Applications of Soft Matter

Drug Delivery

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Information about your instructor

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Shen Research Group

Single-Molecule Catalysis and Biophysics

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The Shen Research Group Innovations

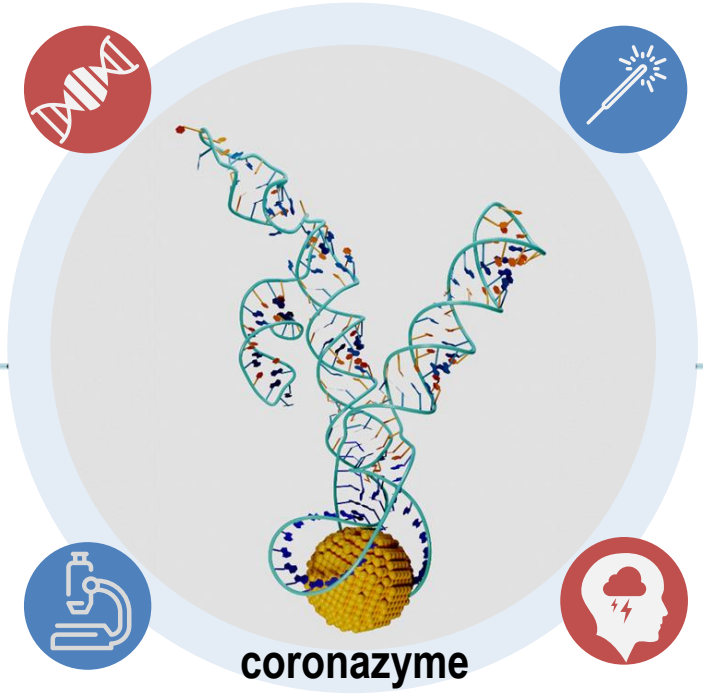
Electron Spin Catalyst

Novel Materials

Electron spin catalyst
Ligand-free nanoparticles

Novel Approach

SMART-MOTION:
Kinetic analysis for nonfluorogenic reactions

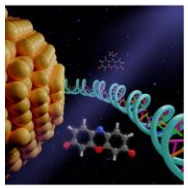
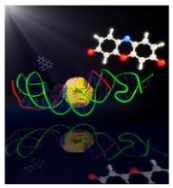
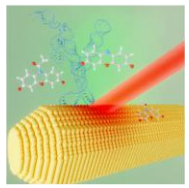
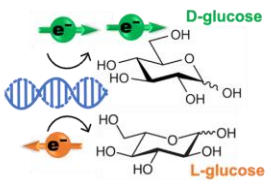


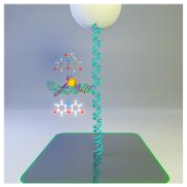
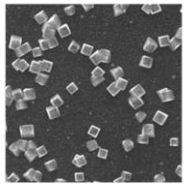
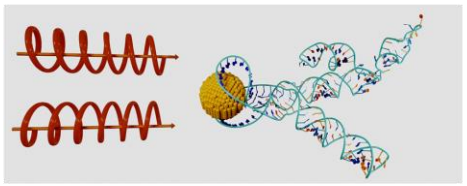
Novel Instrument

MT-HILO microscopy:
the combination of force and 3D super-res imaging

New Insights

CISS catalysis:
Chirality modulates reactivity;
Force and field dependence

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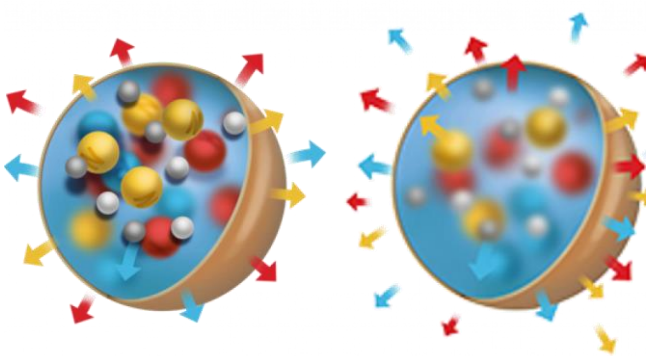
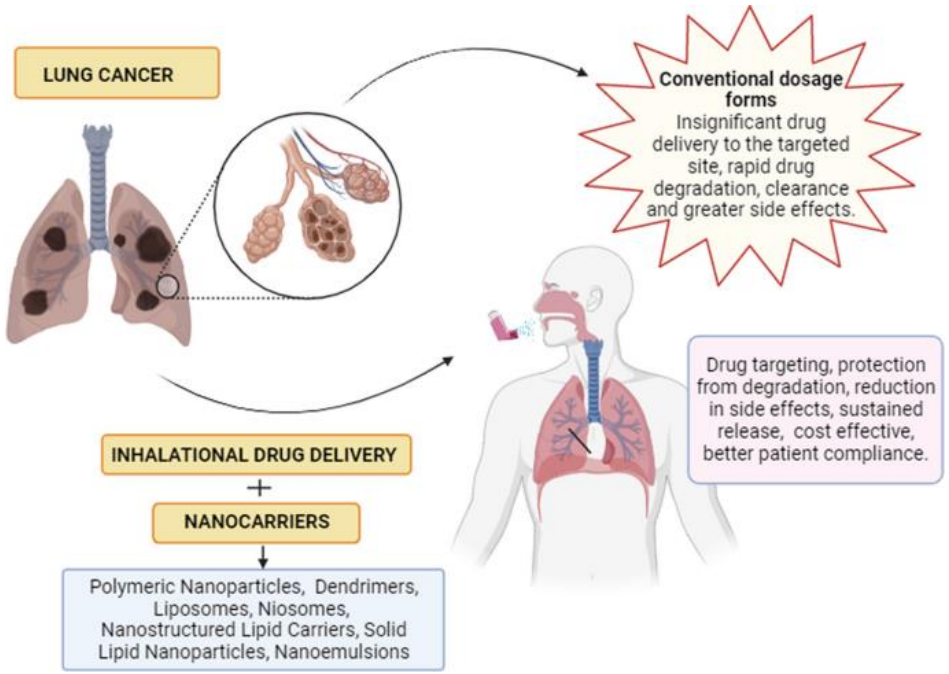
Drug Delivery

- Targeted therapy: use carriers to deliver the drug to a specific cell type or tissue.

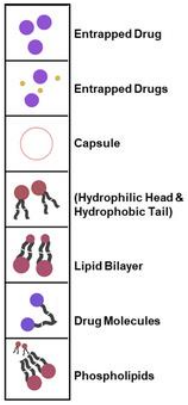
- Controlled release.
- Solubility and bioavailability.
- Patient compliance and comfort.
- Protection of sensitive drugs.
- Cost-effectiveness.
- Reduction of side effects.

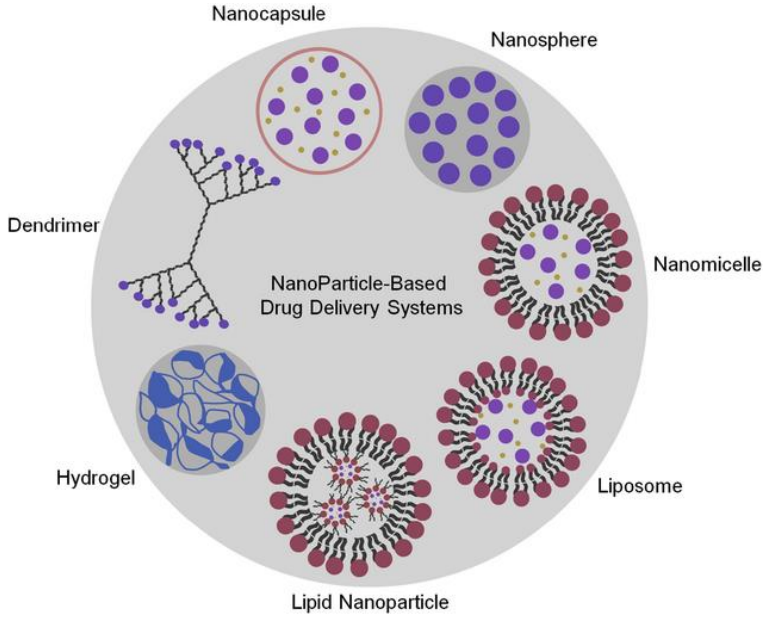




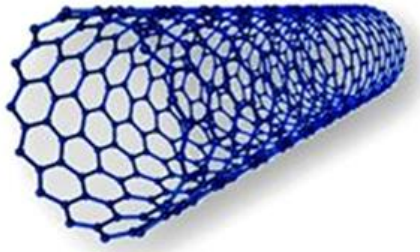
Targeted Drug Delivery Strategy

- **Nanosized carriers:** nanoparticles such as liposomes, dendrimers, and polymeric micelles encapsulate drugs for controlled release.
- **Ligand-receptor targeting**: use ligands that can bind to specific receptors.
- **Magnetic targeting:** magnetic nanoparticles are combined with a drug.
- **pH-Sensitive delivery:** sensing the subtle pH changes and release the drug at desired location.
- **Temperature-Responsive systems:** use materials that change properties in response to temperature changes.

