Intelligent Micro- and Nanocapsules

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Coating colloids and Hollow capsules

Release properties

Encapsulation of macromolecules

Organic dye precipitation by pH-gradient

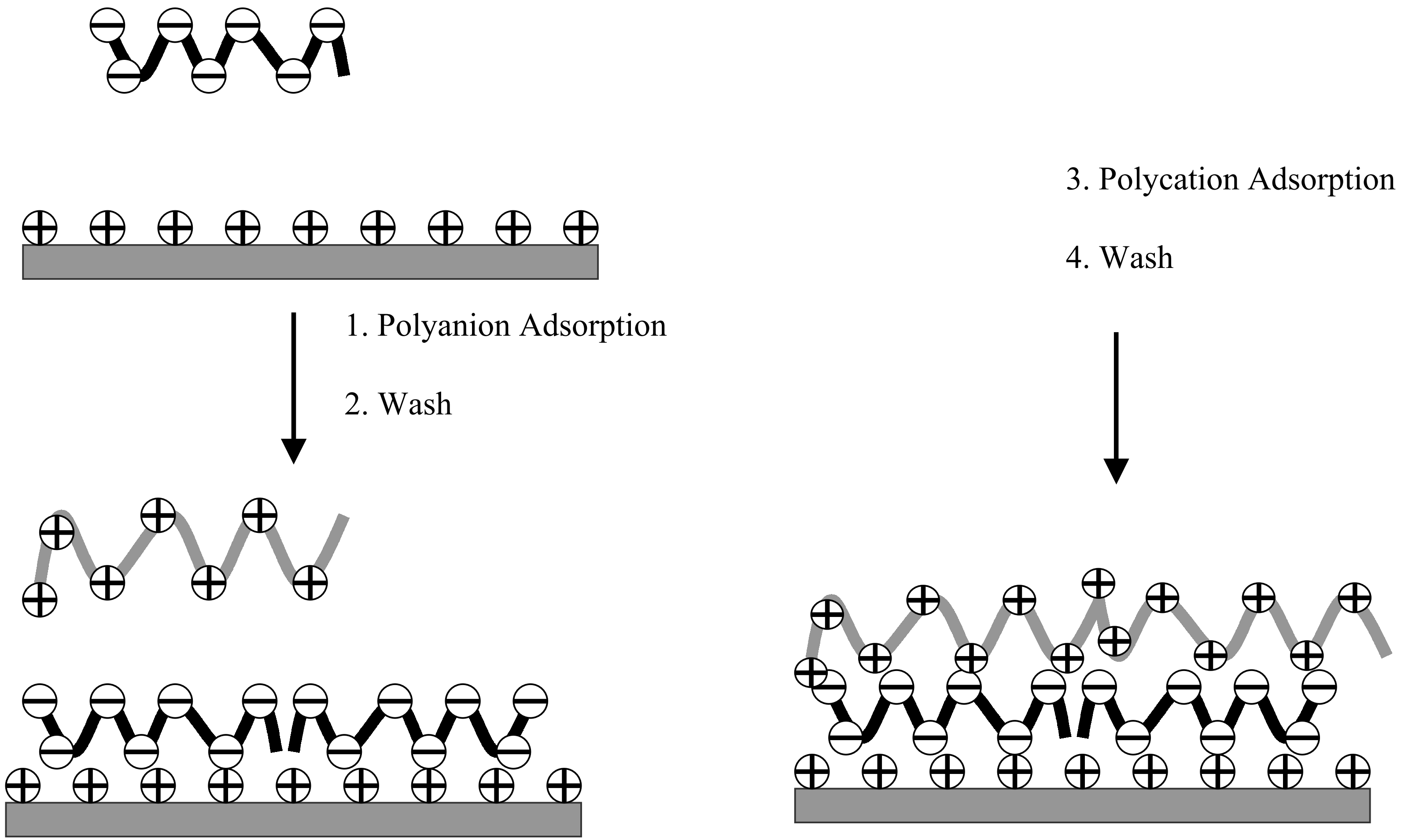
Inorganic particles synthesis in capsules

Poor-water soluble dye precipitation

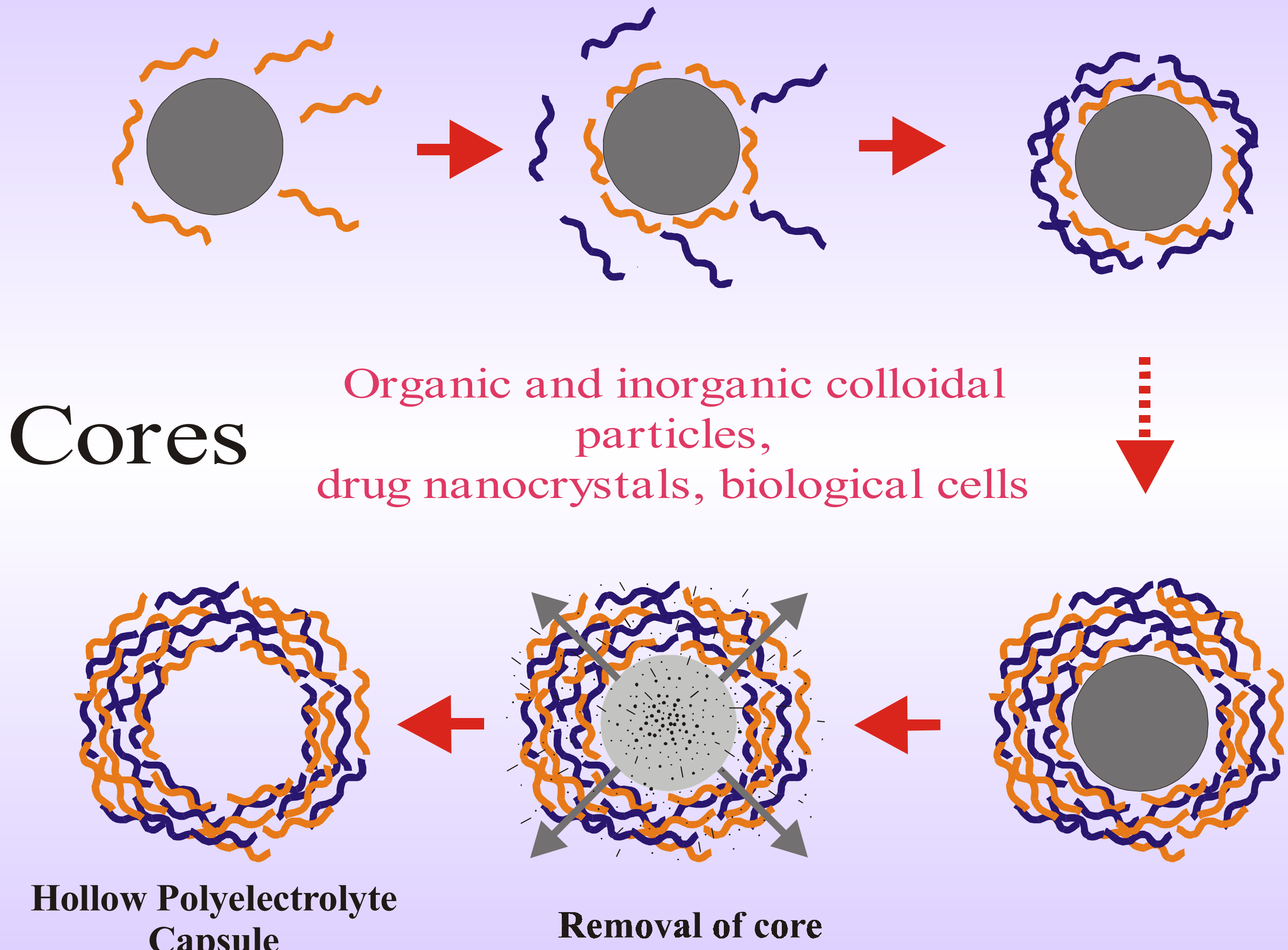
Capsule based combinatorial libraries

Enzymatic reaction in capsules

Polyelectrolyte Layer-by-layer assembly



Capsule preparation



The core (template) is a dissolvable colloidal particle, a drug particle a dye particle or even a biological cell

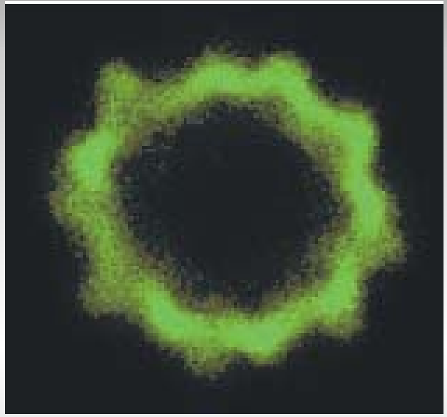
- Melamin resin cores
- Inorganic cores, carbonates, oxides
- Dye and drug particles
- Droplets
- Erythrocytes, others biological cells

Layer constituents

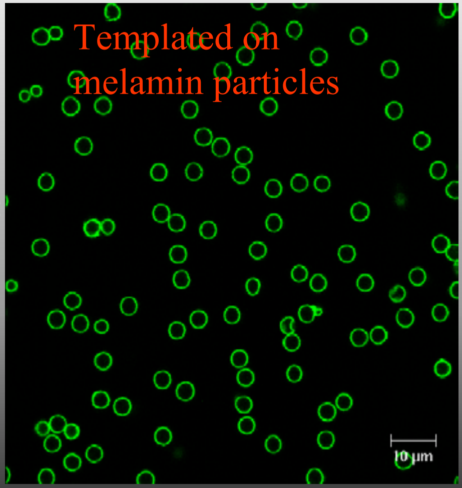
- Synthetic polyelectrolytes
- Biopolymers (proteins, polysacharides, nucleic acids)
- Lipids,
- Inorganic nanoparticles
- The wall can be tuned in thickness, composition and functionality by choosing various constituents and adjusting the layer number

Advantage of the technique

Templated on red blood cell



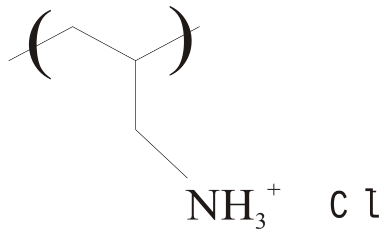
- The size and shape of the capsules is controlled by the SIZE and SHAPE of the TEMPLATE



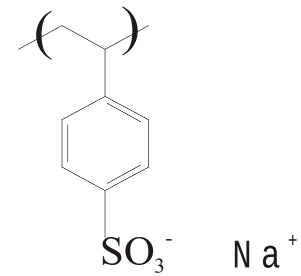
Templated on melamin particles

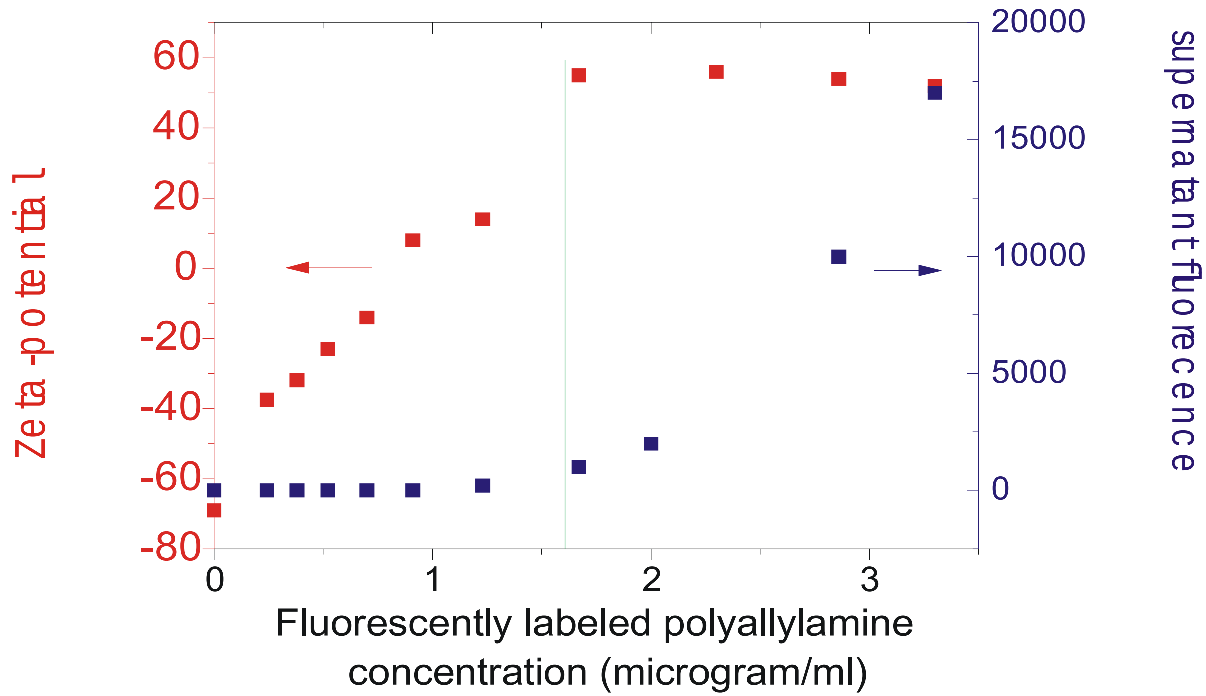
- Rather monodisperse capsule dispersions can be prepared

