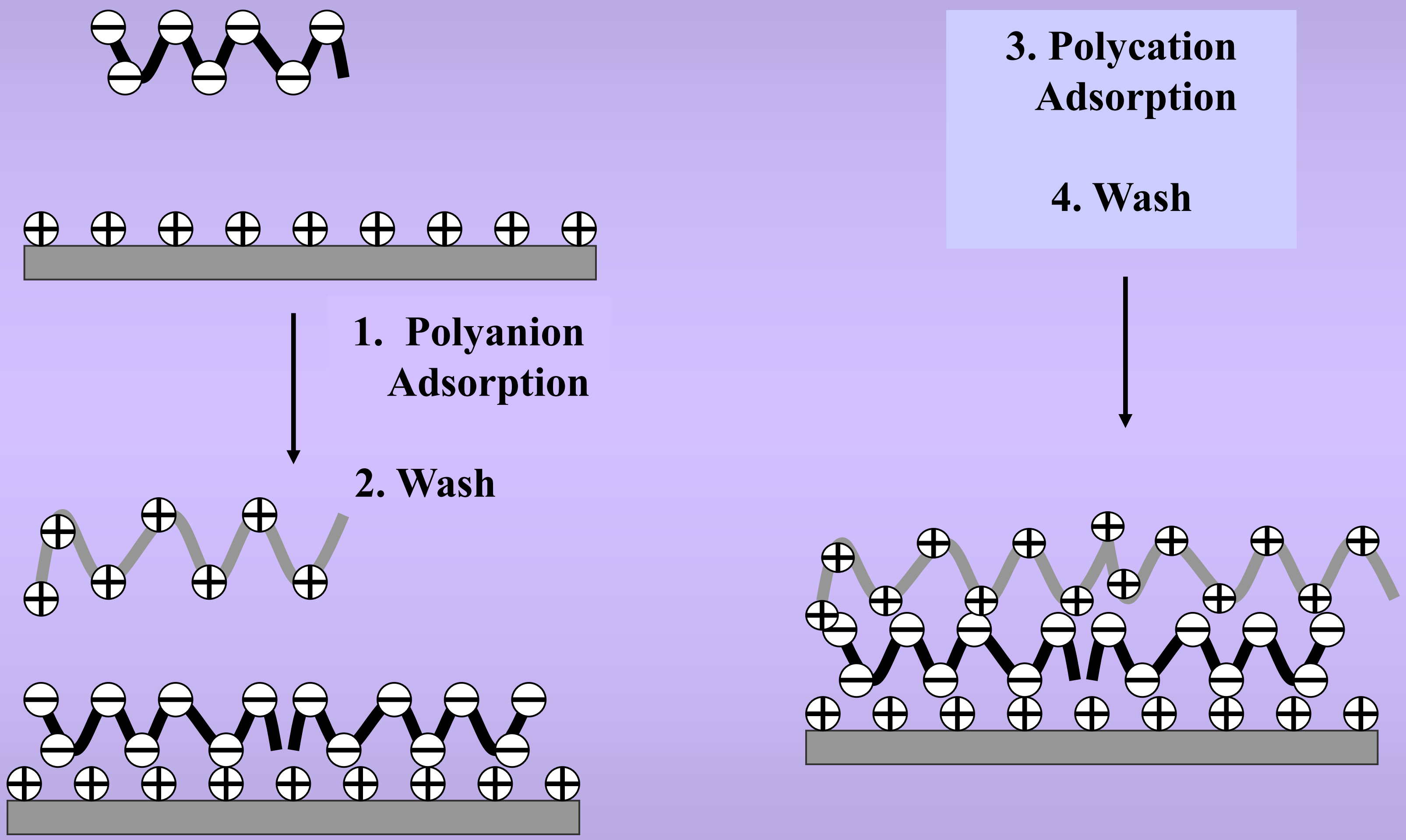
Microencapsulation technology with multifunctional responses and applications

Gleb Sukhorukov

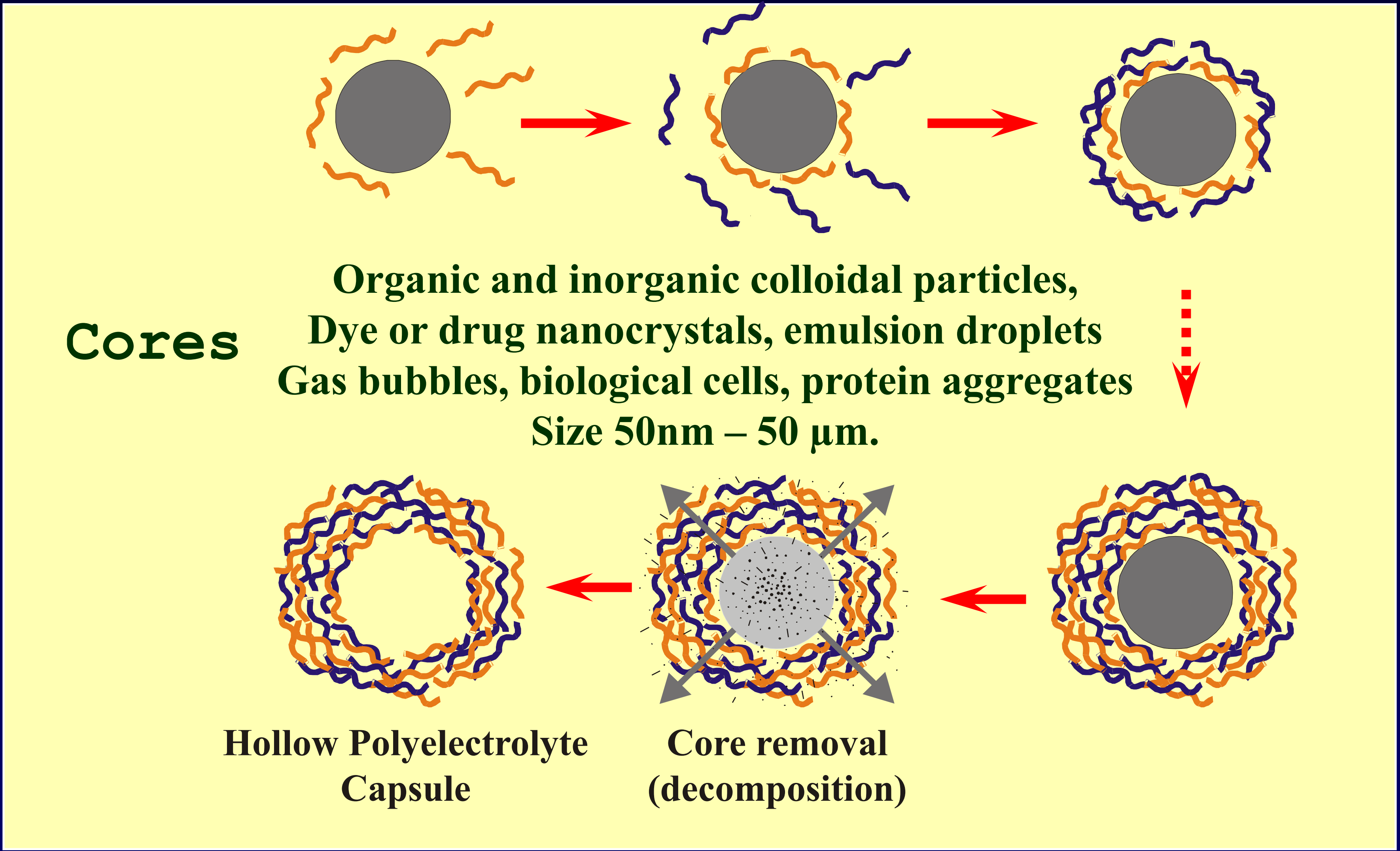
School of Engineerng and Materials Science

Queen Mary University of London

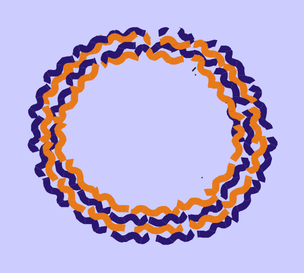
Polyelectrolyte Layer-by-layer assembly



Hollow Capsule Fabrication



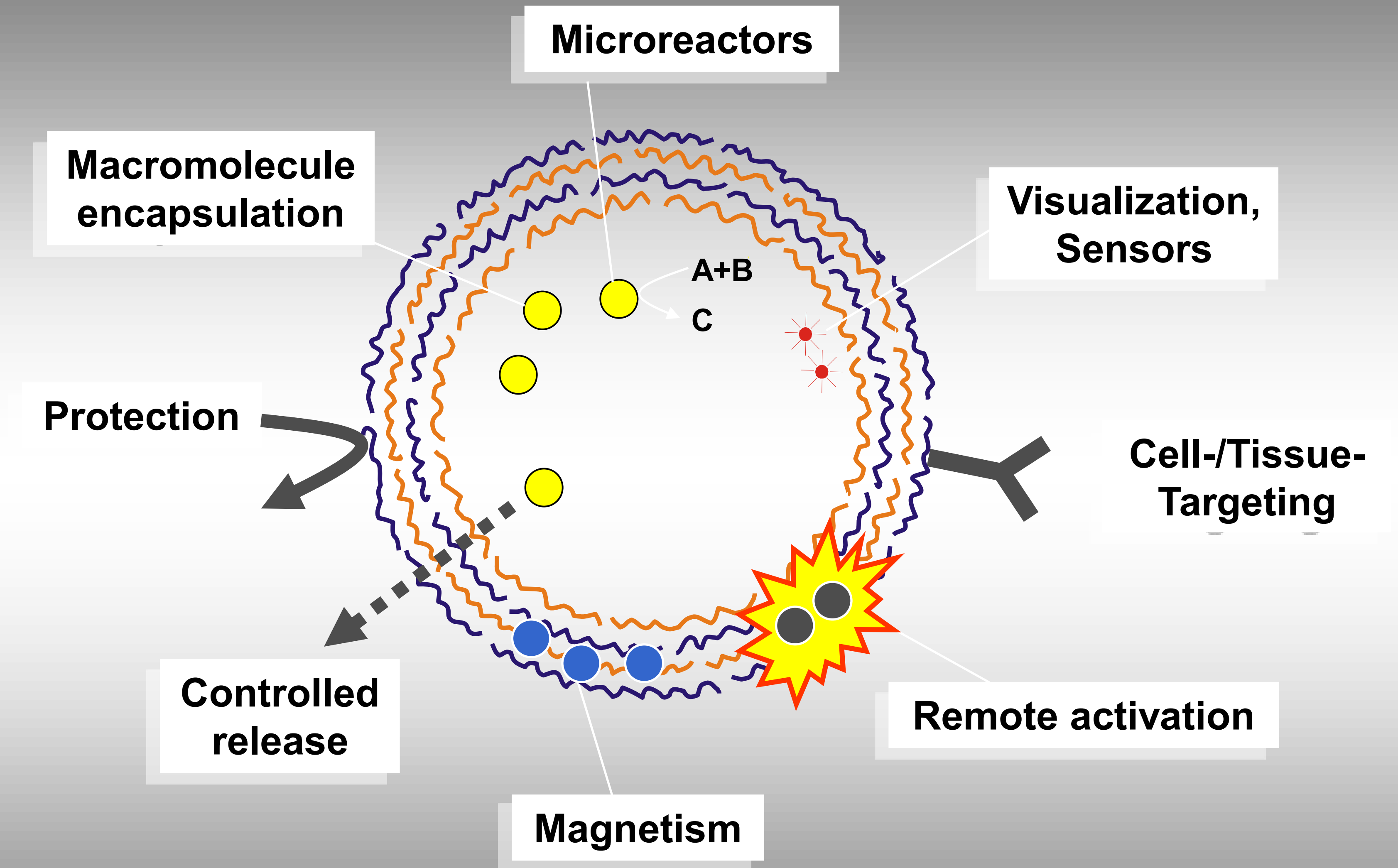
Layer-by-layer Capsules



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

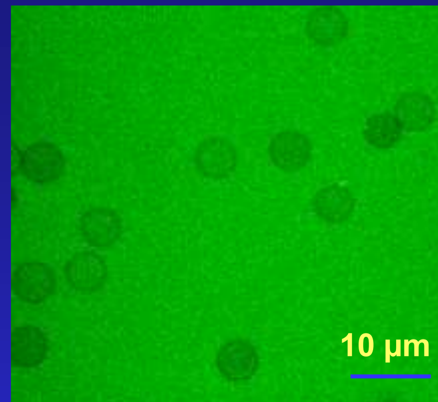
- **Encapsulation → micro- and nanoreactor engineering**
- **Controlling permeability for wide class of molecules**

