Tayloring functions in microcapsules: Responsiveness and remote controlling

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Coating colloids and Hollow capsules
Responsive capsules
Composite capsules - Remote activation
Two compartmental capsules
Capsules delivery in living systems
Intracellular sensing
Conclusions and Perspectives

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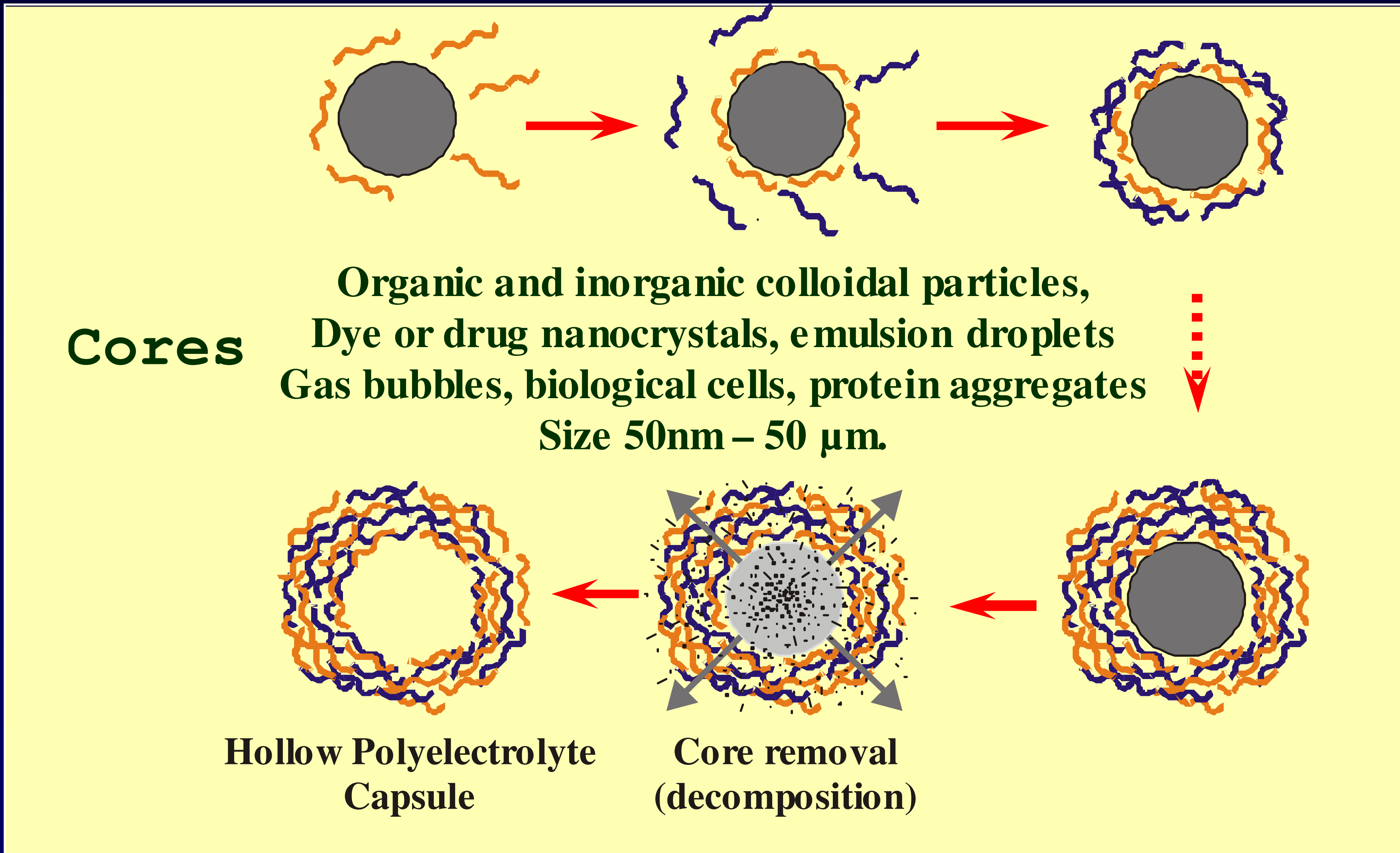
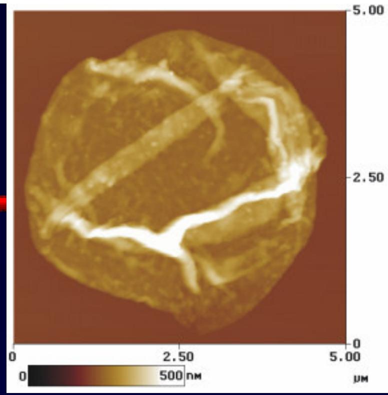
Hollow Capsule Fabrication

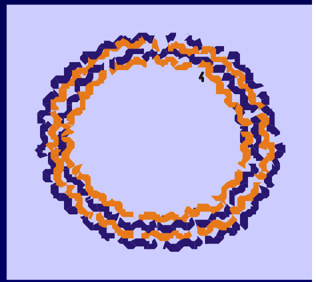


Sukhorukov, et al (1998) *Colloids and Surfaces A* **137**, 253.
Donath, et al (1998):. *Angew. Chemie* **37** (16), 2202

Layer-by-layer Capsules



- Size and shape are determined by templating colloid particle.
- Layer constituents:
  - → synthetic polyelectrolytes and biopolymers
  - → inorganic nanoparticles
- The Capsule Wall is tunable in <u>Nanometer</u> range Thickness, composition and functionality are controlled by constituents and the layer number
- 1 layer of polyelectrolyte → 1-2 nm



- Encapsulation → micro- and nanoreactor engineering
- Controlling permeability for wide class of molecules

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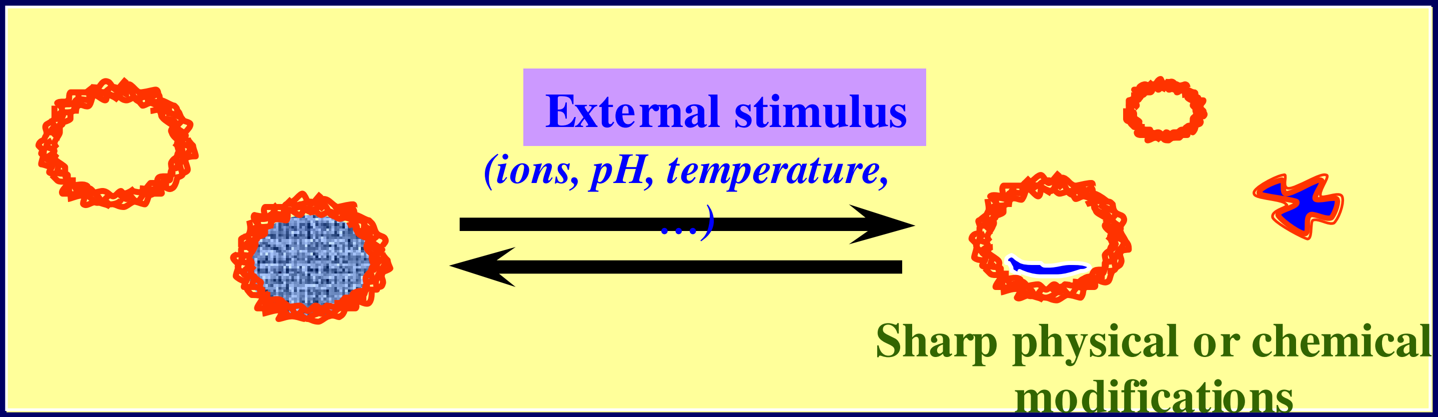
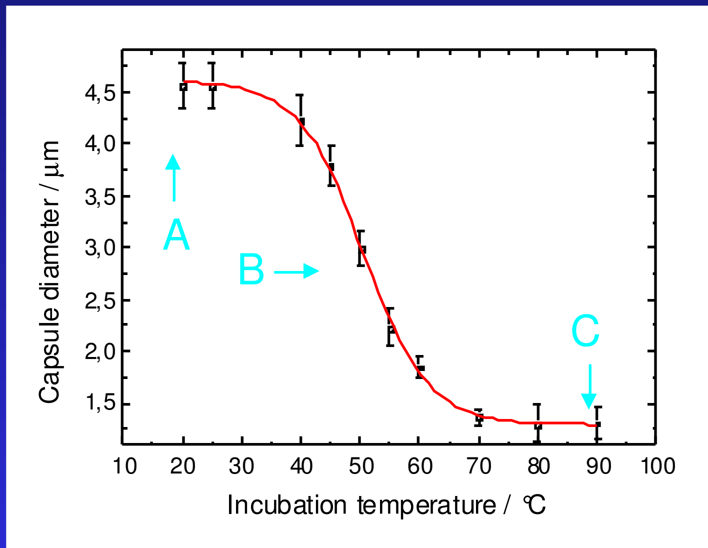
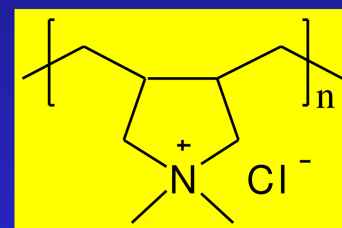


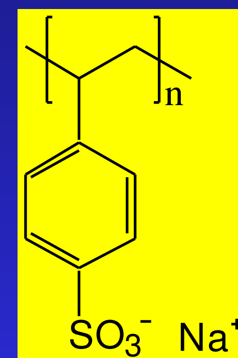
Temperature induced capsule shrinkahe



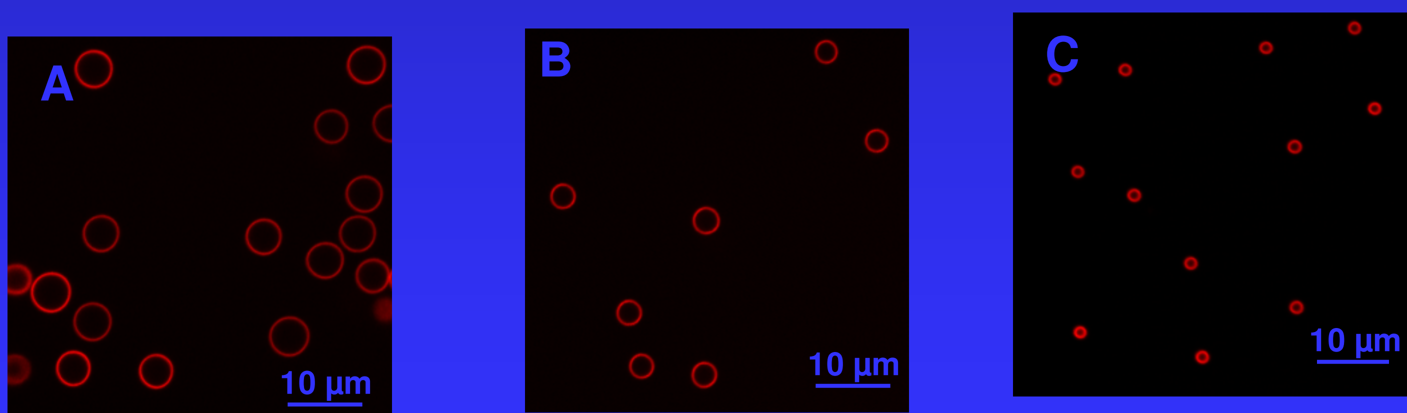
PDADMAC



PSS



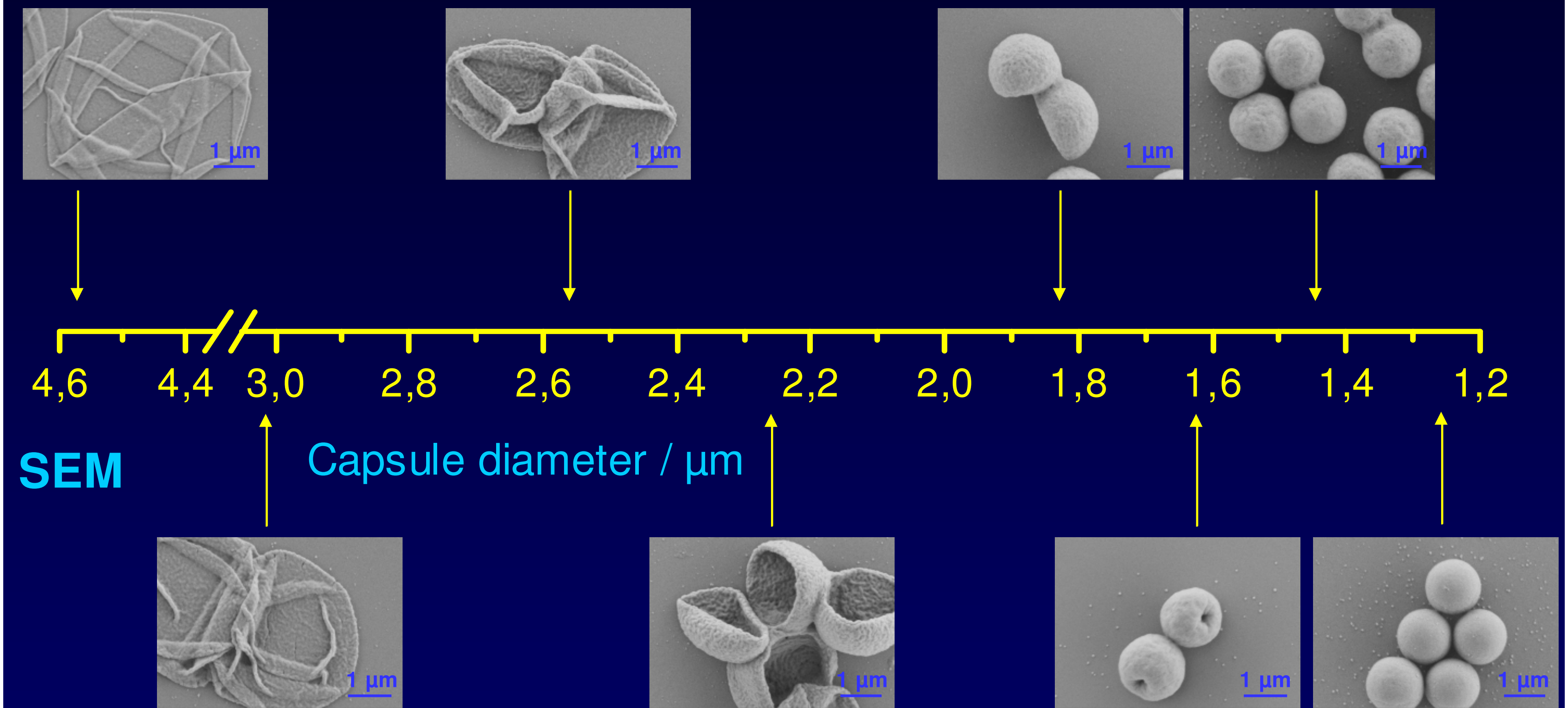
CLSM



Capsule diameter depends on incubation temperature

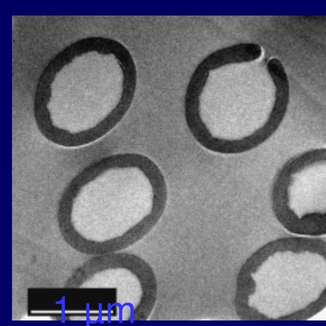
Dr. Karen Köhler

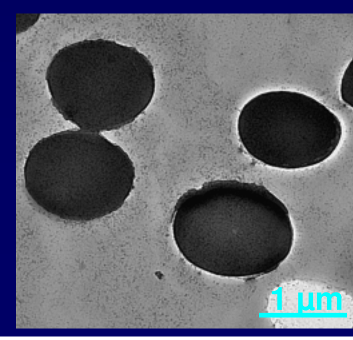
Morphology of (PDADMAC/PSS)$_4$ capsules



TEM

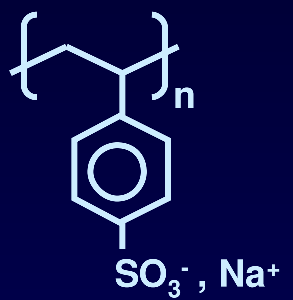
Temperature induced transition from a hollow shell to a full sphere