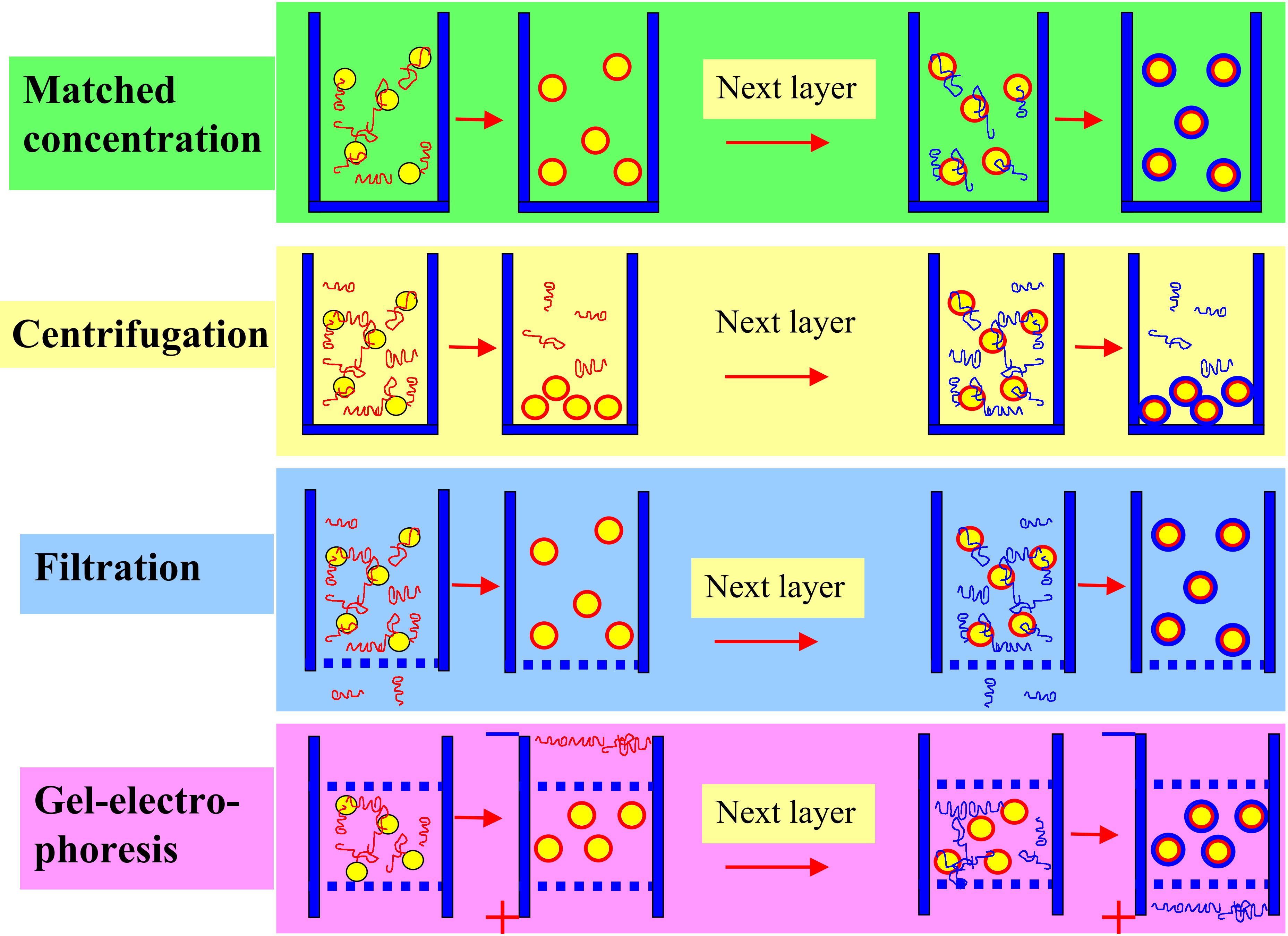
Poly(allylamine hydrochlorid) PAH



Poly(styrenesulfonat) PSS

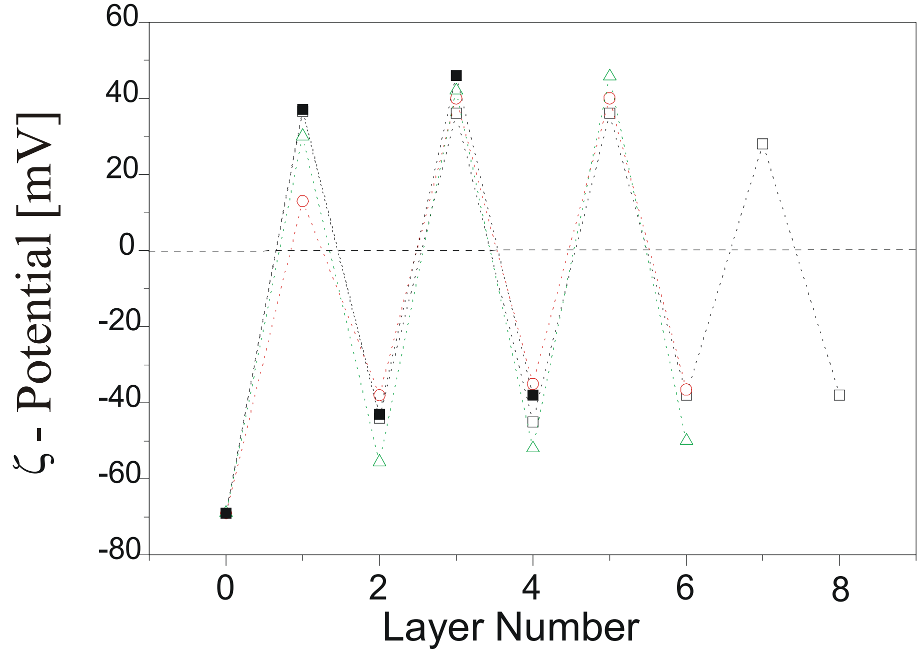






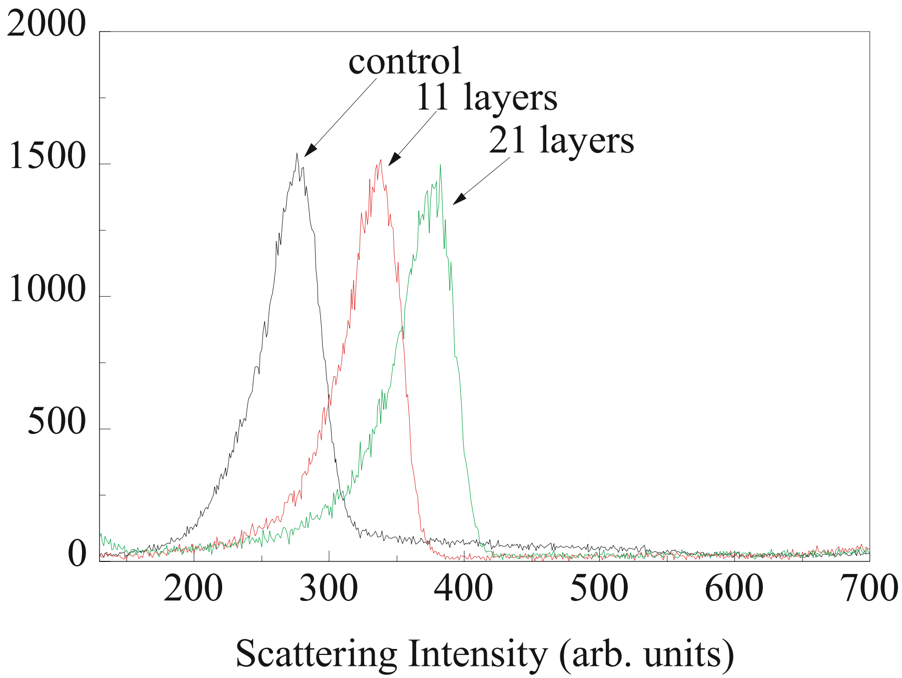
Matched concentration
Next layer
Centrifugation
Next layer
Filtration
Next layer
Gel-electro-phoresis
Next layer

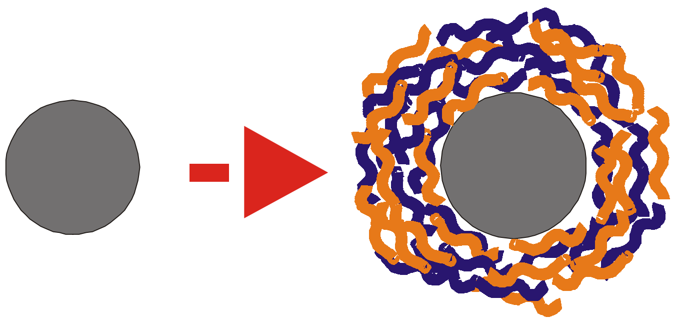
Electrophoretic Mobility measurements as means to follow Layer Growth

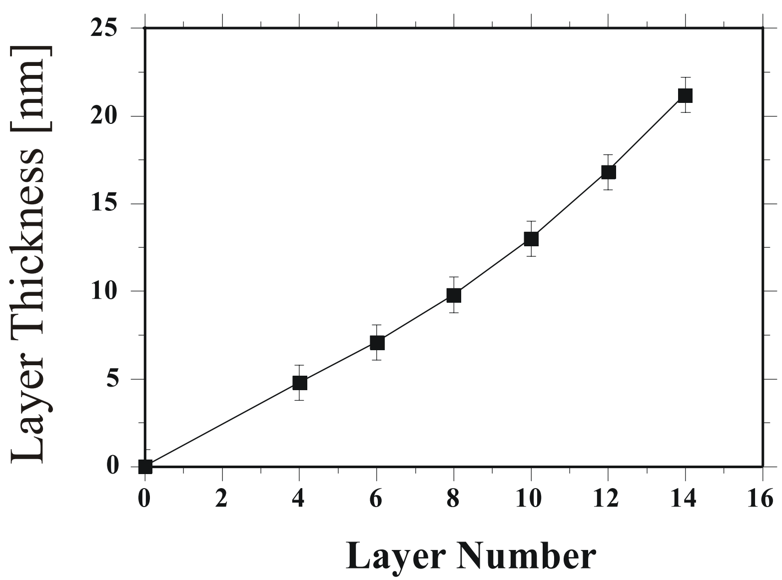


Various Polyelectrolytes: □ PDADMAC - PSS
■ BSA - PDADMAC, ○ PSS - PAH, △ DNA - PDADMAC

Layer Thickness - Monitoring of Multilayer Formation by Single Particle Light Scattering