Multifunctionality to Microcapsules (50nm – 50 mkm)

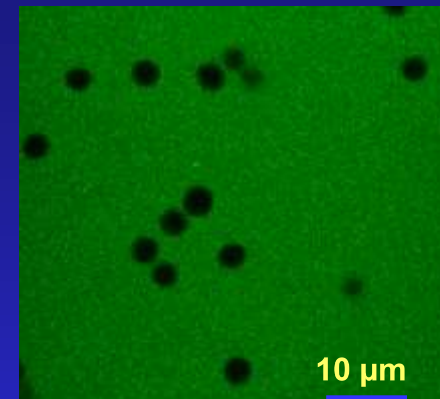


Encapsulation and release

Confocal fluorescence Laser Scanning Microscopy

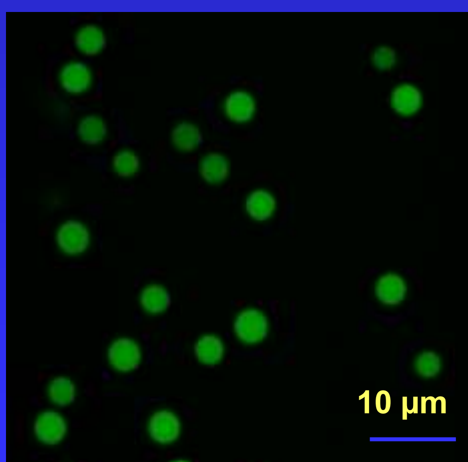


ΔT, pH, light

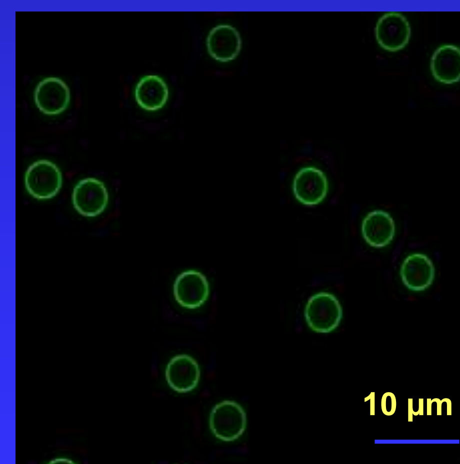


Permeable
„Open gate“

Impermeable
„Closed gate“



pH, light, salt



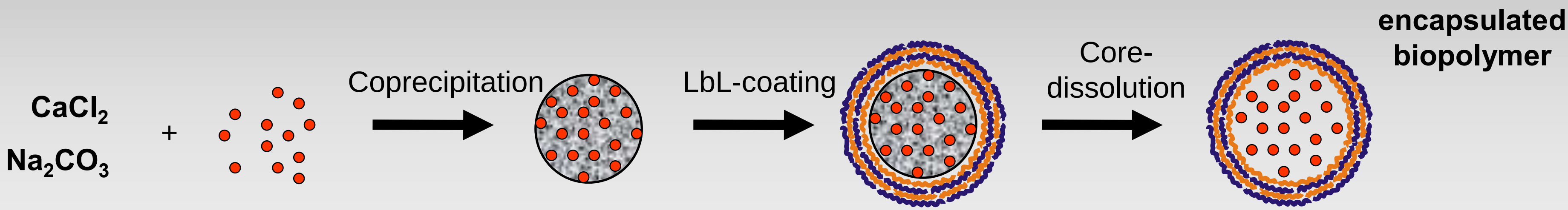
Encapsulated

Release

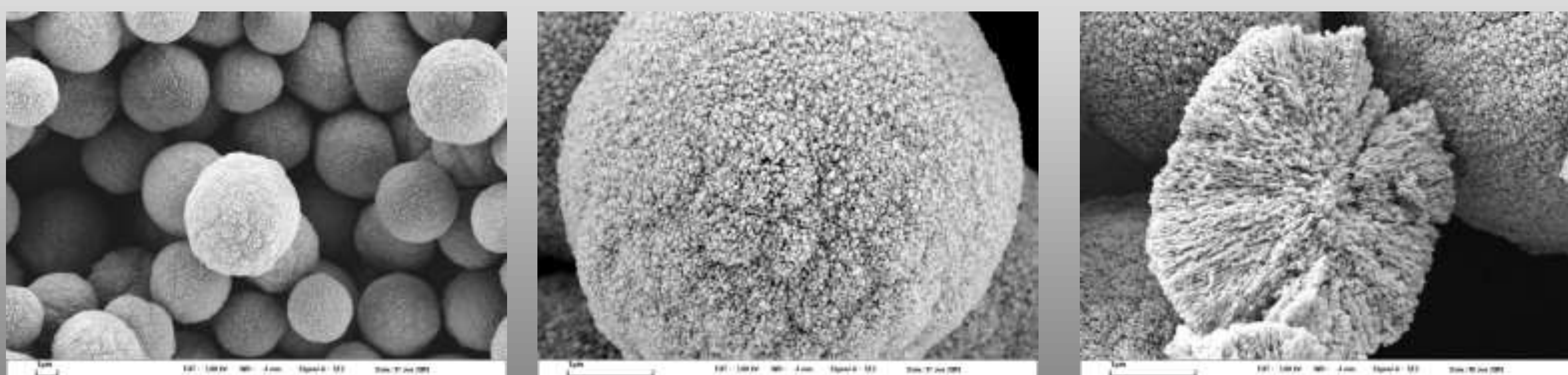
Köhler, K., Sukhorukov, G. B. ***Advanced Functional Materials*****, 2007**

Encapsulation Using Porous Carbonate-Templates

Encapsulation of macromolecules by incorporaton into calcium carbonate microparticles ("coprecipitation method")

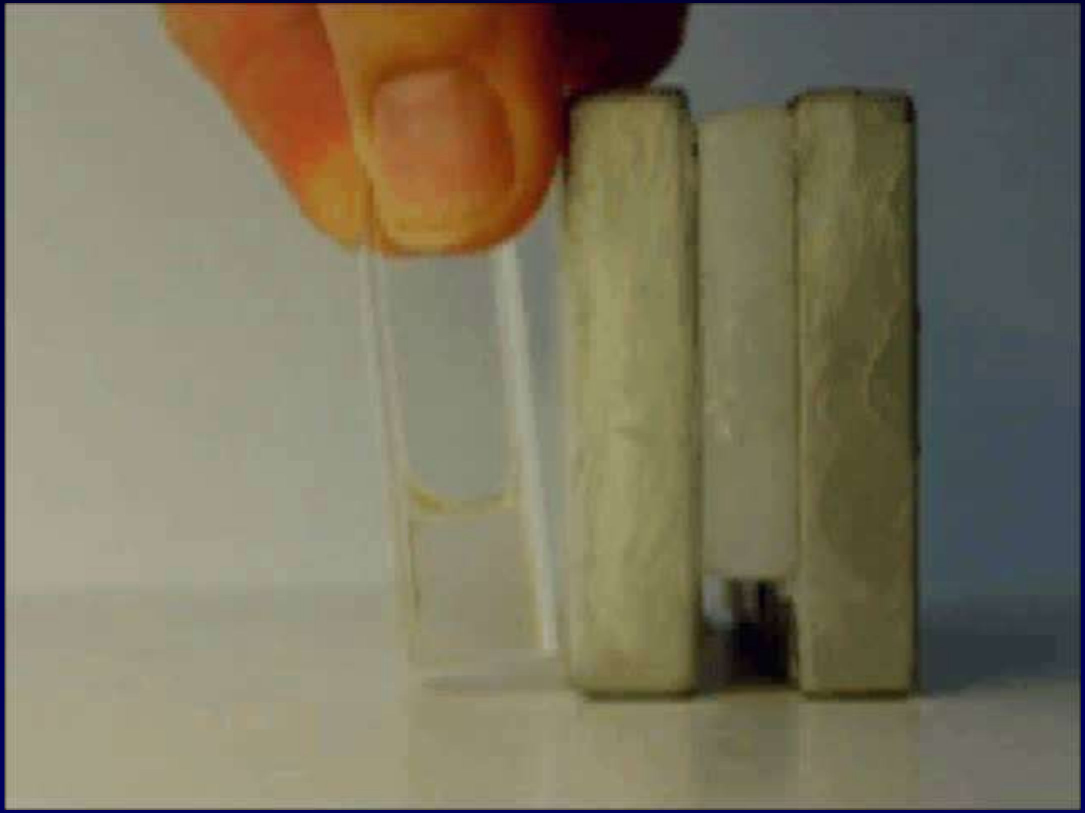


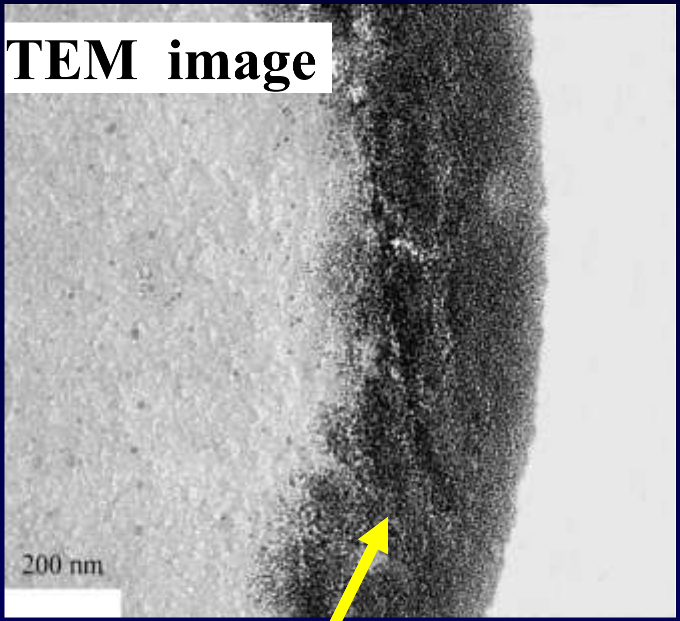
Porous calcium carbonate microparticles (∅ 500nm - 10µm)



Petrov, A.I., Volodkin, D.V., Sukhorukov, G.B. (2005): *Biotechnol. Prog.,* 21(3), 918