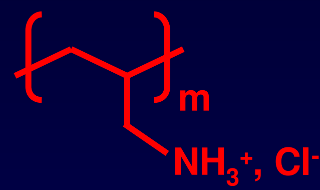
pH-sensitive hollow capsules

PSS

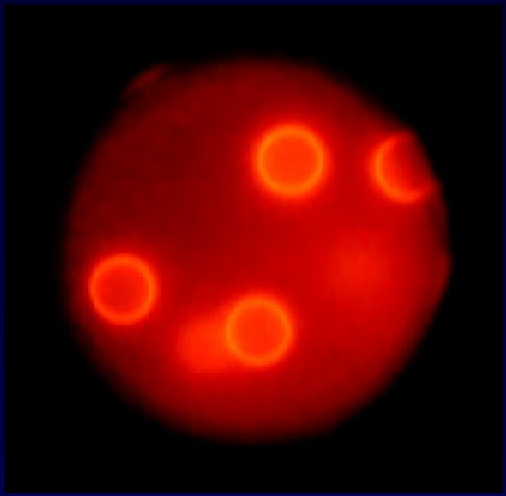


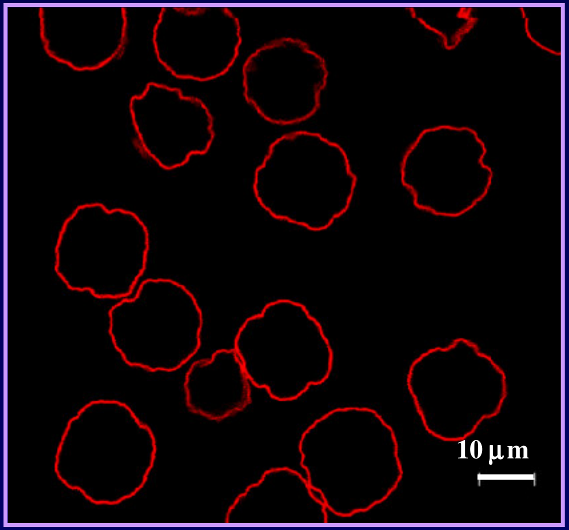
Sodium Poly (Styrene Sulfonate)

PAH



Poly (Allylamine Hydrochloride)





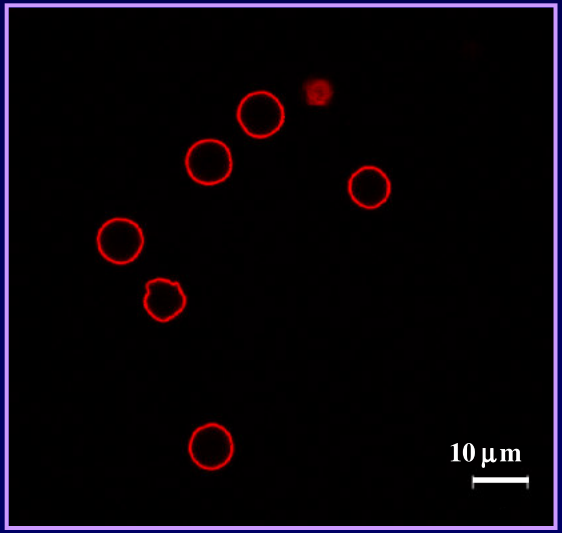
SWOLLEN STATE
(18 µm)

pH ↘

HCl 0.1 M

NaOH 0.1 M

pH ↗

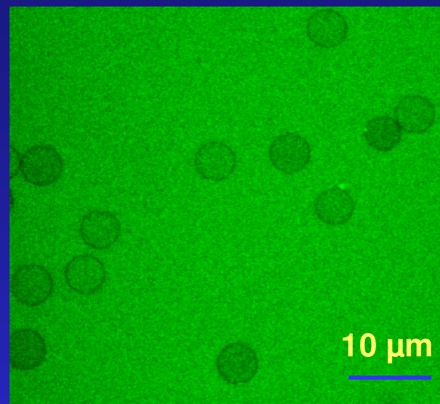


SHRUNK STATE
(8 µm)

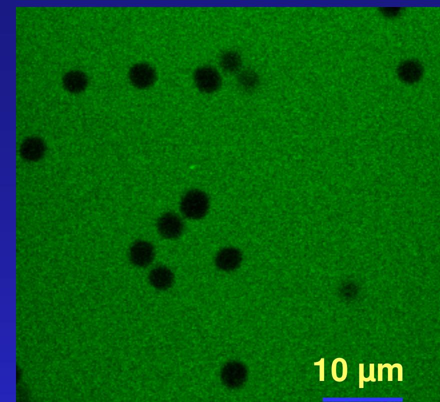
Christophe Dejugnat

Encapsulation and release

Confocal fluorescence Laser Scanning Microscopy

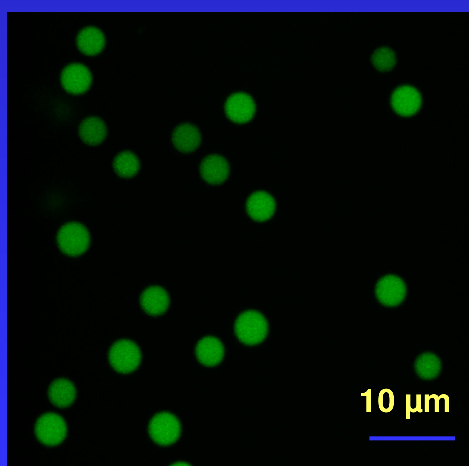


ΔT, pH →



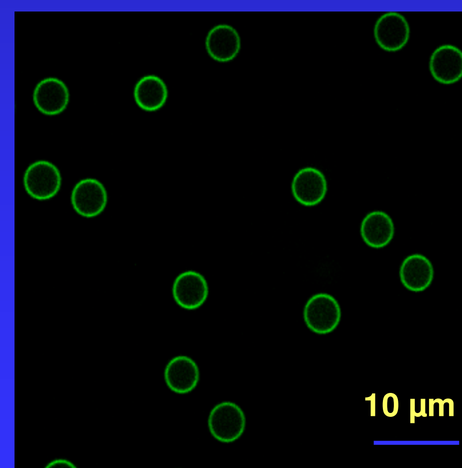
Permeable
<u>„Open gate“</u>

Impermeable
<u>„Closed gate“</u>



Encapsulated

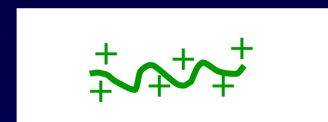
pH, salt →



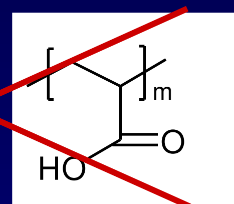
Release

Weak polyelectrolytes

Tuning of electrostatic interactions by pH

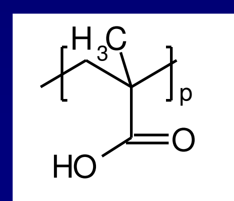


~~PAA~~



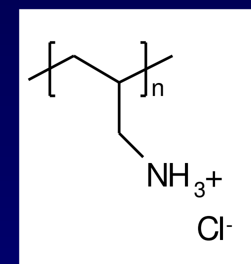
Poly(acrylic acid)

PMA



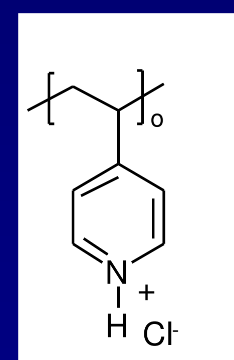
Poly(methacrylic acid)

PAH



Poly(allylamine hydrochloride)

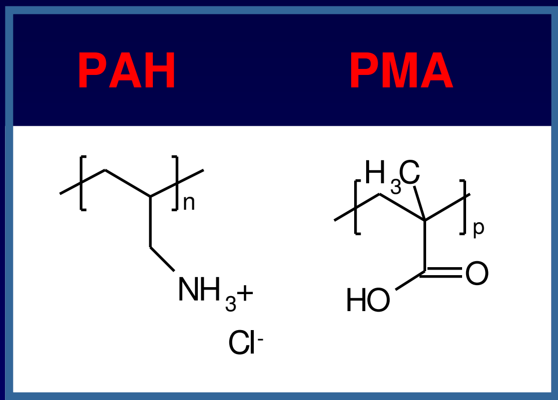
PVP

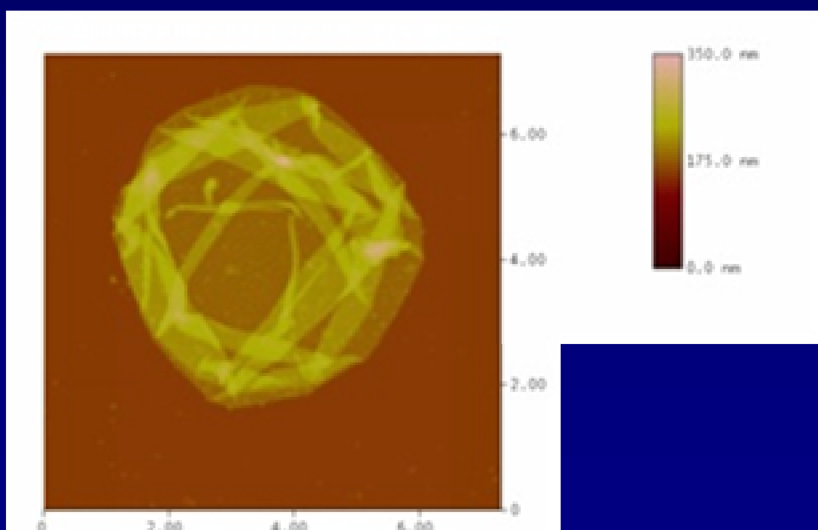


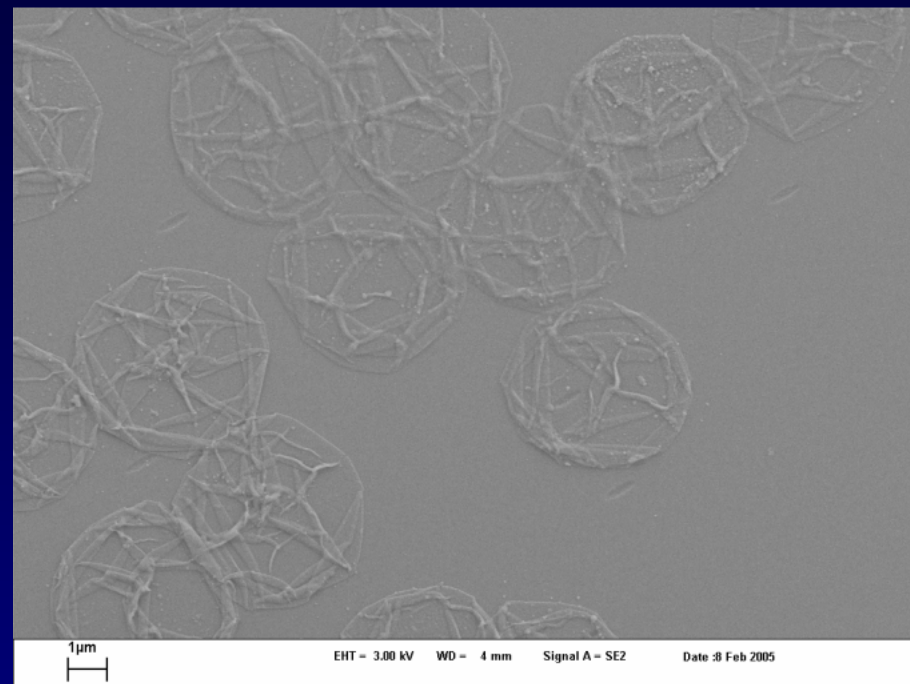
Poly(4-vinylpyridine hydrochloride)

Increasing hydrophobicity

$(PAH/PMA)_5$ capsules templated on SiO2



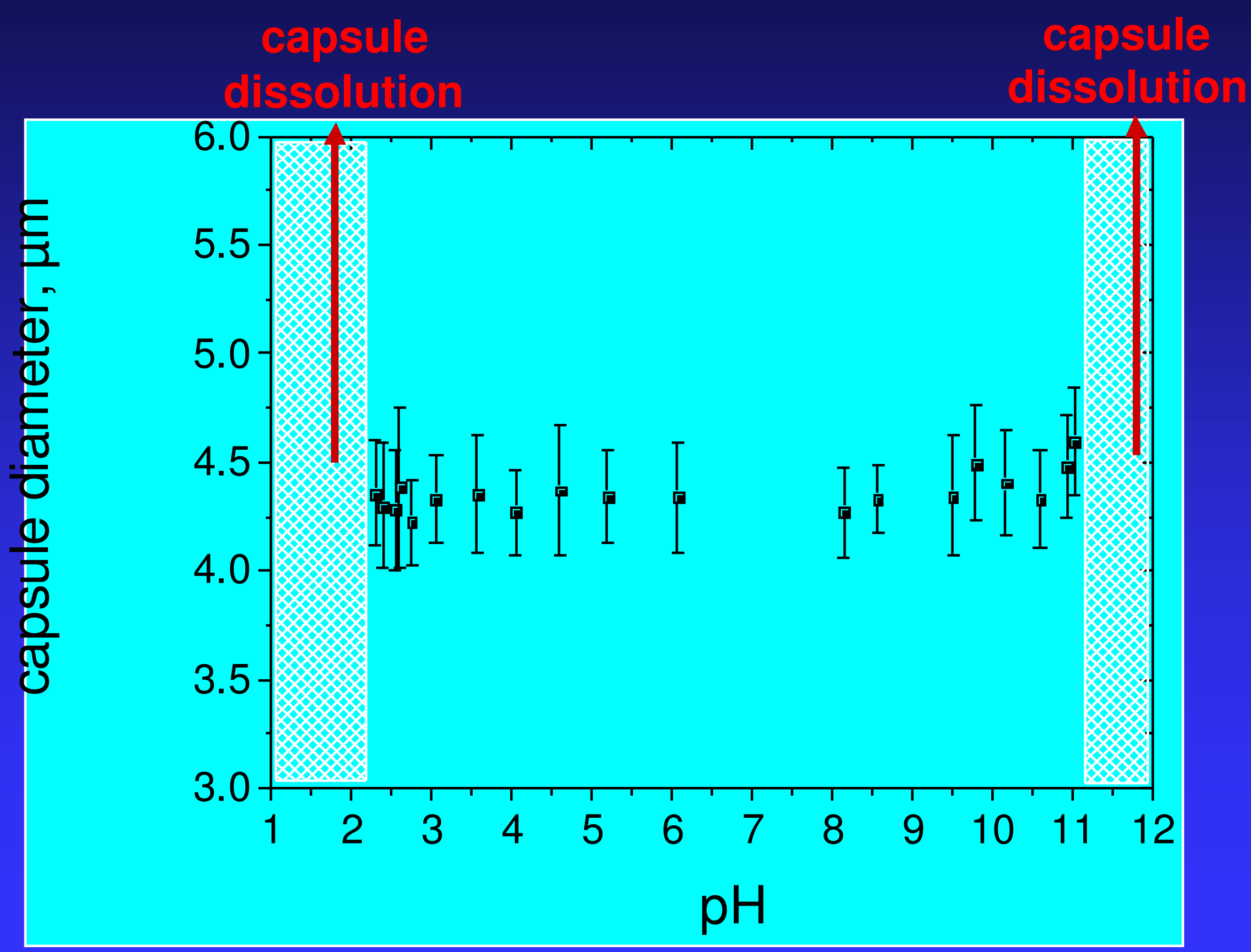


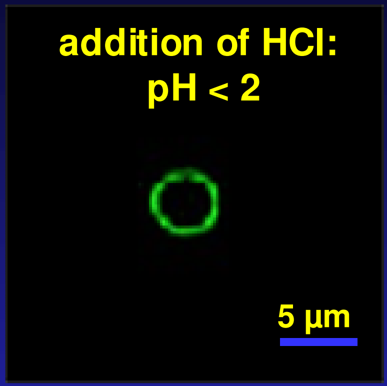


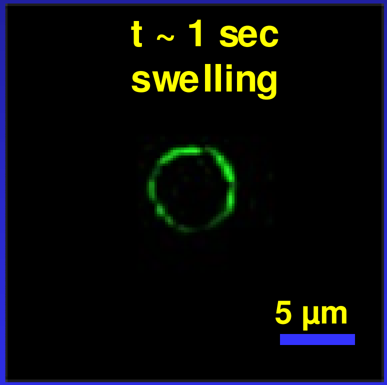
- thin shells
- d_{2L} = (3 ± 0.2) nm
- smooth surface