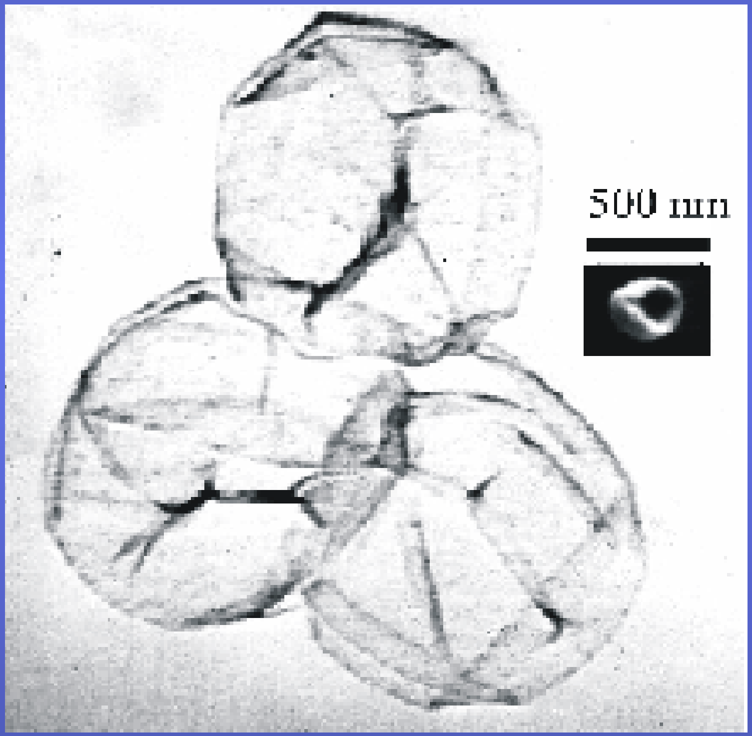




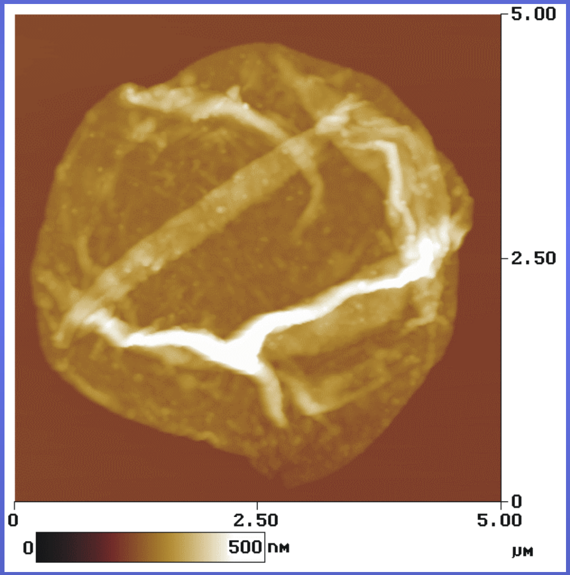


Hollow Polyelectrolyte Capsules

Layer-by-Layer approach



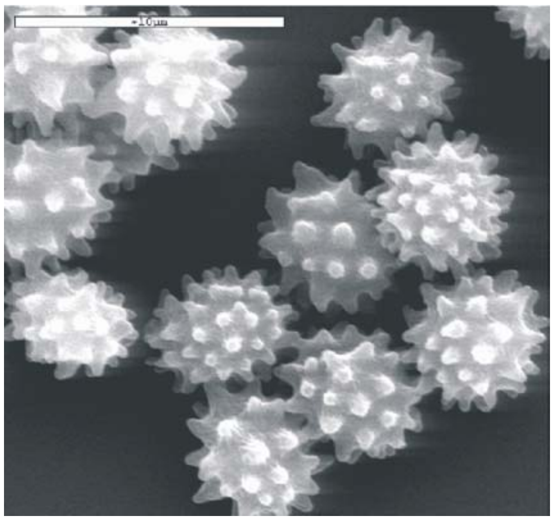
Scanning electron microscopy



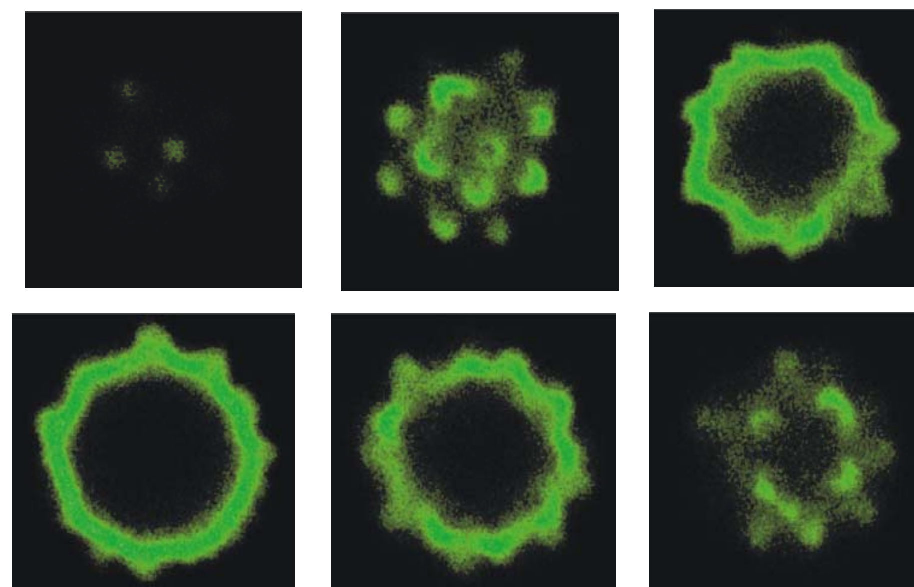
Atomic force microscopy

Templating on biological cells - MICROREPLICA

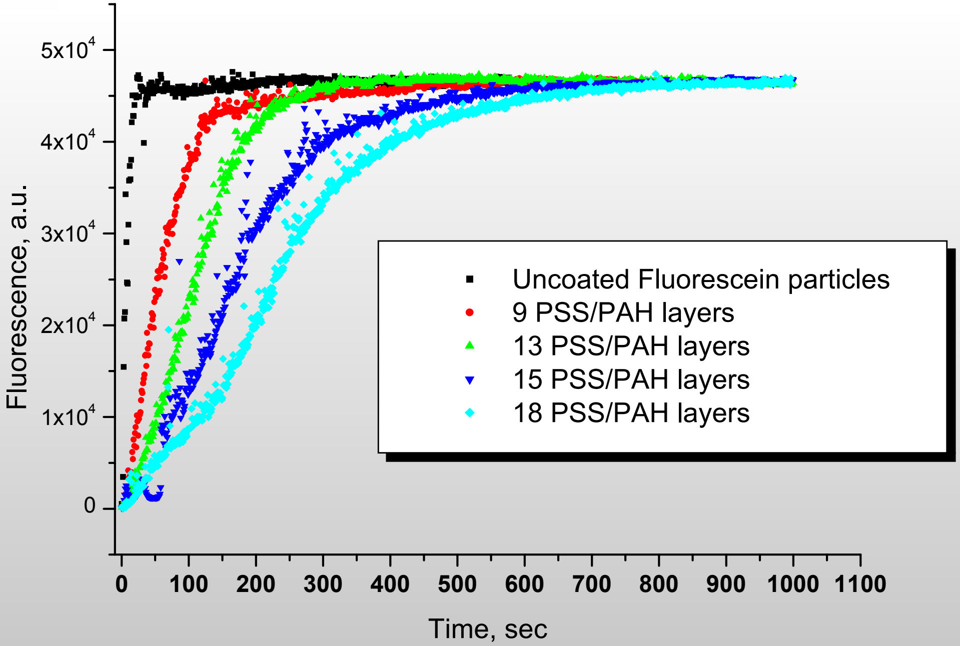
Echinocyte cells

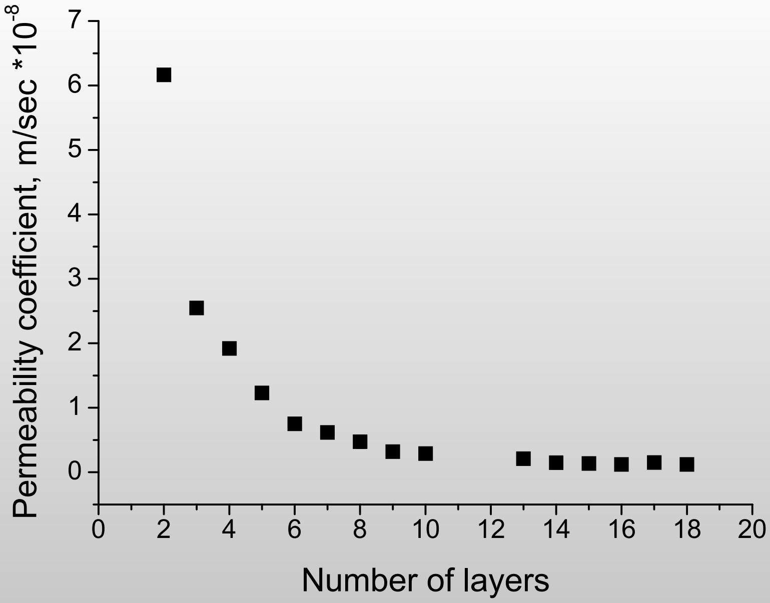


Confocal Scans through an Echinocyte templated polyelectrolyte shell

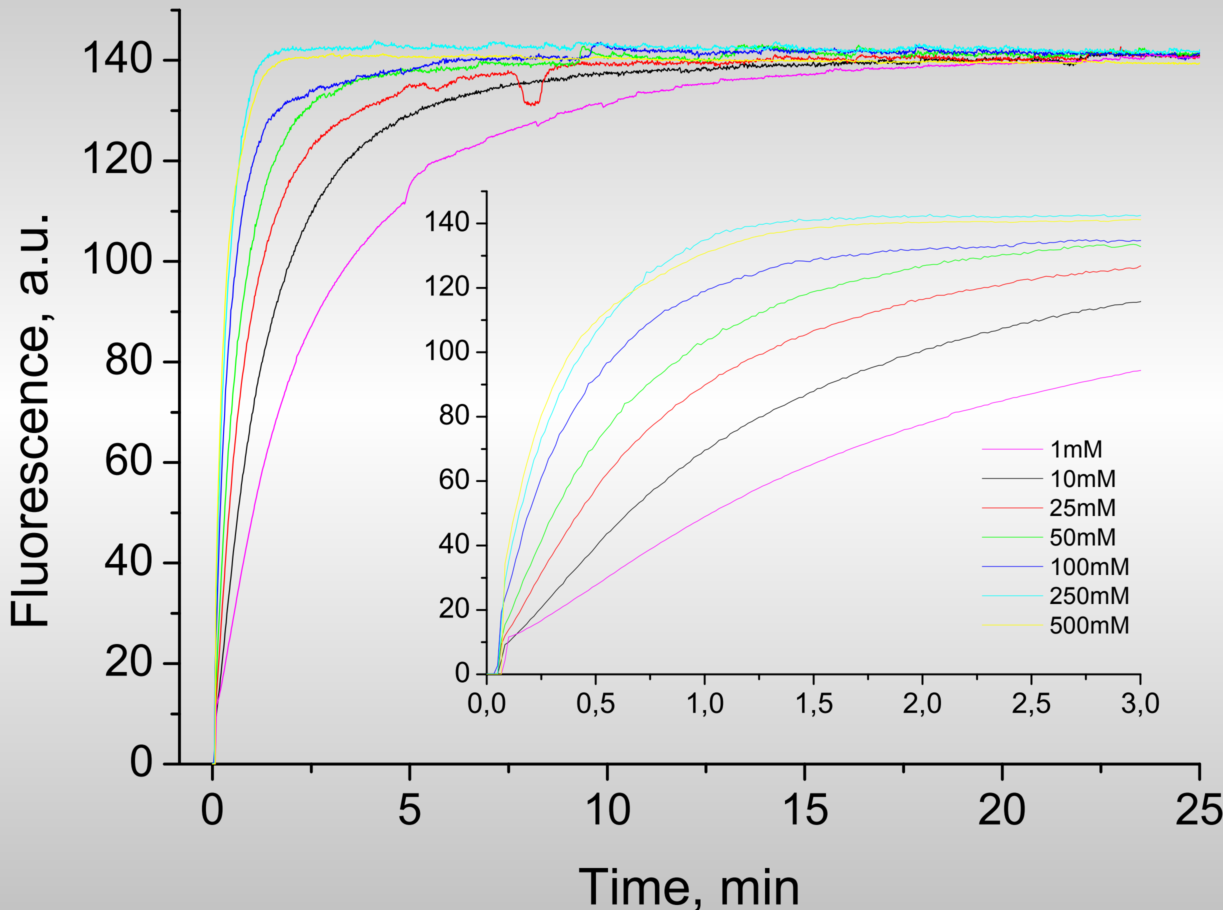


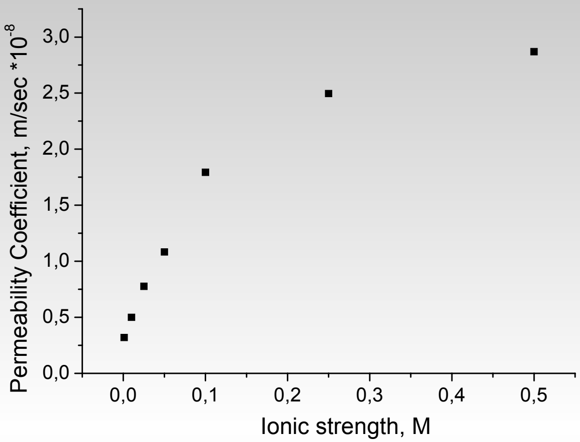
Release Control by Multilayers





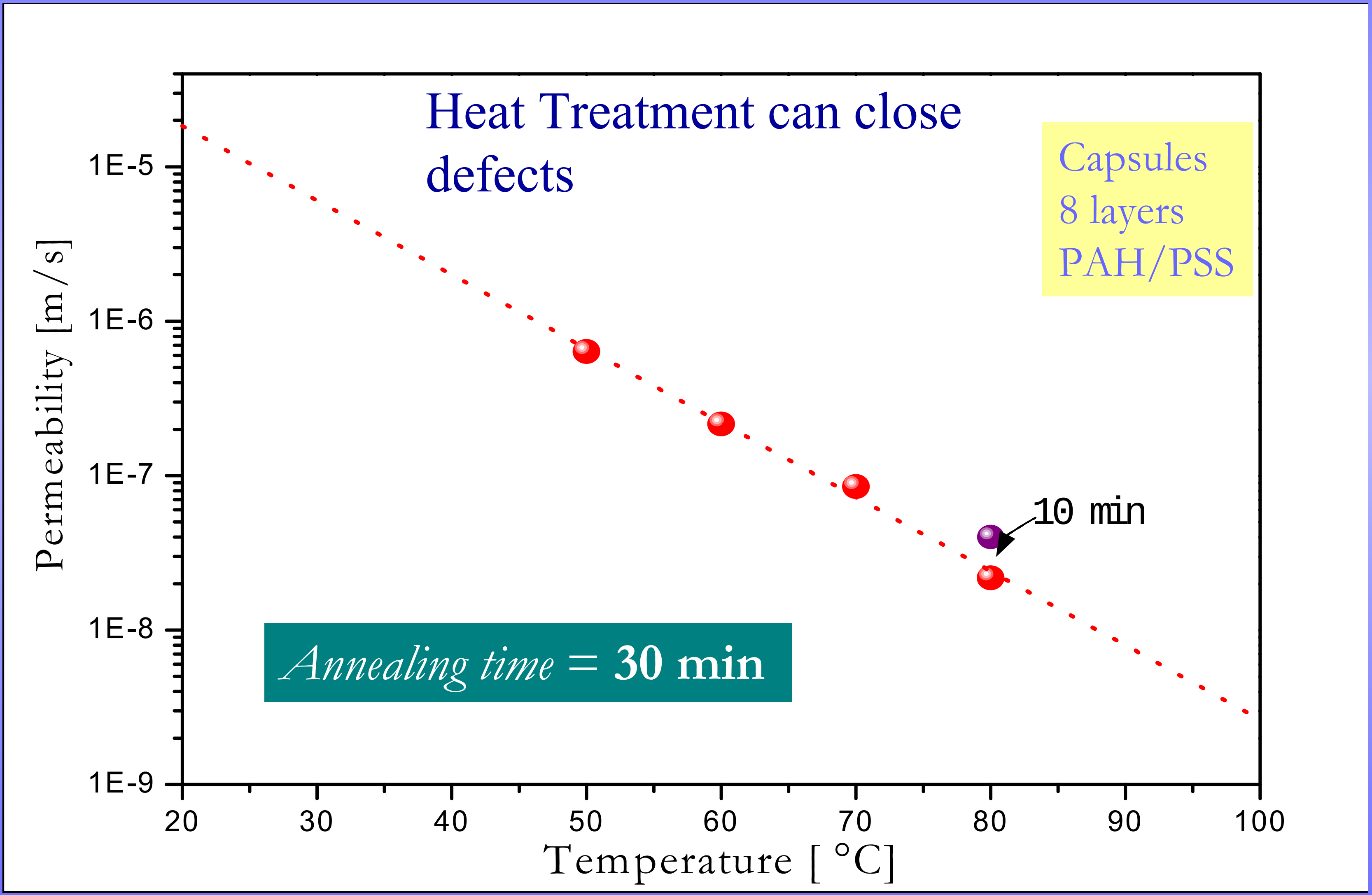
Permeability Coefficients: Ionic Strength



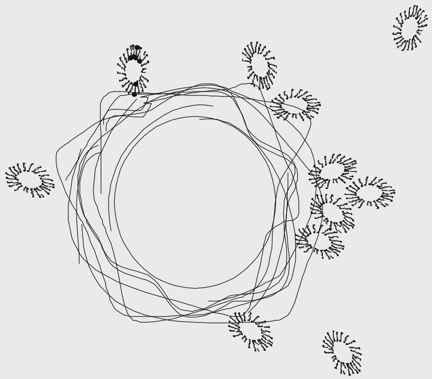


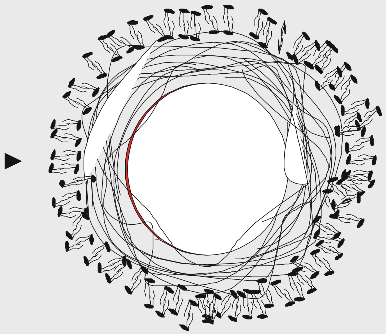
Ionic strength influences drastically (one order of magnitude going from 1 to 500mM) the properties of PEM.

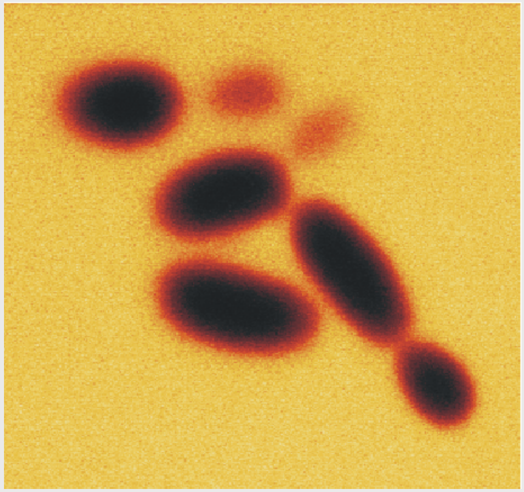
Permeability behavior of annealed shells



The Presence of the Lipid Bilayer Decreases the Permeability





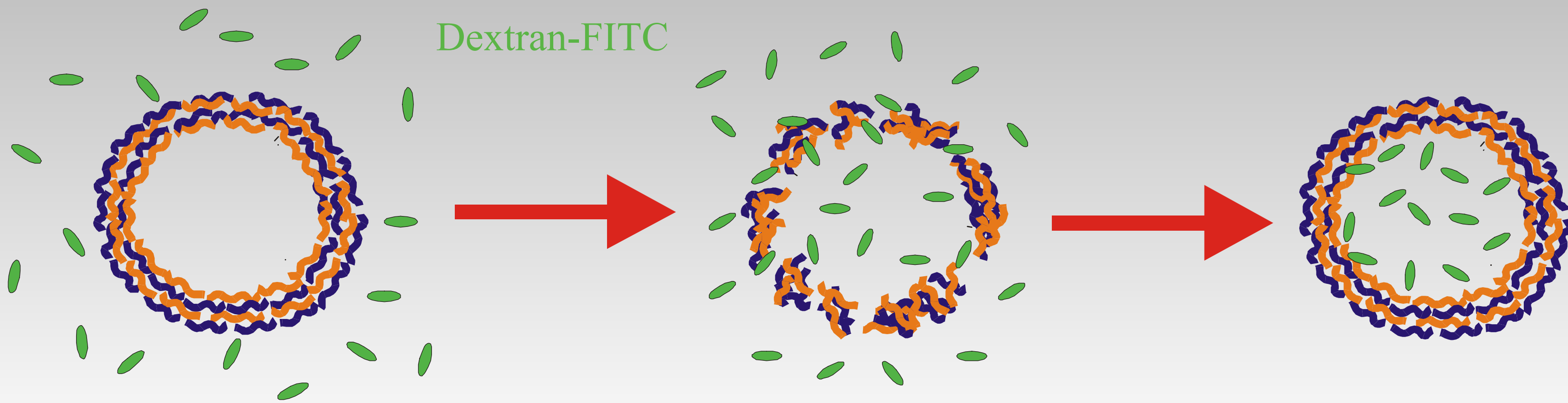


Capsules with 8 Polyelectrolyte Layers

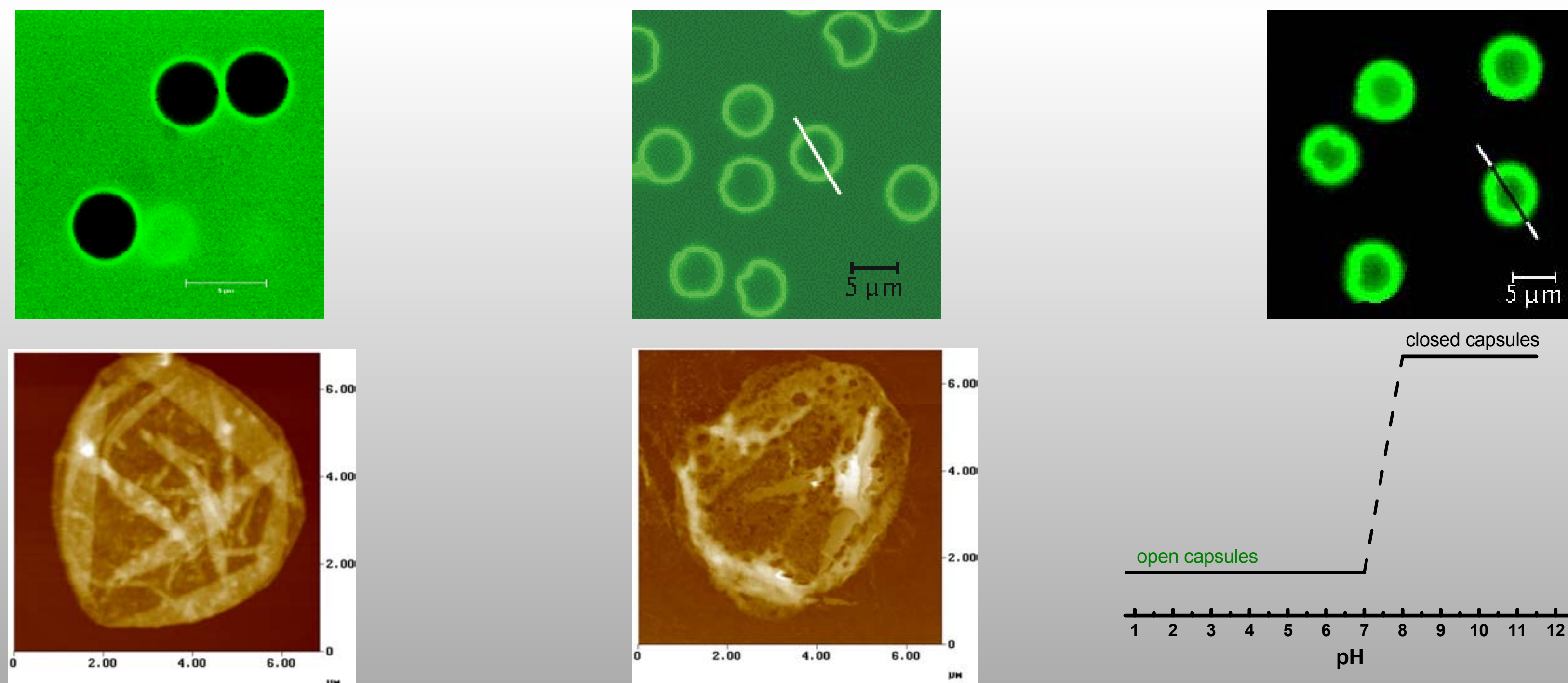
Capsules with a Phospholipid Bilayer

The fluorescent polar marker 6-carboxyfluorescein is excluded

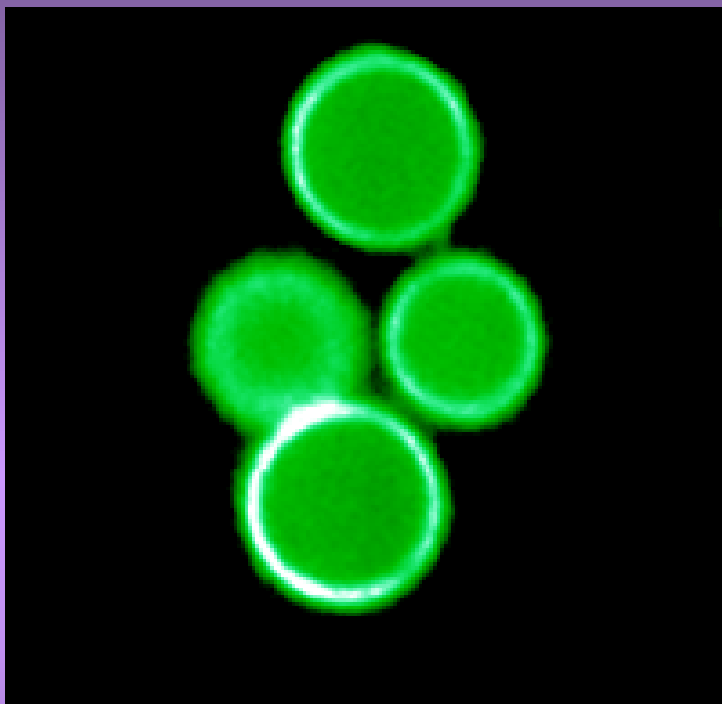
Encapsulation via Permeability Regulation