Magnetite nanoparticles assembled in capsule wall



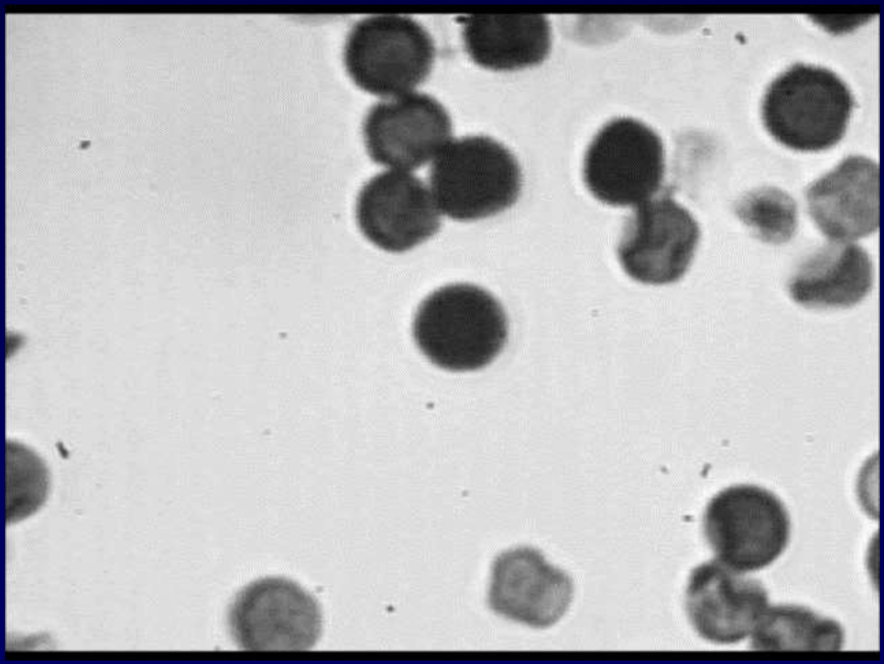


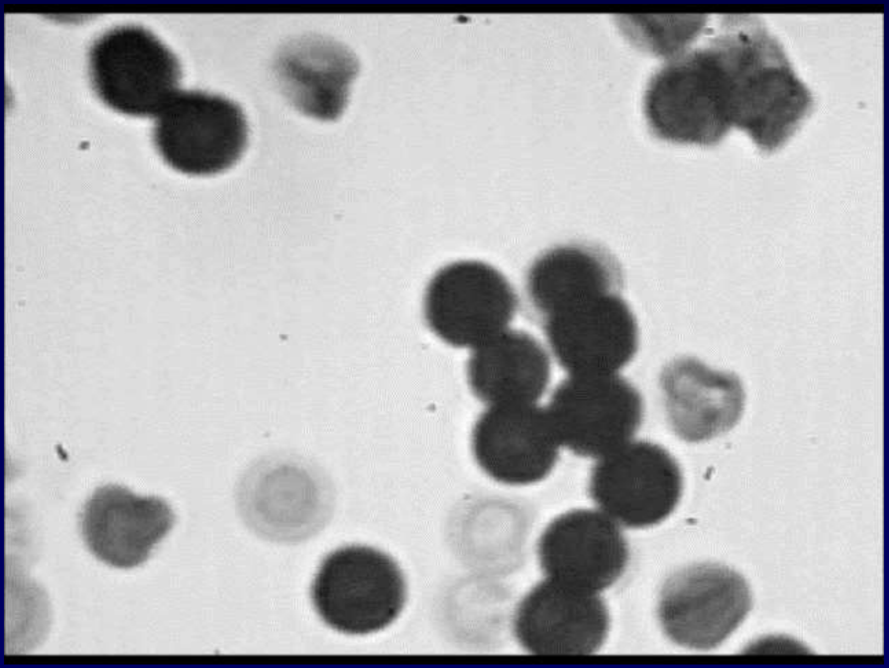
Magnetic NPs in shell

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 Infrared Laser 830nm

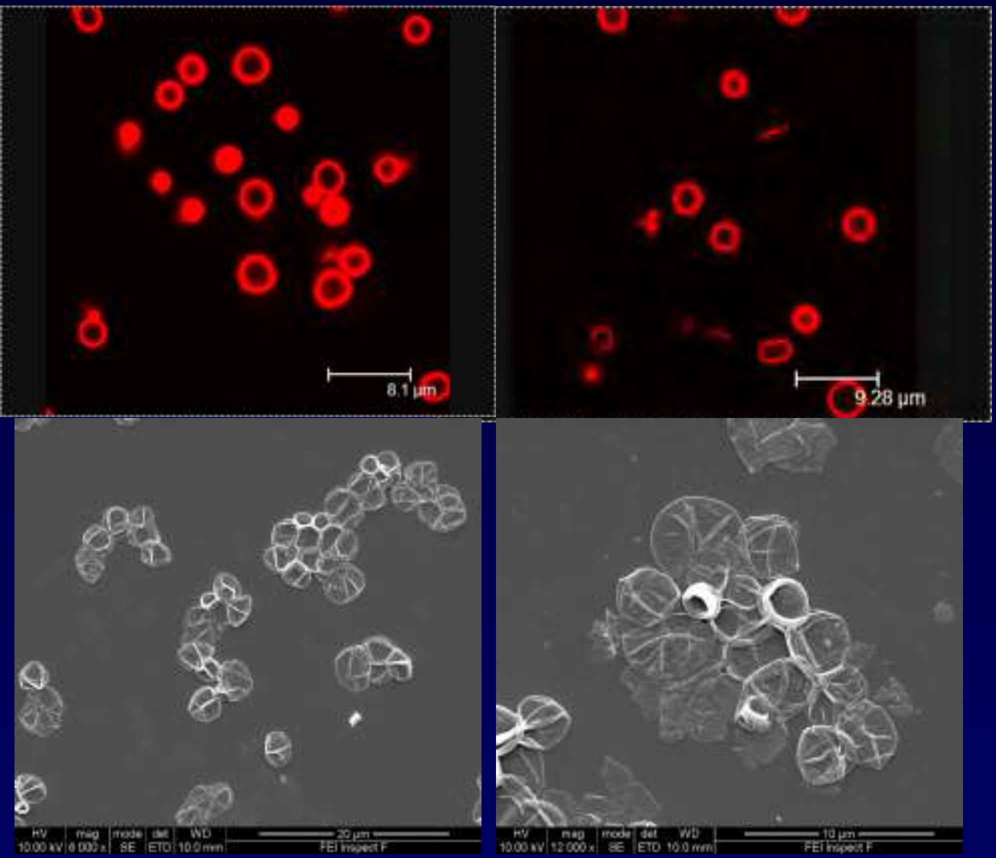




→Optically activated release;
→Infrared window for biomedical application

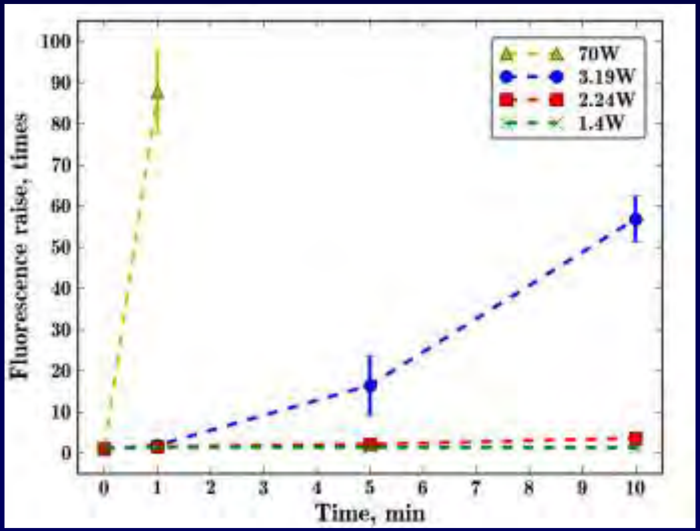
Ultrasound stimulated release – Medical range

before **10 min**



~1MHz, 1 - 3W

Au-NPs in LbL shell,
BSA-TRITC encapsulated

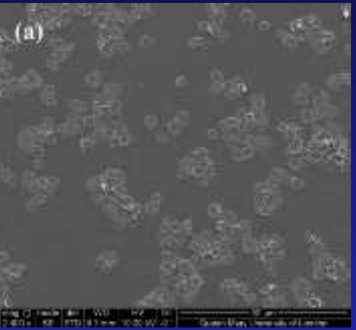


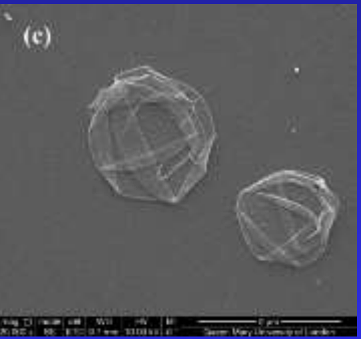
– Induced release without damage of tissues
– Higher depth of operation inside the body

A.Pavlov et al, PCCP, 2011

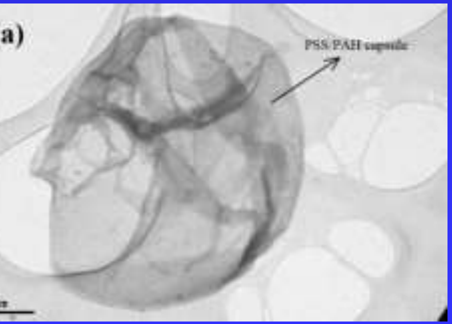
Composite Silica/polyelectrolyte microcapsules