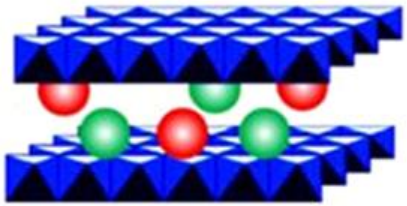




0-D Material

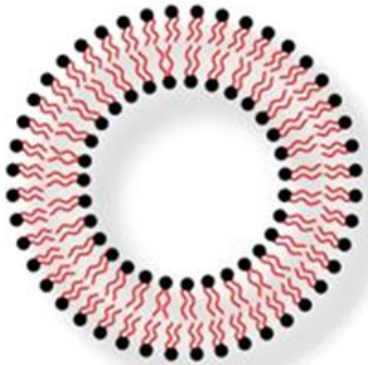


1-D Material

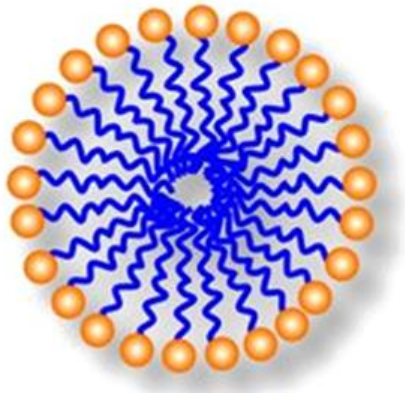


2-D Material

Mesoporous



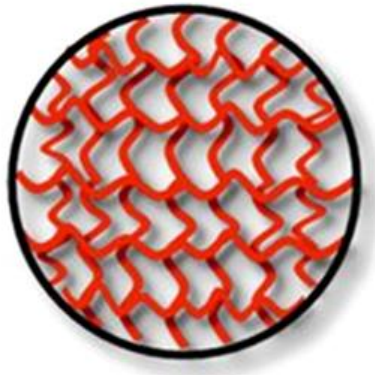
Liposome



Micelle

Dendrimer

Polymeric nanoparticles



Hydrogel

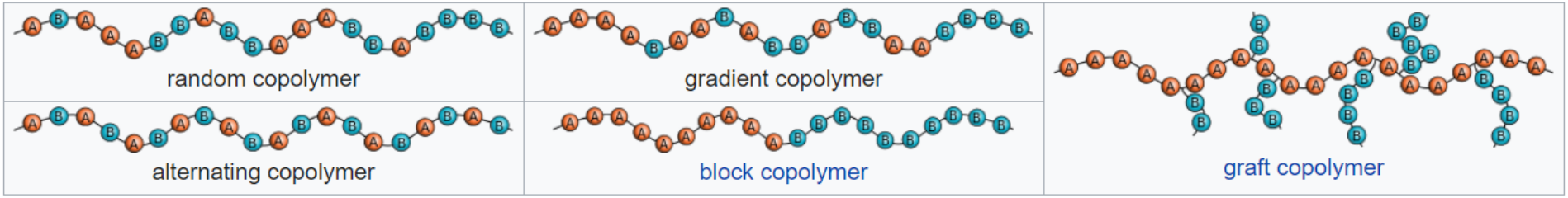
Different types of nanocarriers

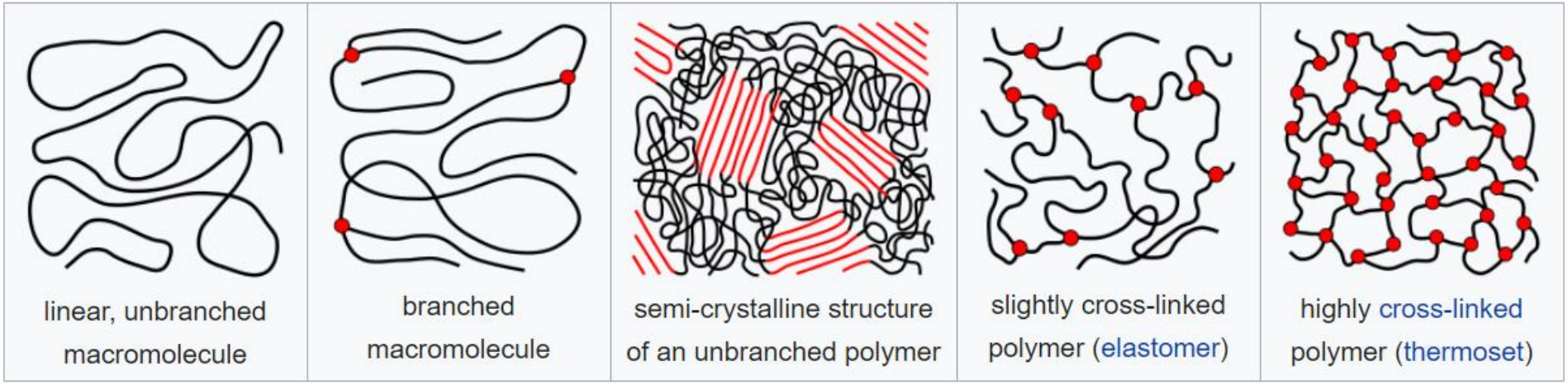
Maiti et al. *Signal Transduction and Targeted Therapy*, 2019, 4, 33.

Polymers

Polymers are large molecules (or macromolecules) composed of many repeated subunits, i.g. synthetic plastics, DNA, proteins, etc.

Polymers are difficult to study, because:

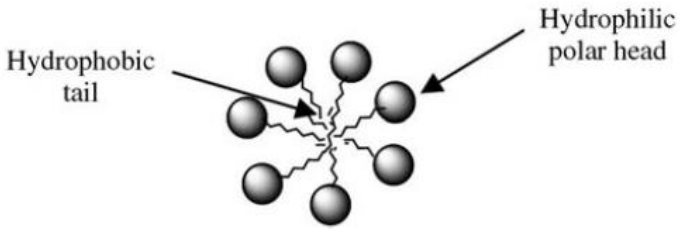




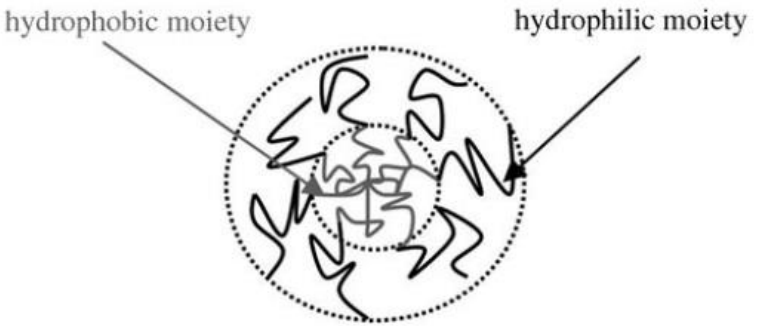
Various compositions.

Micelles

Micelles are aggregates of amphiphilic molecules in which the polar headgroups are in contact with water and the hydrophobic moieties are gathered in the core to minimize their contact with water.



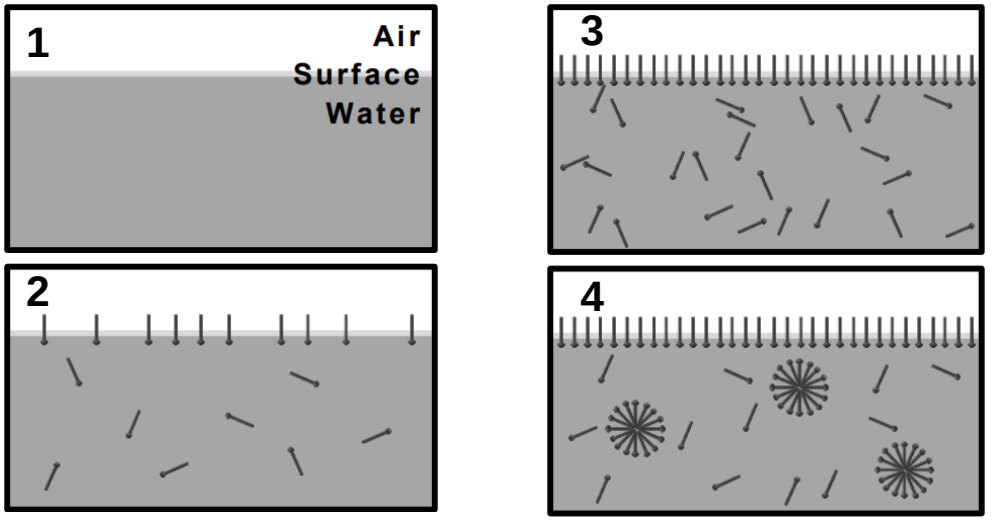
Representation of a surfactant micelle.