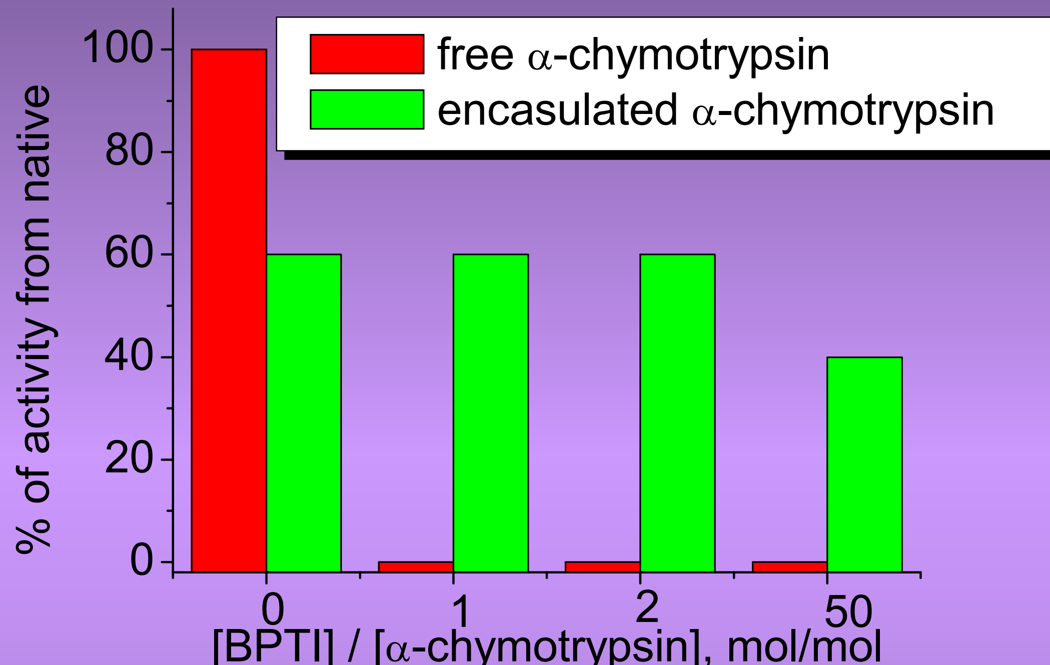


pH >7.5, closed state | **pH <6.5, open state** | **pH>7.5 Encapsulated**



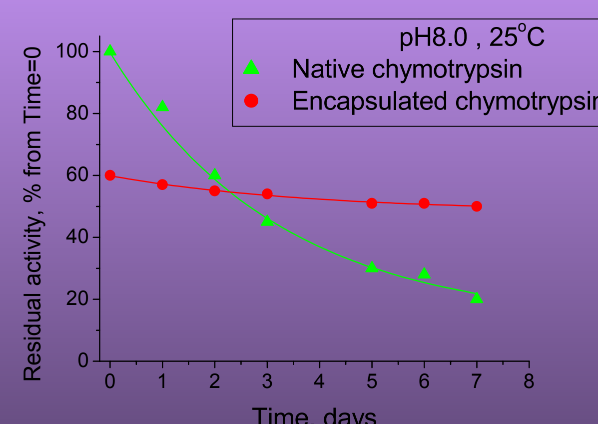
Encapsulation of Enzymes





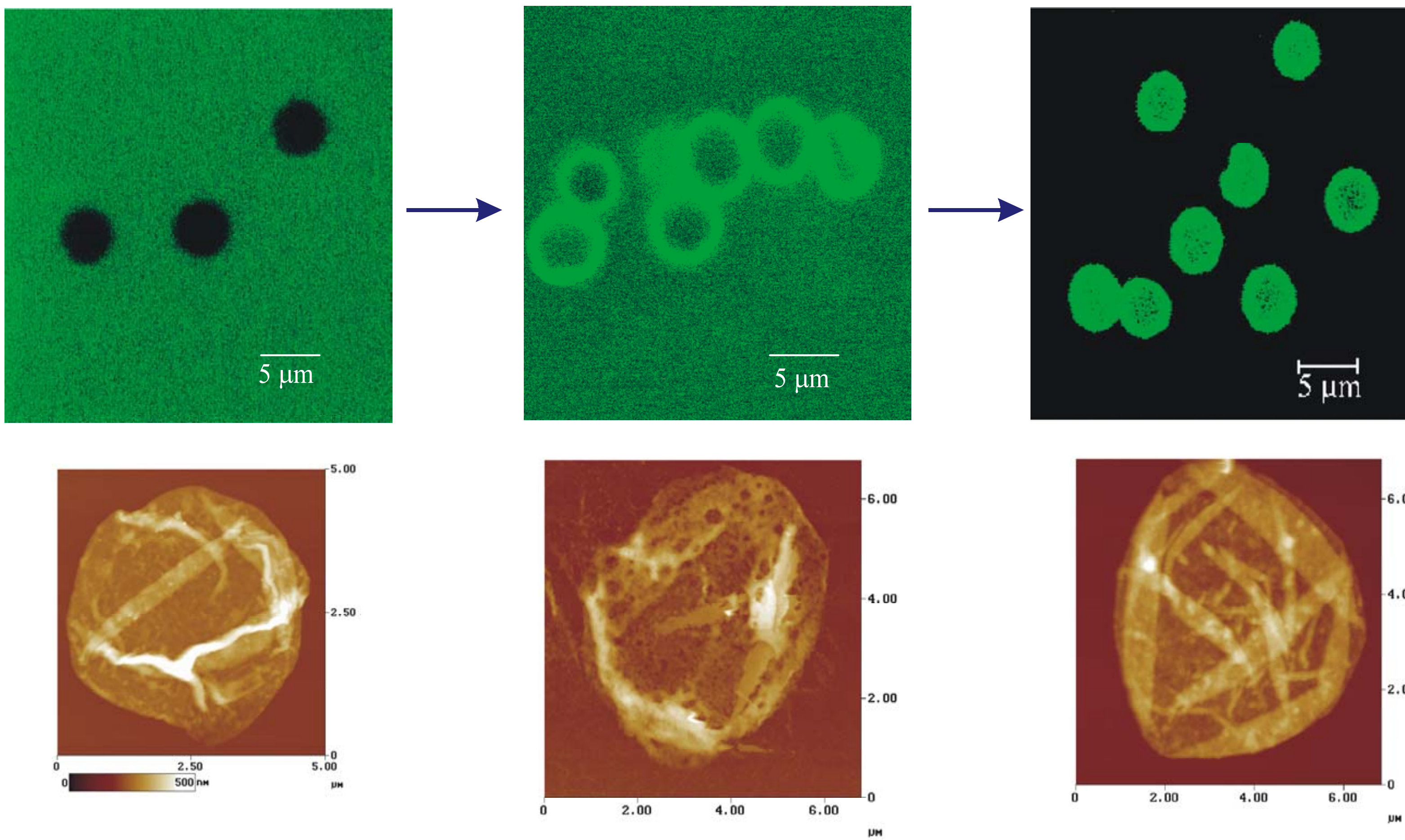
 Inhibitor

 Enzyme



Encapsulation of Urease in Polyelectrolite Multilayer shells

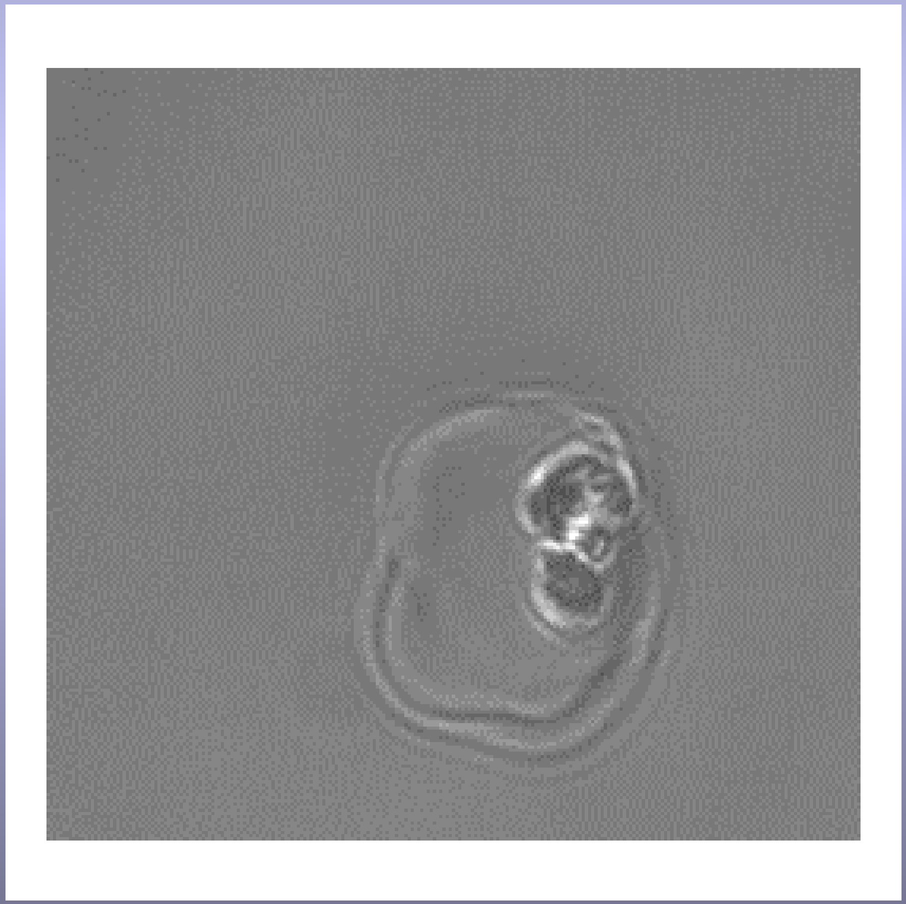
In Water | **Ethanol/Water 1:1** | **In Water. Encapsulated**

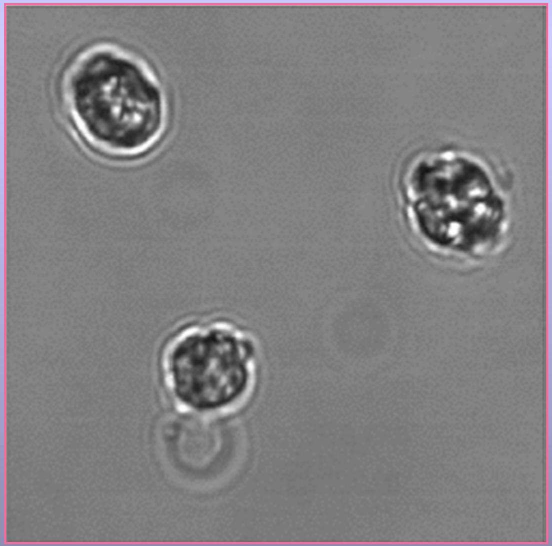


Calcium carbonate growth into polyelectrolyte capsules by urease catalyzed reaction

$$CH_4N_2O + 2H_2O \xrightarrow{\text{urease}} 2NH_4^{+} + CO_3^{2-}$$

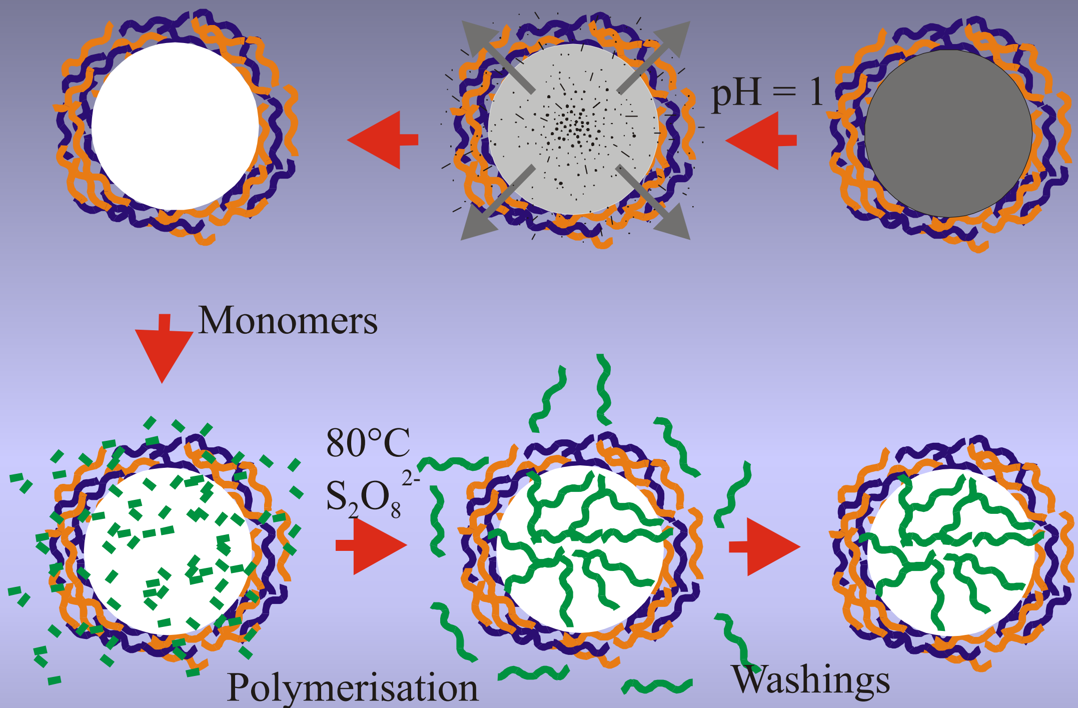
$$Ca^{2+} + CO_3^{2-} \rightarrow CaCO_3$$

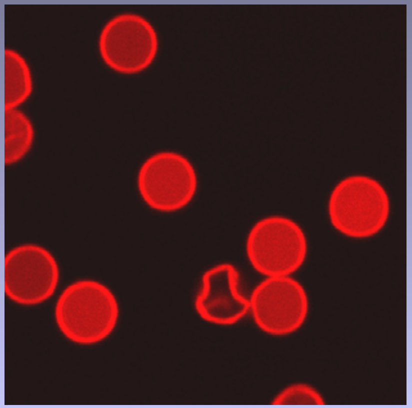




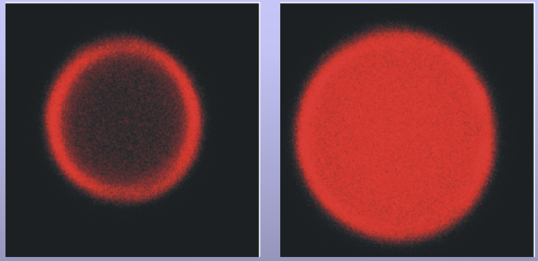
A final stage of precipitation

Polymer Synthesis inside Capsules





Broken and Empty Capsules

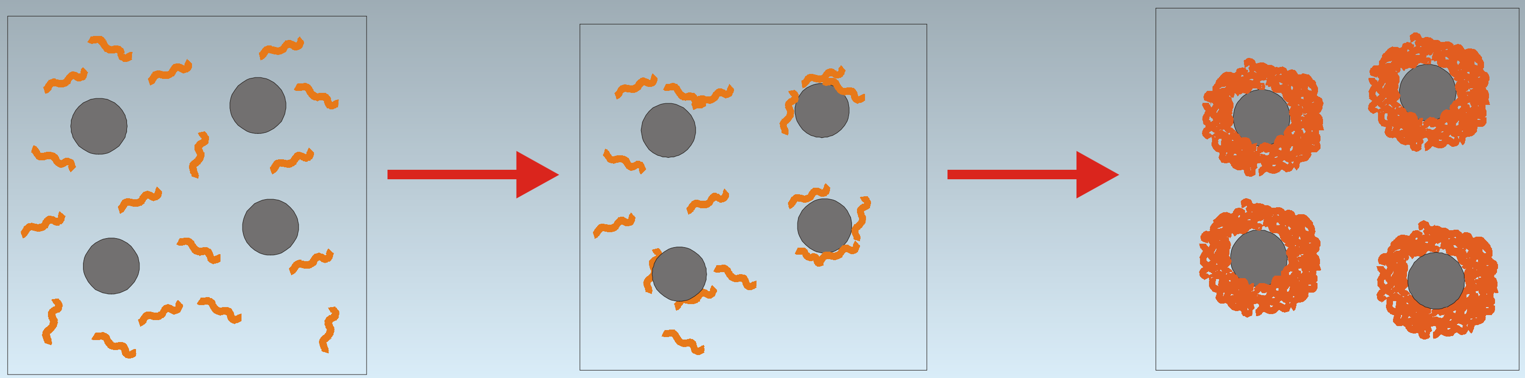


Swelling as a result of osmotic pressure increase.

- •The capsules were filled with a fluorescent (rhodamin) copolymer
- •The permeability difference between substrate and product is always employed

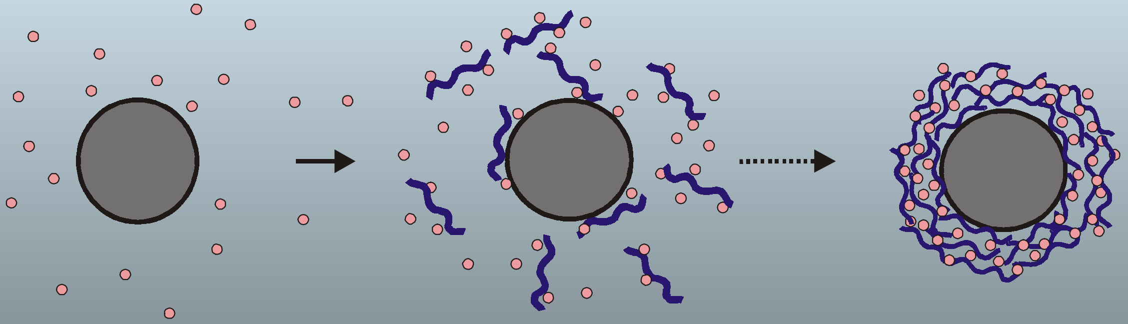
Encapsulation of macromolecules.