SEM

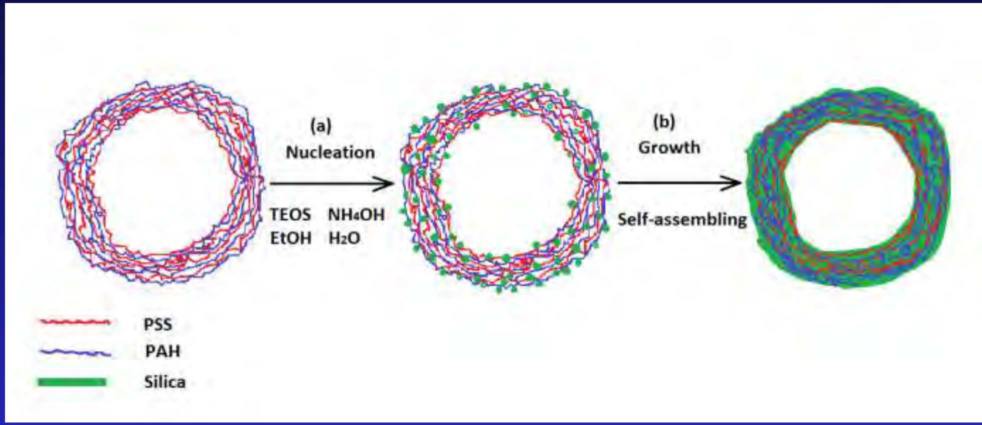




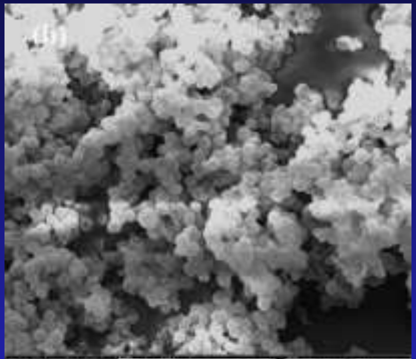
TEM

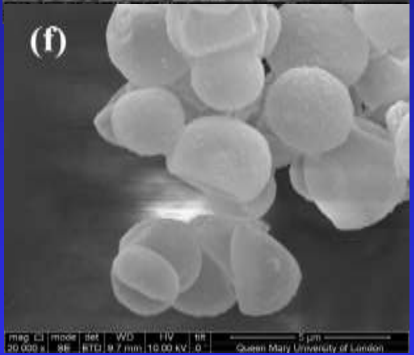


Polyelectrolyte capsule silanisation

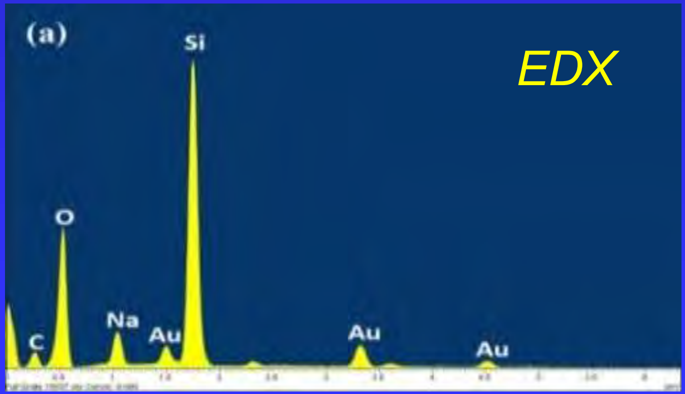


SEM





EDX



TEM

H. Gao, D. Wen and G.B. Sukhorukov, J. Materials Chemistry B, 2015

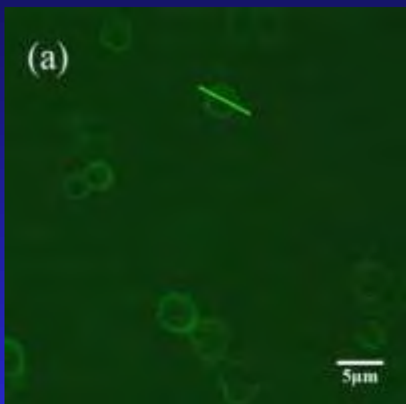
Composite Silica/PE microcapsules

Encapsulation and Ultrasound stimulated Release

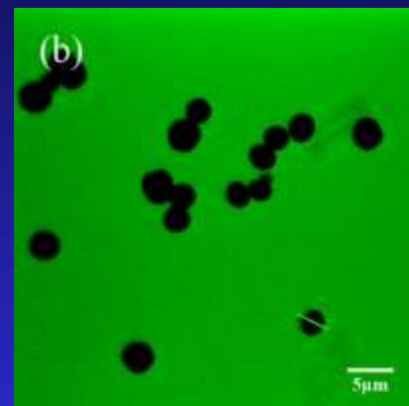
Bare capsules

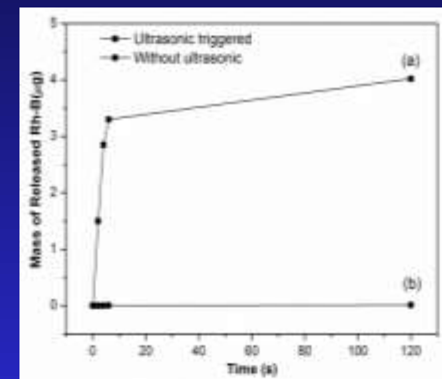
Silica composite capsules

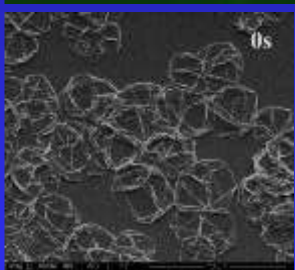
Encapsulated Rhodamine



Fluorescein solution



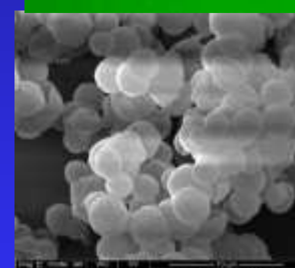




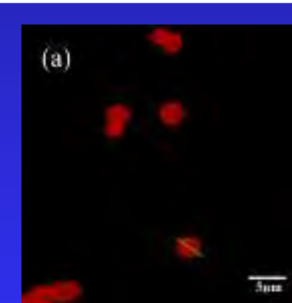
0s

Ultrasound probe

0s

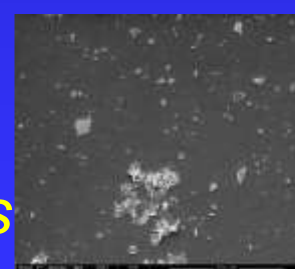


0s

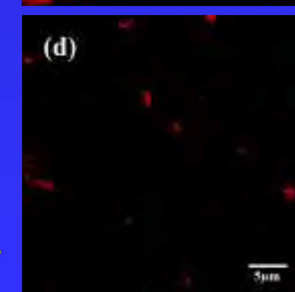


6s

6s

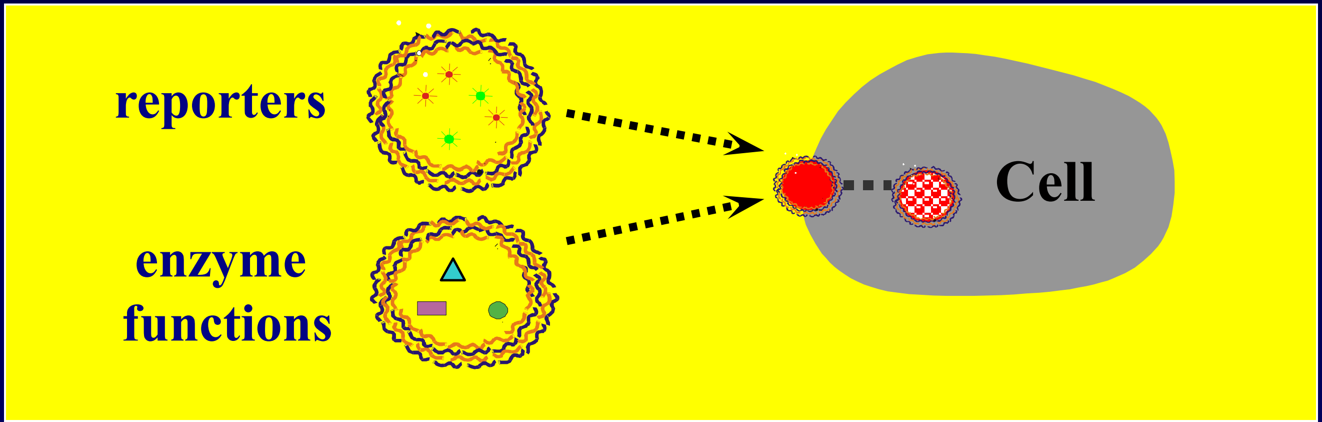


6s



H. Gao, D. Wen and G.B. Sukhorukov, J. Materials Chemistry B, 2015

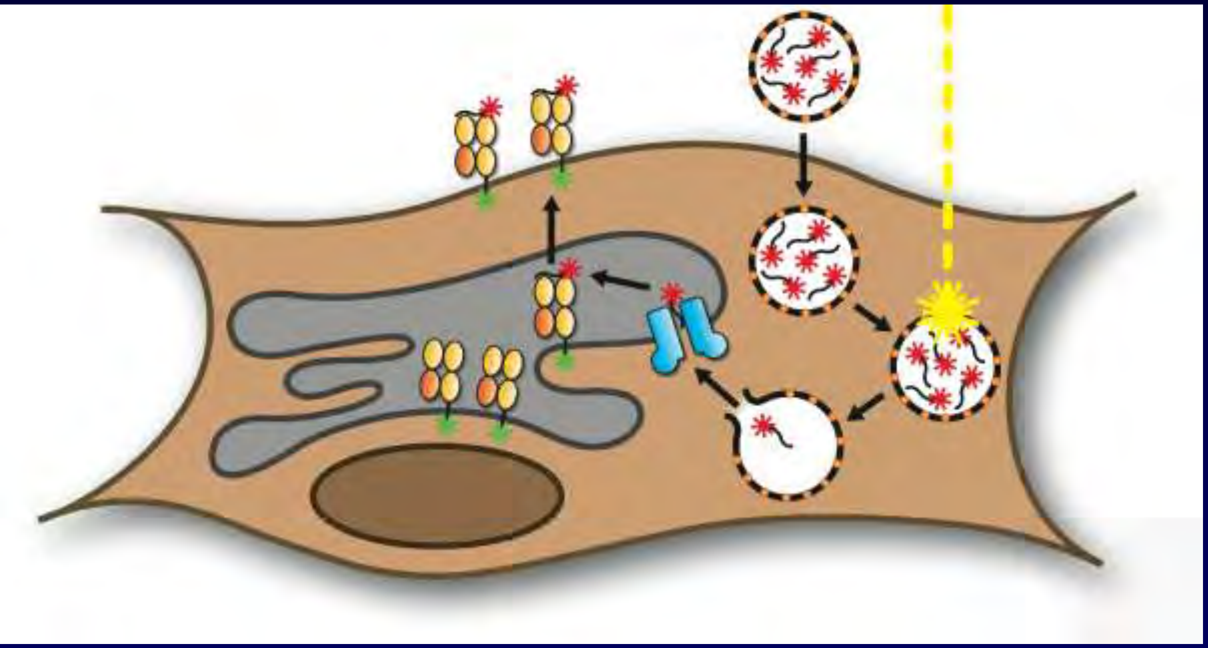
Intracellular Delivery of polyelectrolyte Capsules for On-site Sensing and Manipulation



Capsules in cells - Artificial organelles
Reporting on cell interior

n cooperation with group of Prof. Wolfgang Parak *Small 2005 1(2), 194-200*

Intracellular Release of Antigenic Peptides to Follow their Presentation on MHC Class I Molecules