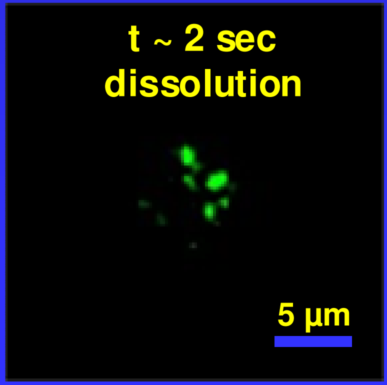
Tatjana Mauser

Influence of pH on $(PAH/PMA)_5$ capsules



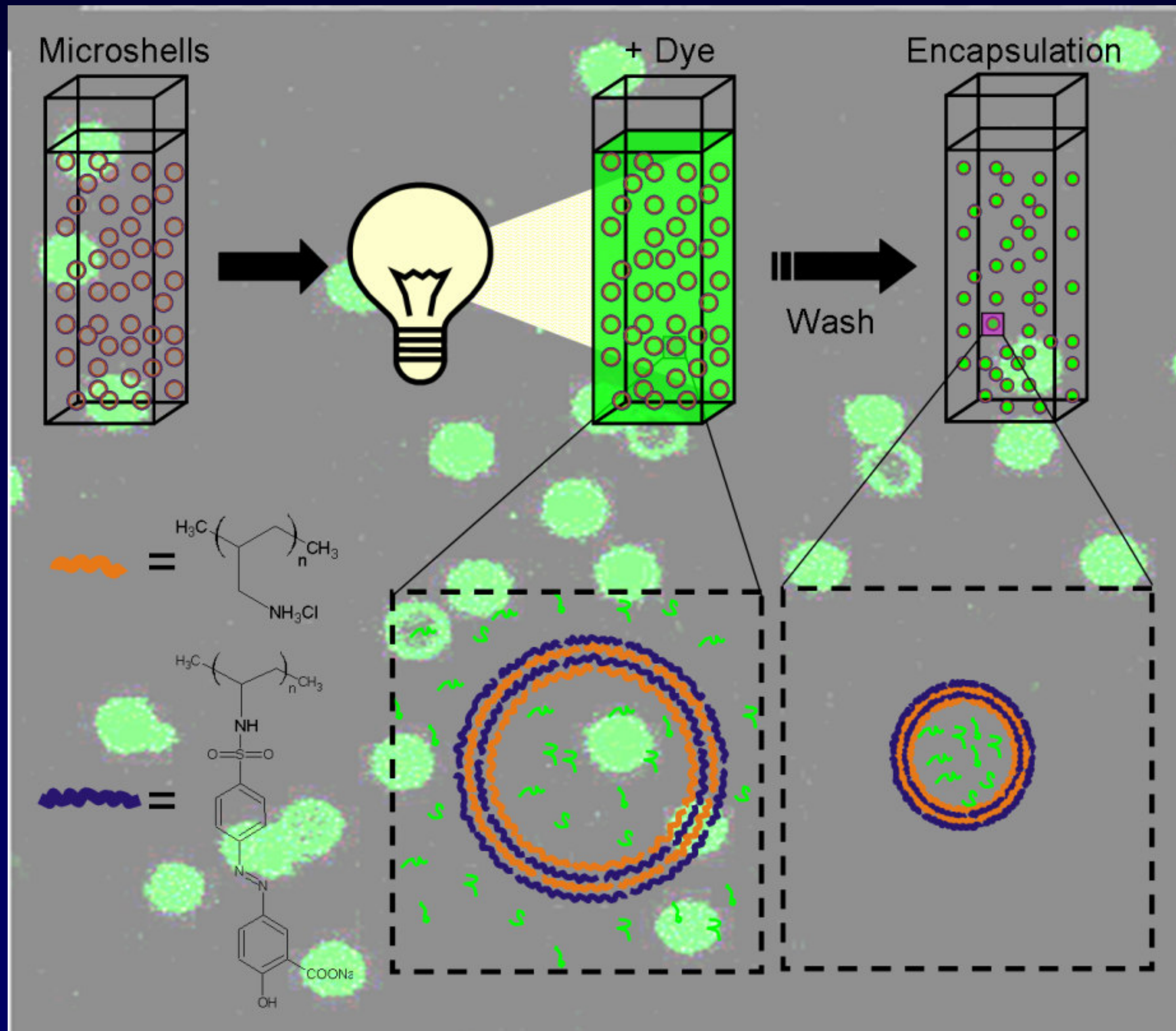






Tatjana Mauser

Optically driven Encapsulation



Matthieu Bedard – Optically addressable microcapsules

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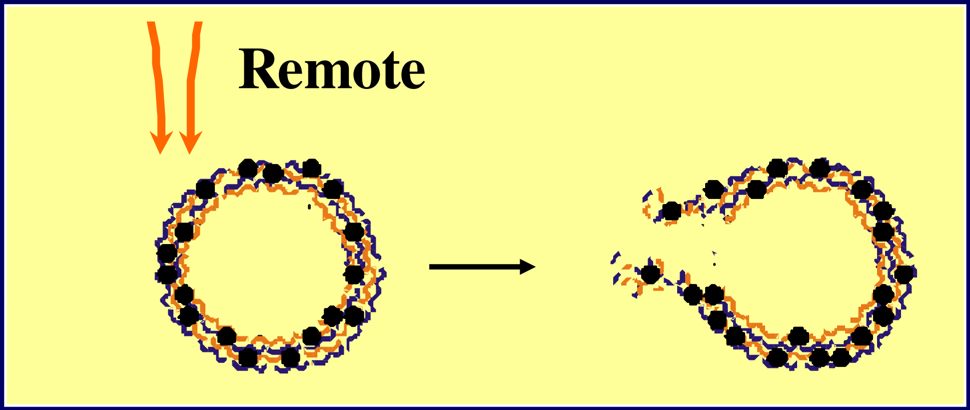
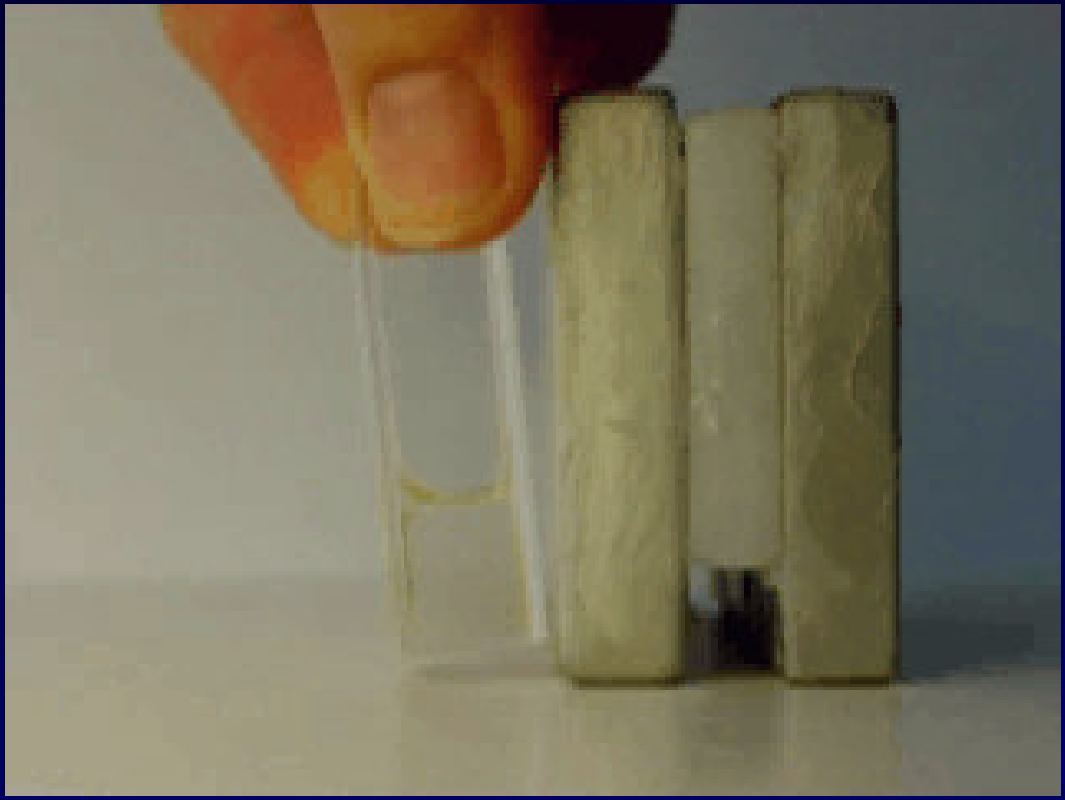
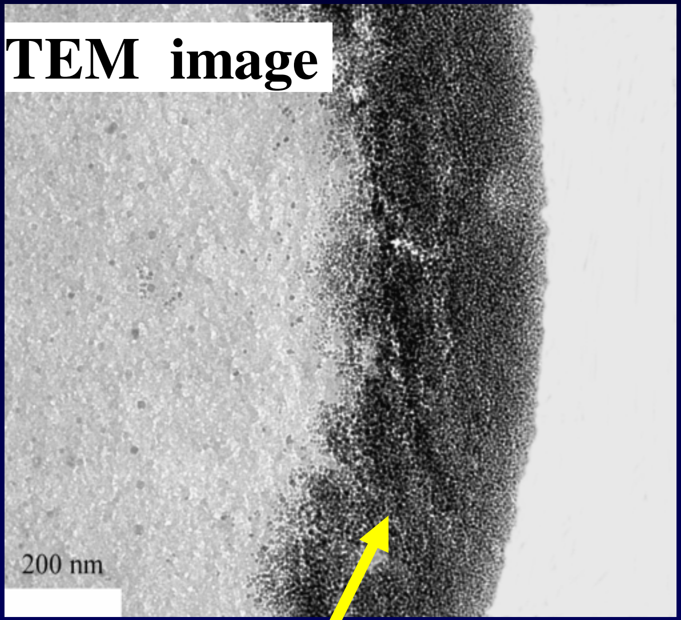


Magnetite nanoparticles assembled in capsule wall



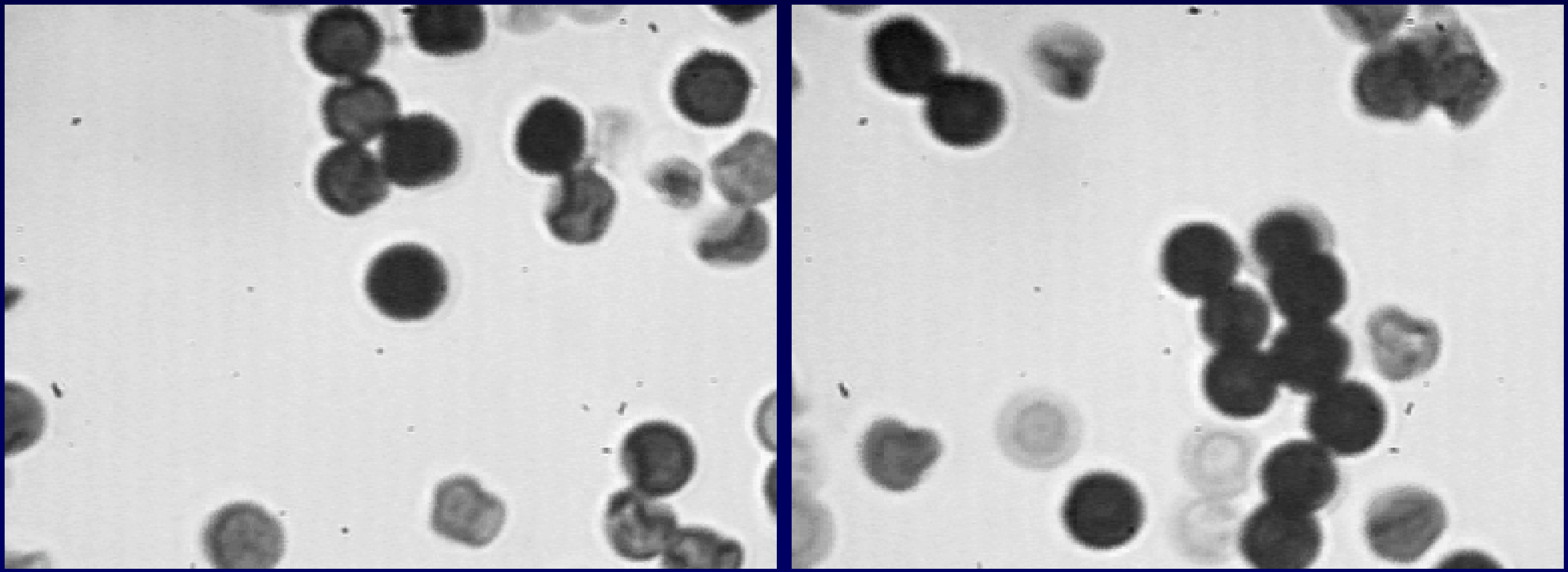


Magnetic NPs in shell

Targeted capsule delivery via magnetic field to tissues

Capsules with Composite Shell are Susceptible to Remote Activation

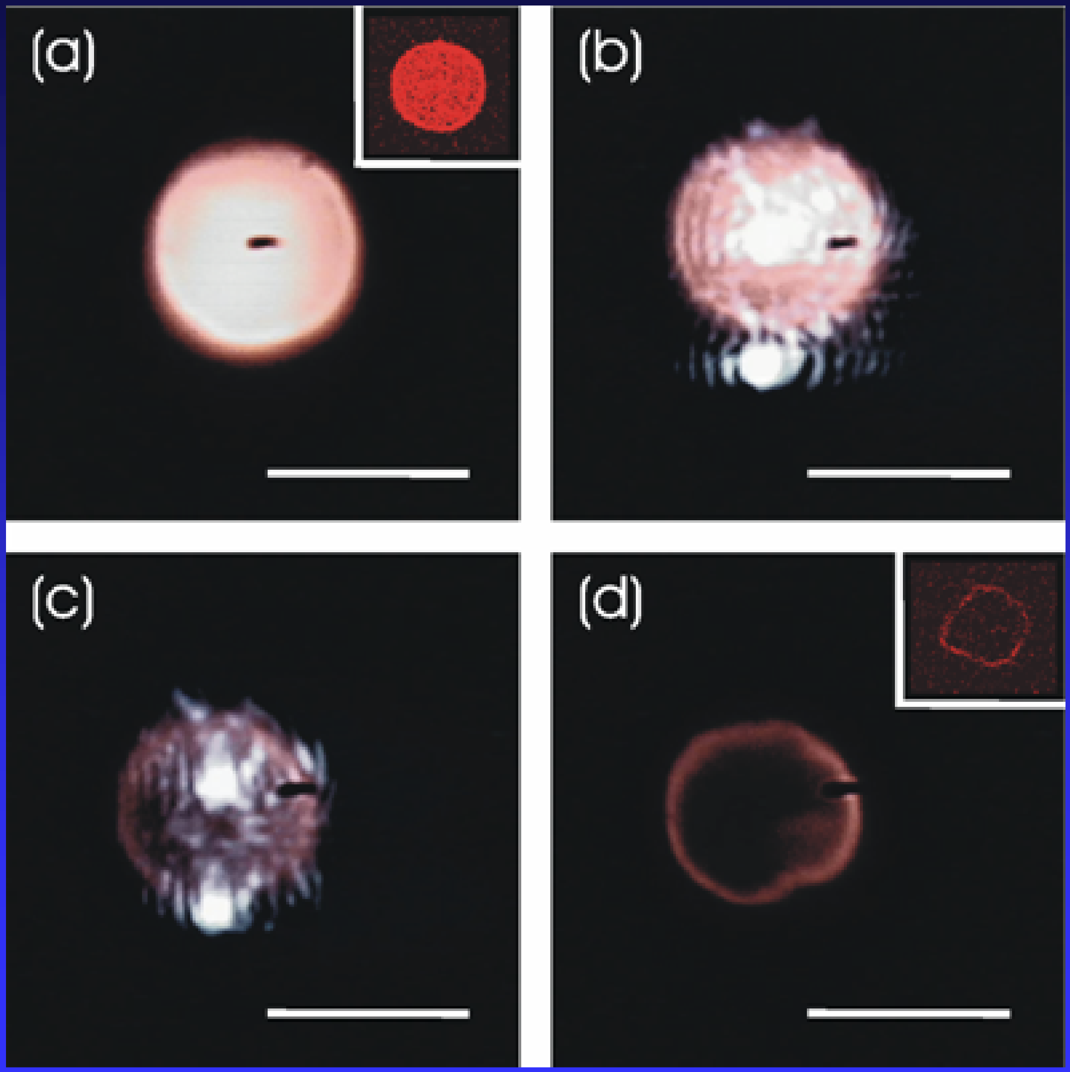
Ag-nanoparticles doped capsules can be ruptured by <u>Infrared Laser 830nm</u>