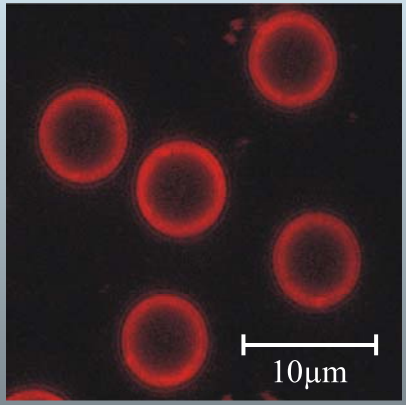
1. Controlled precipitation of polymers on colloidal particles



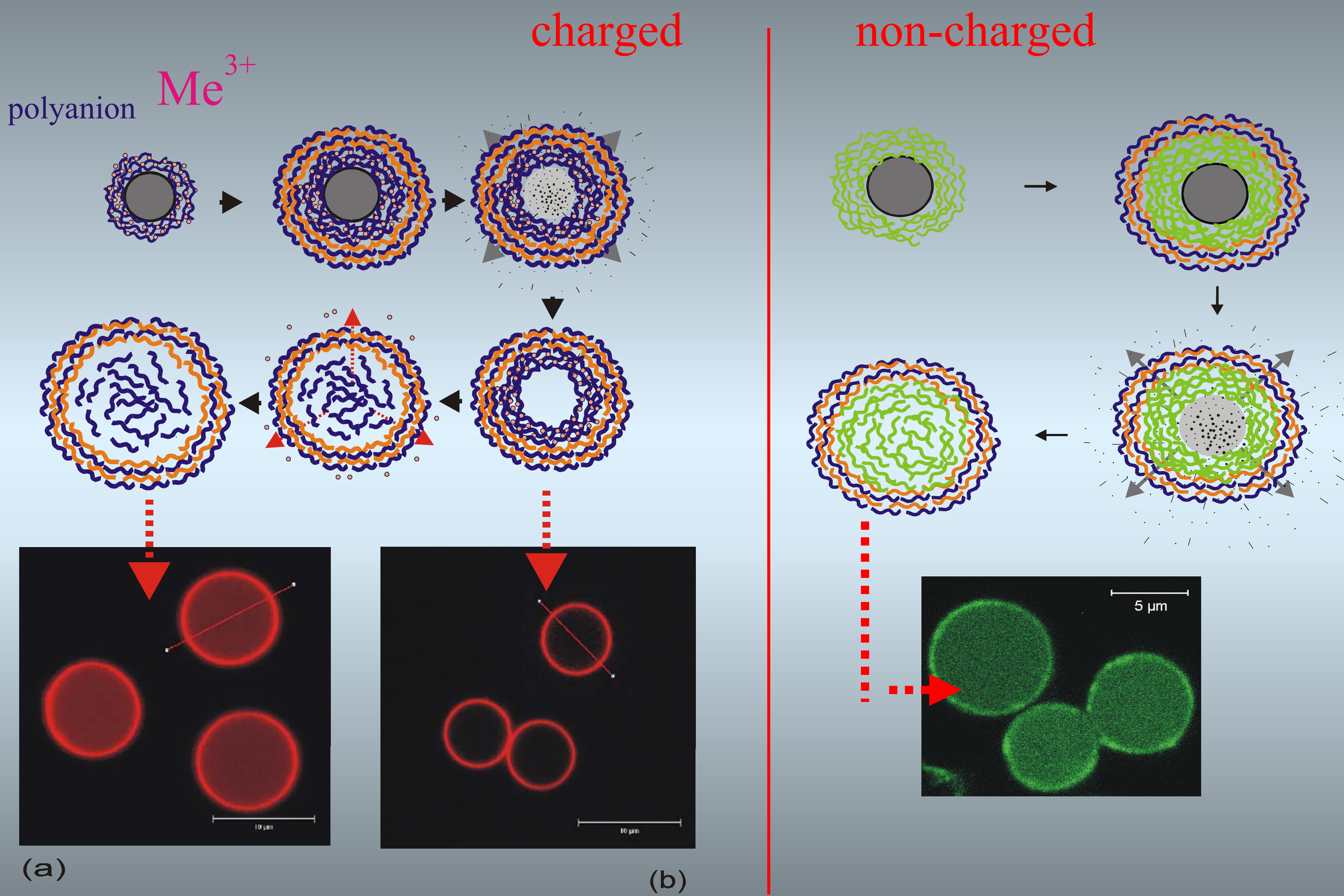
Precipitating condition

Solvent or complex-ion

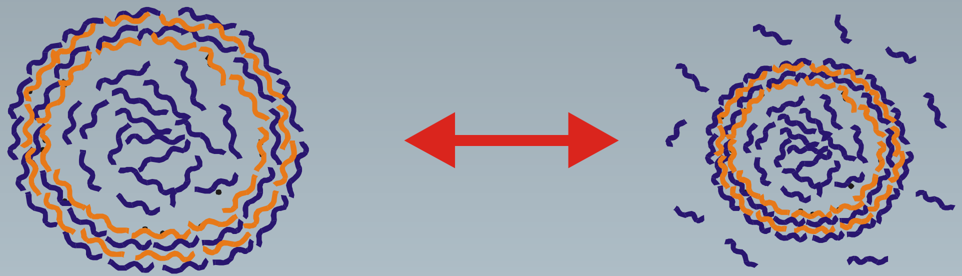


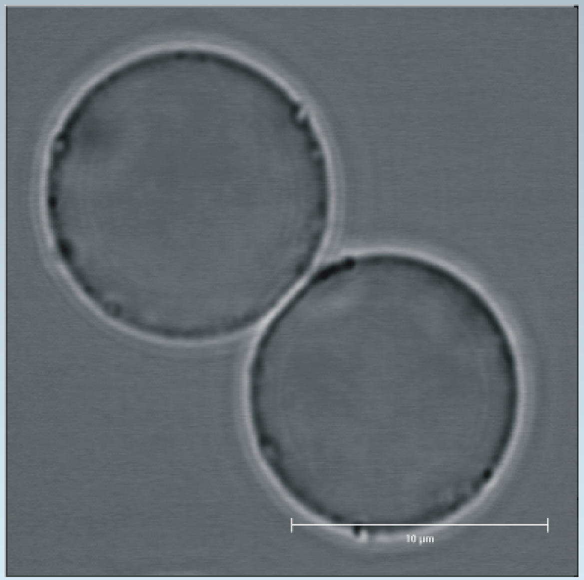


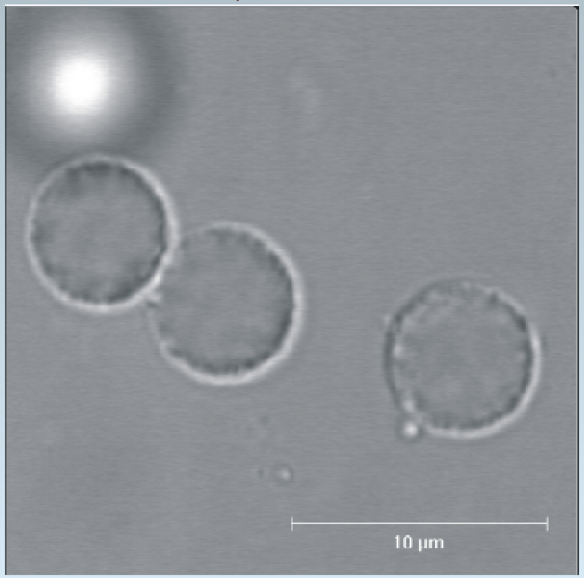
Encapsulation of macromolecules. 2. Inner shell decomposition

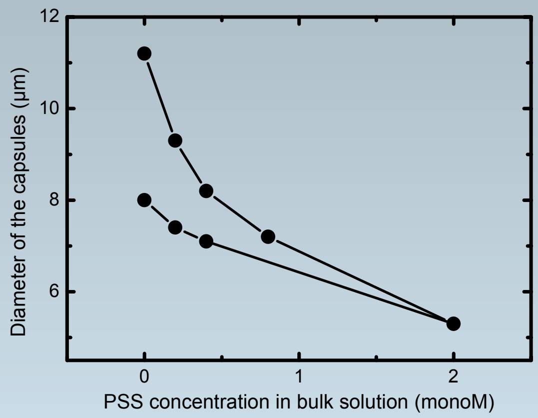


Reversible shrinkage - swelling of the loaded with polyelectrolyte (PSS) capsules induced by osmotic pressure

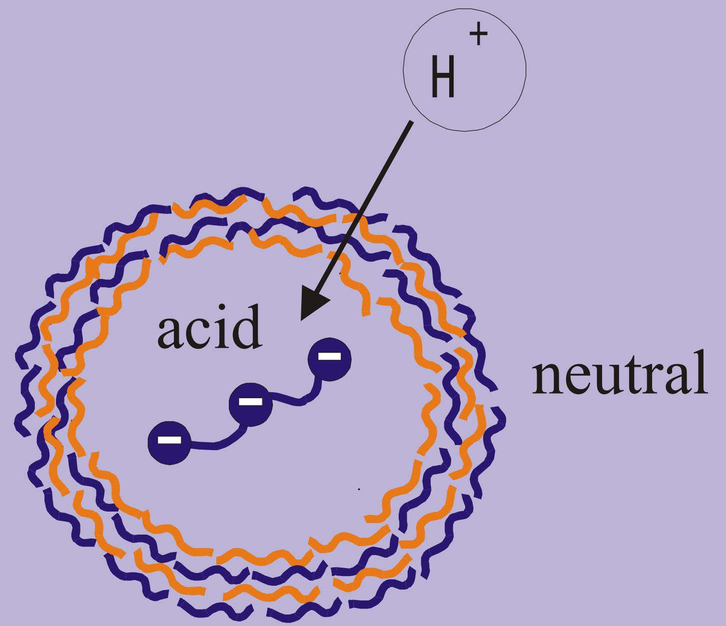






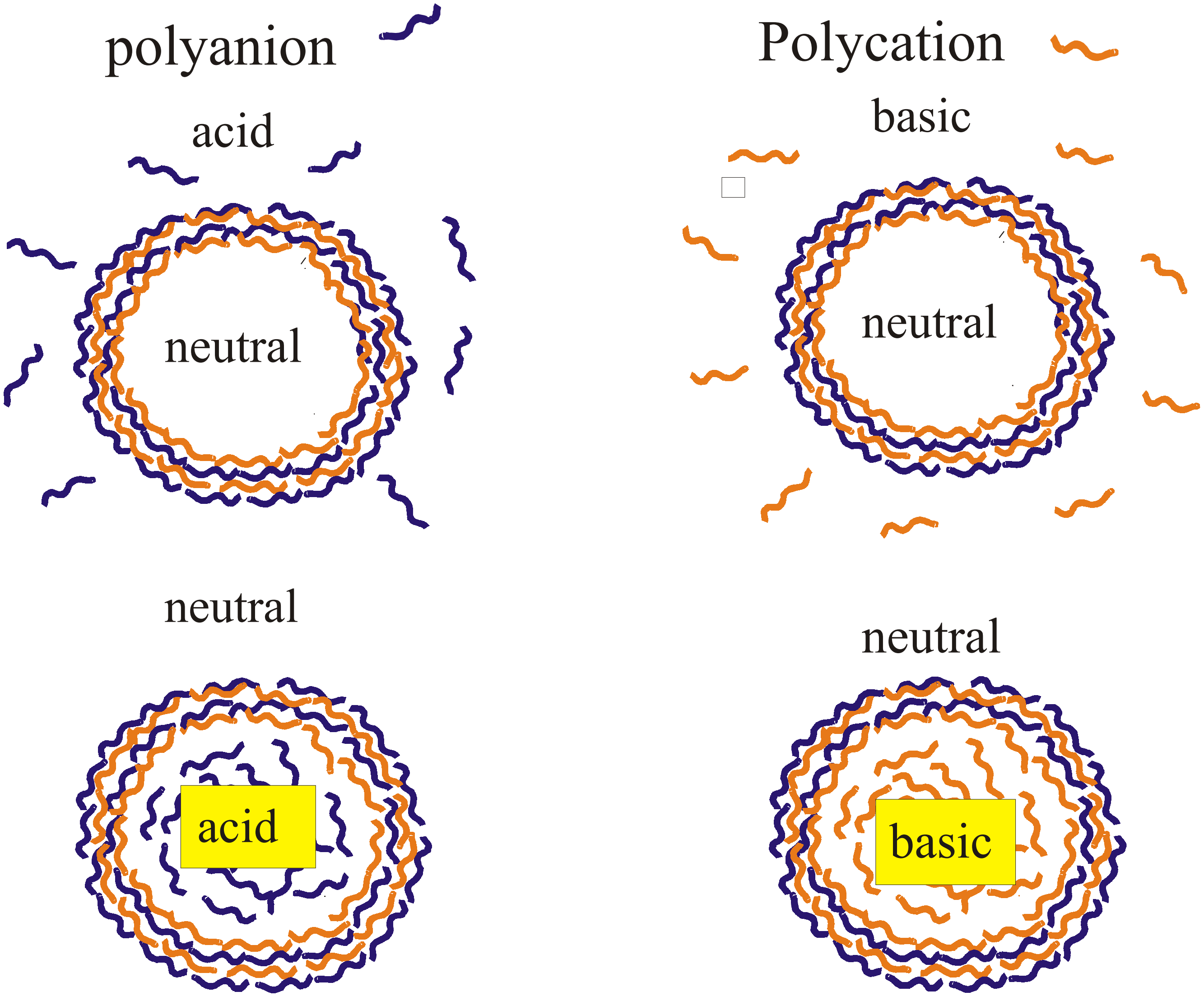


Organic dye precipitation by pH-gradient

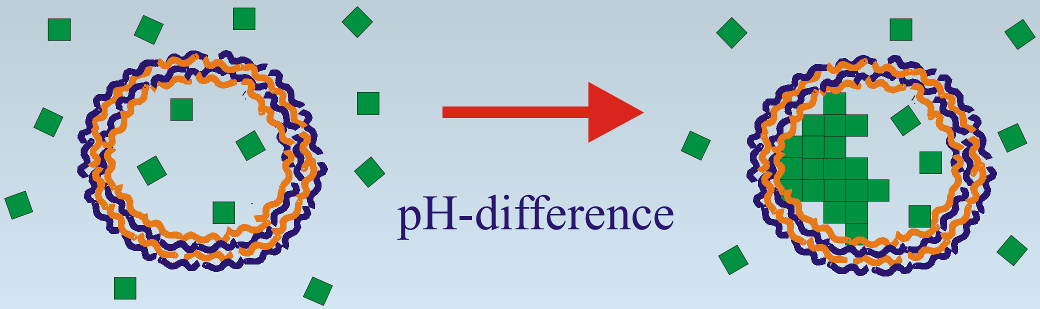


Electroneutrality ($C_{OH} = C_H$)
yields pH = 7

pH- difference through capsule wall established by Donnan equilibrium



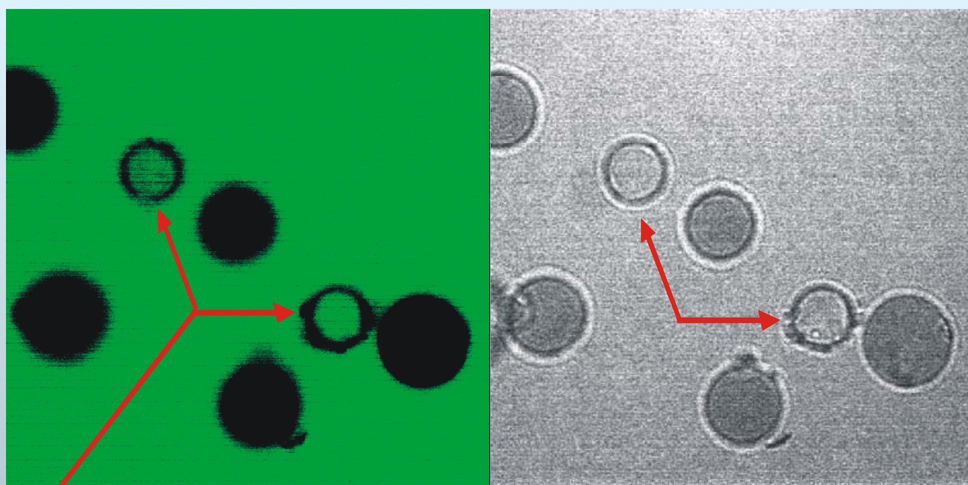
Organic dye precipitation by pH-gradient



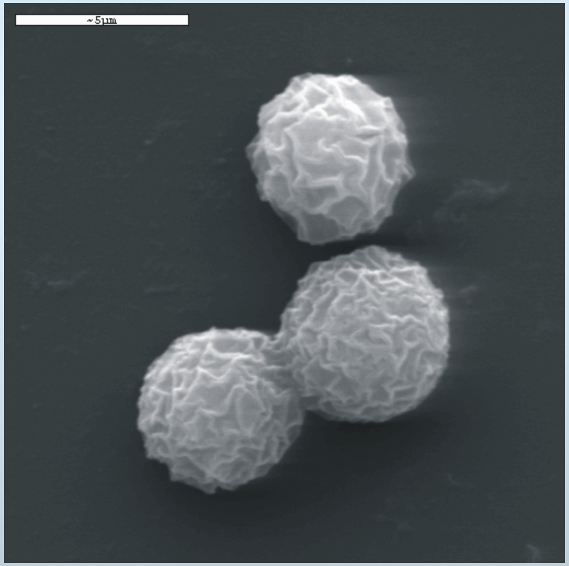
Polyelectrolyte Shells as templates for controlled crystallization and precipitation of small organic molecules. Model of drug loading

Fluorescence Confocal Image (self-quenching)