Insertion of the capsule via electropermeabilization

Opening by IR laser pulse

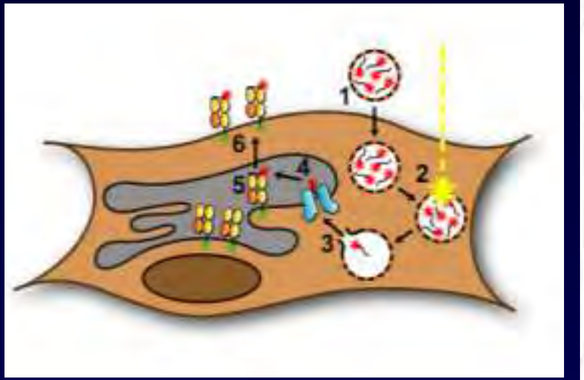
Peptide recognition

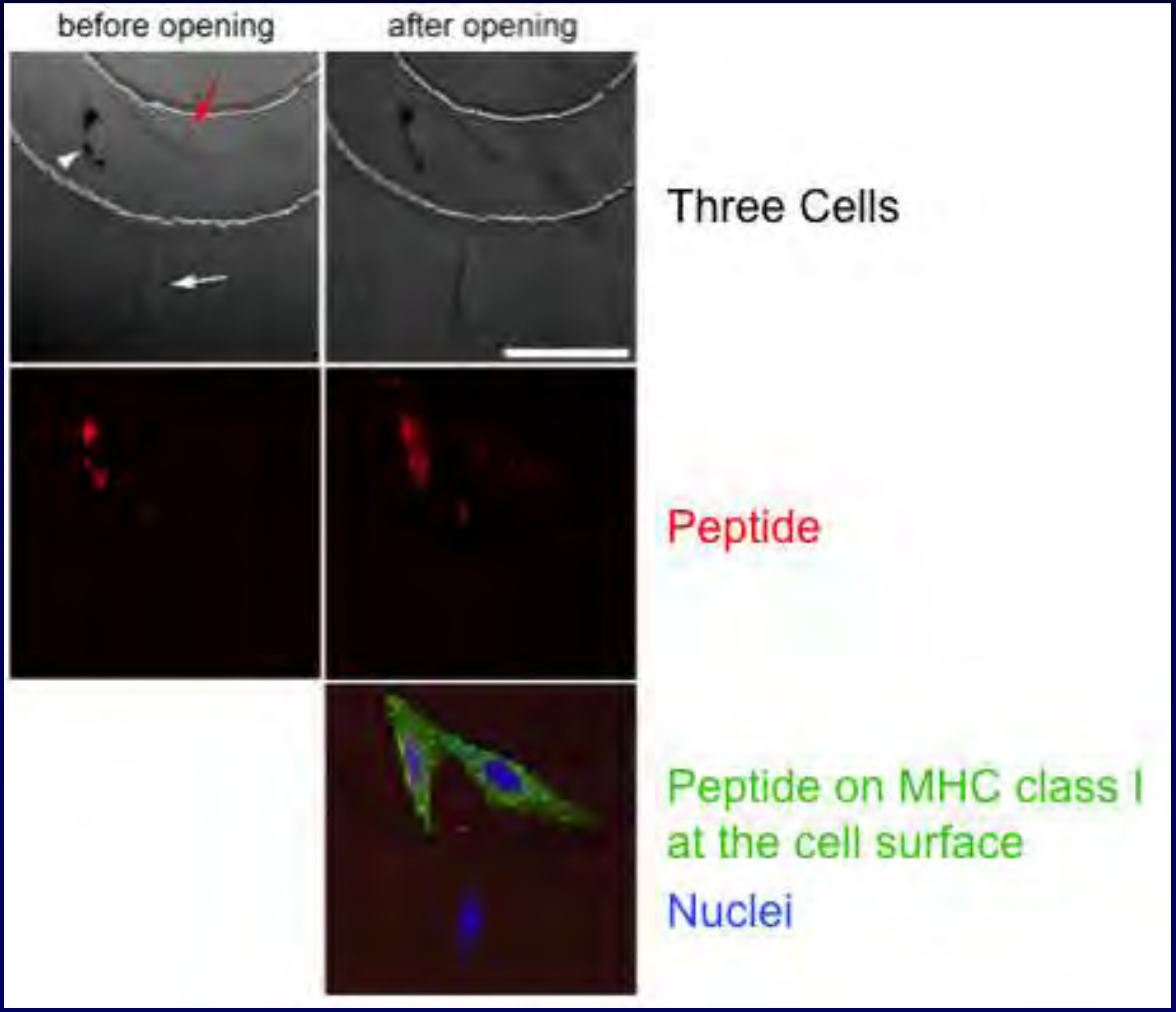
Transport to the cell surface

In cooperation with Prof. Mathias Winterhalter, Prof. Sebastian Springer, Dr. Ragu Palankar - Jacobs University Bremen

Palankar, *et al. Small, 5* (2009), *2168.*

Intracellular Release of Antigenic Peptides to Follow their Presentation on MHC Class I Molecules



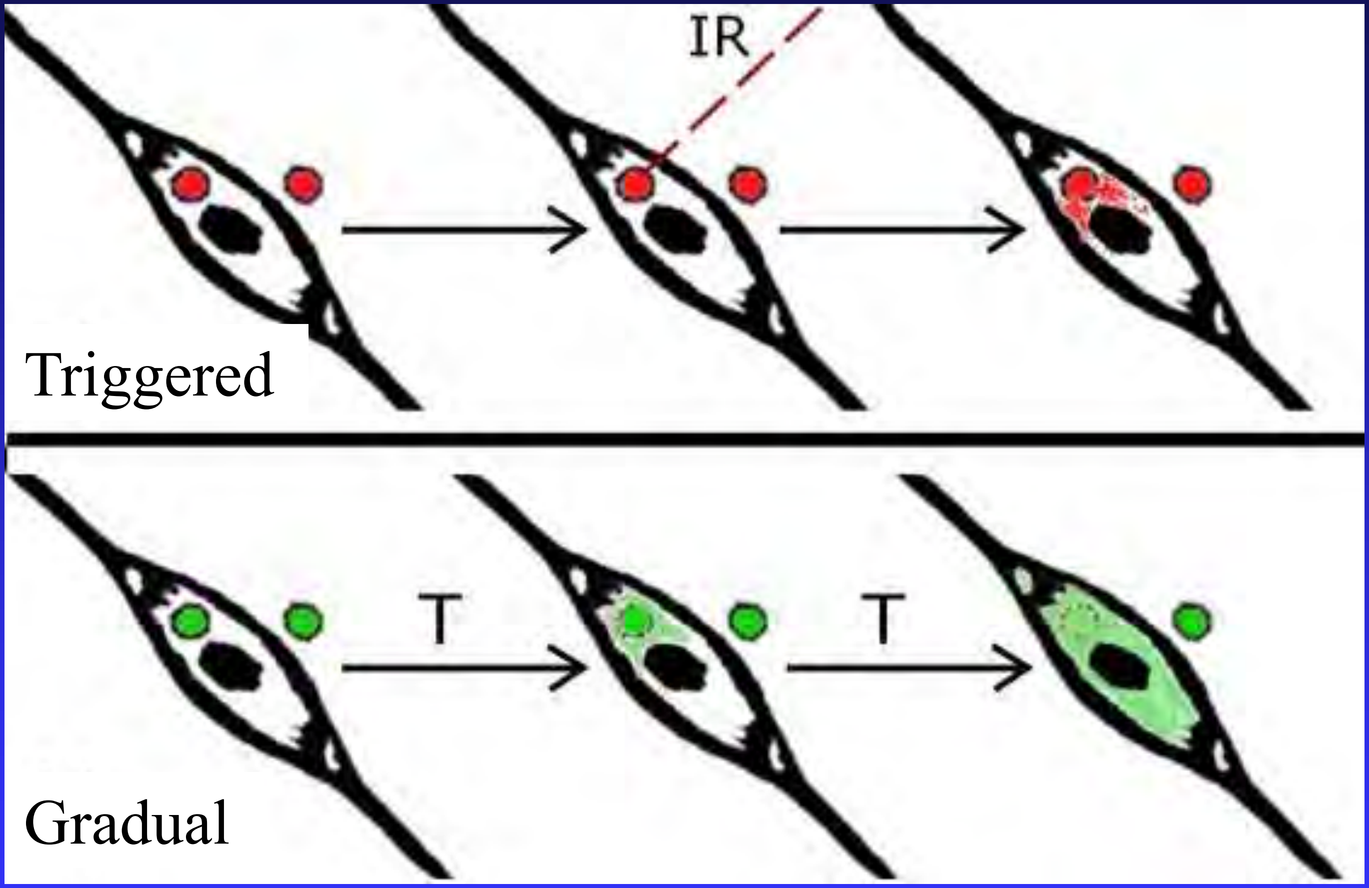


Advantage:
allows separation of uptake vs. trafficking

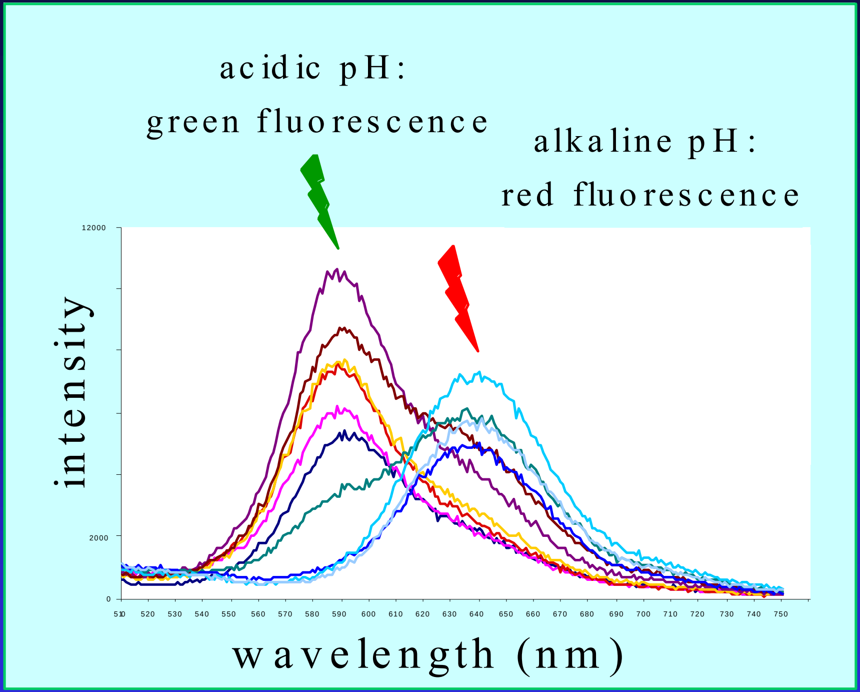
Future:
tool for single cell manipulation

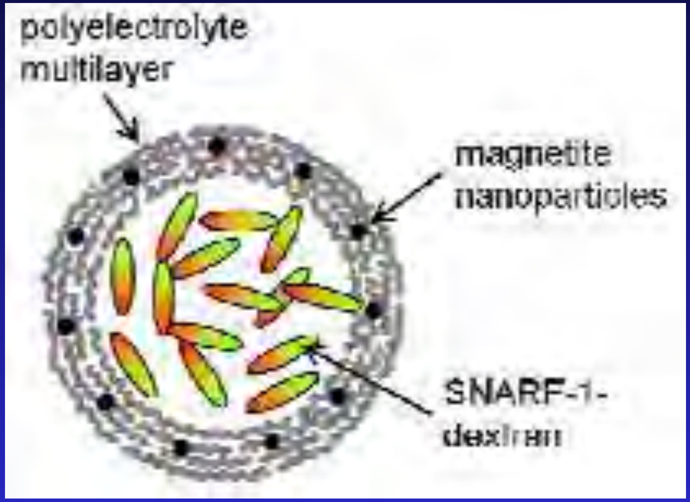
Palankar, *et al. Small, 5* (2009), *2168.*

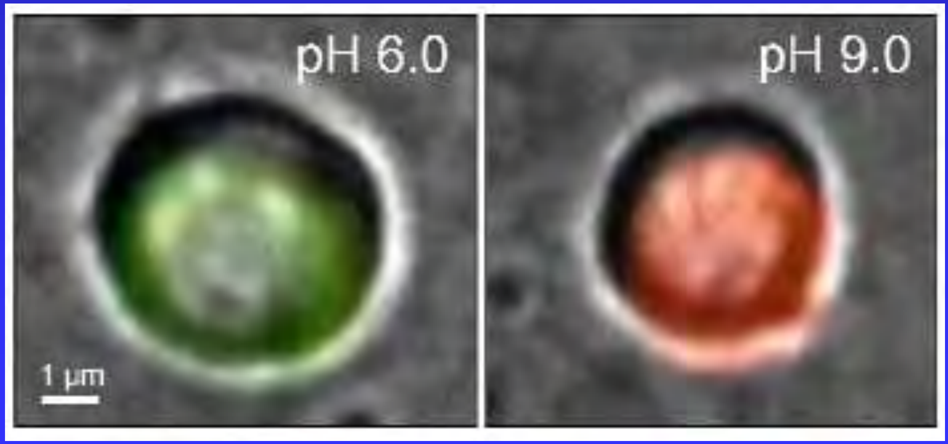
Intracellular Release from polyelectrolyte capsules