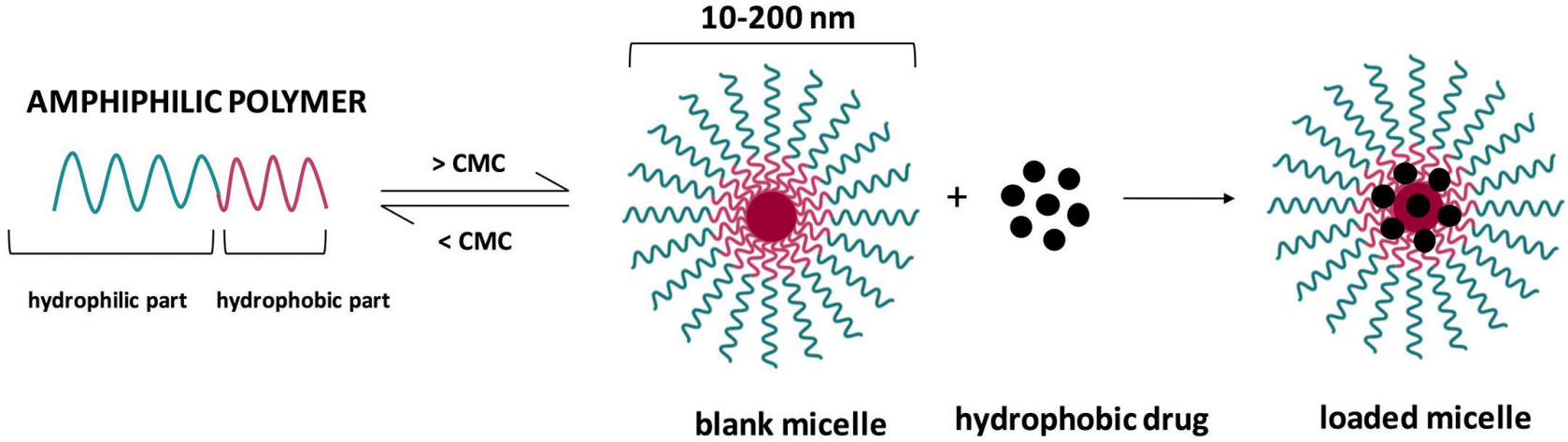
Representation of a block copolymer micelle.

Micelles form only when the concentration of surfactant is greater than the critical micelle concentration (CMC), and the temperature of the system is greater than the critical micelle temperature.

Increasing concentration of surfactant in water first leads to the formation of a layer on the surface. After reaching the CMC micelles begin forming.

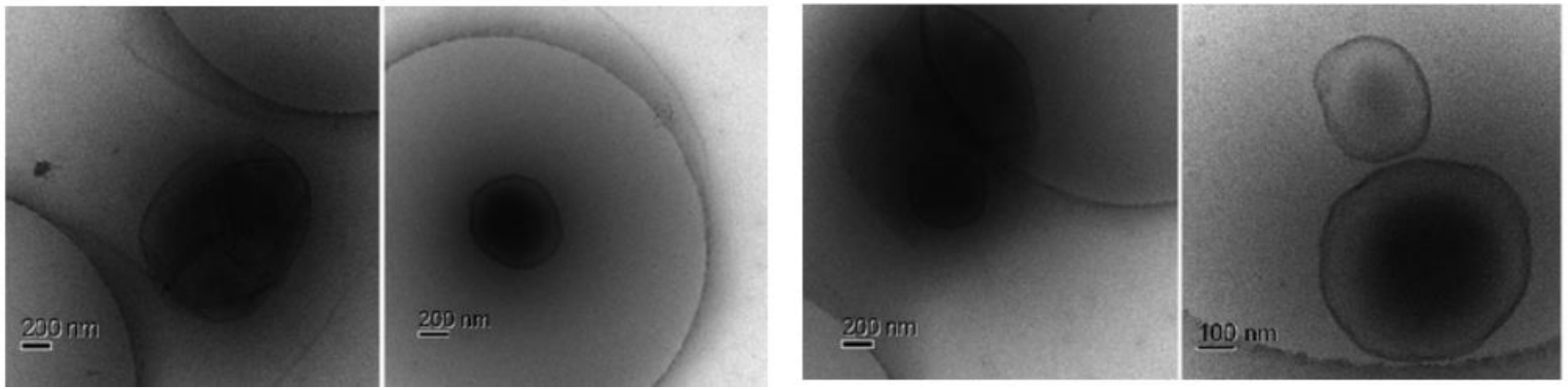


Functional Micelles



Temperature responsive micelles

- poly(ethylene oxide) Micelle forms above 70 °C, or below 5 °C.



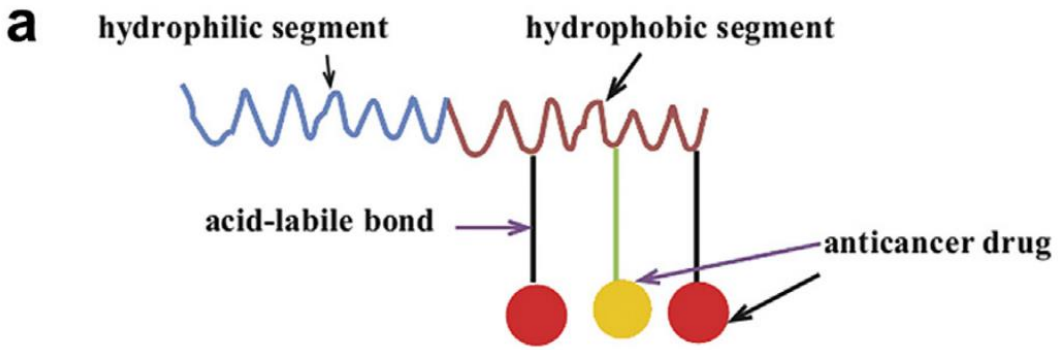
Cryp EM images for programmed cooling of PEO micelles.

***Soft Matter*, 2009, 5, 1812.**

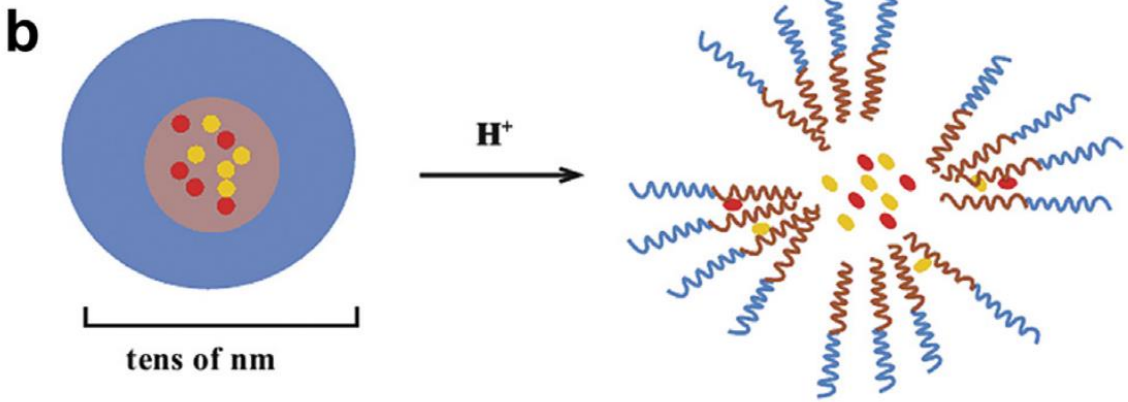
Functional Micelles

pH responsive micelles

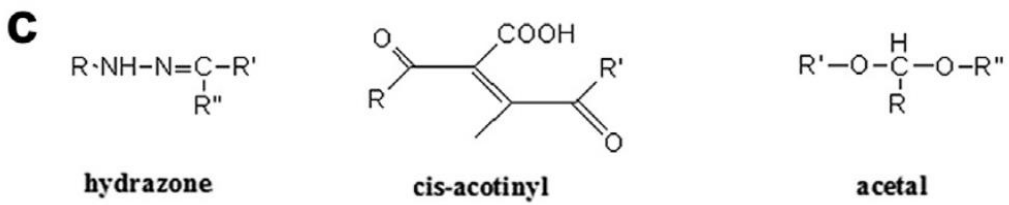
Copolymers by inclusion of amine or acid functional groups.