→ Optically activated release;
→ Infrared window for biomedical application

Andre Skirtach

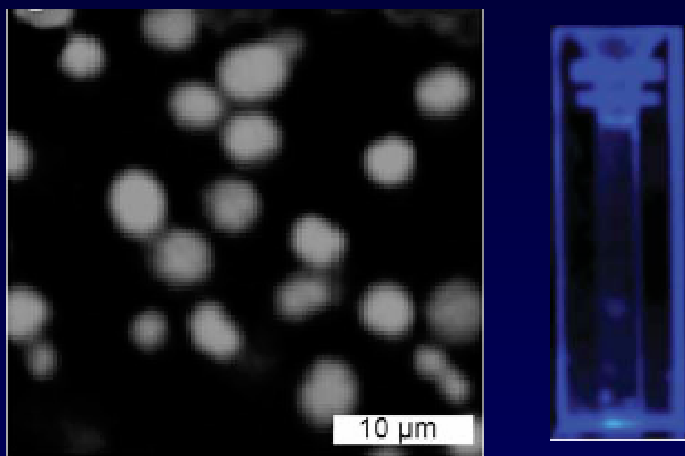
Fluorescence Imaging



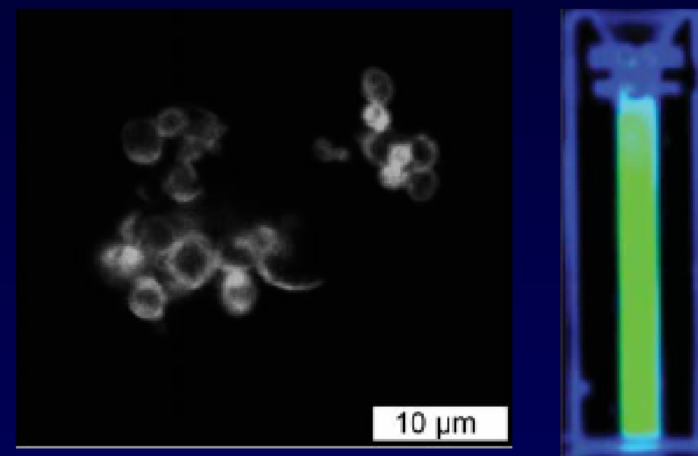
A.Skirtach et at, Nanoletters, 2005

Ultrasound stimulated release.

Before - encapsulated



After – released



– Power of Ultrasound for capsule rupture is compared to medical use without damage of tissues
– Higher depth of operation inside the body

Skirtach, A.G., De Geest, B.G., Mamedov, A.A., Antipov, A.A., Kotov, N.A., *Sukhorukov, G.B.*
J. Mater. Chem., *2007, 11, 1050-1054*

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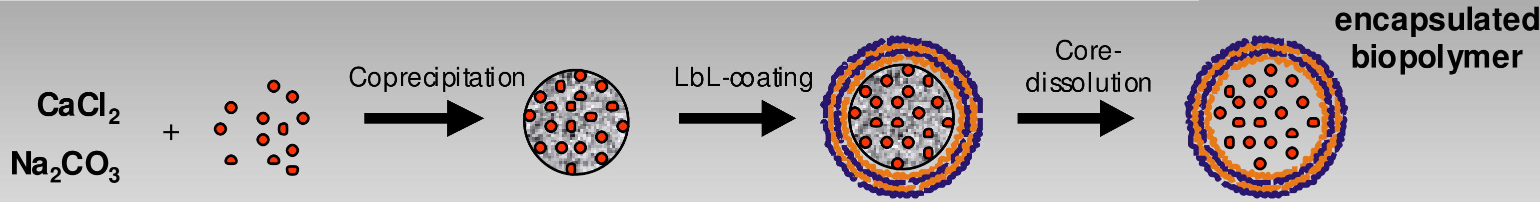
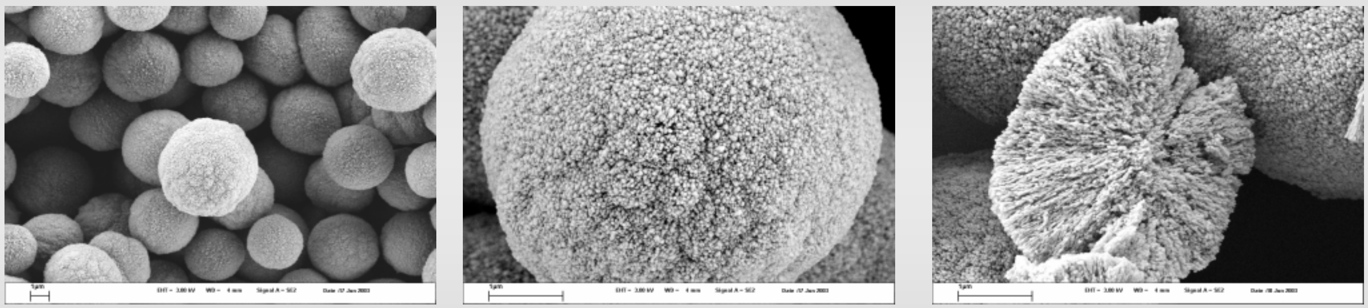
Encapsulation Using Microcrystalline Carbonate-Templates

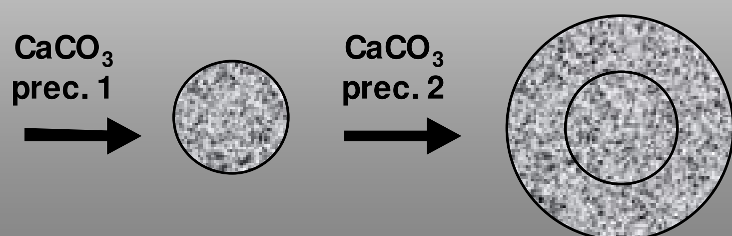
1. **Encapsulation of macromolecules after incorporaton into calcium carbonate microparticles (”coprecipitation method”)**



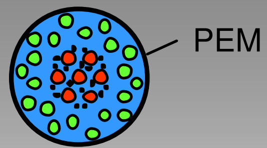
Porous calcium carbonate microparticles (∅ 5µm)



2. **Fabrication of multicompartment „ball-in-ball“particles calcium carbonate microparticles**

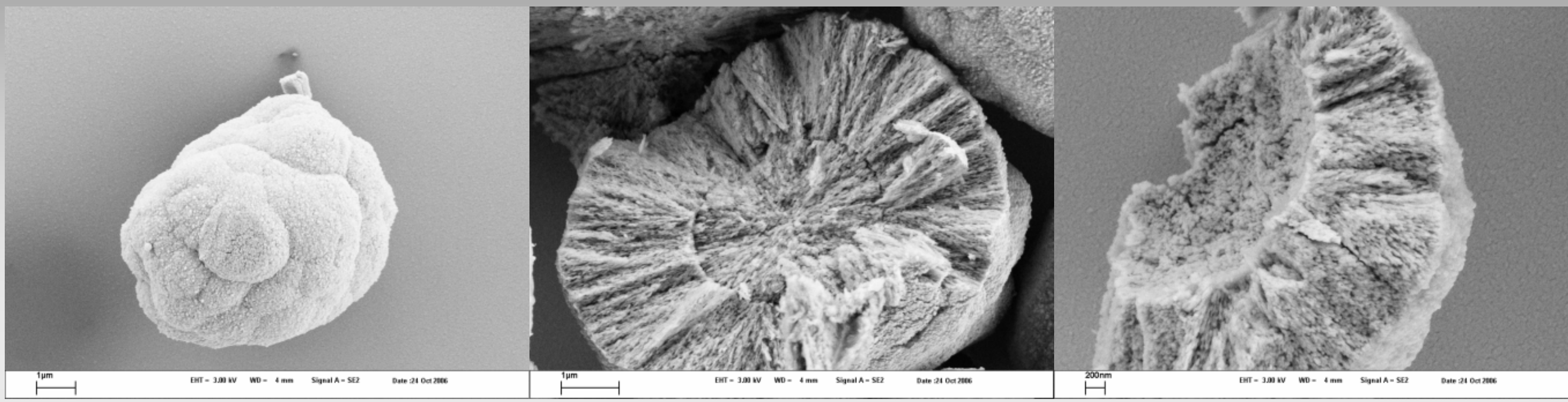


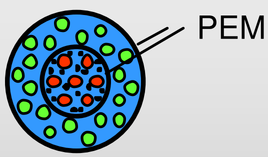
Fabrication of two-compartment calcium carbonate particles



ball-in-ball particle (type III)

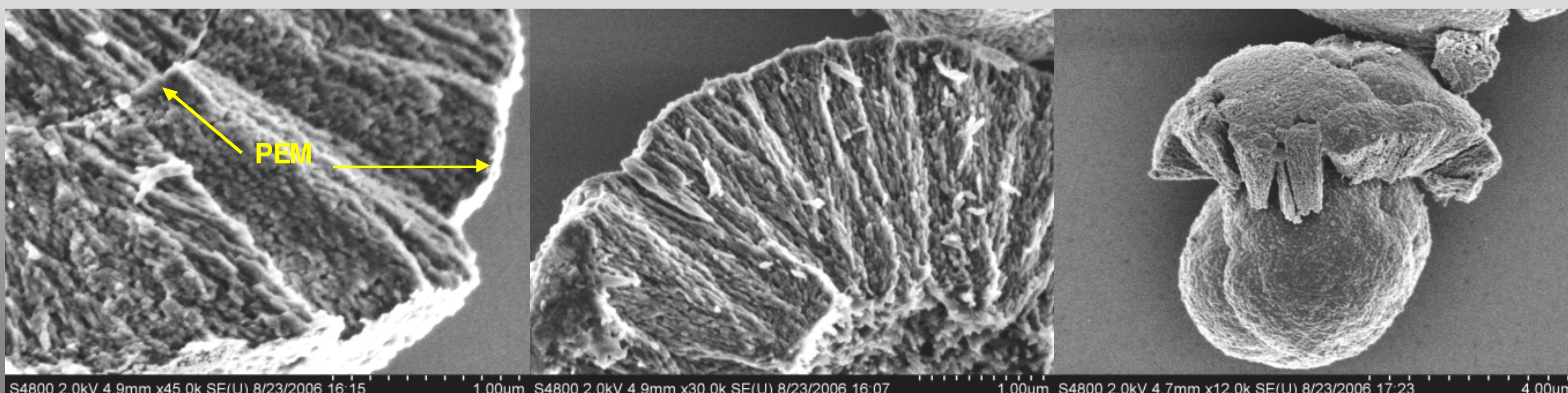
SEM-images



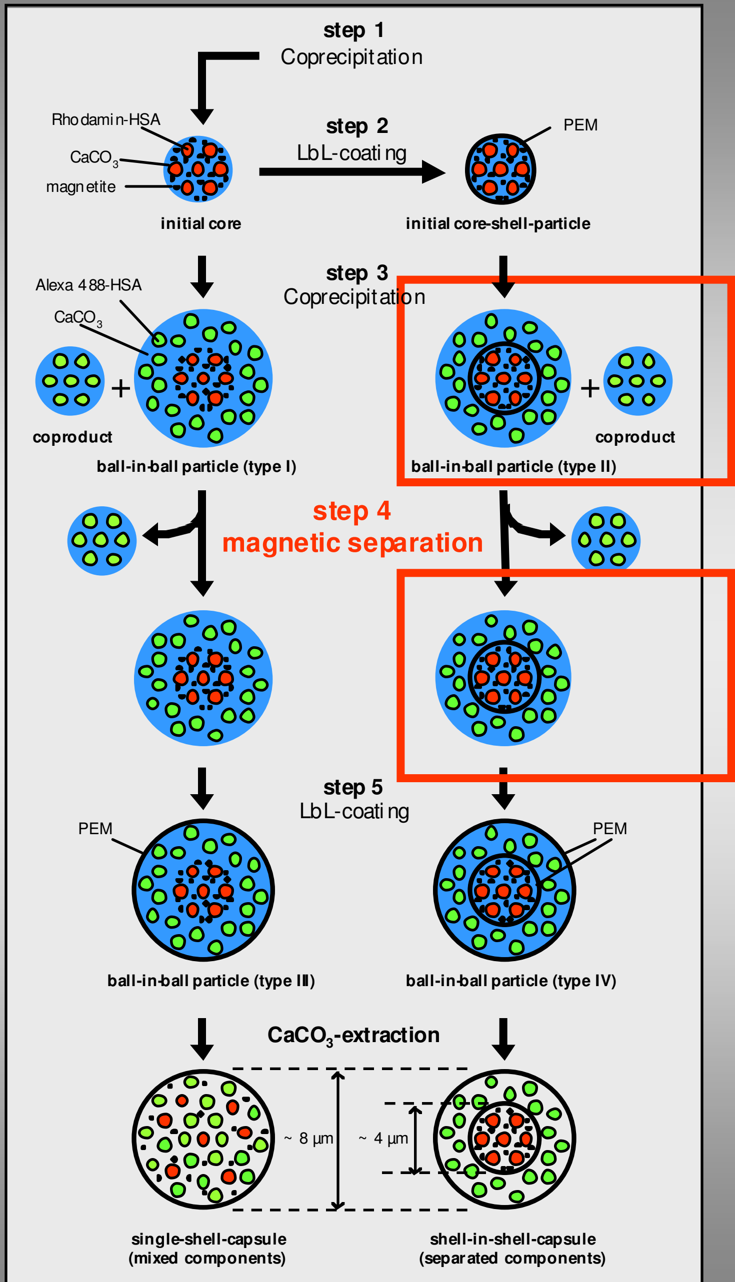


ball-in-ball particle (type IV)

