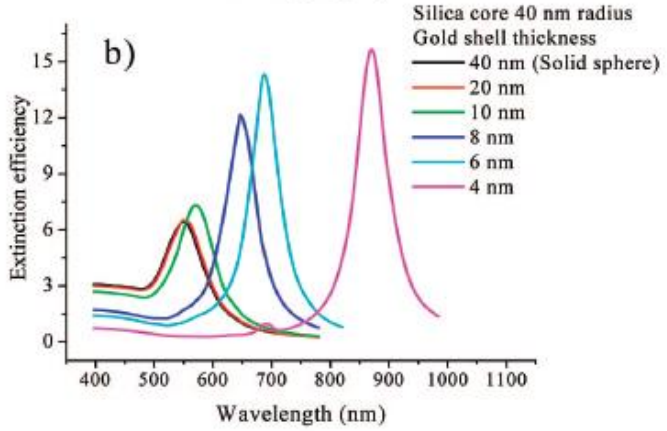
Journal of Controlled Release 142 (2010) 108–121

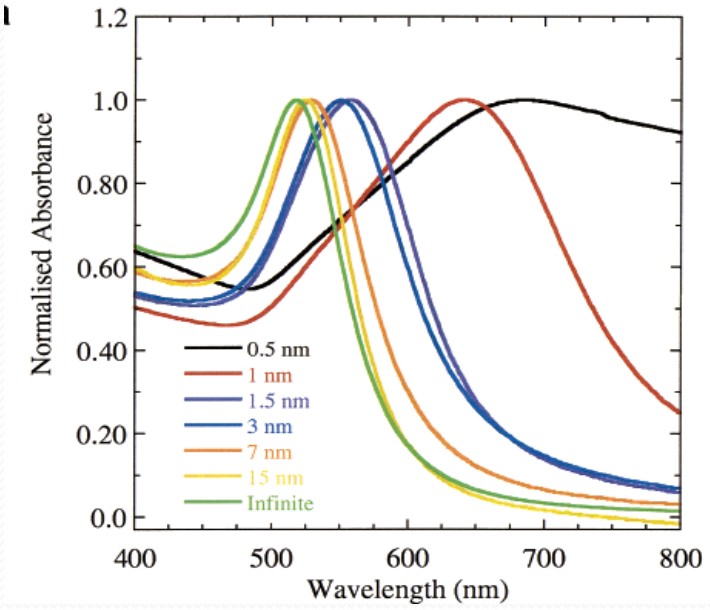
# Plasmonic Nanoparticles Au NPs



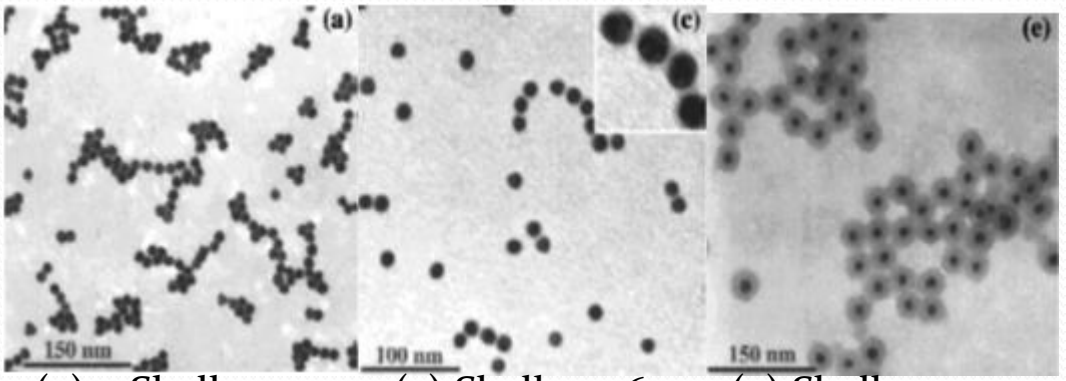

Accounts of Chemical Research 41 (2008), 1578



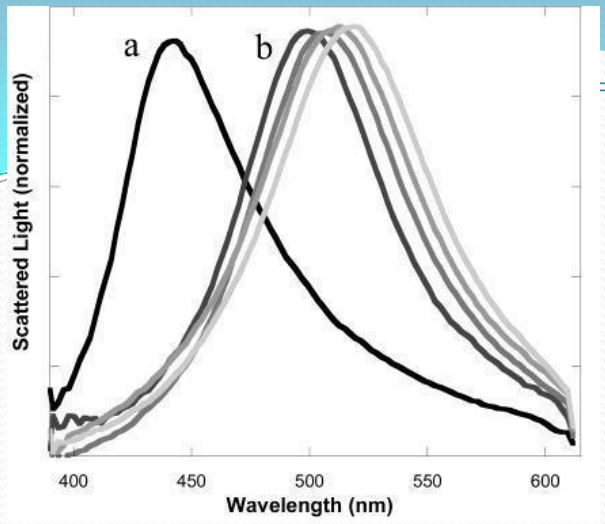




## Silica coated gold nanoparticles

*J. Phys. Chem.* B 105 (2001), 3441-3452




(a) Shell = 0 nm (c) Shell = 4.6nm (e) Shell =12.5nm (13.2 nm Au particles)



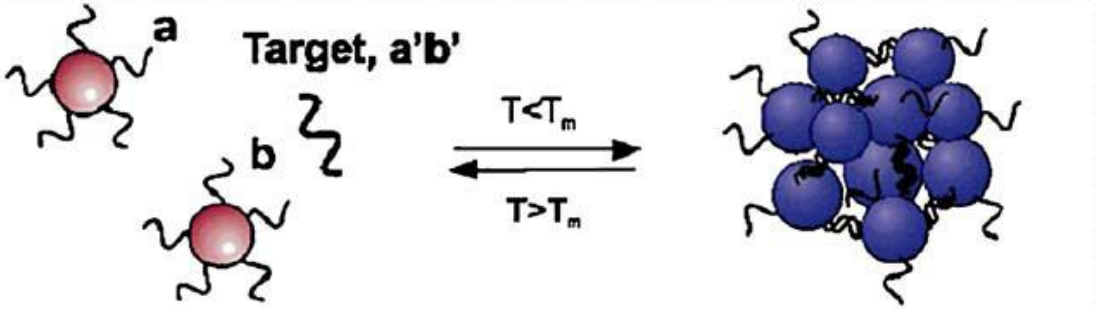

Spectral shift for individual silver nanoparticles. Typical particle absorption spectrum as it is shifted from (a) air to (b) 1.44 index oil, and successive oil treatments in 0.04 index incremental increases.