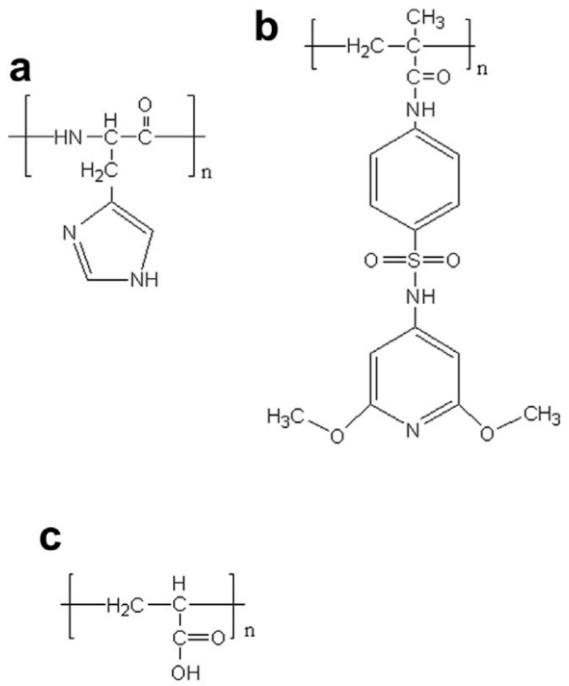
Design of amphiphilic block copolymer



Slow drug release at low pH environment



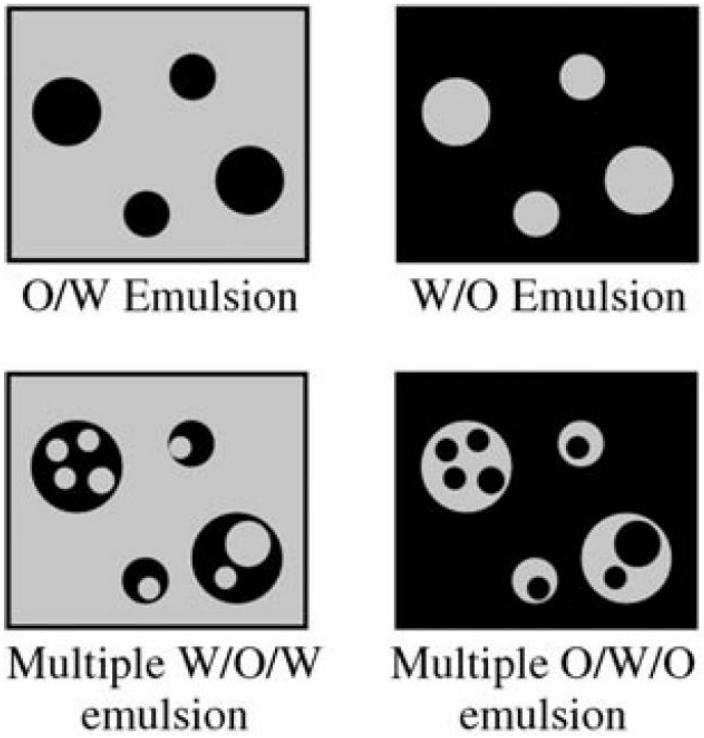
Acid liable functionalities



Representative pH-sensitive polymers.

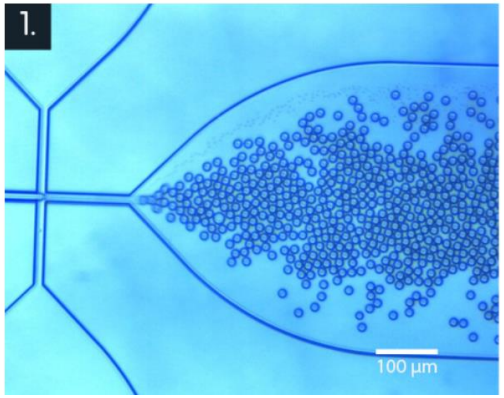
Emulsions

Emulsions are heterogeneous dispersions of two immiscible liquids, such as oil in water (O/W) or water in oil (W/O).

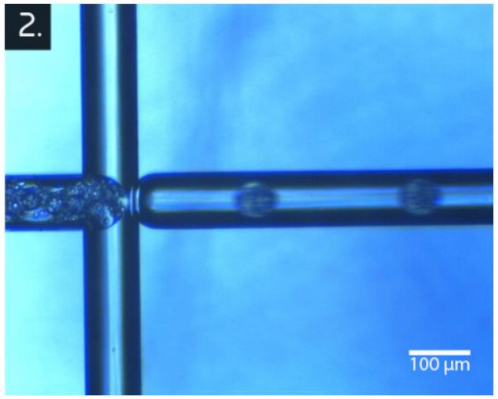


Representation of different types of emulsions (gray: aqueous phase, black: oil phase)

Emulsions usually require polymer surfactants for stabilization



Poly(lactic-co-glycolic acid) a.k.a PLGA, stabilizes the water droplets in dichloromethane (DCM).



Producing the water/PLGA in DCM/water emulsion (w/o/w).

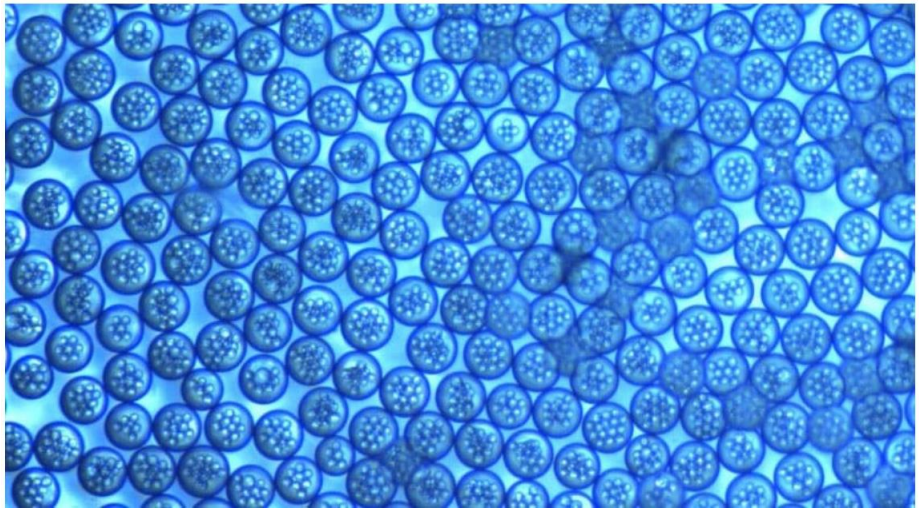
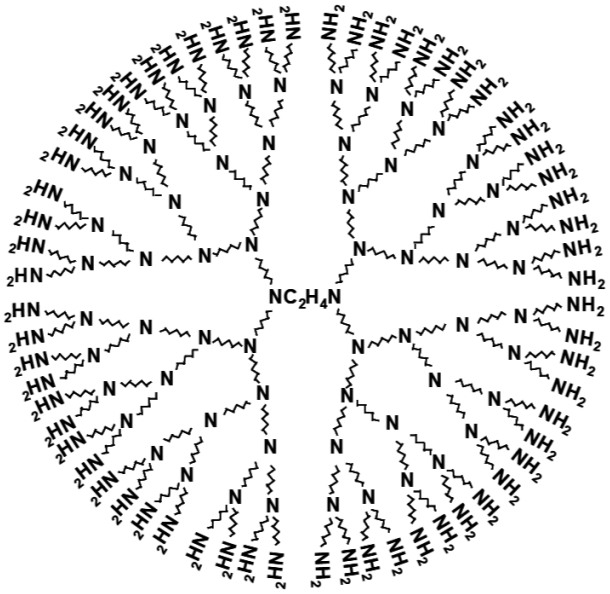


Image of resulting emulsion (w/o/w).

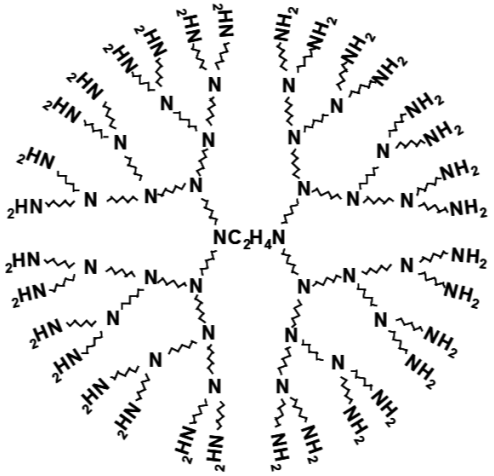
Dendrimers

A **dendrimer** is a molecule composed of monomers that associate according to a tree-like process around a central plurifunctional core.

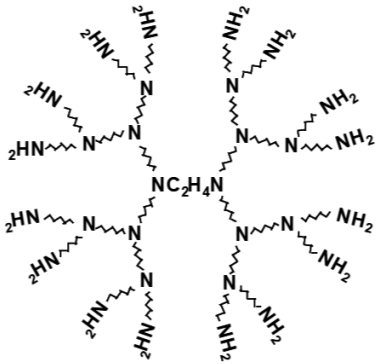
Dendrimers are classified according to their generation, which corresponds to the number of repeating layers.