Transmission Image

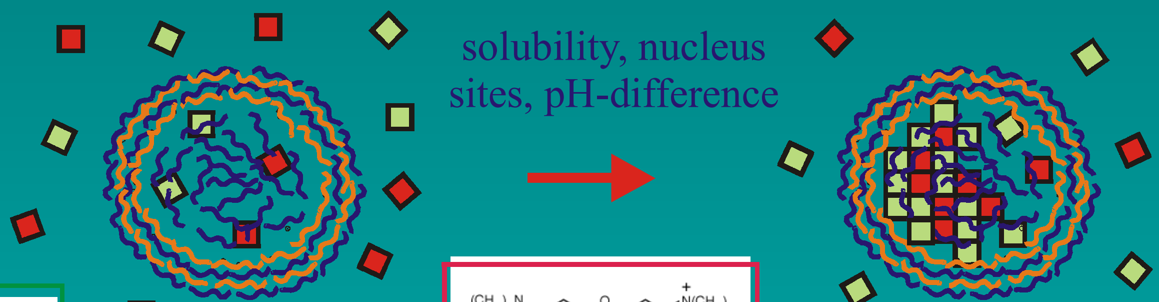


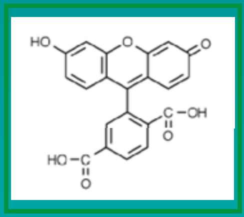
6-carboxy-fluorescein



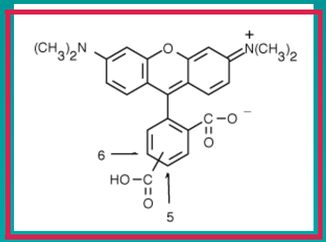
Scanning electron microscopy image of carboxytetra-methylrhodamine precipitates

Organic dye precipitation inside capsules caused by pH-gradient



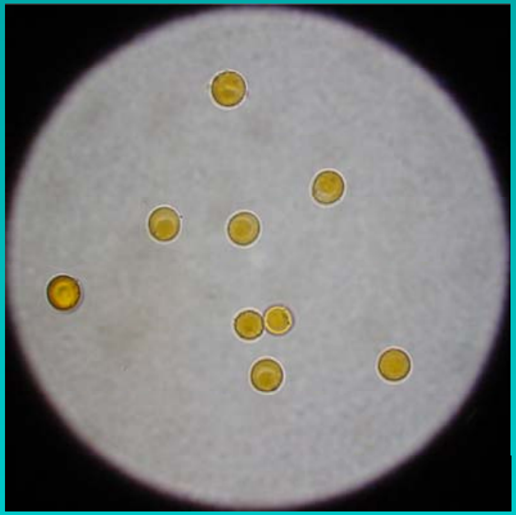


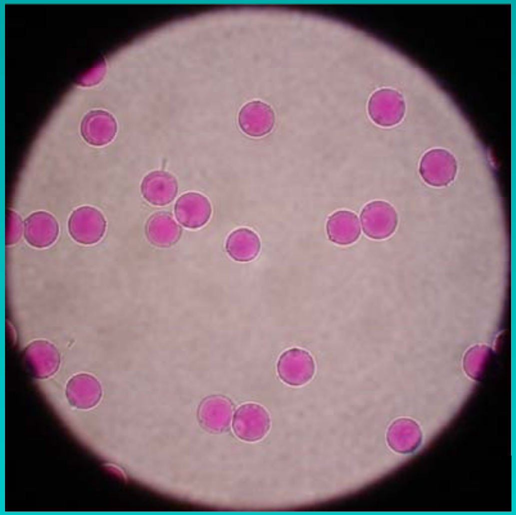
6-CF

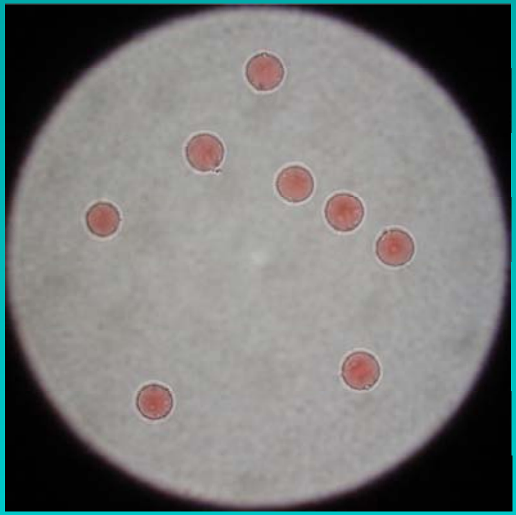


5(6)-TAMRA

MIXTURE

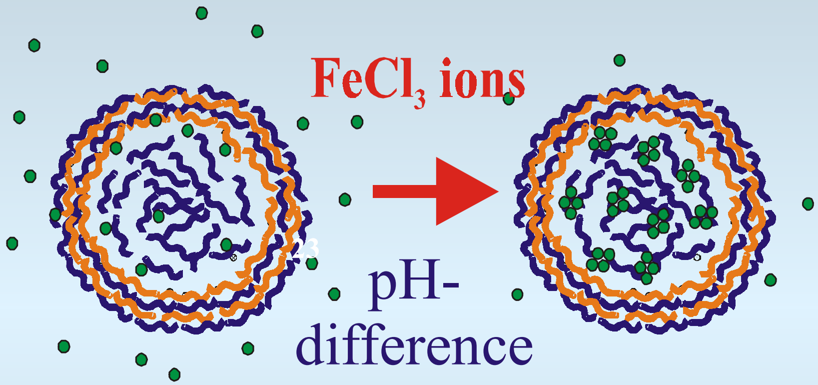


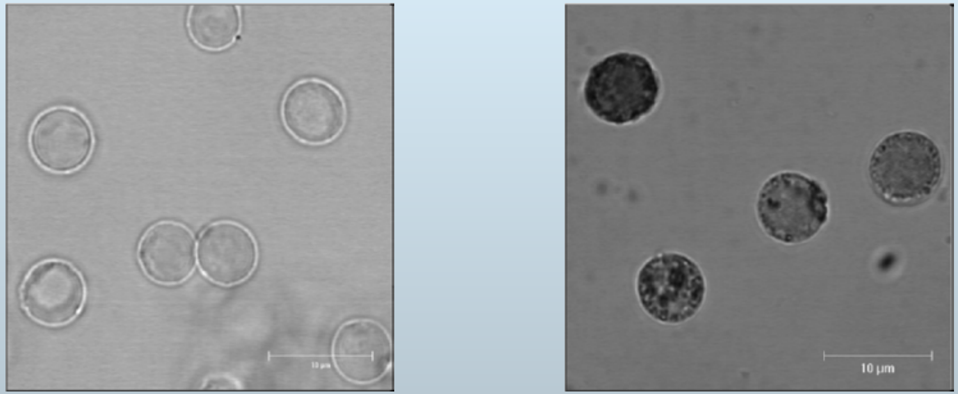




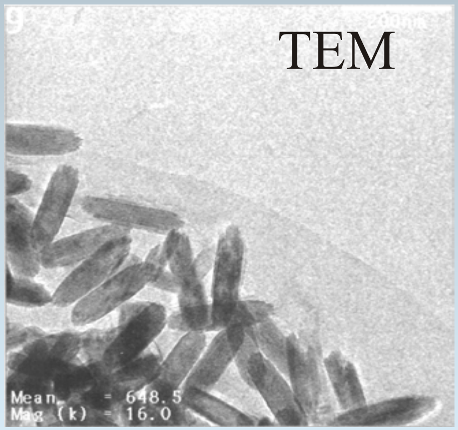
Inorganic particles synthesis inside capsules

Selective pH-induced formation of Iron oxide crystals into capsule filled with polycation

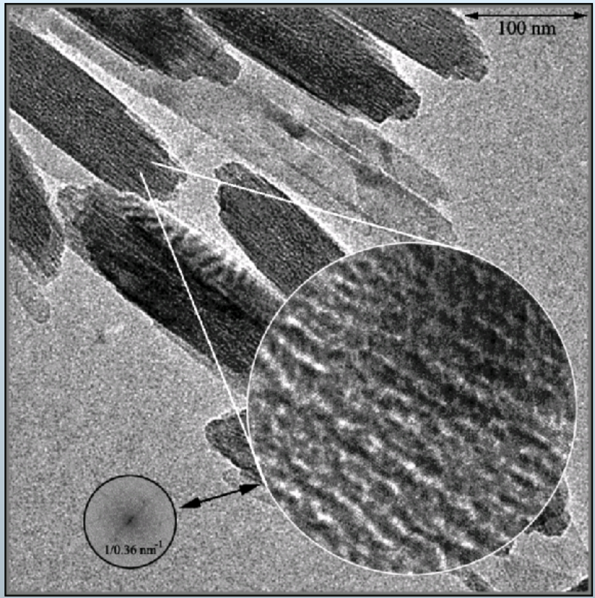




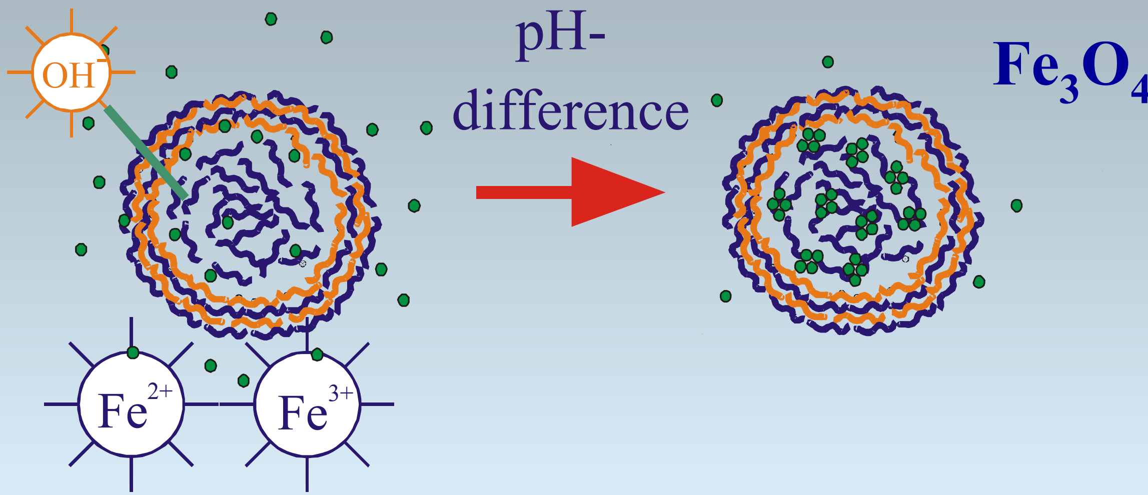
Optical microscopy

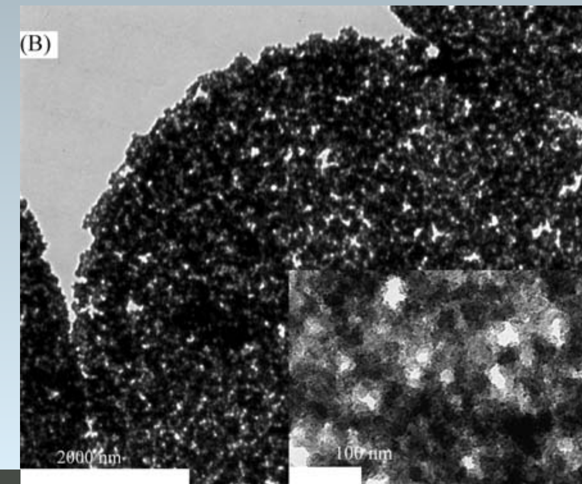


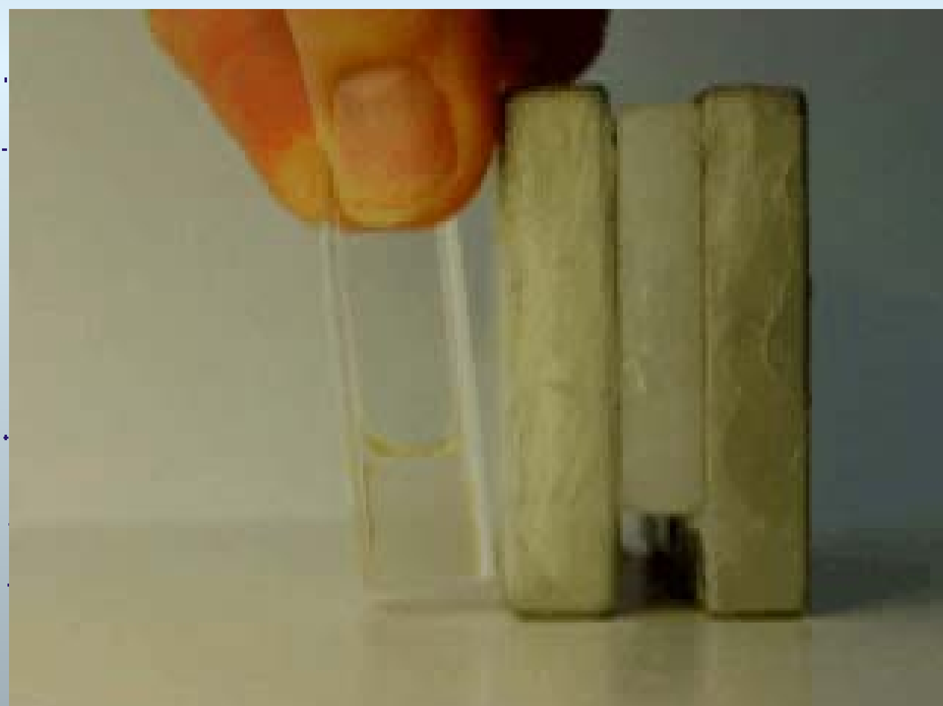
Hematite Fe_2O_3-particles



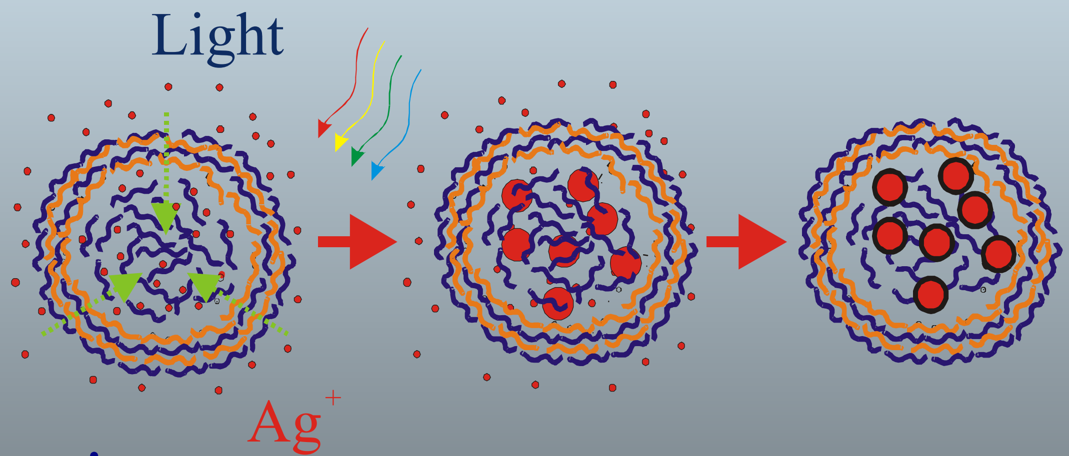
Magnetite particles synthesis in capsule interior



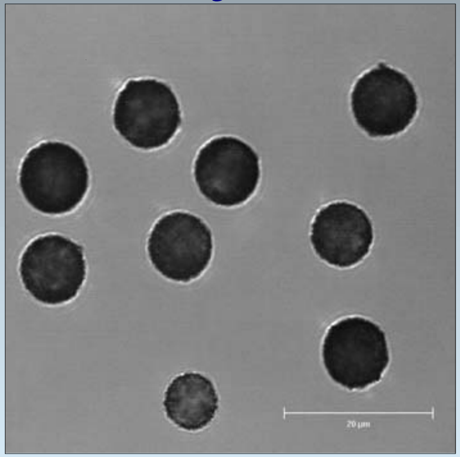




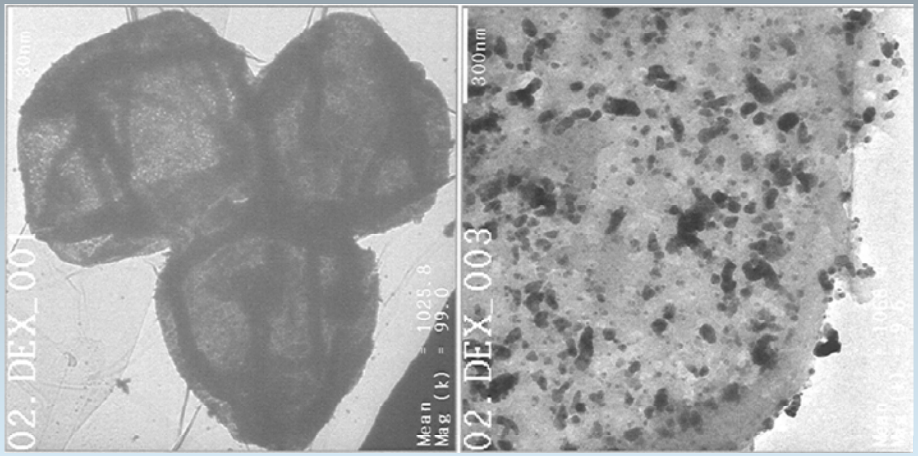
Selective polymer/light-induced Silver particles formation into PSS and dextran filled capsules