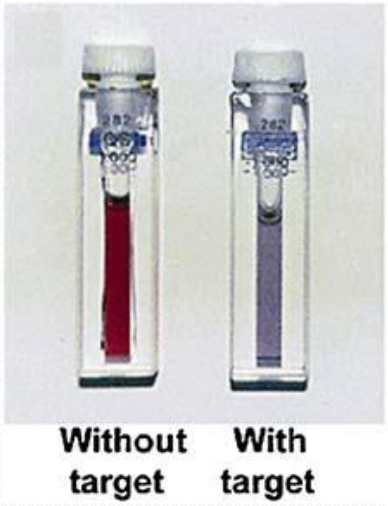
Nano letters 2003 Vol. 3 No. 4 485-491

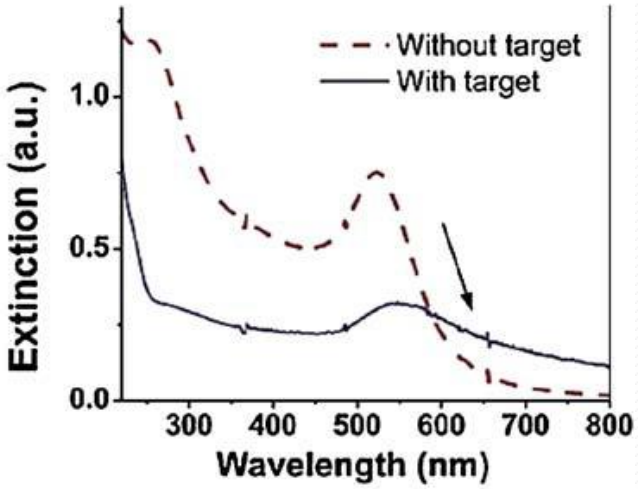
## Application

**specific DNA detection (hybridization assay)**

J. Am. Chem. Soc. 125 (2003), 1643–1654

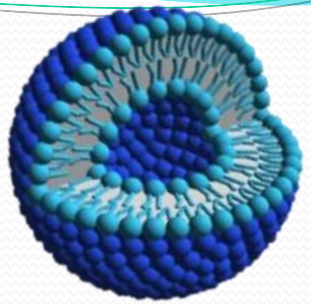


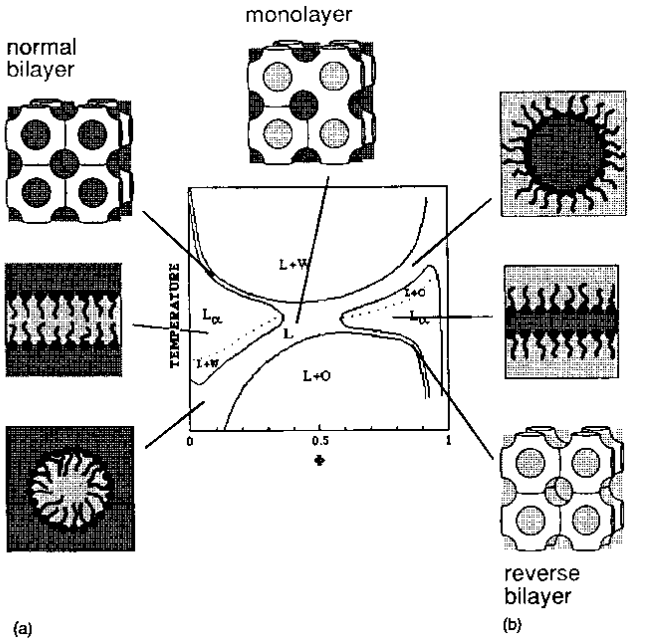



# Self-Assembled Nanostructures

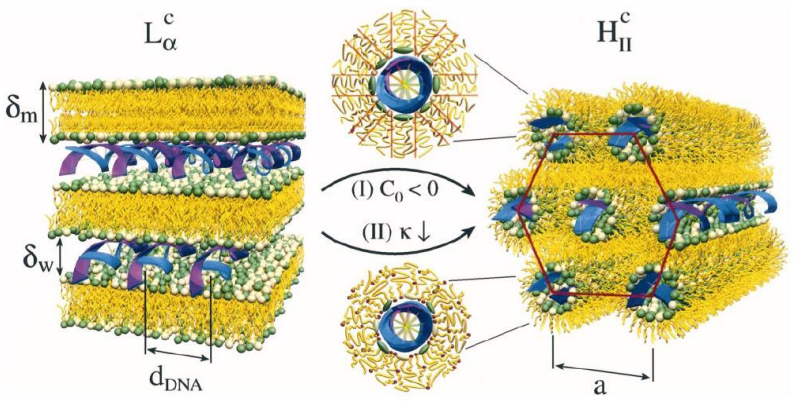