Generation 4



Generation 3

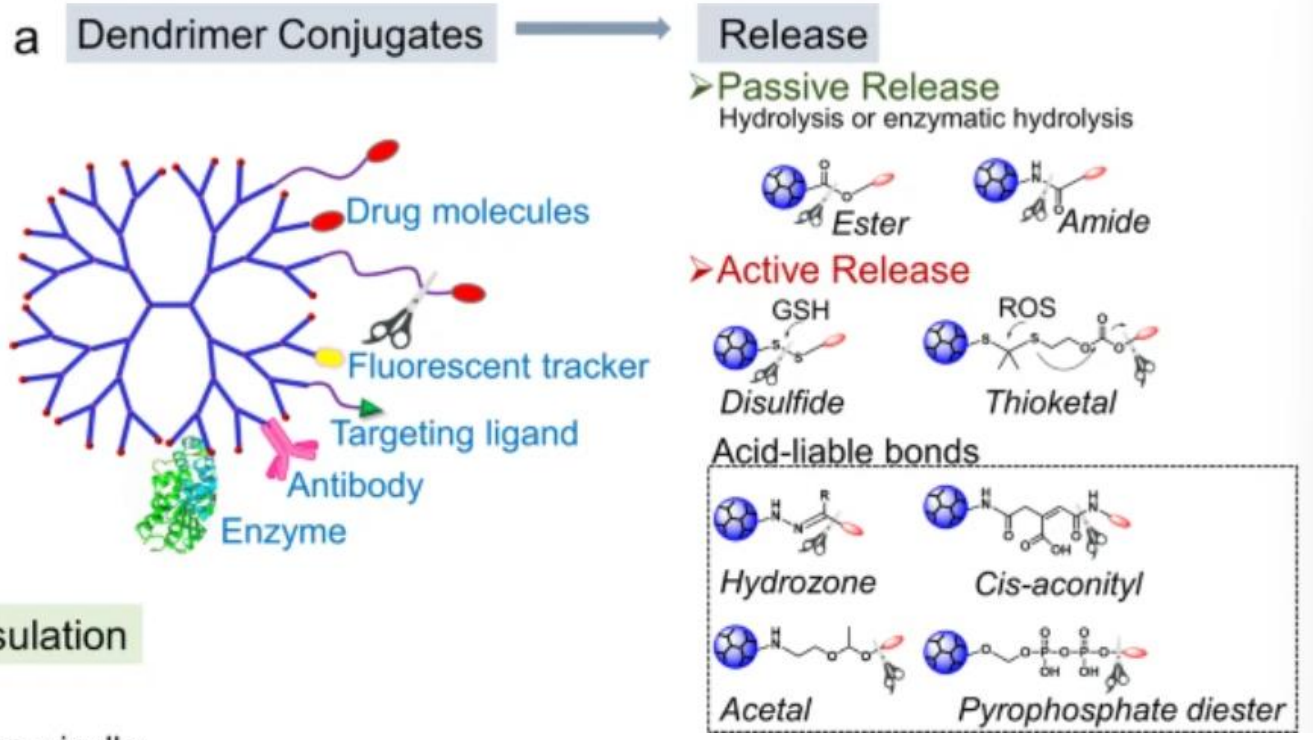


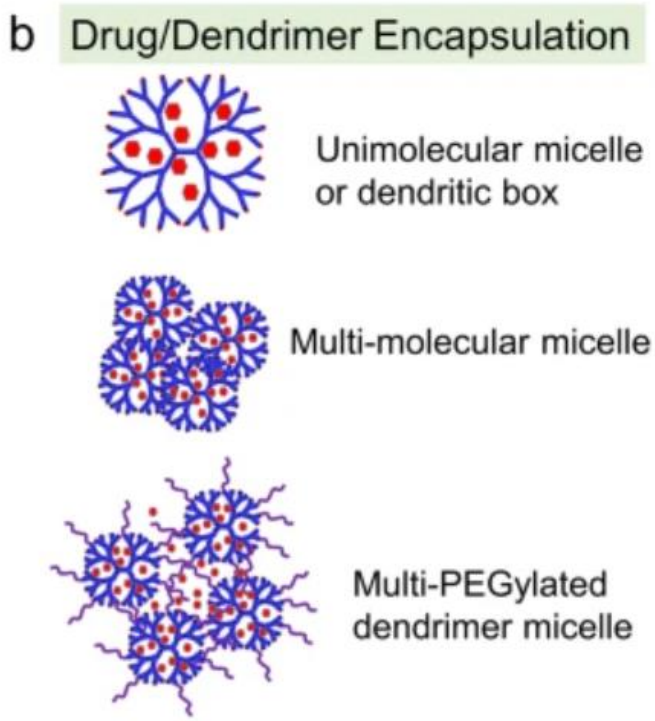
Generation 2

Dendrimers

Chemically link drugs →

Physically encapsulate drugs ↓





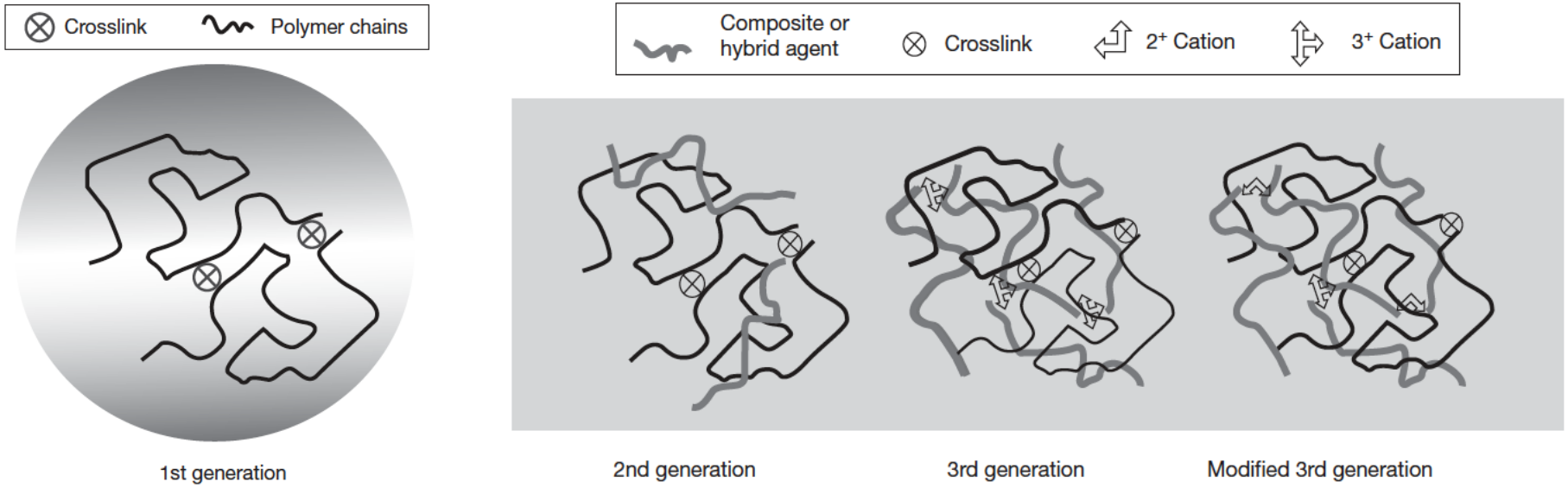
Building up the complexity and increasing the overall stability

Easy to manipulate the interactions through electrostatic interactions.

Hydrogels

A **hydrogel** is a network of polymer chains that are hydrophilic, meaning they can absorb and retain significant amounts of water while maintaining their structure.

Hydrophilic monomers e.g. carboxylate or amide in acrylic acid and acrylamide.



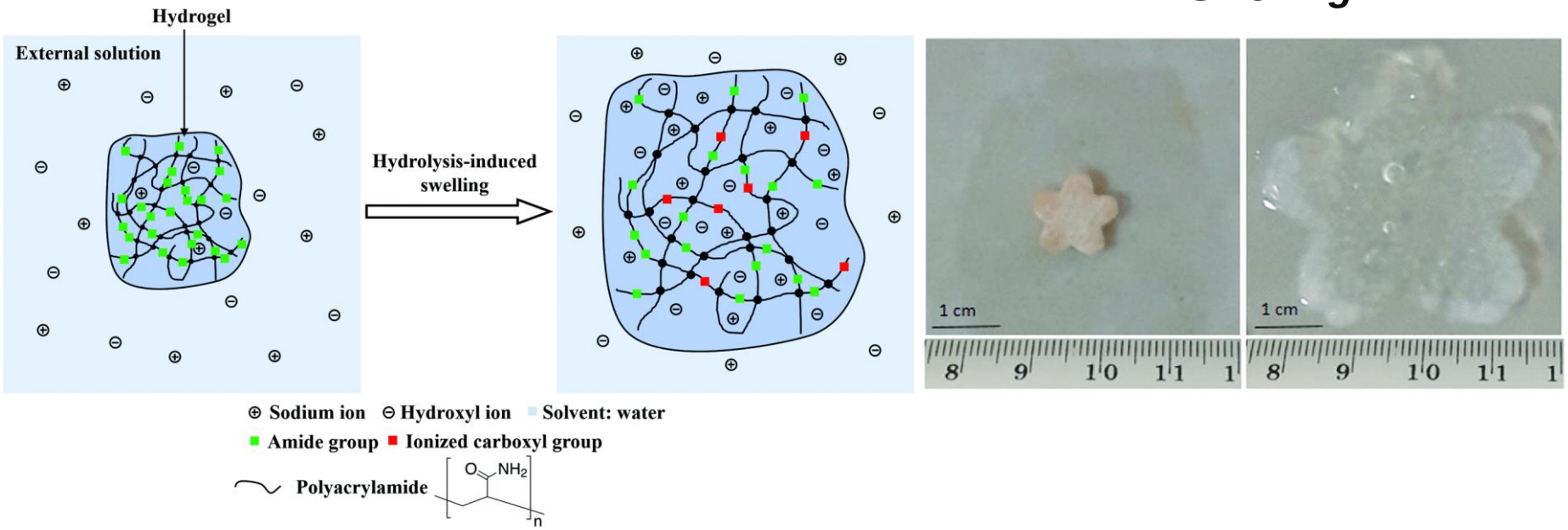
Bad mechanical stability

Add fillers (a different polymer) to increase mechanical strength

Super strength
Add ionogelling polymer and treat in an ion solution after gel formation

Hydrogels

Swelling



Hydrogels can partially hydrolyze and switch from neutral to ion-group containing. The electrostatic interactions enables significant swelling.