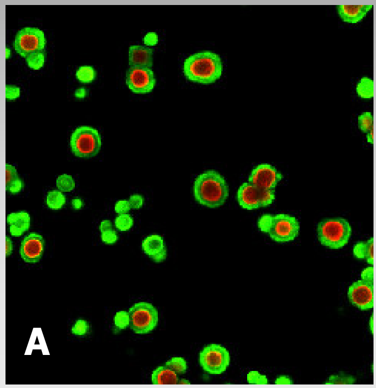
SEM-images



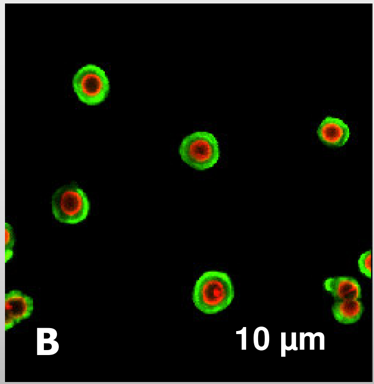
Magnetic separation



unpurified raw-product



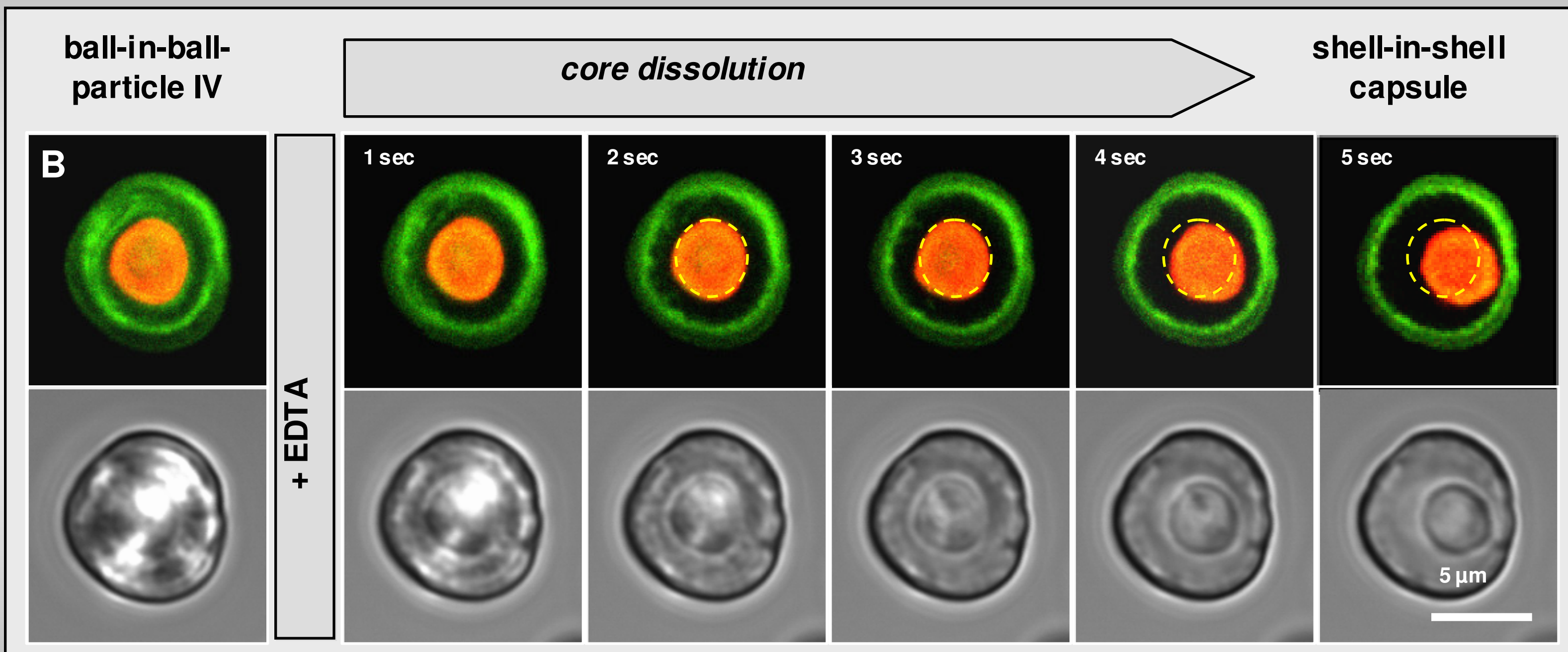
ball-in-ball particles after magnetic separation



Product purification by an external magnetic field.

Oliver Kreft

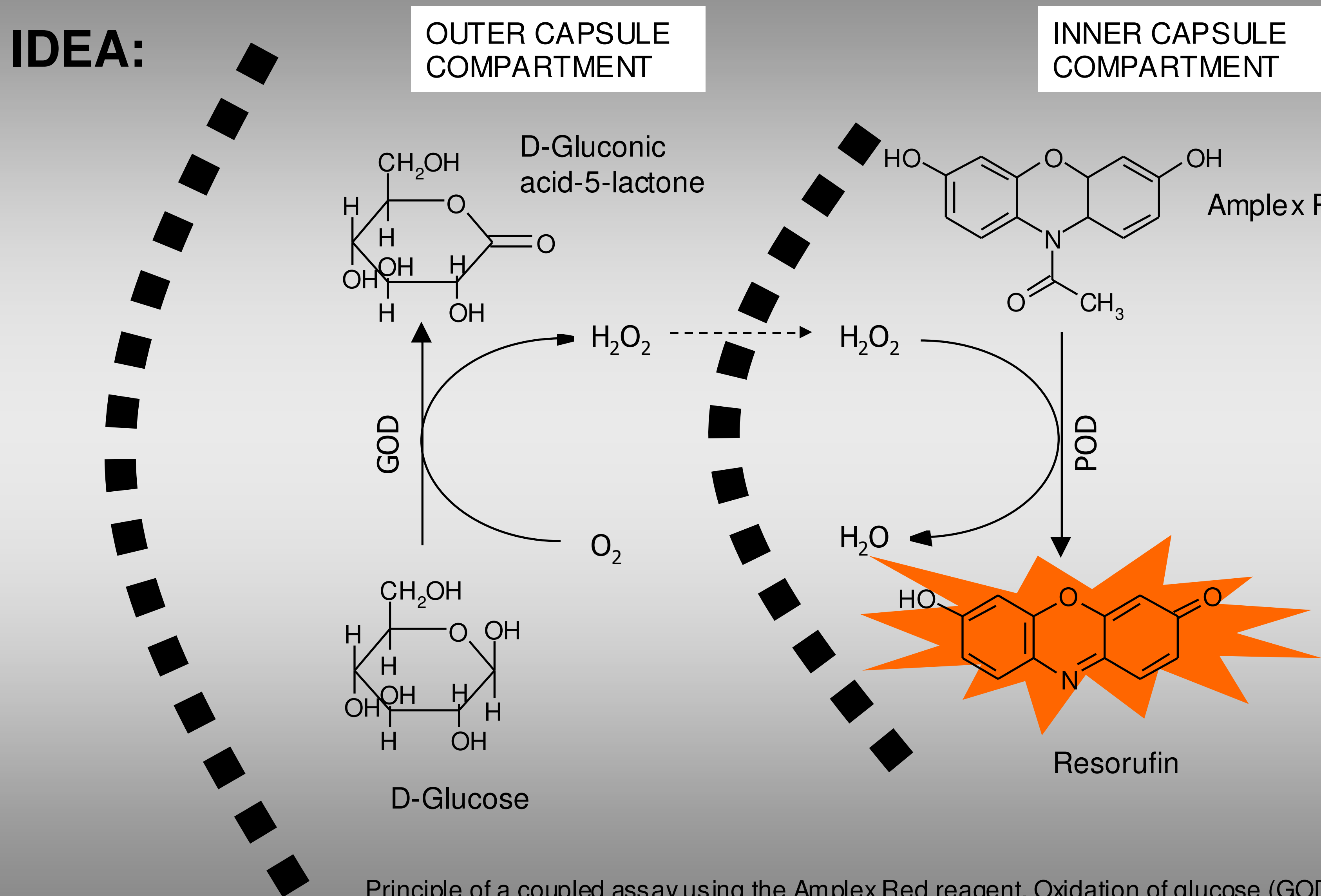
Controlled Mixing or Separation of Biomolecules



Stable separation

Oliver Kreft

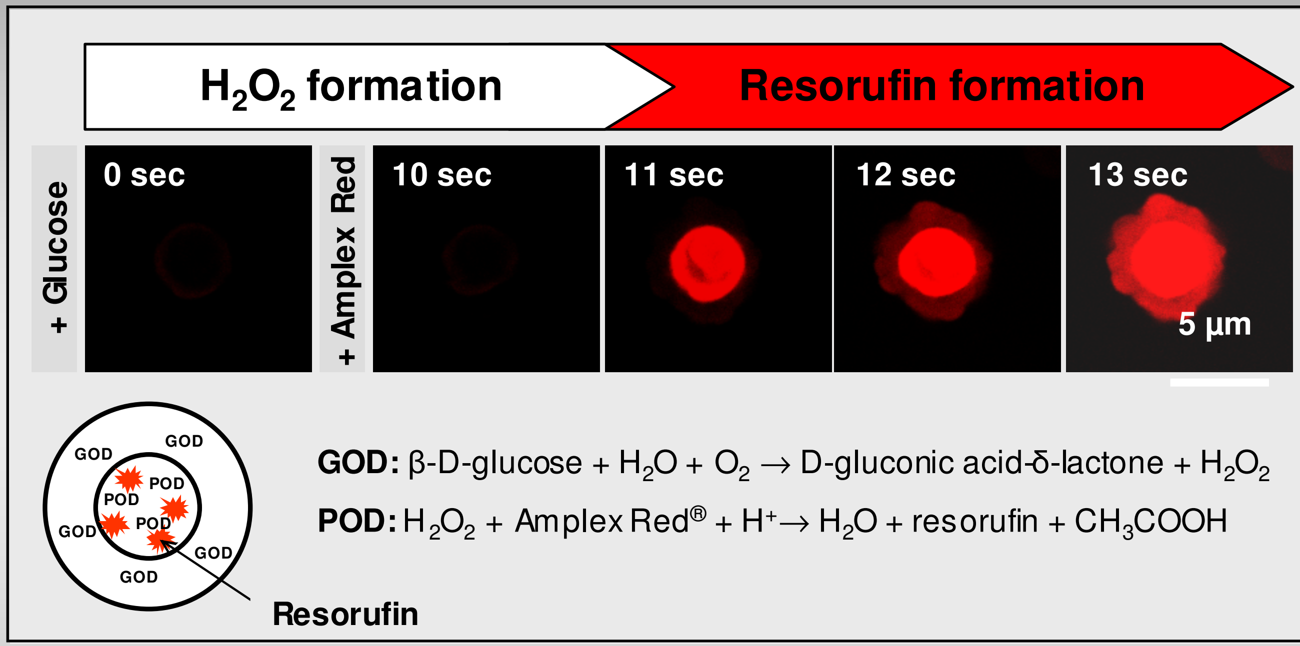
Preliminary example for prospective applications:
Coupled enzyme assay with glucose oxidase (GOD) and peroxidase (POD)



Principle of a coupled assay using the Amplex Red reagent. Oxidation of glucose (GOD) by glucose oxidase results in generation of H2O2, which is coupled to converion of the Amplex Red reagent to fluorescent resorufin by peroxidase (POD).

Example for prospective applications:

Coupled enzyme assay with glucose oxidase (GOD) and peroxidase (POD)



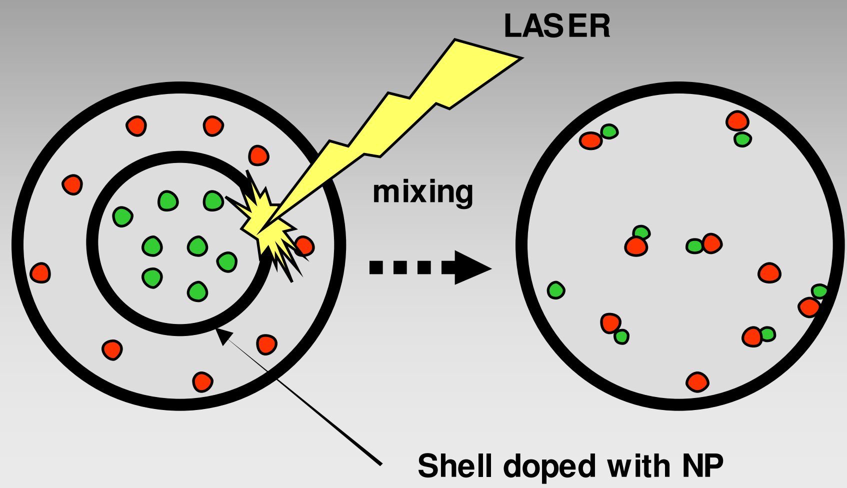
CLSM image of a shell-in-shell capsule containing GOD and POD, after adding glucose and Amplex Red. Resorufin formation results in red fluorescence of the capsule interior.

Separate compartments for biochemical reactions

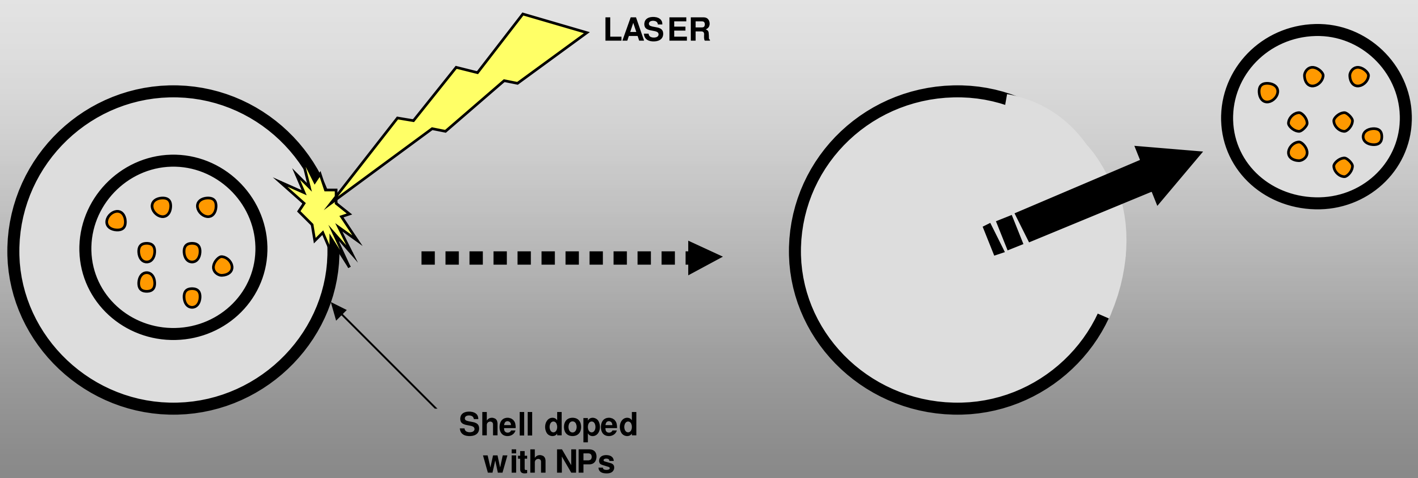
Kreft, O. et al. *Angewandte Chemie Intern. Ed., 2007,*46 (29), 5605-5608

Shell-in-Shell Microcapsules/Outlook:

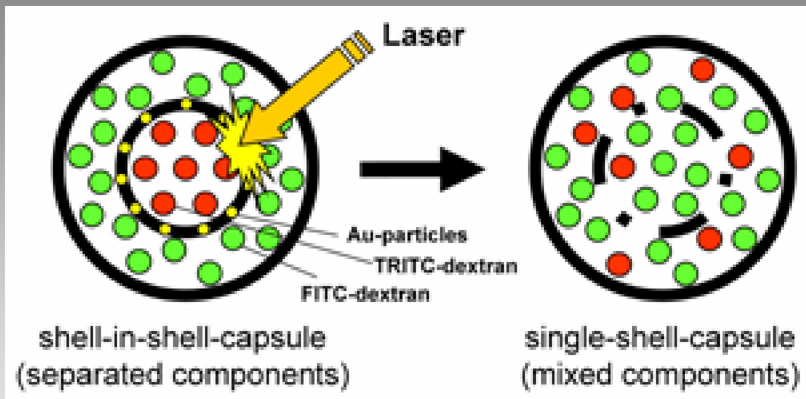
Mixing of reaction partners by physical triggers:

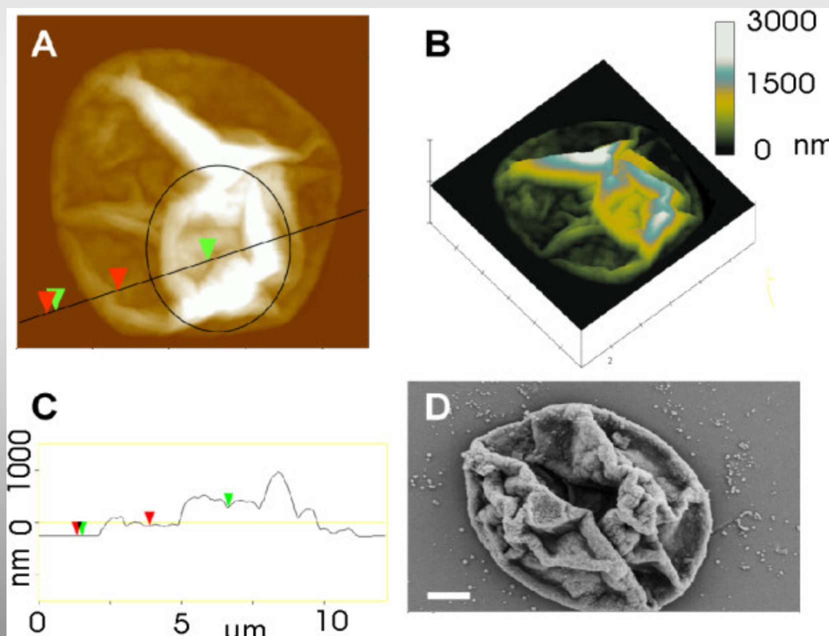


Release of inner capsules by external trigger:

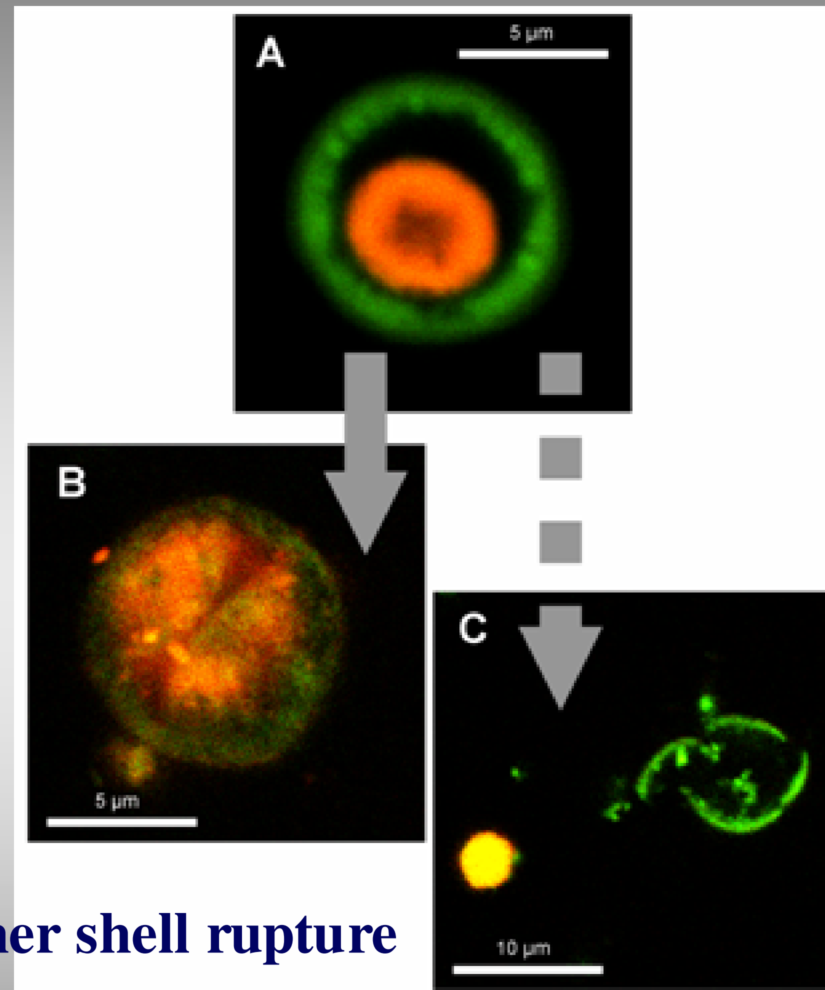


Shell-in-Shell Microcapsules/Outlook:





AFM & SEM images of shell-in-shell microcapsules



Inner shell rupture

Outer shell rupture
- release of nner capsule

O. Kreft et al, Advanced Materals, 2007, 19, 3142

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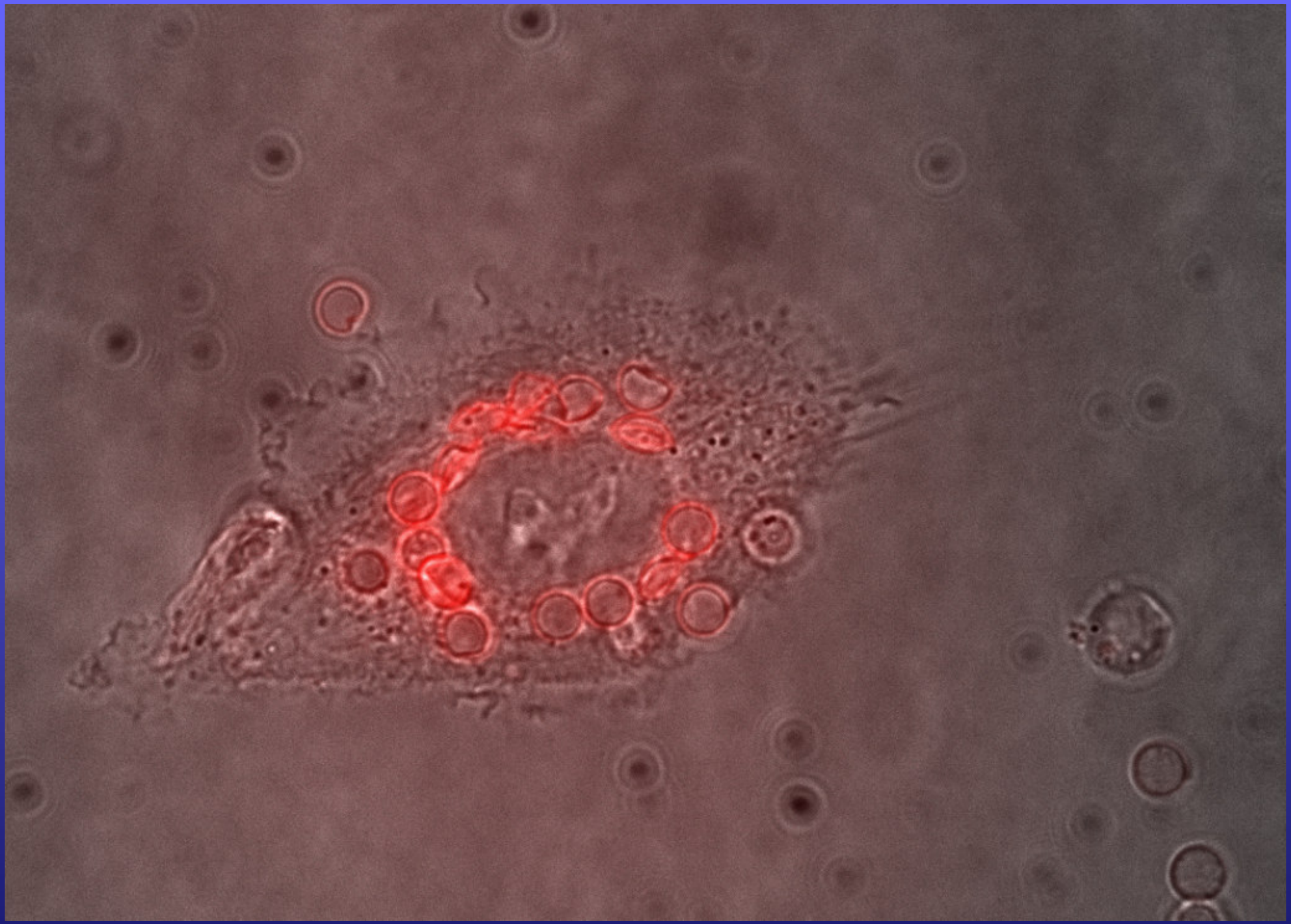
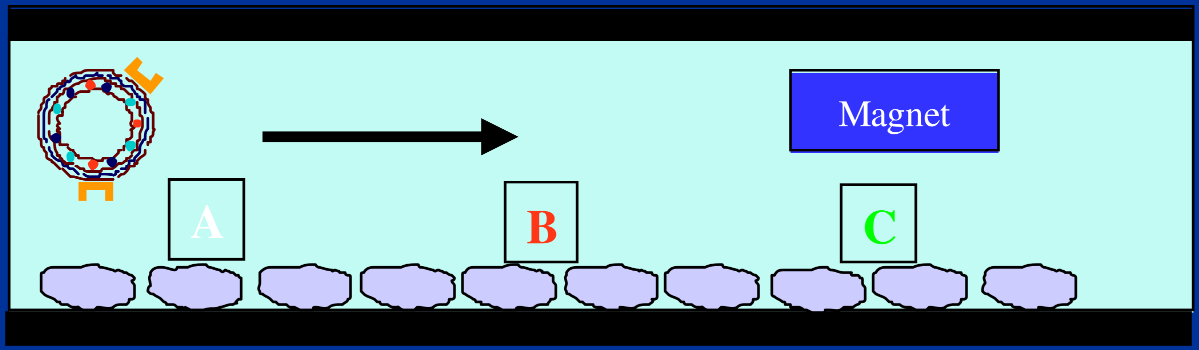
Capsules in cells - Artificial organelles
Reporting on cell interior

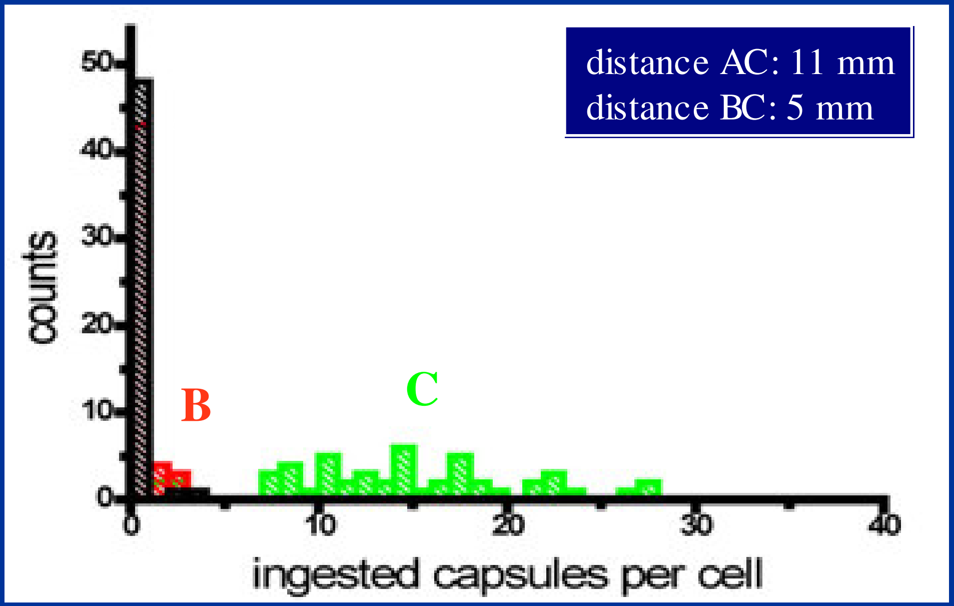


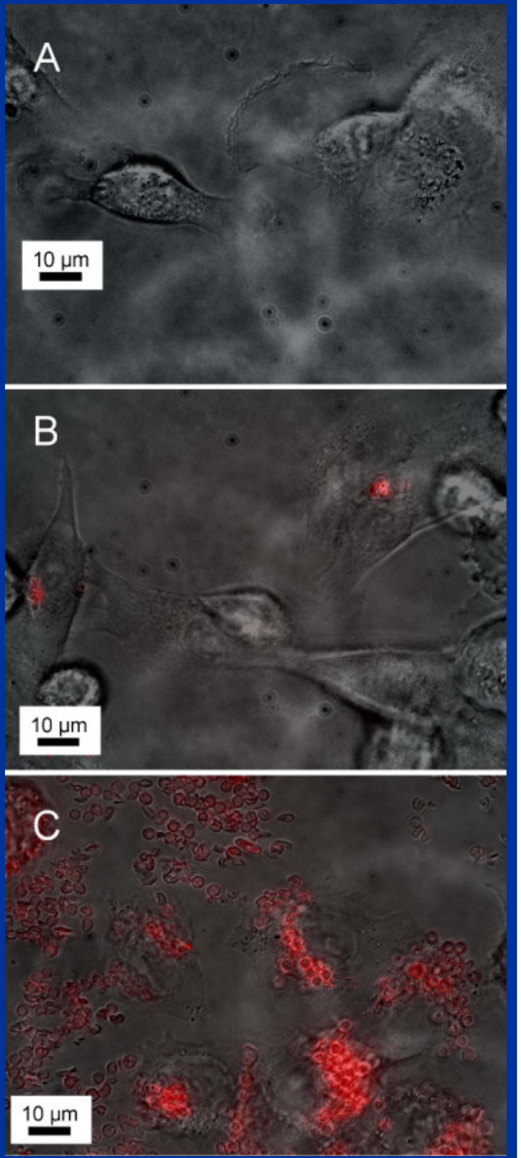
Capsules Uptake by Breast cancer cells

Small 2005 1(2), 194-200

Targeted drug delivery - Use of polymer capsules as multifunctional (magnetic, labeled) carrier systems