## Liposomes



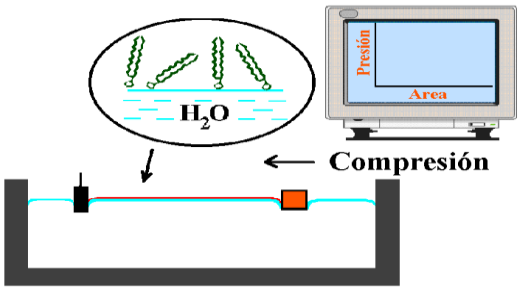
## w/o or o/w microemulsions

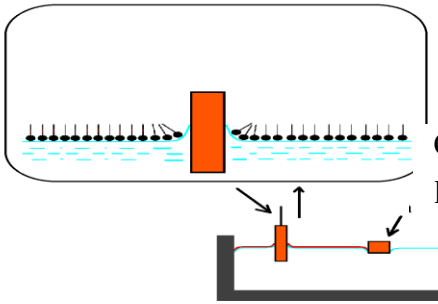



## Lipoplexes (Lipid + DNA complexes)



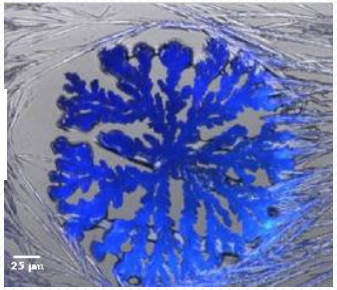

## Langmuir-Blodgett isotherms and films



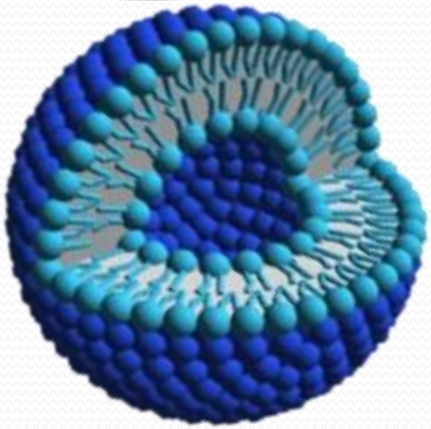
Constant Surface Pressure ( $\Pi$ )