Gen 3

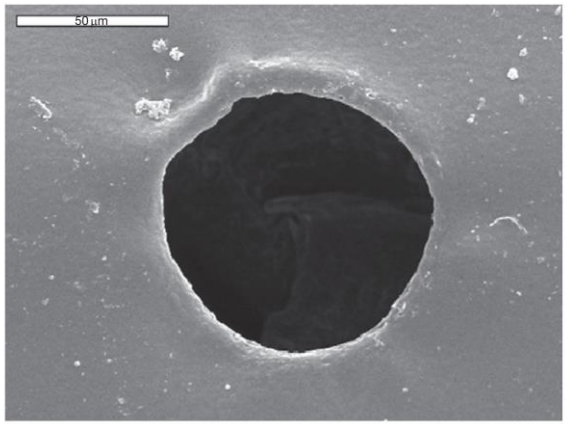


Figure 1 A typical superporous hydrogel with an average pore size of 50 μm.

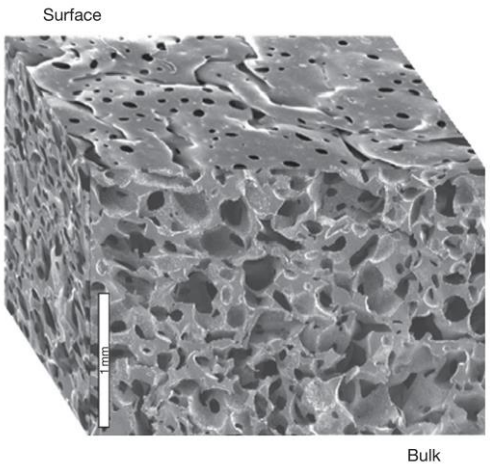


Figure 2 A three-dimensional porous structure of a typical superporous hydrogel.

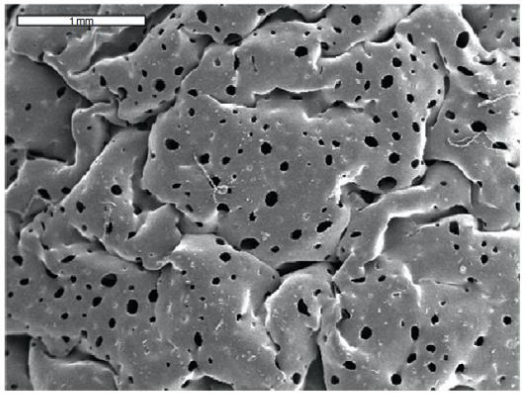
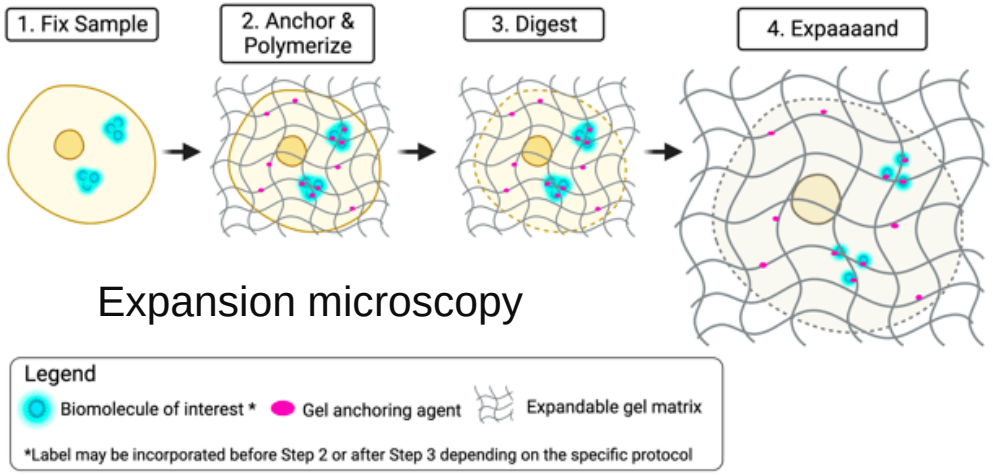
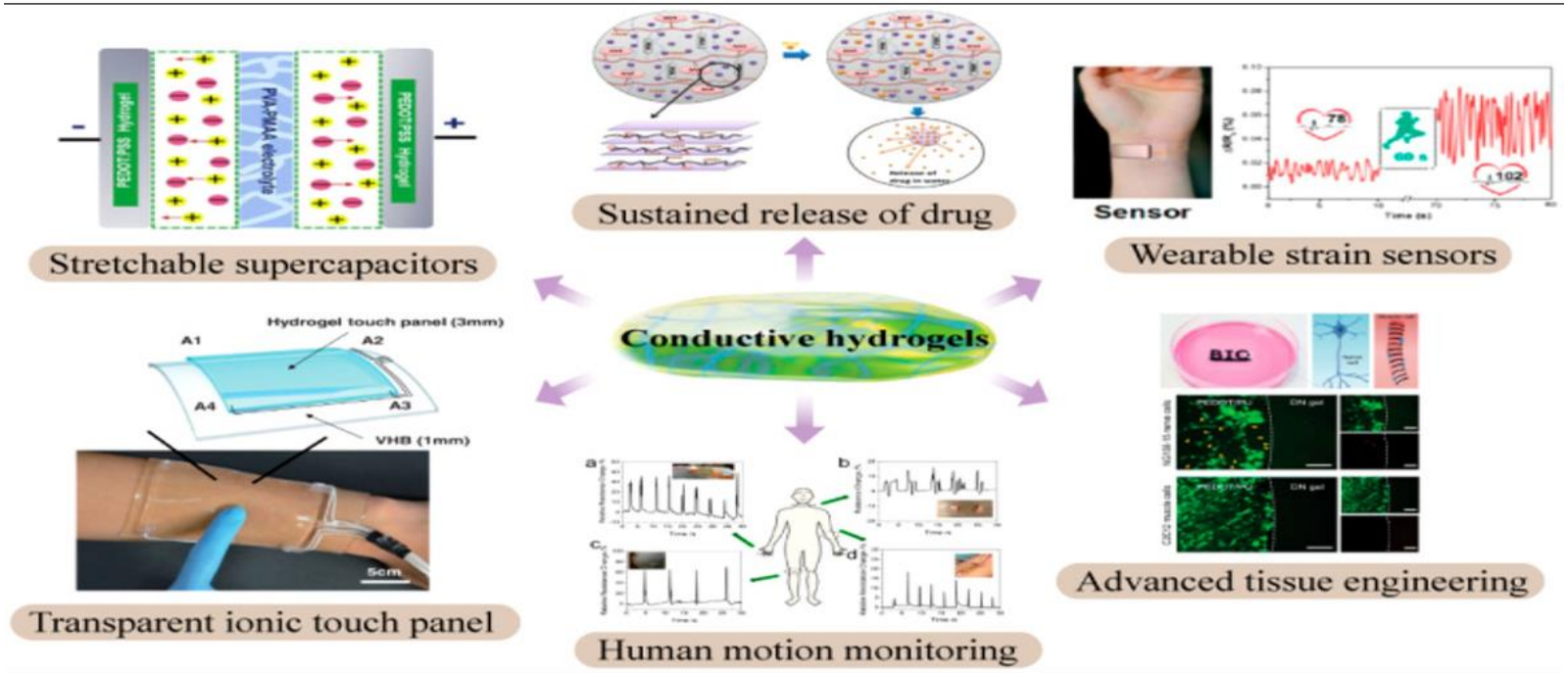


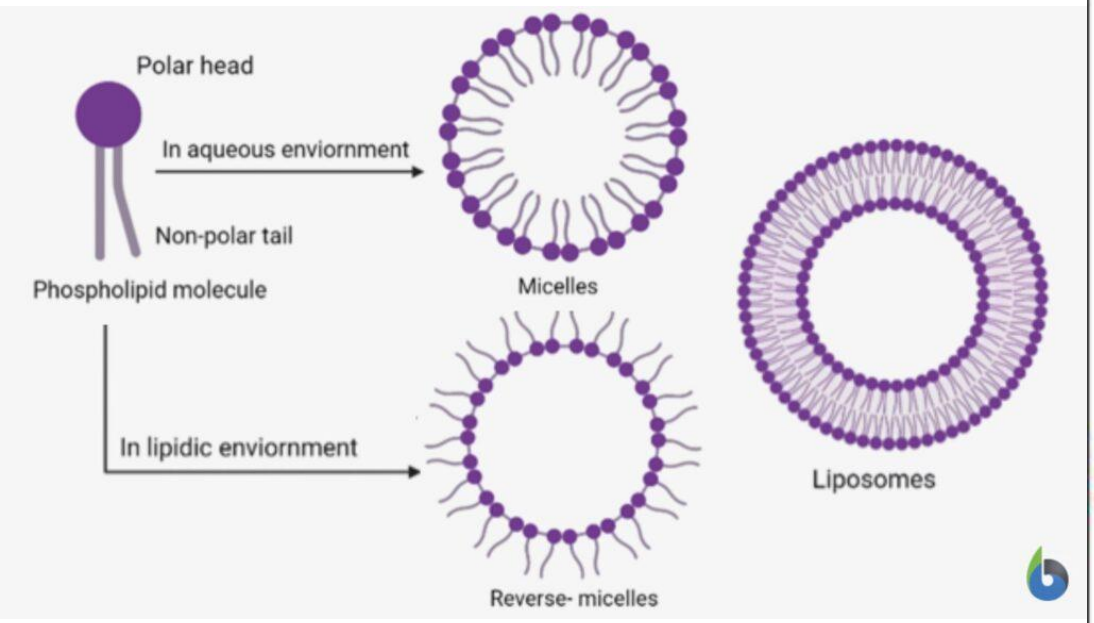
Figure 8 The surface morphology of a typical superporous hydrogel hybrid.