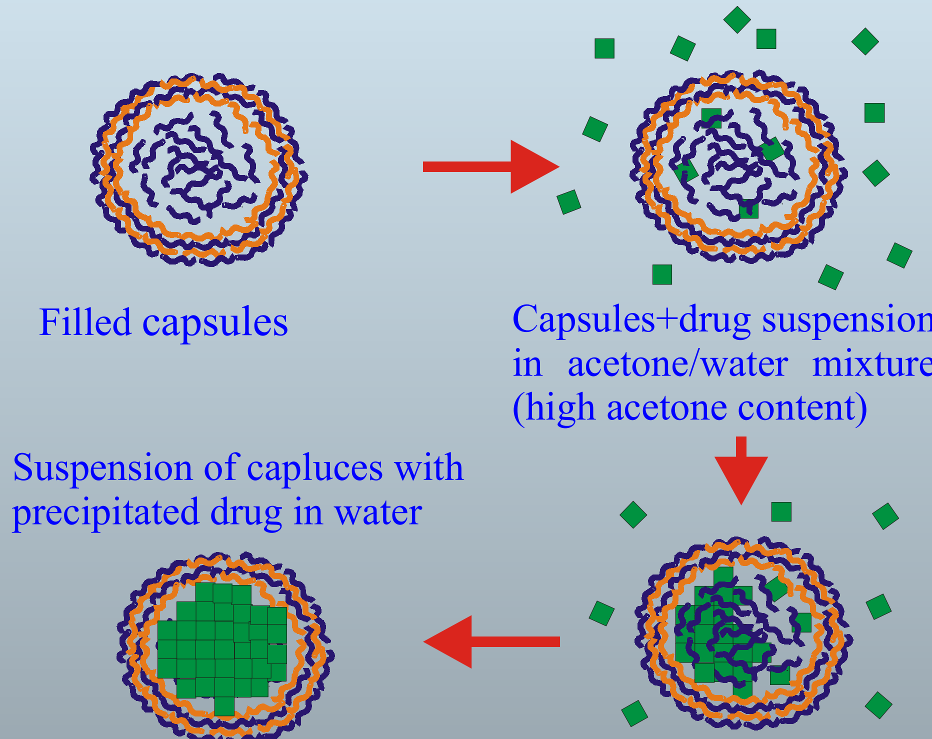
Optical microscopy image of dextran filled capsules in $AgNO_3$ solution

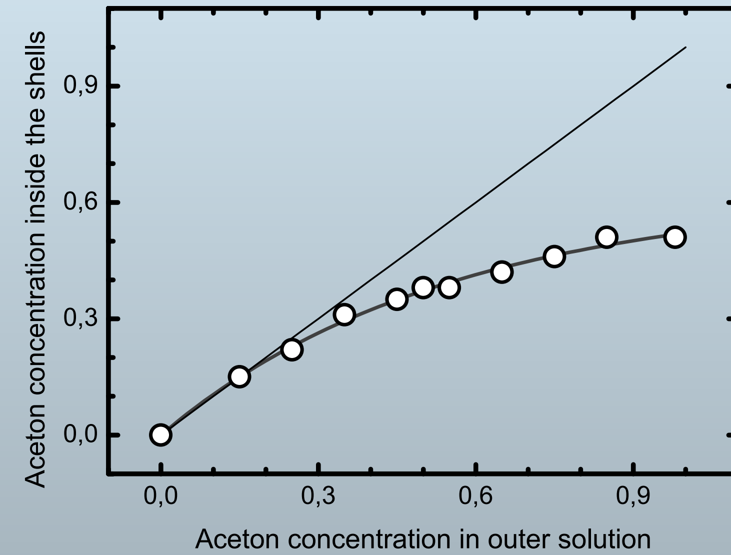


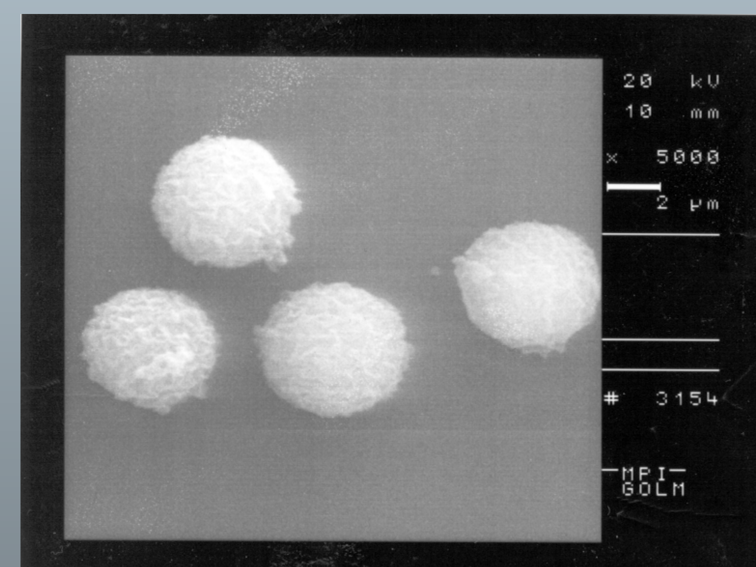
TEM image of dextran filled capsules in $AgNO_3$ solution

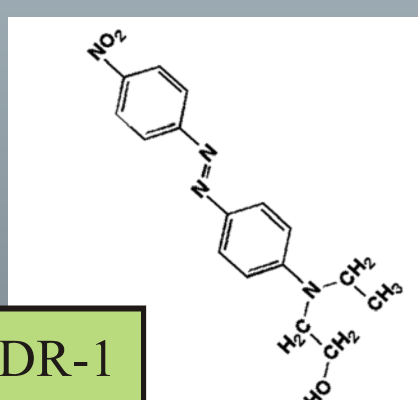


Precipitation poor-water soluble dyes in capsules caused by polarity gradient







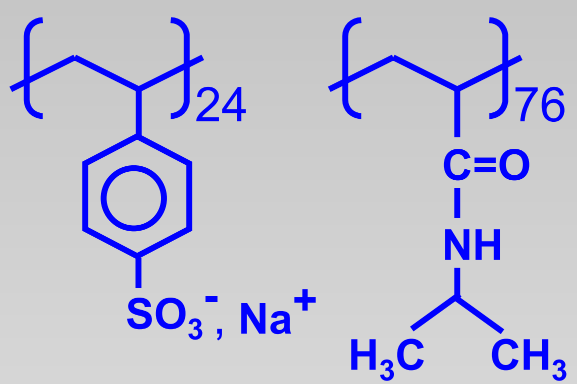


DR-1

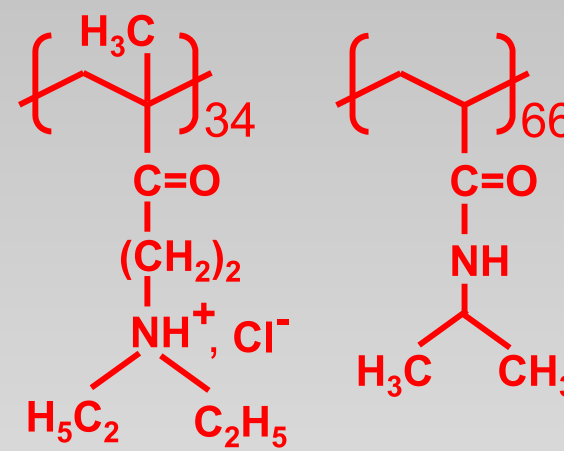
LbL of Thermosensitive Polyelectrolytes

use of charged PNIPAM derivatives
for the preparation of thermosensitive microcapsules

anionic
***block* copolymer**
(SS_{24}-$NIPAM_{76}$)



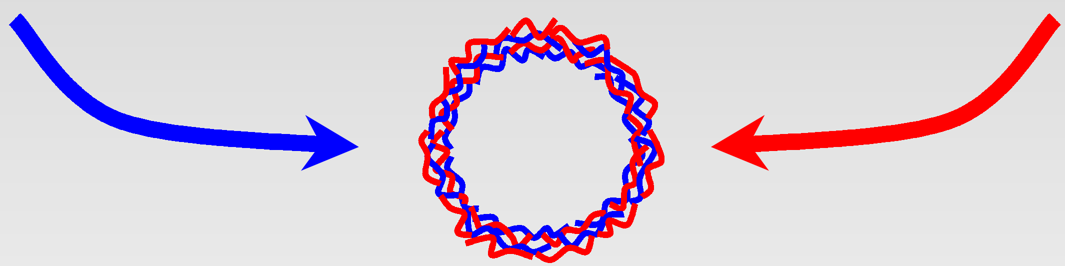
cationic
***block* copolymer**
($DEAEMA_{34}$-$NIPAM_{66}$)



LCST = 31.9ºC

(determined by DSC measurements)

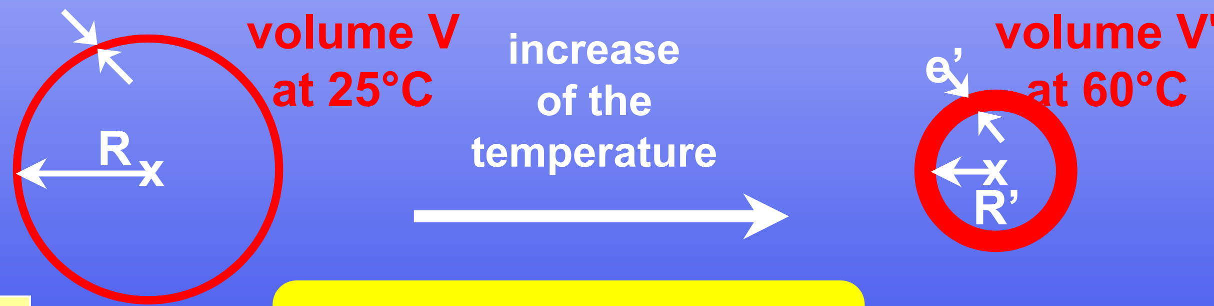
LCST = 31.8ºC



Influence of the Temperature on the Capsule

size measured by confocal microscopy (8 deposited layers)

shrinking of the hollow capsules with the increase of the temperature



$e << R$

$\Downarrow$

$V = 4\pi e R^2$

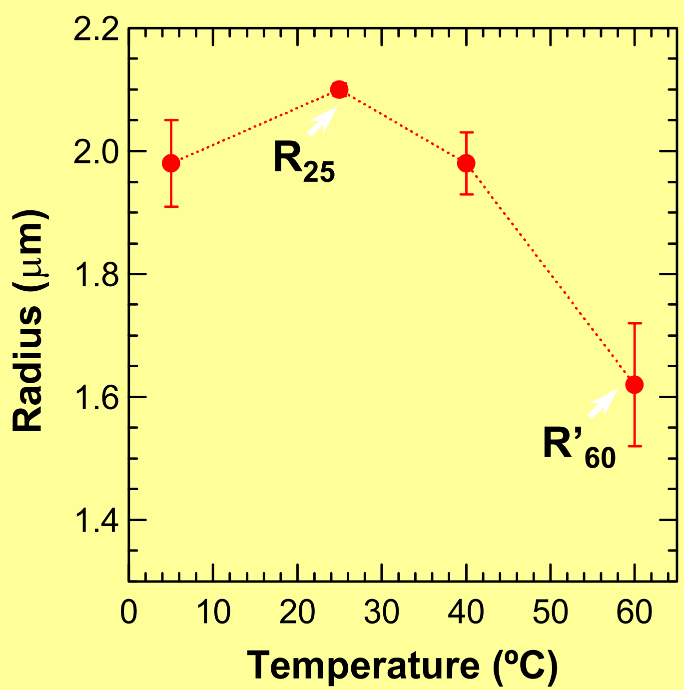
$V = V' \Rightarrow (e/e') = (R'/R)^2$

ratio $R'_{60}/R_{25} = 0.77$

$e' << R'$

$\Downarrow$

$V = 4\pi e' R'^2$

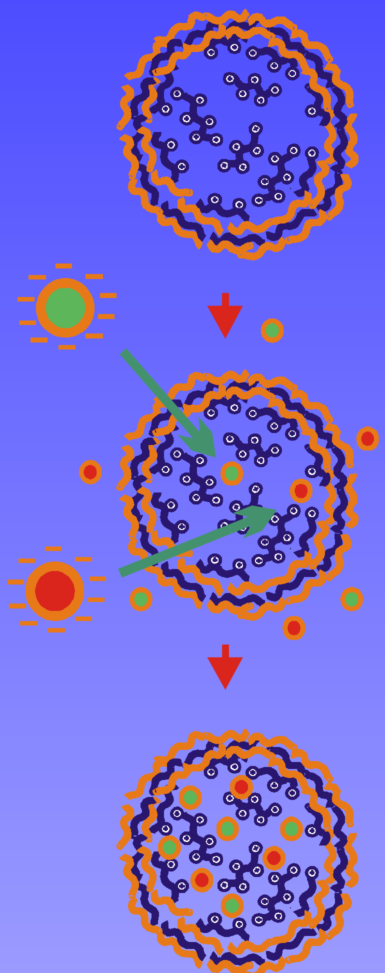


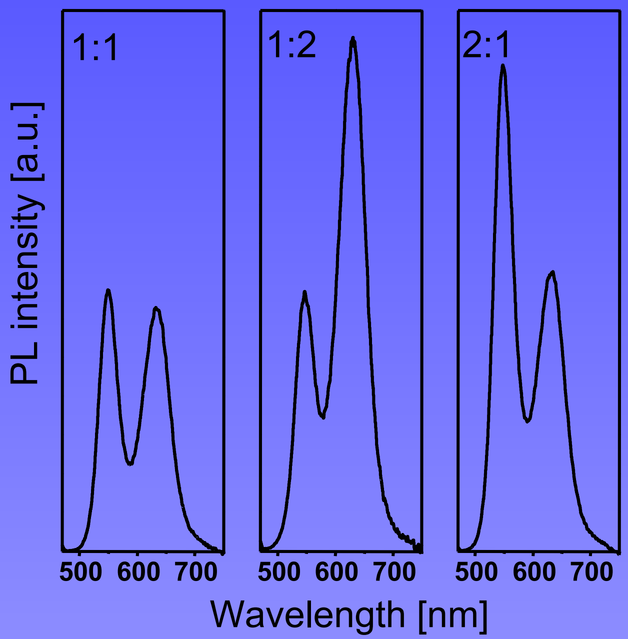
-the thickness of the wall measured by AFM increases with the temperature

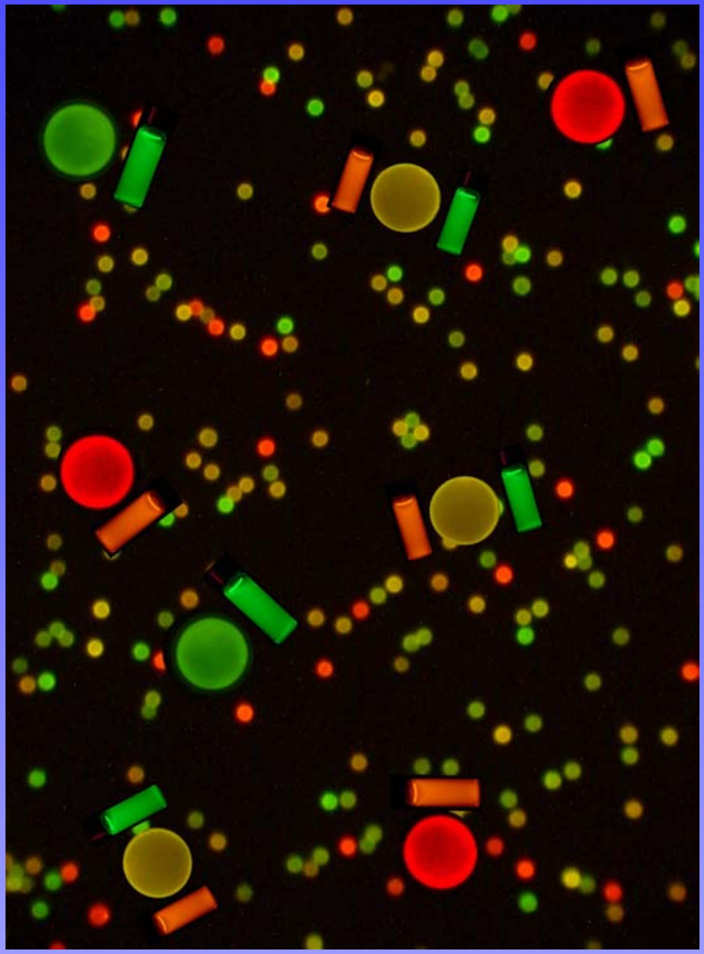
-Ratio of thickness ≈ 0.5

⇒ decrease of the permeability of the wall

Combinatorial library based on Doping of Capsules with Fluorescent nanoparticles (quantum dots) and their mixture