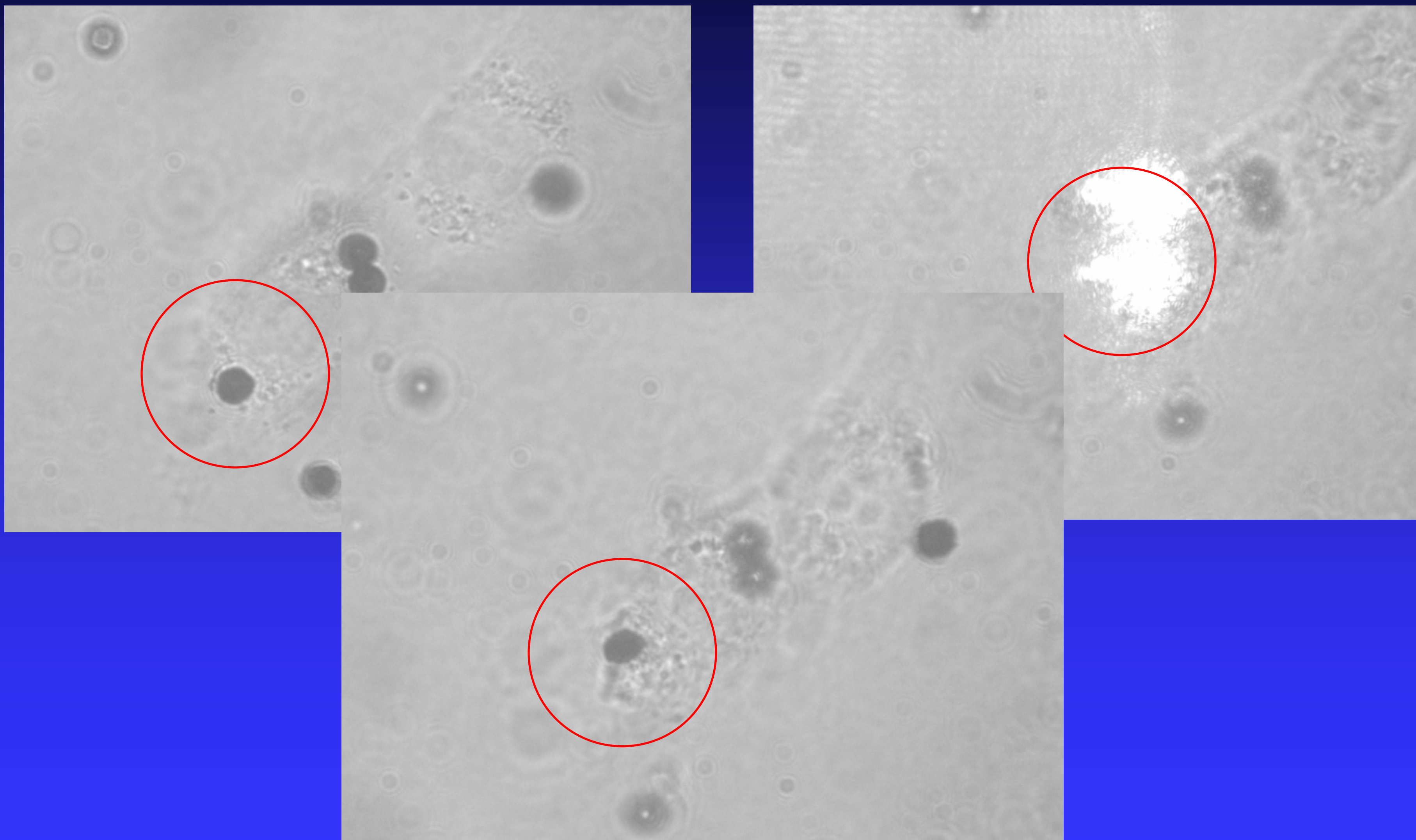






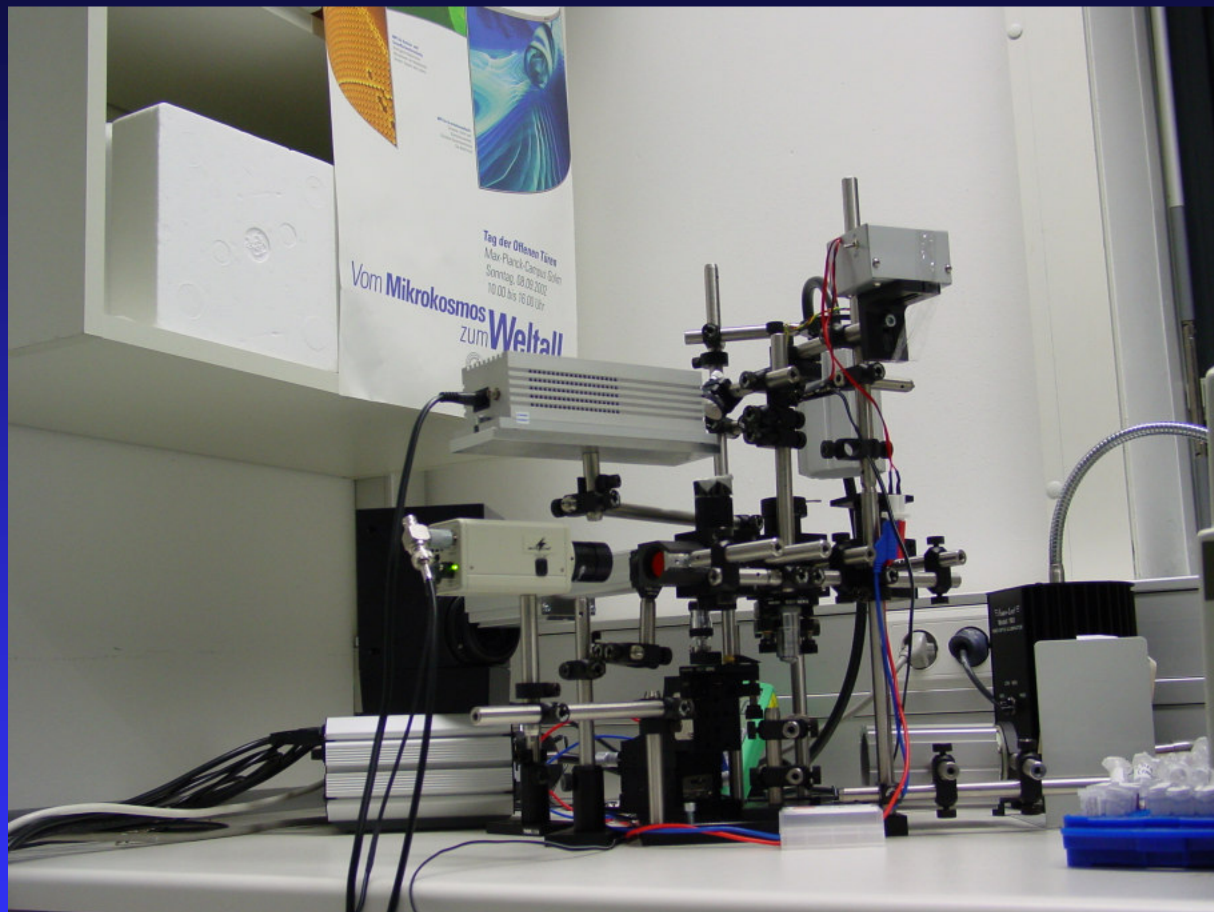
B. Zebli, A. S. Susha, G. B. Sukhorukov, A. L. Rogach, W. J. Parak, *Langmuir*, 2005, 21, 4262

Capsules in cells - Artificial organelles
Remote activation in the cells



In cooperation with Dr. Wolfgang Parak, (LM Uni-München) Dr. Andre Skirtach

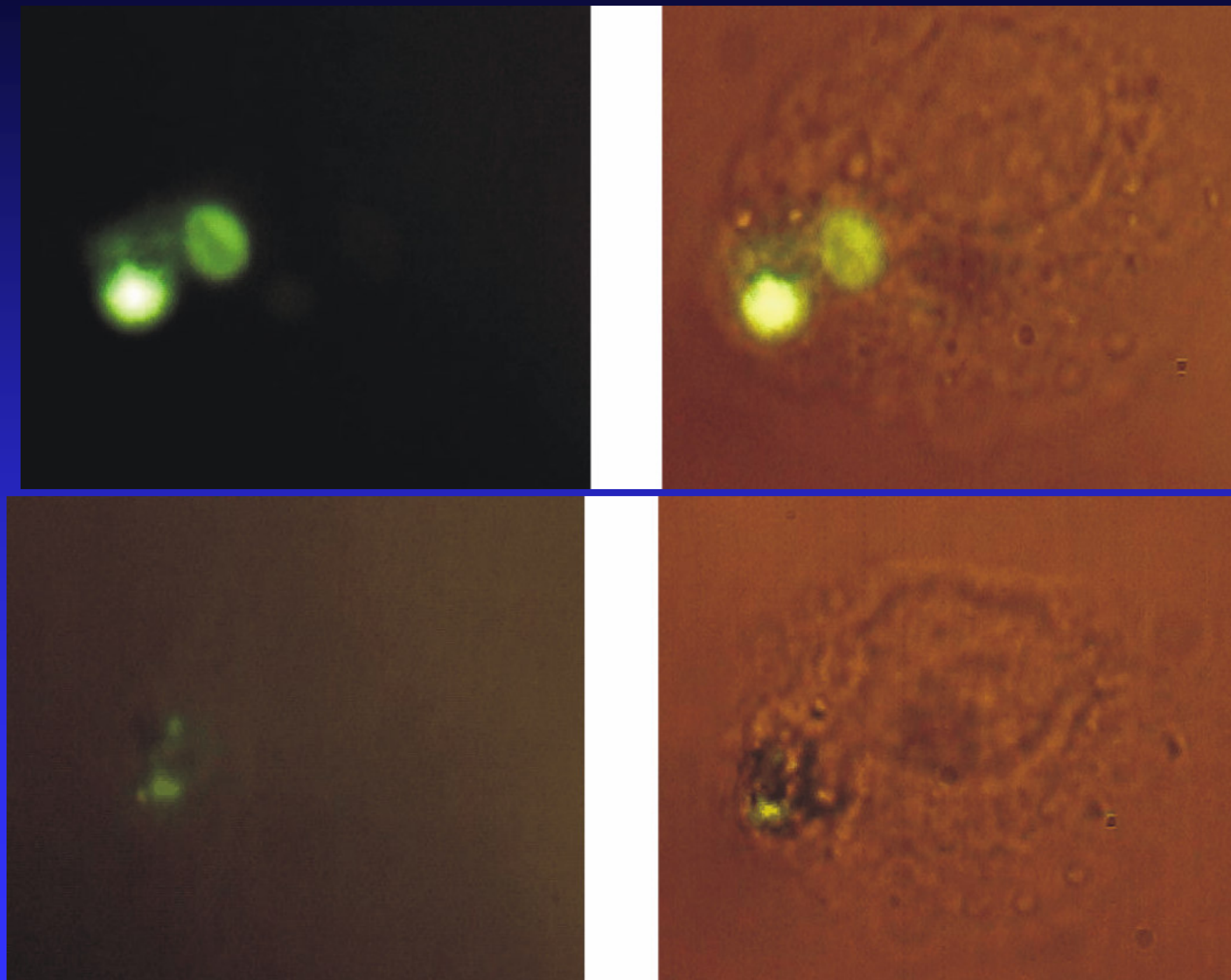
In-house developed optical setup for remote release experiments



Various sources, CCD, real-time imaging, portable, easy tranferable to new location

Andre Skirtach

Optically induced release inside cells



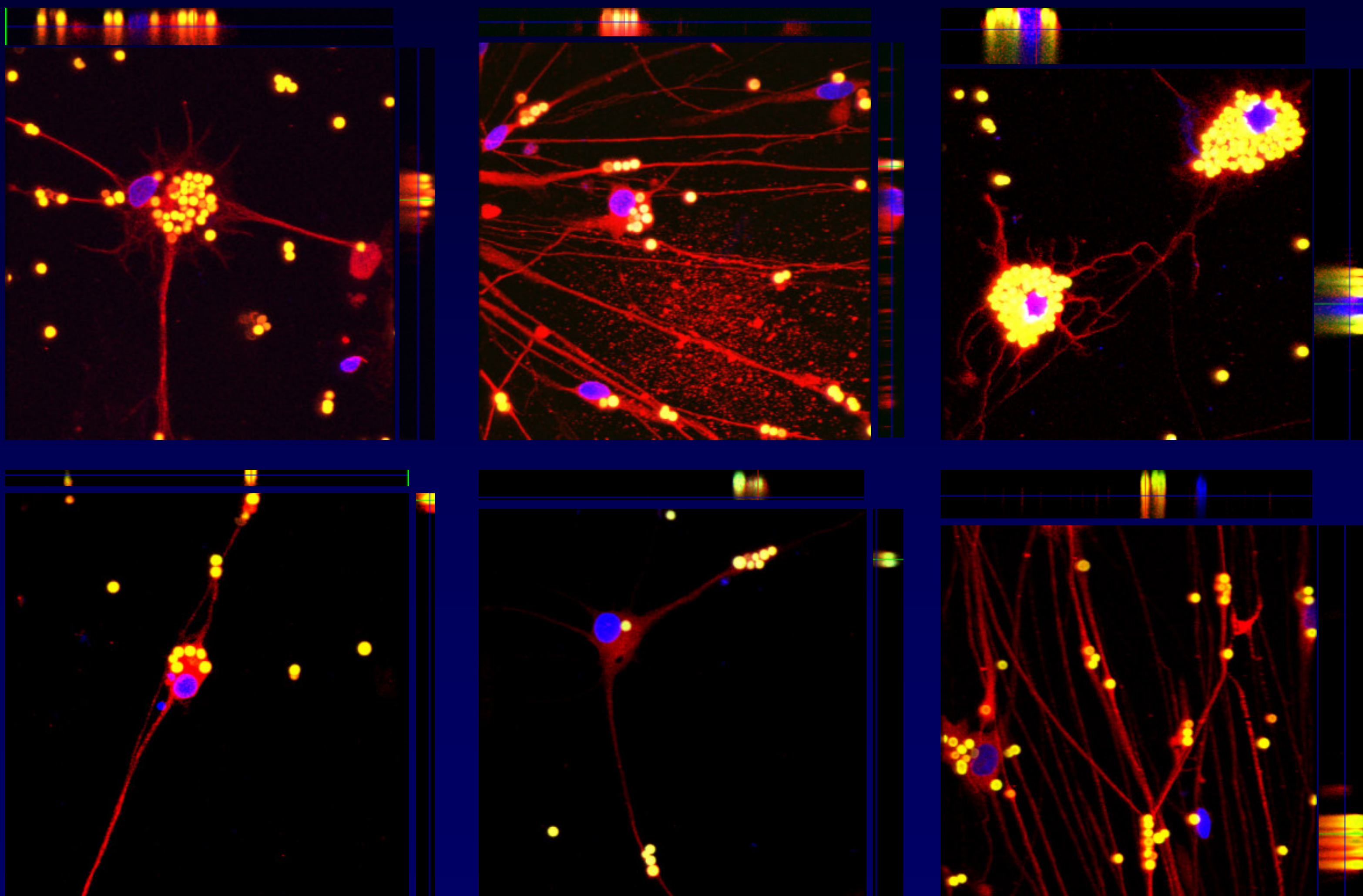
Before

After

Skirtach, A.G., Muñoz Javier, A., Kreft, O., Köhler, K., Piera Alberola, A., Möhwald, H., Parak, W.J., Sukhorukov, G.B. Angewandte Chemie Intern. Ed., 2006, 45, 4612-4617

Towards Intracellular Capsule Delivery to Neurons

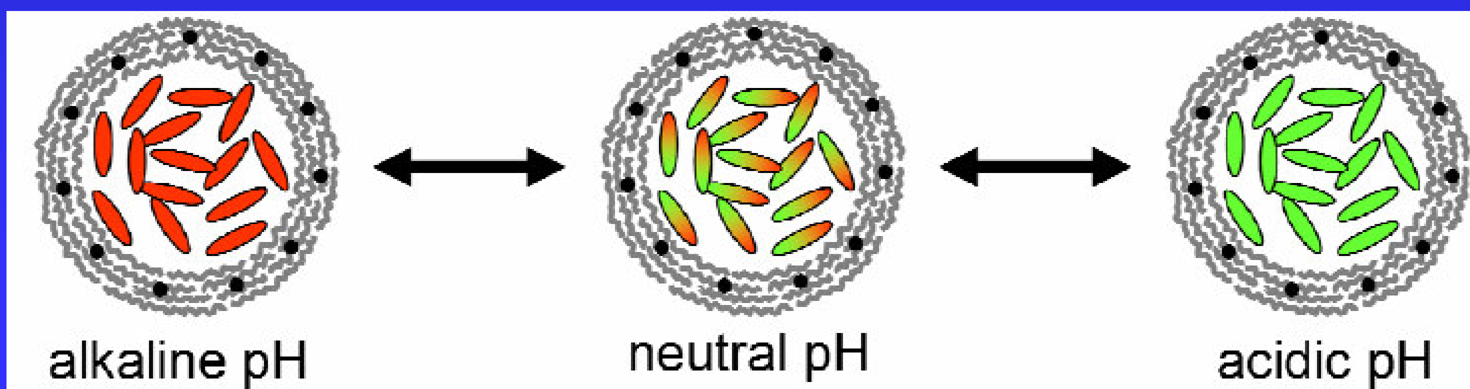
PSS/PAH capsules filled with labelled BSA



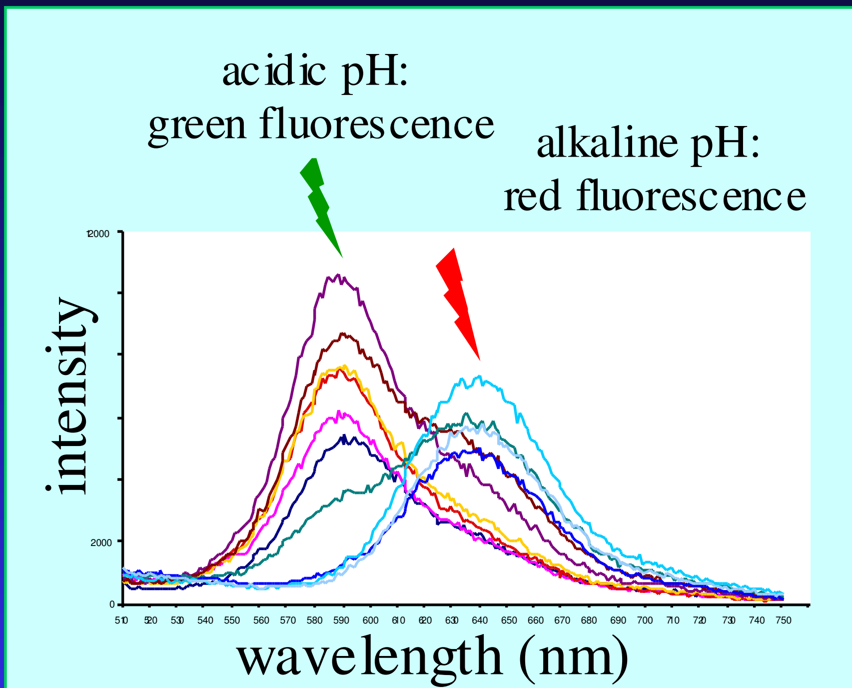
In cooperation with Prof. Jo Martin and Dr. D.Davidson
(Queen Mary, Neuroscience Center)