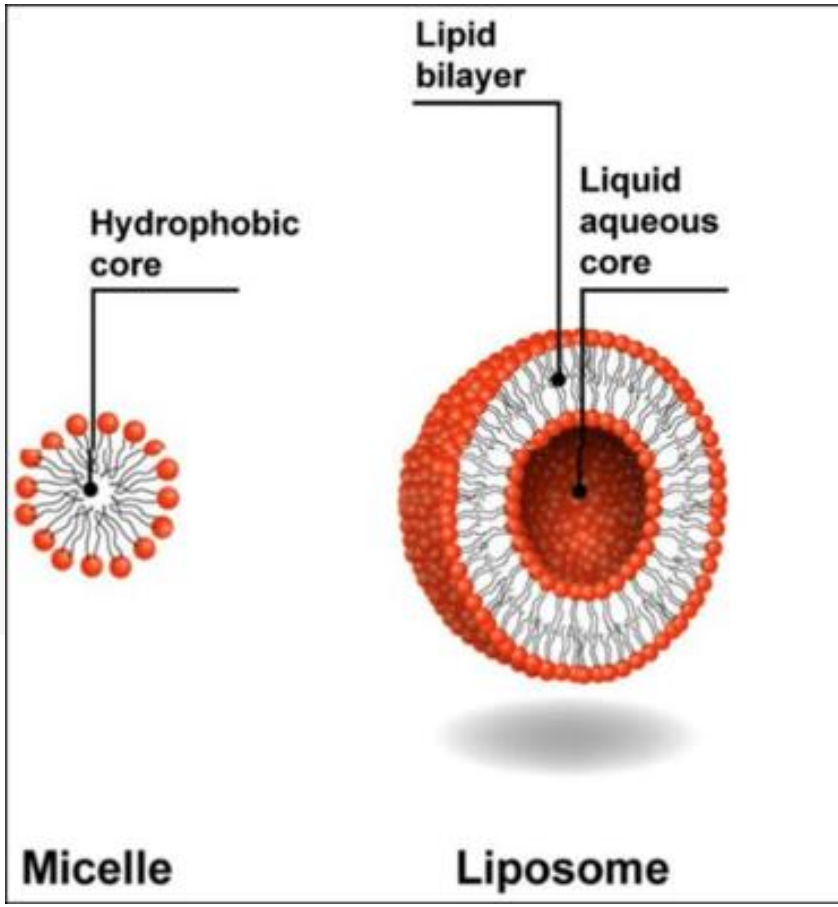
More about Hydrogels





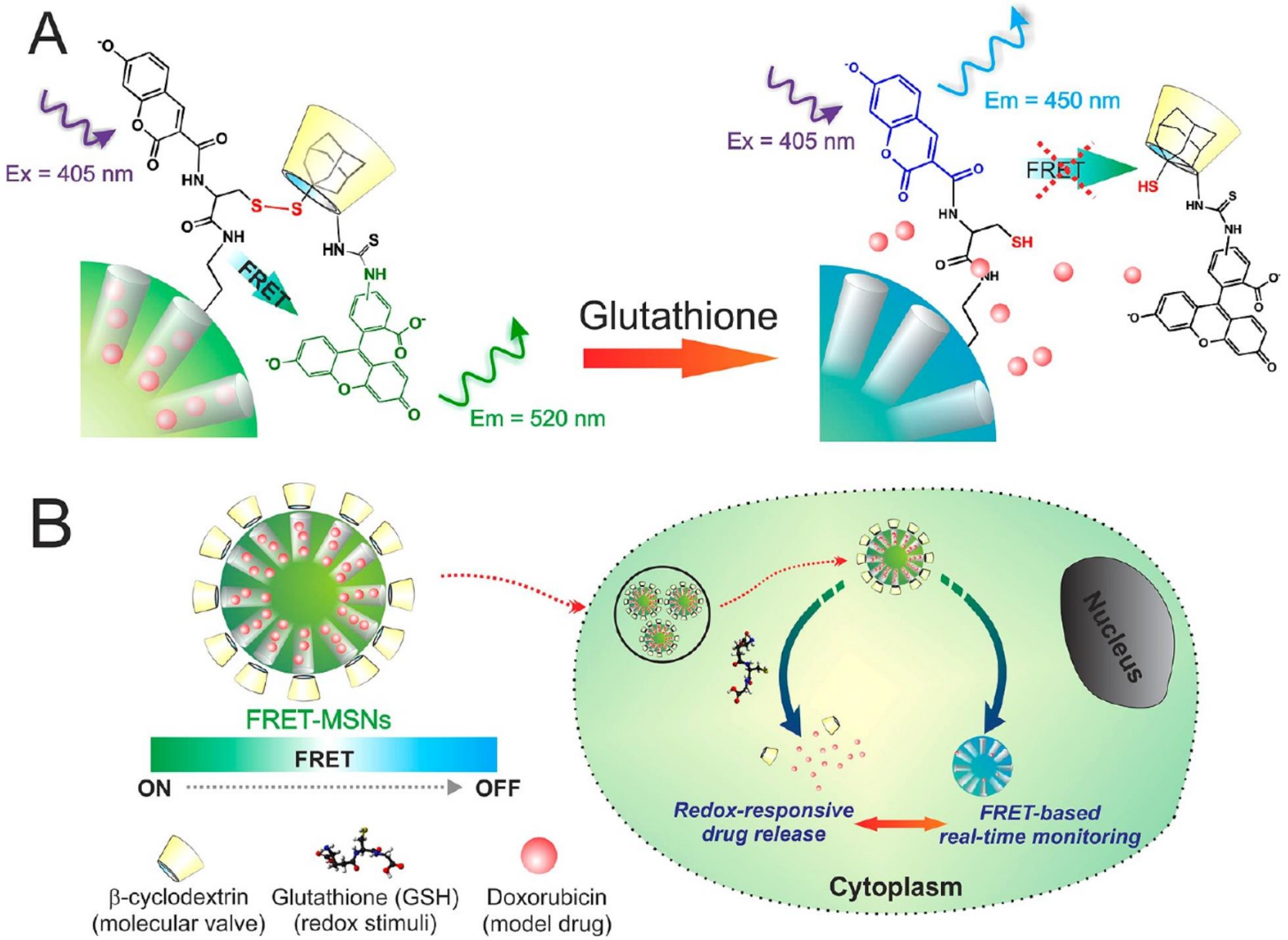
Extracellular Vesicles (Liposome)



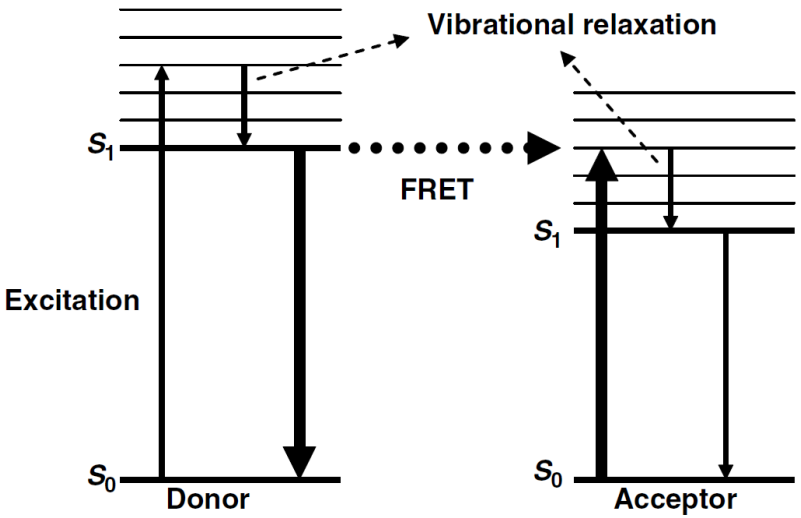


More bio-compatible, easier to transfer through physical barriers.