## Dendrites of QDs

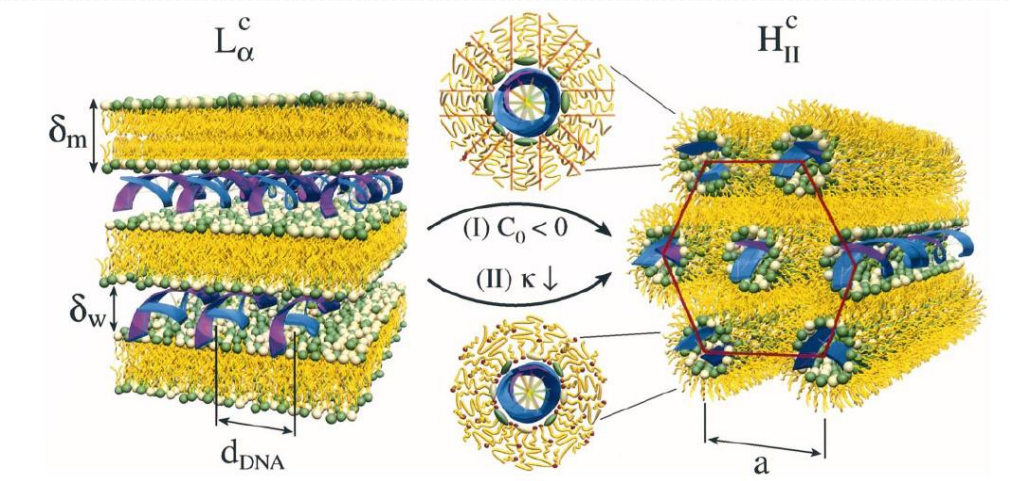


## Applications

(Targeted) drug delivery using liposomes



Non-viral DNA transfection



# Inorganic Nanoparticles

**Quantum Dots** (CdSe, CdSe@ZnS, CdTe, ….)

- Development and biological assays of bionanoconjugates based on CdSe/ZnS quantum dots *(MSc, concluded)*

**Magnetic Nanoparticles** Metallic (Ni, Co, ….)

- Development of magnetoliposomes based on nickel/silica core/shell nanoparticles for antitumoral drug delivery applications *(MSc, concluded)*

Magnetite ($Fe_3O_4$)

- Development of magnetite-based magnetoliposomes for antitumoral drug delivery applications *(MSc, concluded)*

Ferrites ($MnFe_2O_4$, ….)

- Development of manganese ferrite-based magnetoliposomes for drug delivery applications *(MSc, in progress)*
- Development of magnesium ferrite-based magnetoliposomes for drug delivery applications *(MSc, in progress)*
- Development of calcium ferrite-based magnetoliposomes for drug delivery applications *(MSc, in progress)*

**Plasmonic Metallic Nanoparticles** (Au, Ag, Pt, ….)

- *MSc:* Biosensors based on enzime association to plasmonic gold surfaces *(in progress)*

# Self-assembling nanostructures :

(dendrites of QDs, **liposomes, lipoplexes**, Langmuir-Blodgett thin films….)

## Membrane models

- Interaction of new antitumoral drugs with membrane proteins and lipid membranes *(MSc, concluded)*
- Development of pH sensitive liposomes for biomedical applications *(MSc, concluded)*

## Biocompatible liquid crystals

- Biocompatible peptide hydrogels as drug delivery systems *(MSc, in progress)*

## Lipoplexes ( DNA, siRNA + cationic lipids)

- Development of DODAB/MO/PEG-FOL lipoplexes for targeting of cells expressing folate receptors (MSc, *concluded*)
- Lipoplexes incorporating both plasmid DNA and siRNA for improved cell trafficking and therapeutic delivery (MSc, in progress)
- Development of DODAX:MO:PEG nanoparticles containing oncogene BRAF-specific siRNAs for colorectal carcinoma treatment *(MSc, in progress)*
- Development of lipofection vectors based in novel amino acid lysine-cationic gemini surfactants finely tuned by monoolein for therapeutic siRNA delivery *(MSc, in progress)*