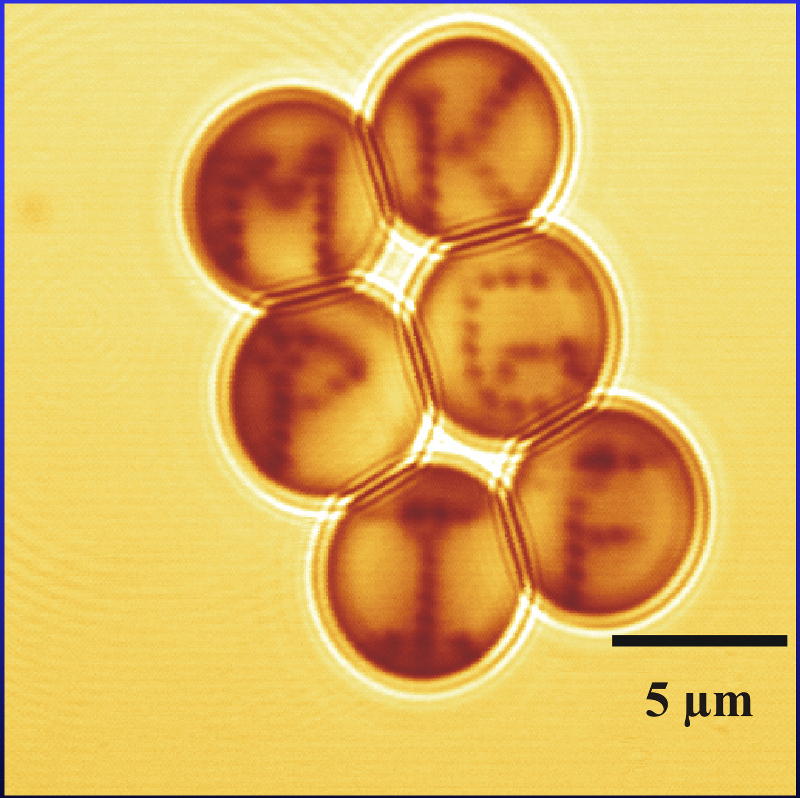




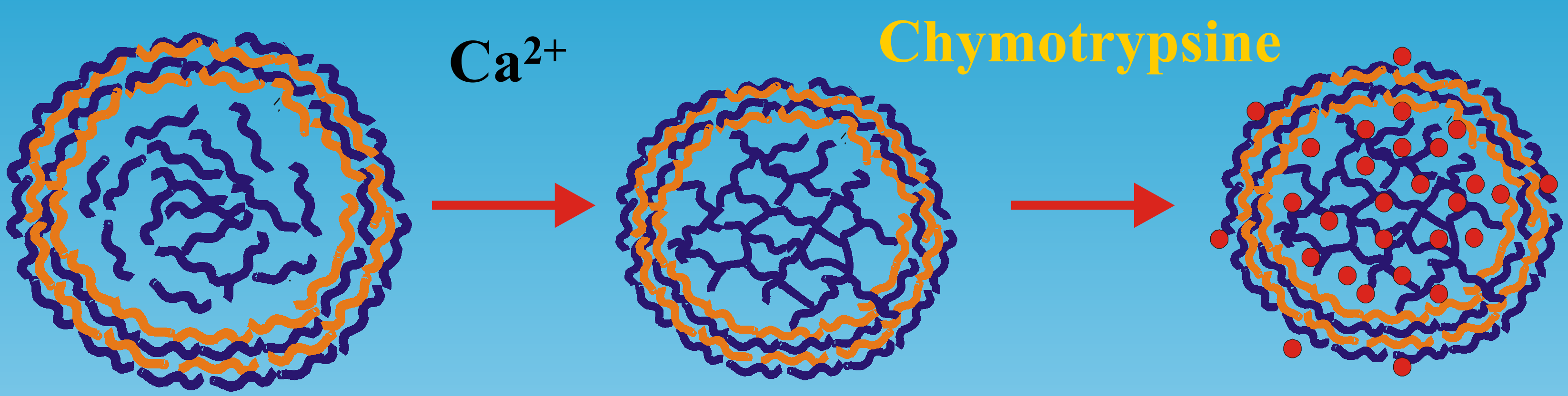
Combinatorial library based on particle signing

Reduction of Ag in film by laser beam on surface of colloidal particles

Ag/PSS film was assembled on colloid particles

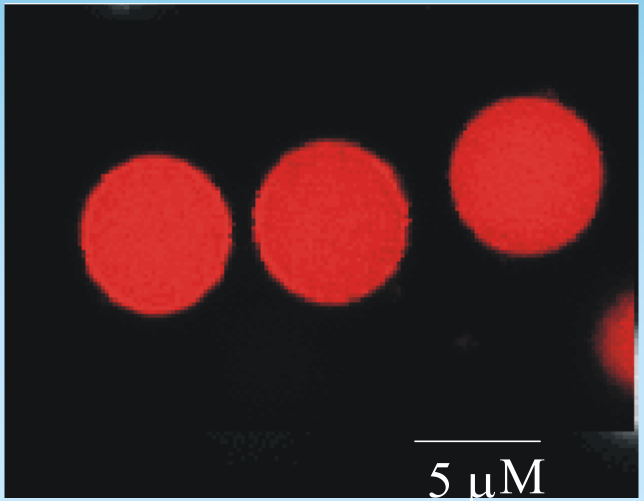


Enzymatic reactions inside capsule



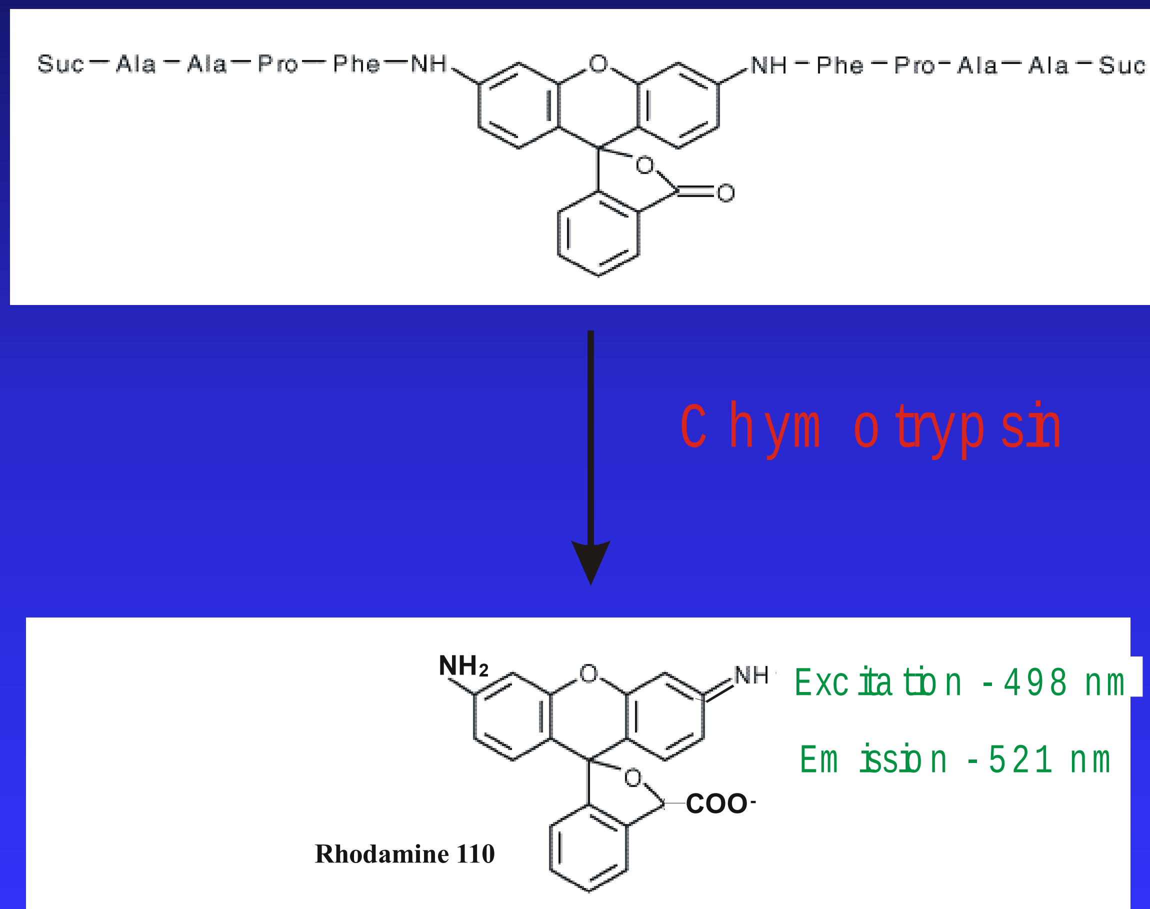
Dextran sulfate/
protamine capsules
filled with alginate

Chymotrypsine embedding in capsules containing alginate gel

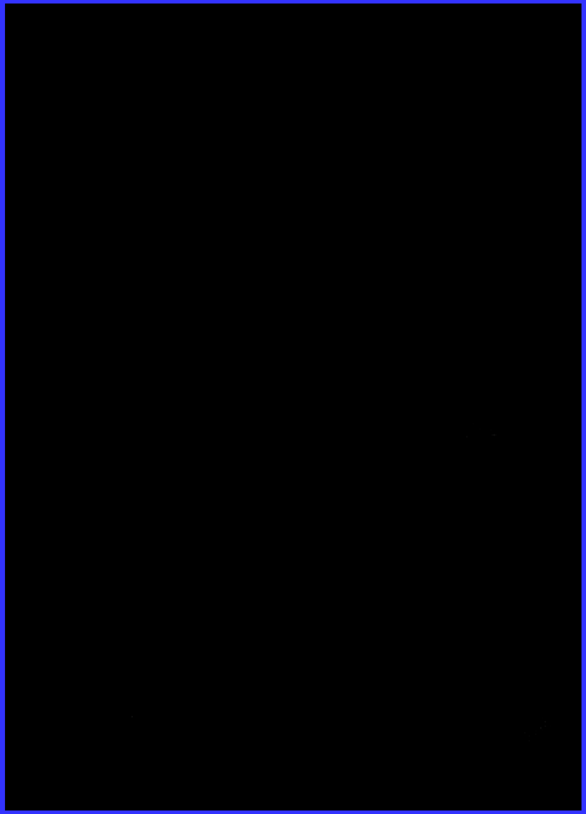


Enzymatic reactions inside capsule

Kinetic scheeme of chymotrypsime function



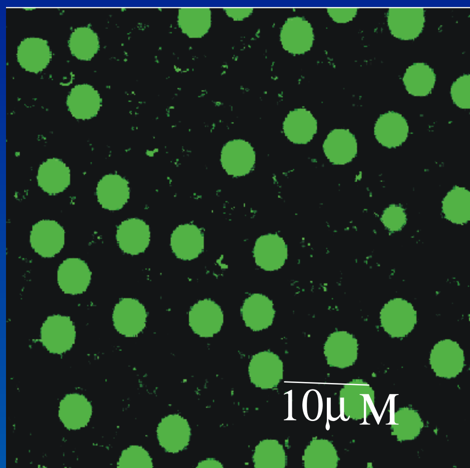
Enzymatic reactions inside capsule



Capsules with embedded chymotrypsine

Bi-enzyme system incorporated in the capsule

Peroxidase fluorescein labeled



Glucose oxidase

beta-D-Glucose + O_2 = D-glucono-1,5-lactone + H_2O_2

Peroxidase

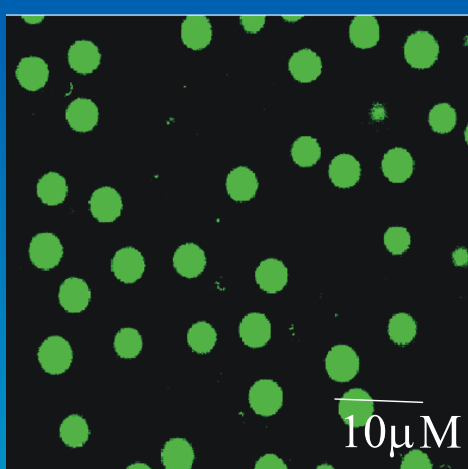
Donor + H_2O_2 = oxidized donor + 2 H_2O

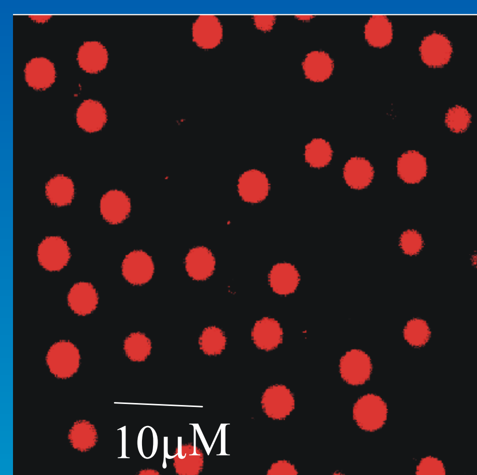
Amplex for glucose
assay, colorless

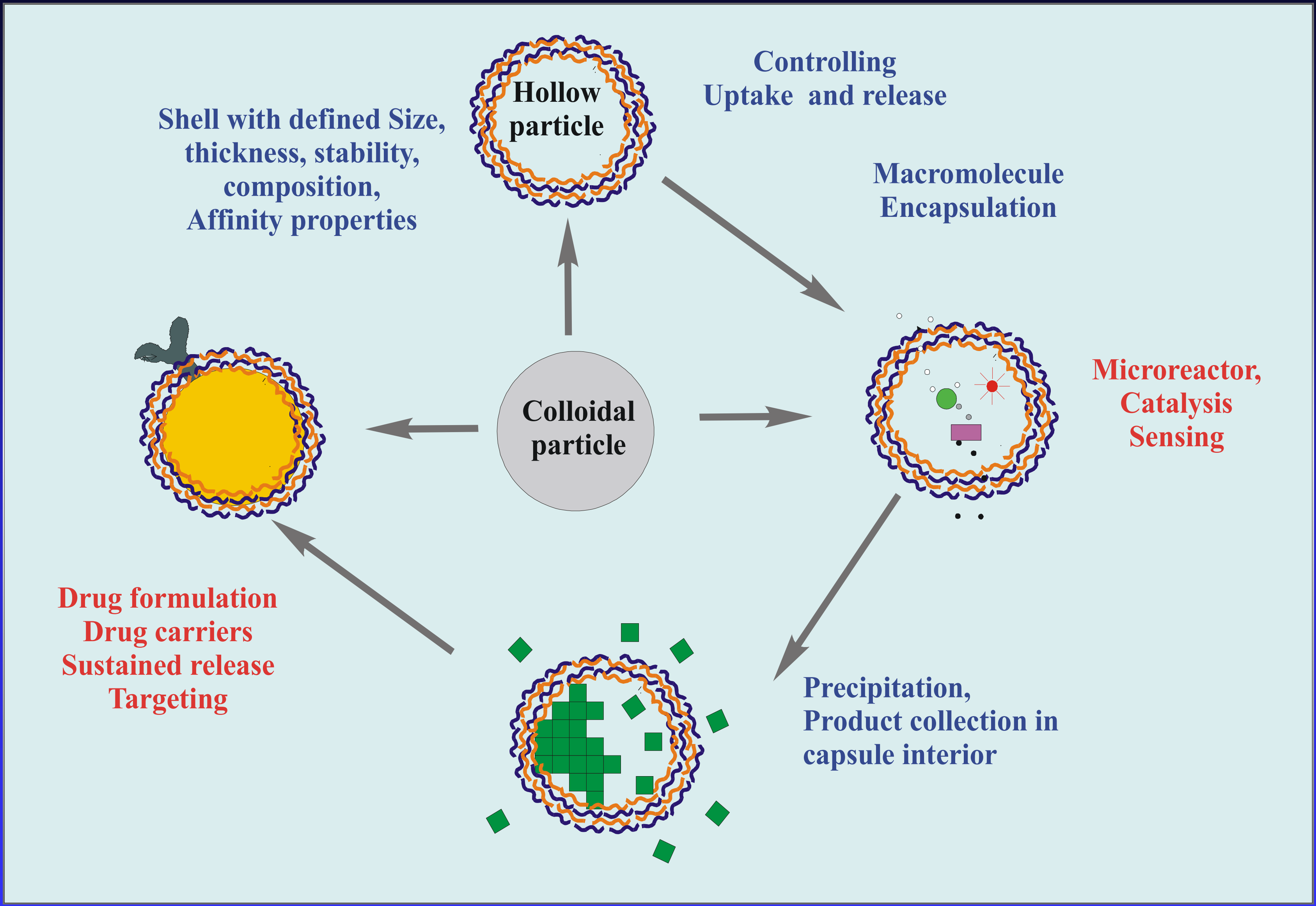
Red

Excitation 563 nm
emission 587 nm

Glucose oxidase rhodamine labeled



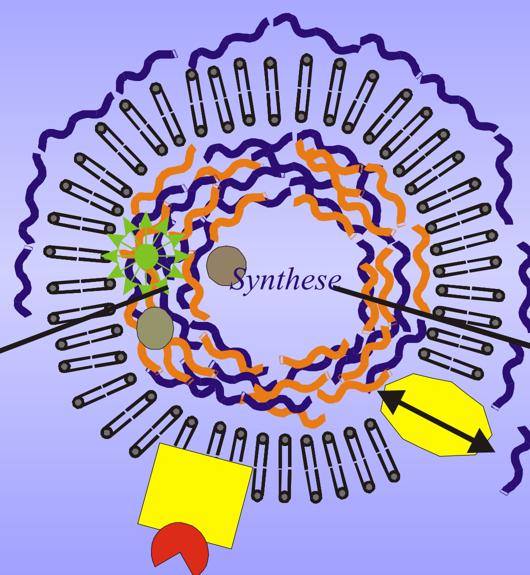



Hollow particle
Controlling Uptake and release
Shell with defined Size, thickness, stability, composition, Affinity properties
Macromolecule Encapsulation
Colloidal particle
Microreactor, Catalysis Sensing
Drug formulation Drug carriers Sustained release Targeting
Precipitation, Product collection in capsule interior

Biological Functions on Polyelectrolyte Capsules - Toward Artificial Cells?

Lipid-Polyelectrolyte Interaction

Tuning the Lipidproperties



Tuning of the polyelectrolyte Layer properties

Capsule or Colloidal Core

Additional Functions:
Nanoparticles, Fluorescent
Reporter Molecules, Magnetic
Particles, etc.

Do the membrane proteins work?

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