Polymer Microcapsules as Mobile Local pH-Sensor





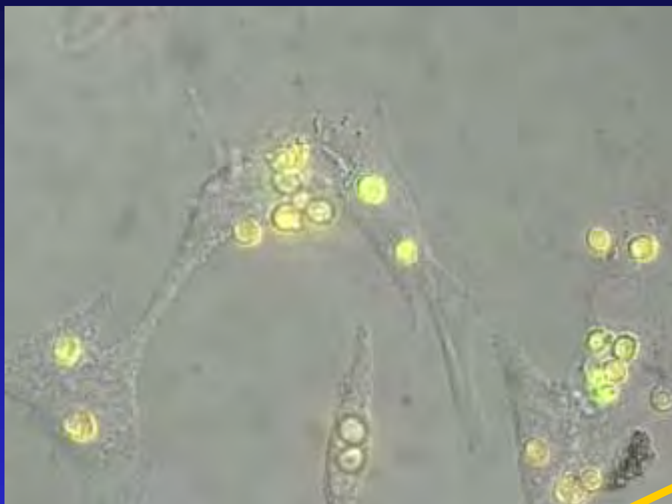


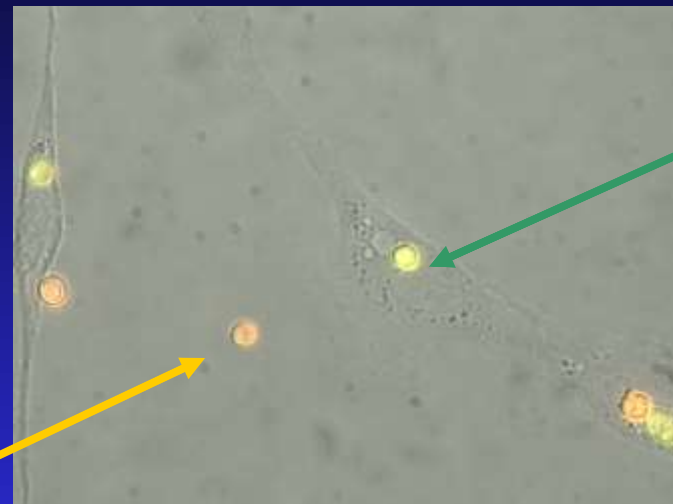
SNARF dye

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

Intracellular Sensors

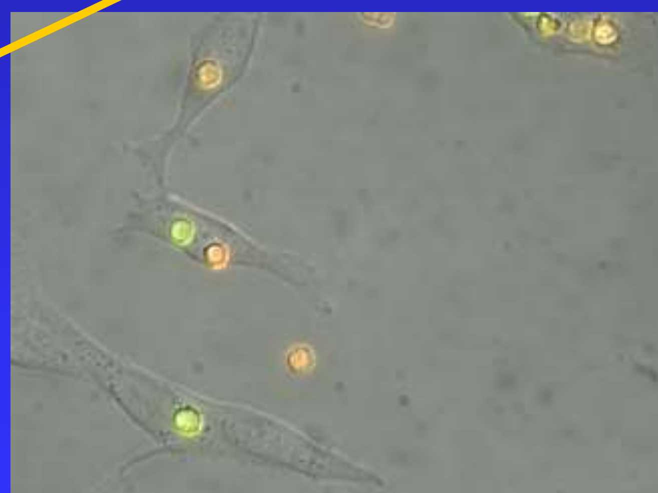
Encapsulated pH – sensor, ***SNARF-based dye***





After Uptake

Before Uptake



Green – low pH

Emission 580nm

Inside cell endosome

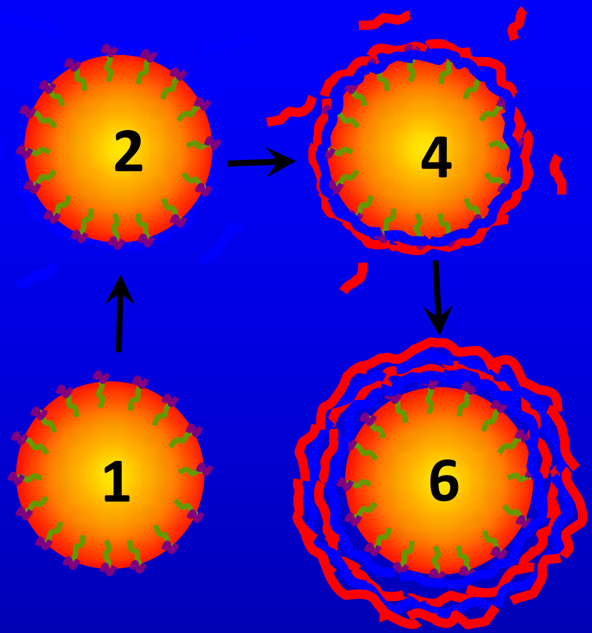
Red – high pH

Emission 650 mn

Outside cell

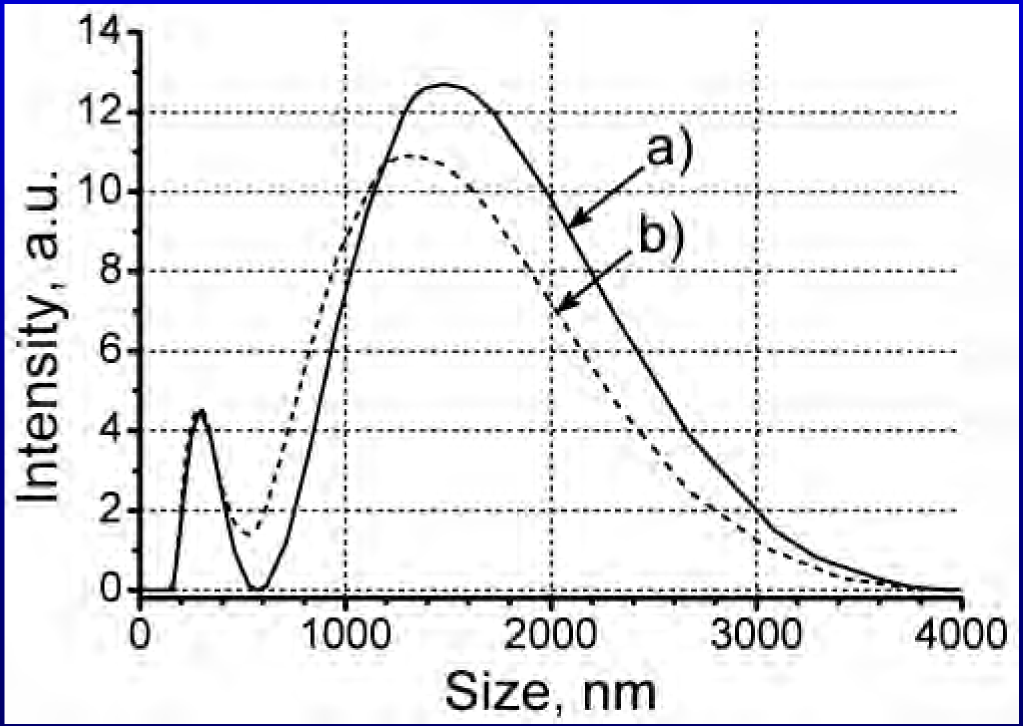
O. Kreft, A.Munoz Javier, G.B.Sukhorukov, W.Parak, J. Mater. Chem., 2007, 42, 4471

Stability and Anti-oxidation protection of Emulsions



Polyelectrolyte LbL shell assembly over droplets of oil-in-water (O/W) emulsion

(a) Particle size distribution of encapsulated linseed-oil-in-water emulsion
(b) After the freeze-drying and resuspending the powder in water

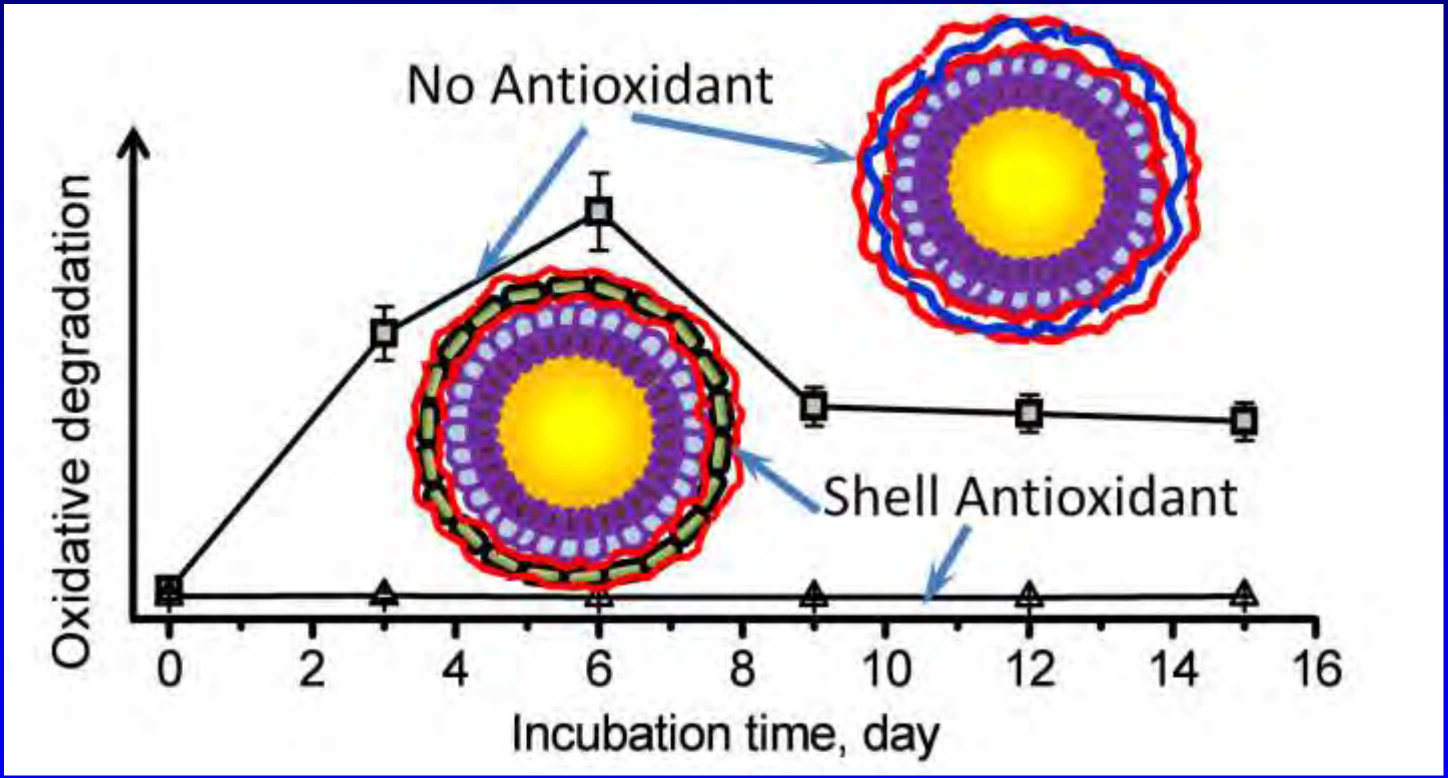


Coated Emulsions can be freeze-dried and re-suspended

Lomova, M.V.; Sukhorukov, G.B.; Antipina, M.N. *ACS Appl. Mater. Interfaces* **DOI:** 10.1021/am100818j

Encapsulation provides protection against the oxidative degradation

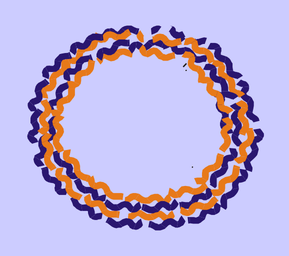
Embedding a layer of Tannic acid as antioxidant into the encapsulating shell prevents lipid peroxidation



Emulsion covered by the polyelectrolyte multilayer shell comprising a single layer of antioxidant (tannic acid) is stable towards oxidation.