FRET Applications: Drug Release

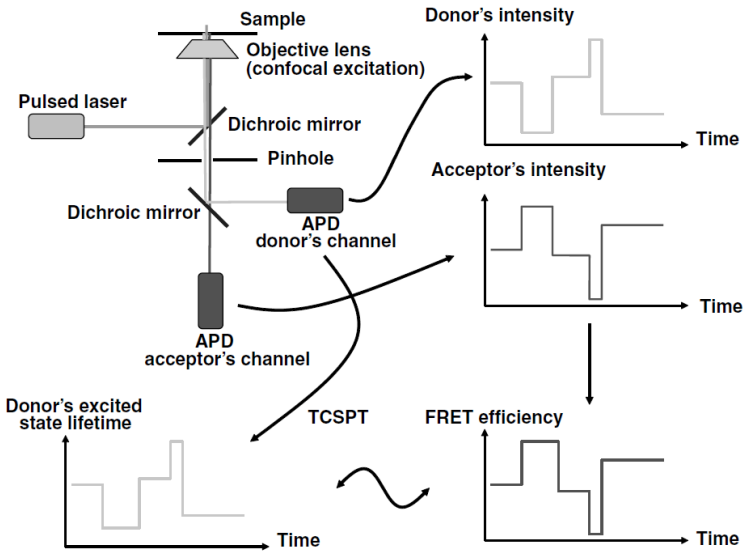


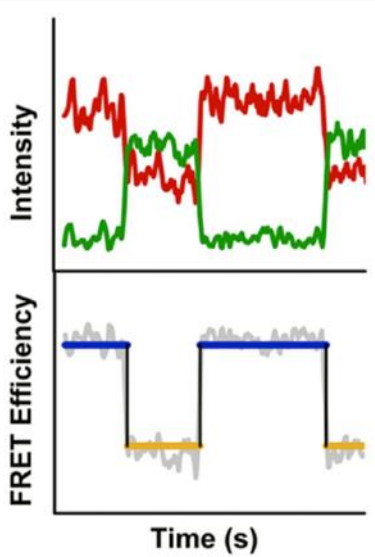
Förster Resonance Energy Transfer (FRET)



Scheme of FRET transfer

- FRET is through long range dipole-dipole interactions.
- Dipolar interactions are in the range of 2-10 nm.
- The orientation factor is between 0 - 4.For randomly oriented molecules, κ^2 equals 2/3 (diffusive) or 0.476 (still).





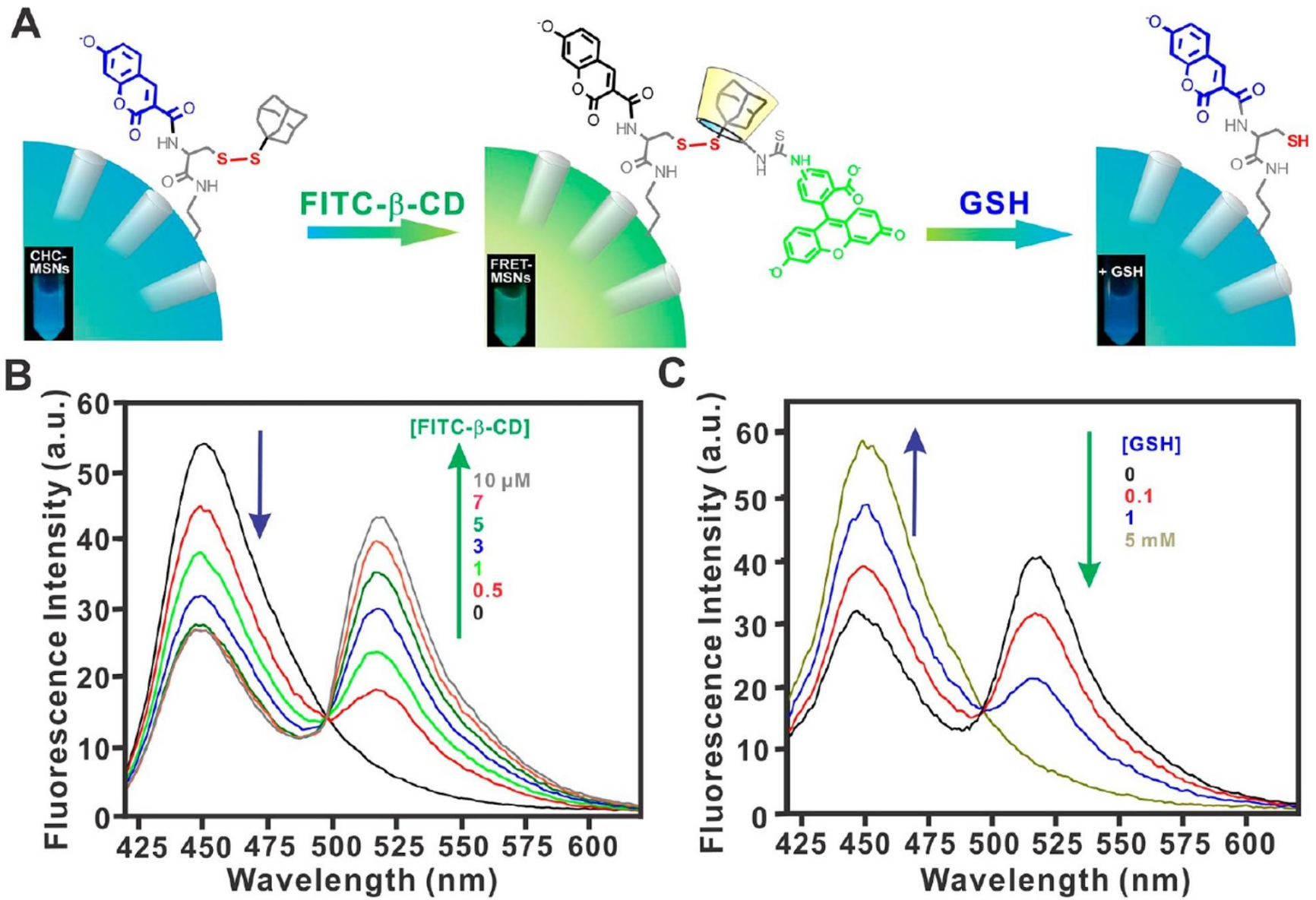
Anti-correlated

$$E = \frac{I_{A,\mathrm{FRET}}}{I_{D,\mathrm{FRET}} + \gamma I_{A,\mathrm{FRET}}}$$

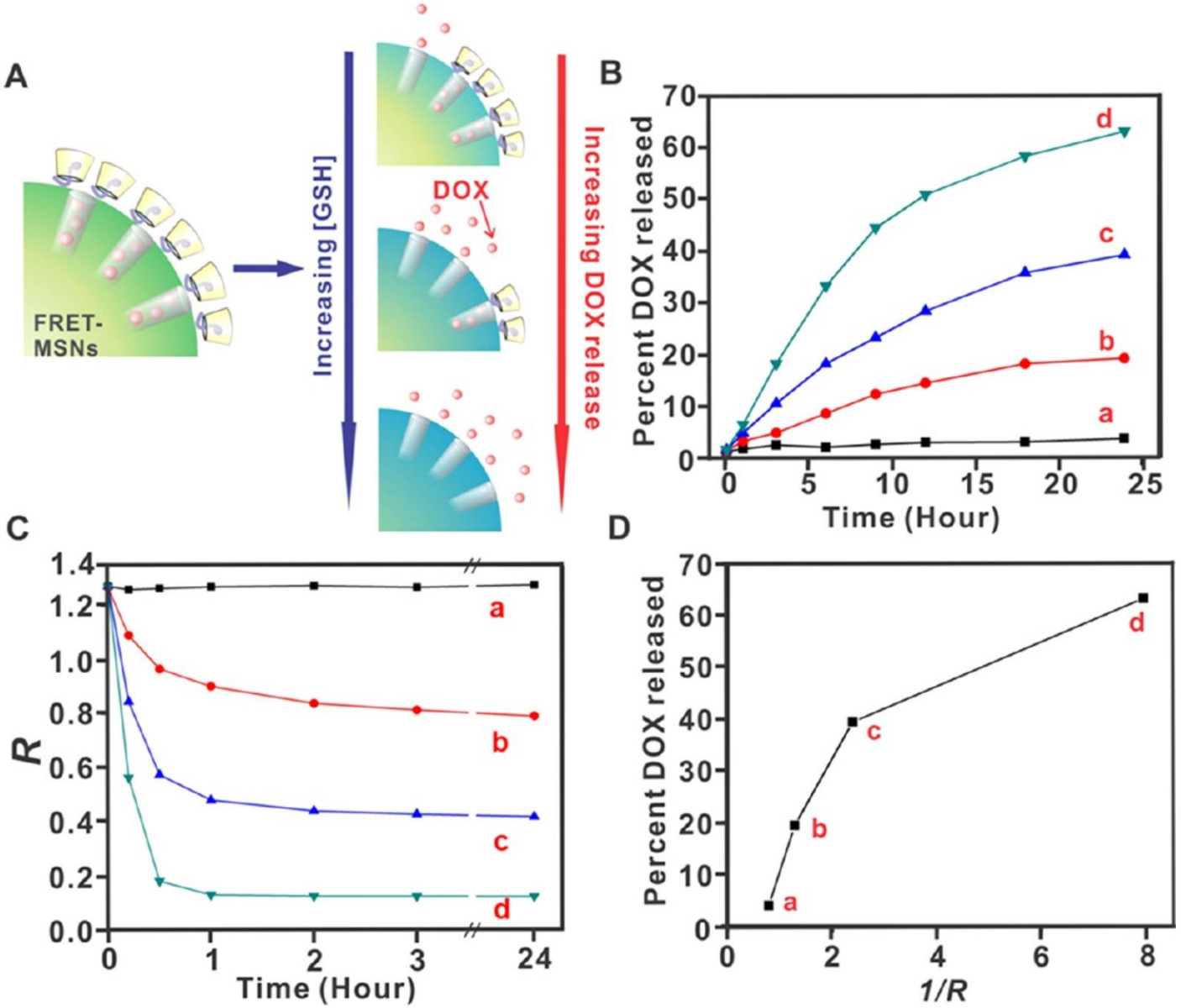
Converting FRET efficiency to distance:

$$E = \frac{R_0^6}{R_0^6 + r^6}$$

FRET Applications: Drug Release



FRET Applications: Drug Release



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