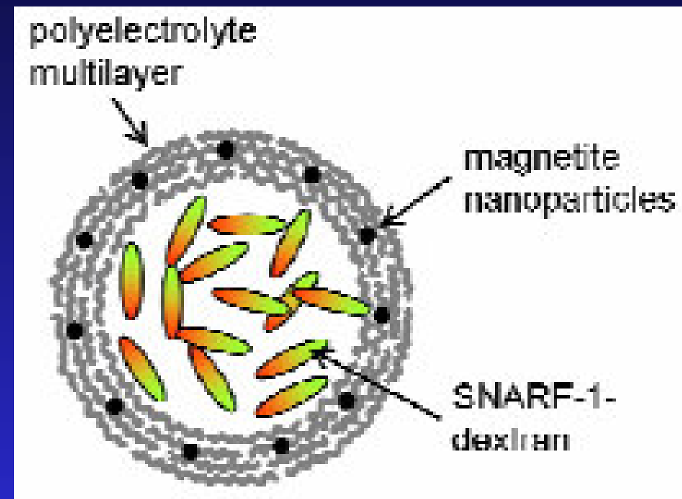
Tayloring functions in microcapsules: Responsiveness and remote controlling

Coating colloids and Hollow capsules
Responsive capsules
Composite capsules - Remote activation
Two compartmental capsules
Capsules delivery in living systems
Intracellular Sensing Systems
Conclusions and perspectives



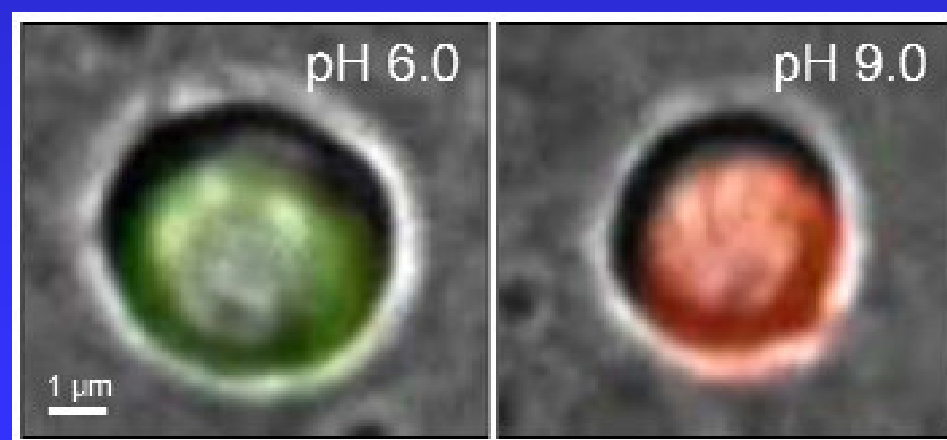
Polymer Microcapsules as Mobile Local pH-Sensor



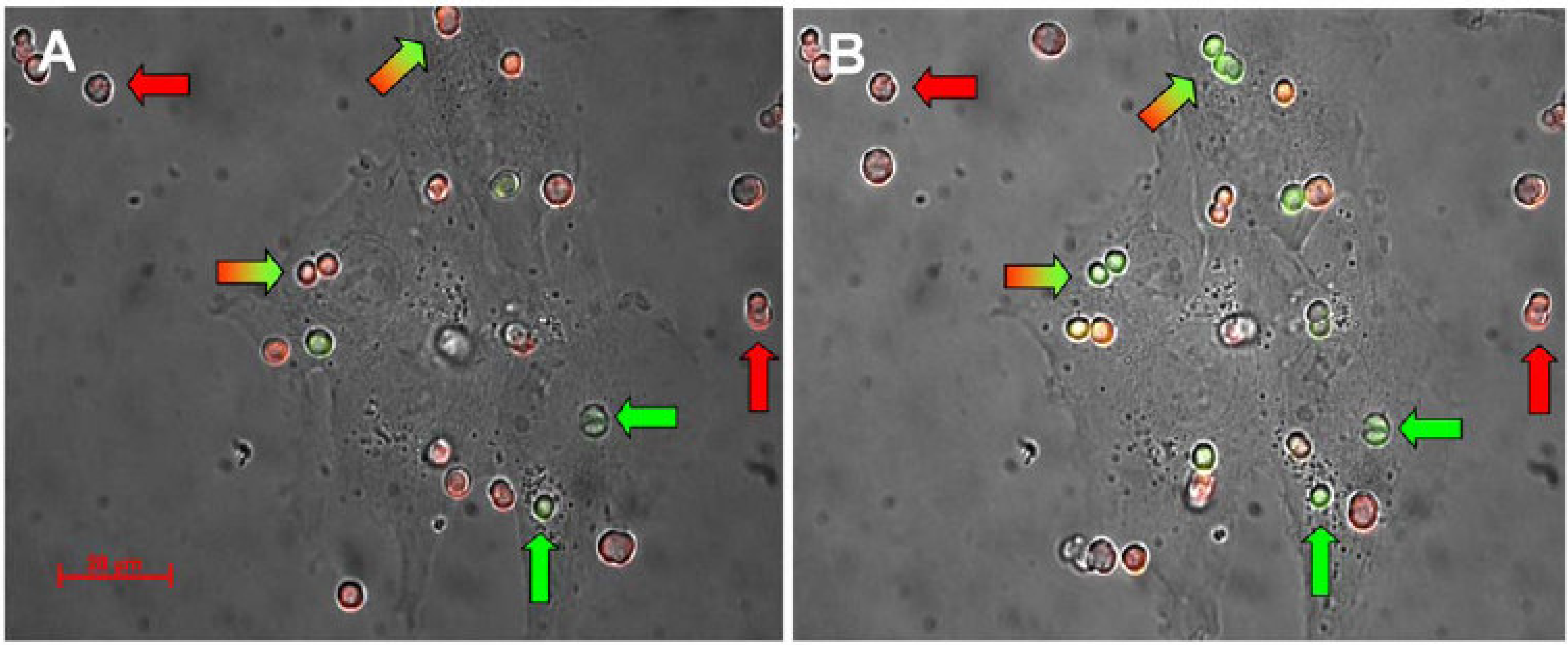


SNARF dye

Ratiometric pH measurement. The dye shifts the maximum of the fluorescence emission from green to red color upon increasing the pH.



On-line monitoring of capsule internalisation



SNARF-loaded capsules change from red to green fluorescence upon internalization by MDA-MB435S breast cancer cells.

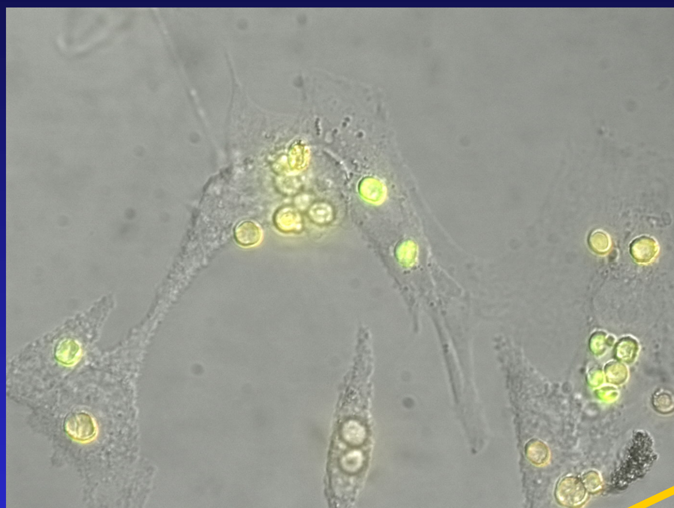
(A) SNARF-fluorescence 30 min after adding the capsules to the cell culture.

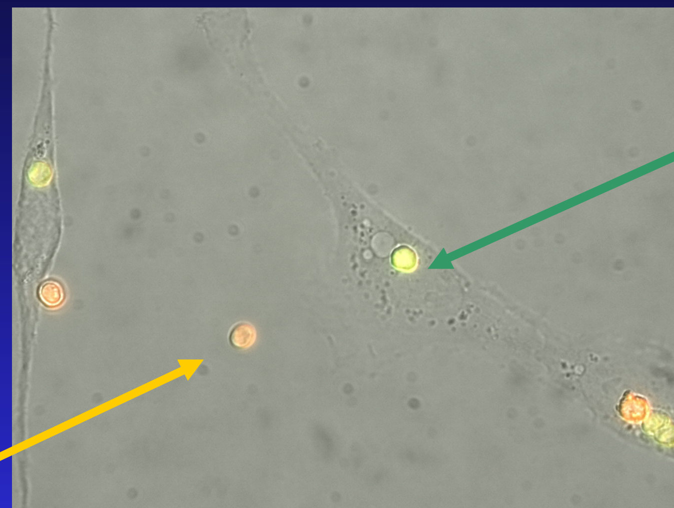
(B) The same cells after another 30 min of incubation.

Kreft, O., Muñoz Javier, A., Sukhorukov, G.B., Parak, W.J.
J. Mater. Chem., 2007, 42, 4471-4476

Intracellular Sensors

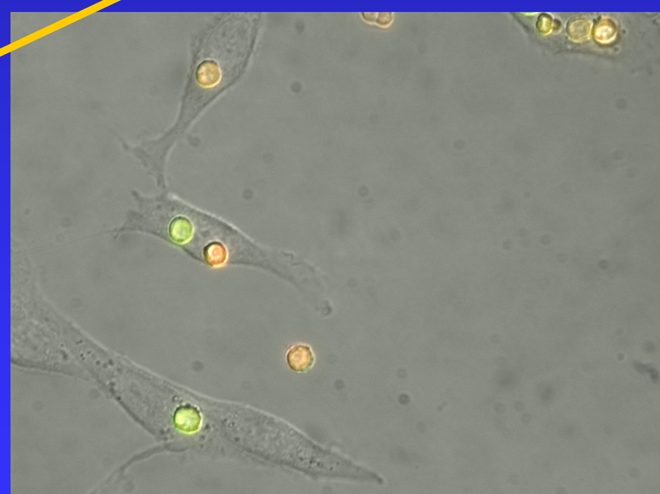
Encapsulated pH – sensor, ***SNARF-based dye***





After Uptake

Before Uptake



Green – low pH

Emission 580nm

Inside cell endosome

Red – high pH

Emission 650 mn

Outside cell

Kreft, O., Muñoz Javier, A., Sukhorukov, G.B., Parak, W.J.
J. Mater. Chem., 2007, 42, 4471-4476

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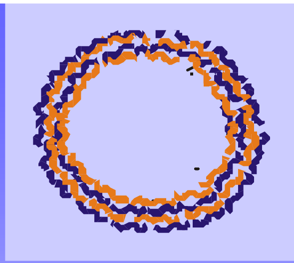
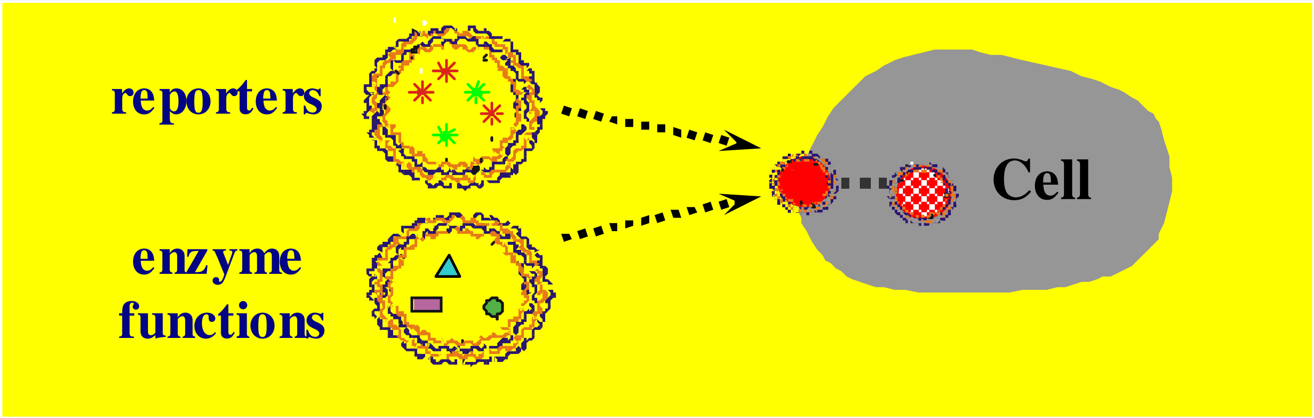
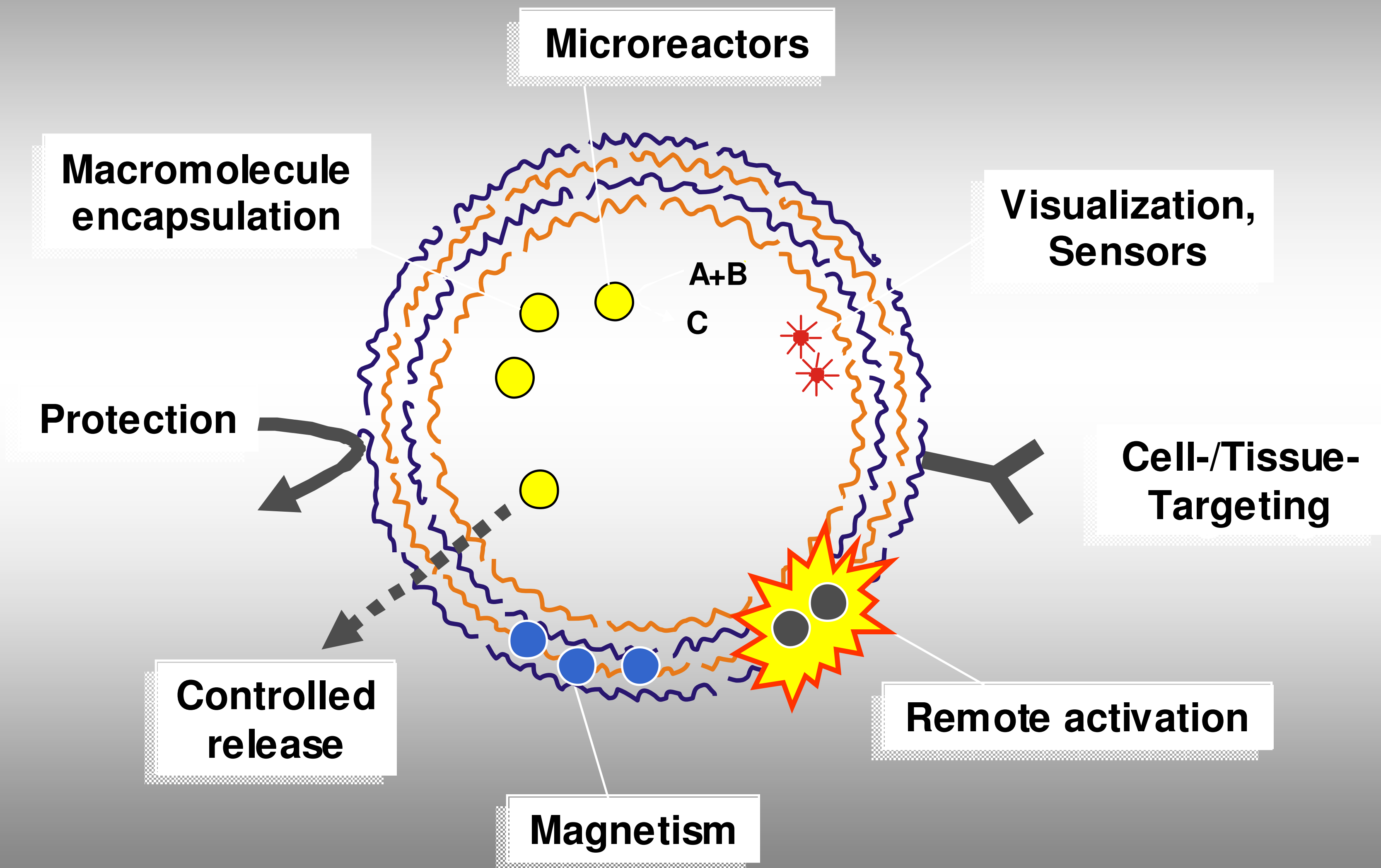
Research strategies



- Design of Nano-engineered shell on colloidal particles/capsules inc. Emulsion, micro- and nanocrystals, bubbles
  Tuning release, delivery systems into cells and tissues,
- Stimuli-responsive capsules Remote (IR-, US, MW) activated release
- Diagnostics/Sensing using encapsulated material
- Modelling biological cells and organelles. Cell residing reporters.



Multifunctionality to Microcapsules



Acknowledgements

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Matthieu Bedard

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University of Ghent – Dr. Bruno de Geest

NeuroScience Centre, QMUL – Prof. Jo Martin, Dr. D.Davidson