Lomova, M.V.; Sukhorukov, G.B.; Antipina, M.N. *ACS Appl. Mater. Interfaces, 2010*

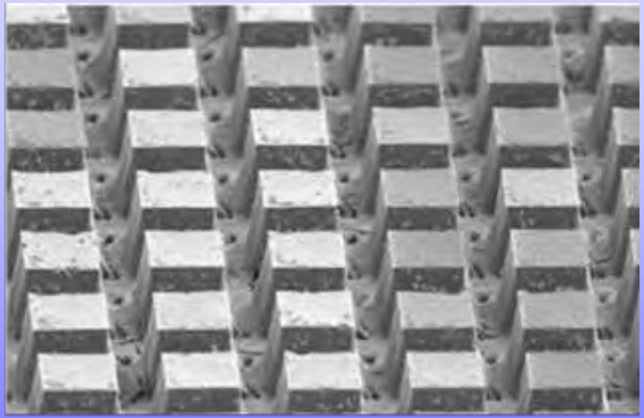
Research strategies



- <u>Design of Nano-engineered shell</u> on colloidal particles/capsules inc. Cells, <u>Emulsion, micro- and nanocrystals, bubbles</u>
  Tuning release, delivery systems into cells and tissues,

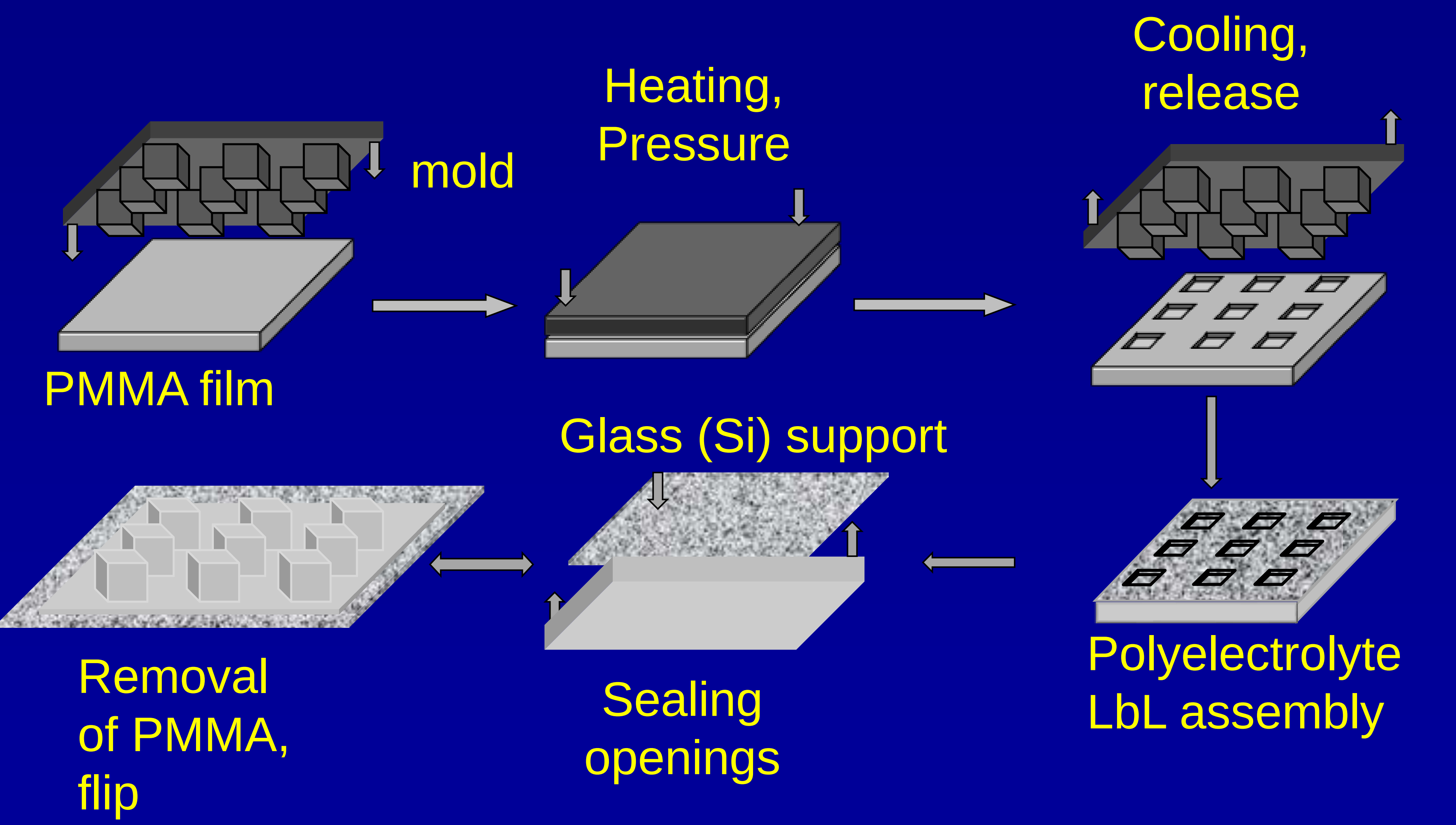
- Stimuli-responsive capsules <u>Remote</u> (IR-, US, MW) activated release

- Diagnostics/Sensing using encapsulated material, Cell residing reporters

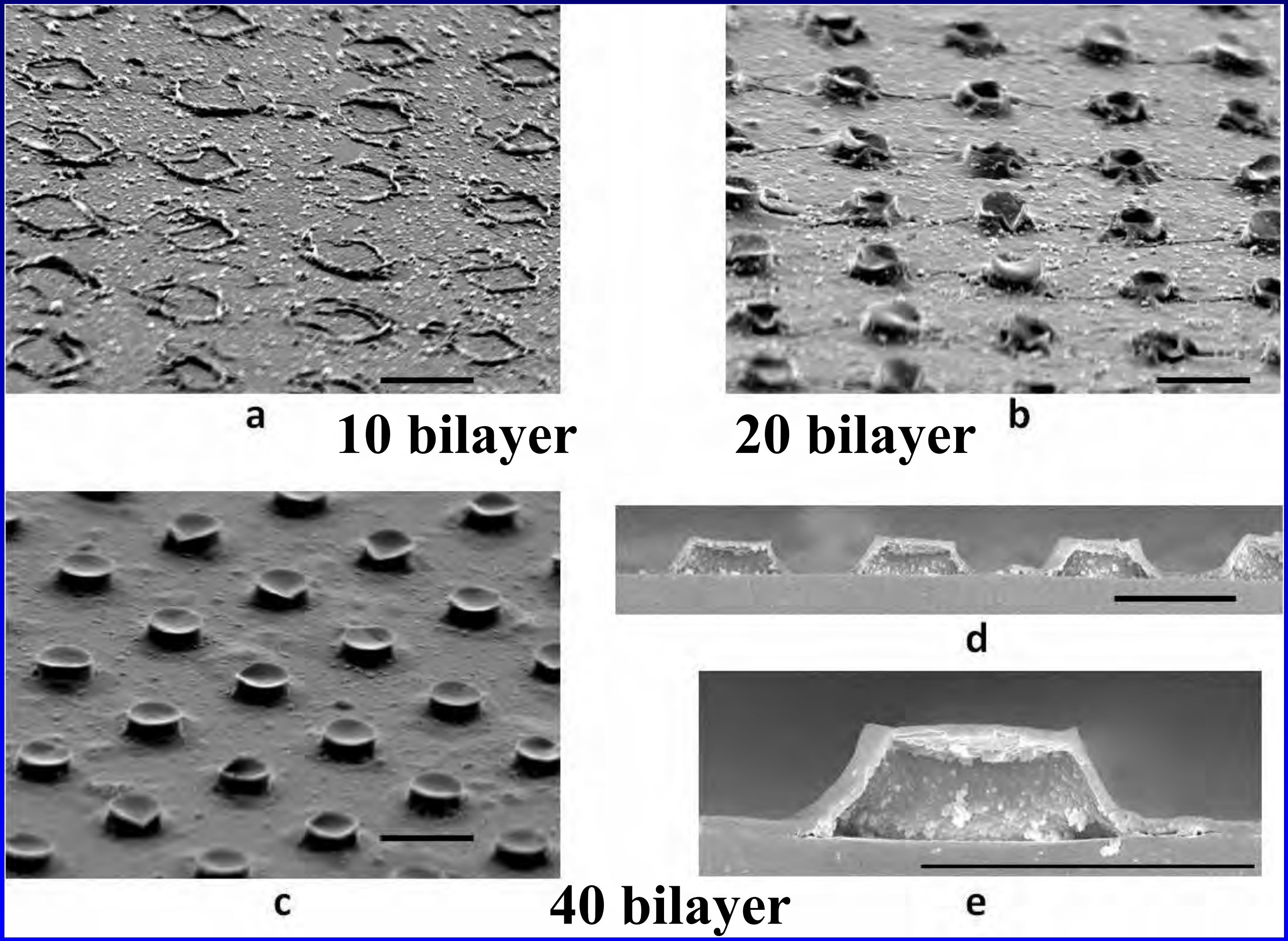


- Fabrication Microchambers films with triggered release/local sensing

Fabrication Polyelectrolyte Multilayer Chambers Using Imprinted Templates

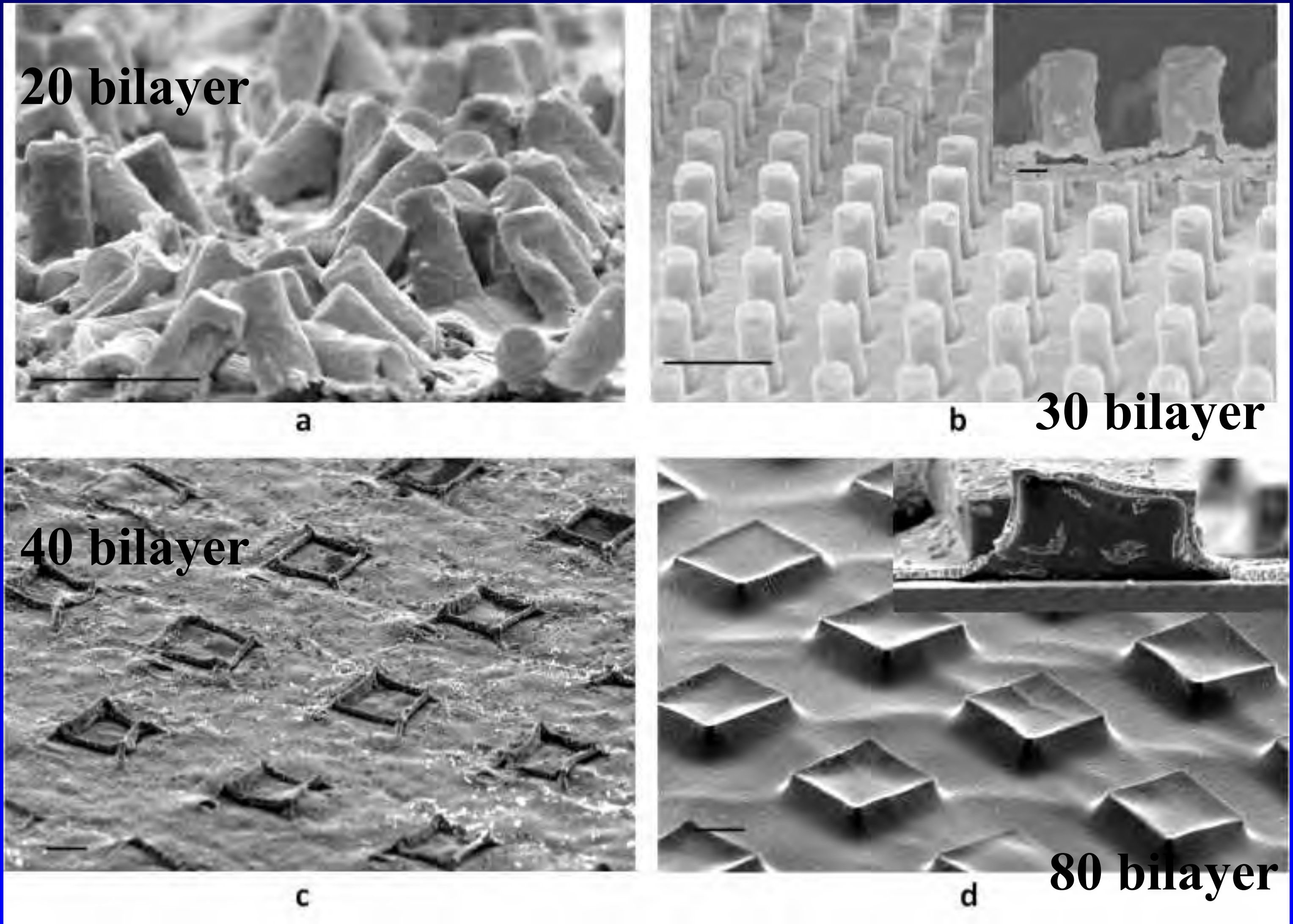


Free-Standing Microchambers at different film thickness



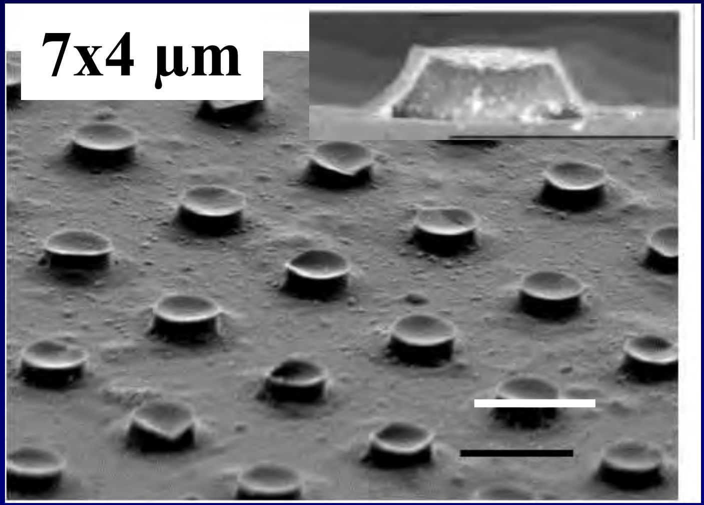
M. Kiryukhin et all, Soft Matter, 2011

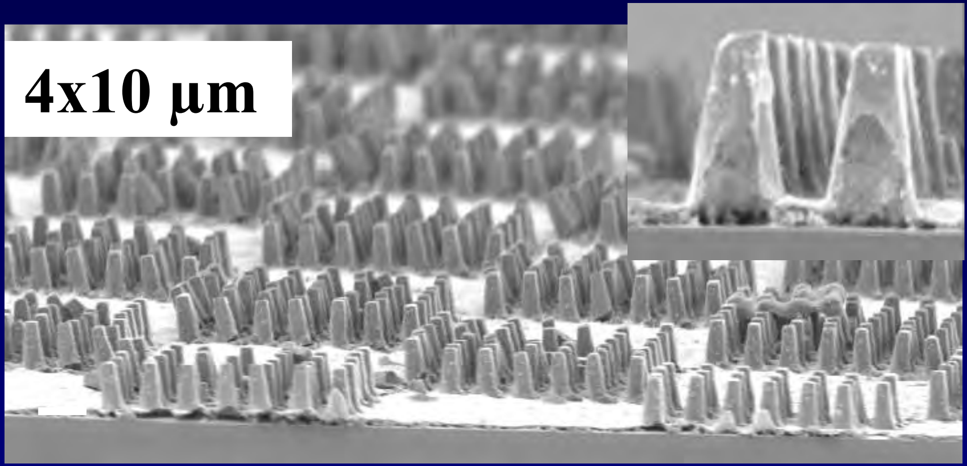
Free-Standing Microchambers of various film thickness

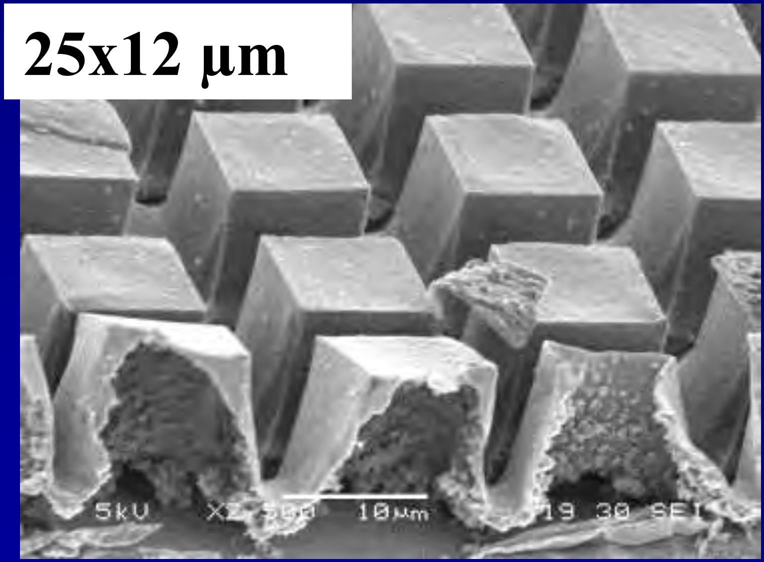


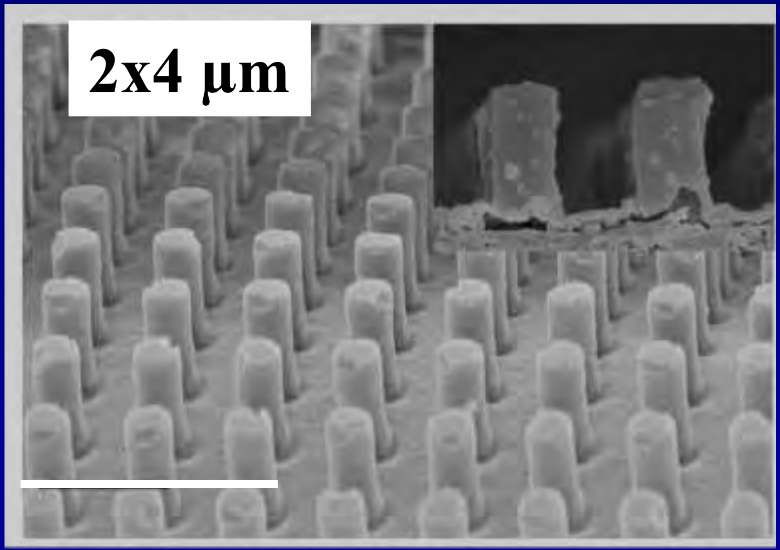
Maxim Kiryukhin et al. Soft Matter, 2011

Microchambers, variety of sizes and shapes
Constant thickness of 40 bi-layers (PAH-PSS)



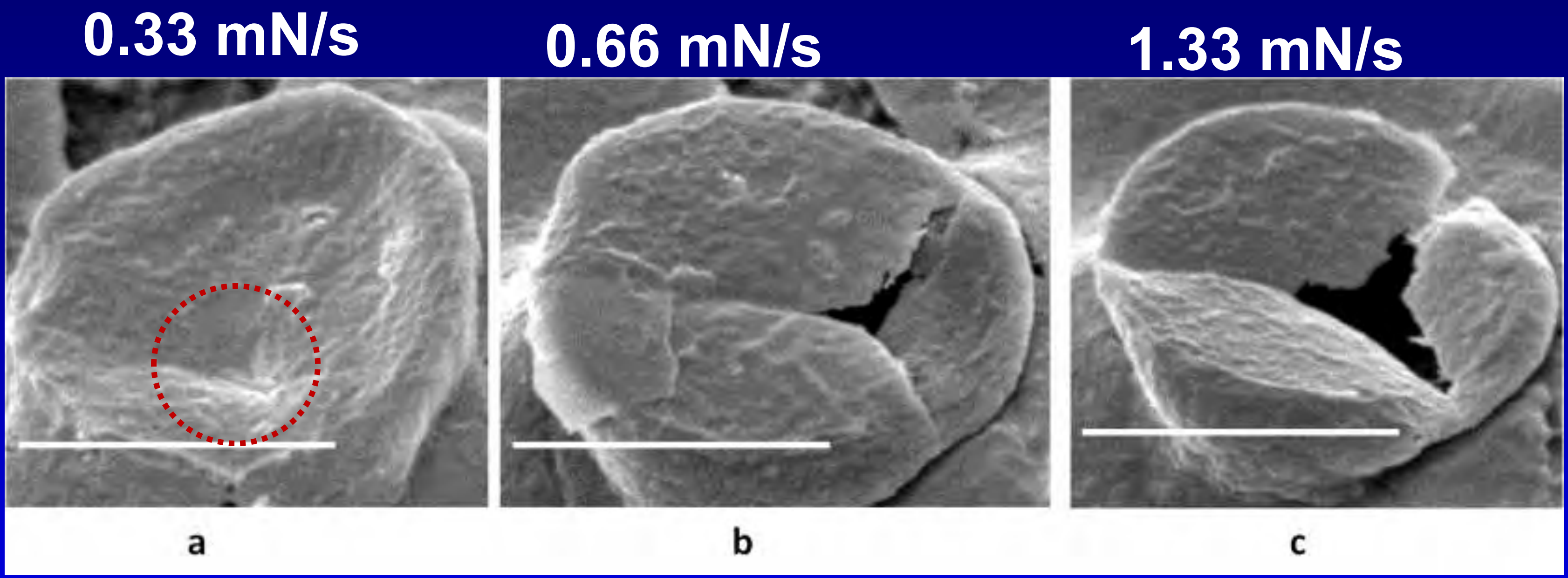






All scale bars: 10 microns

Nano-indentation and “Cap” rupture force



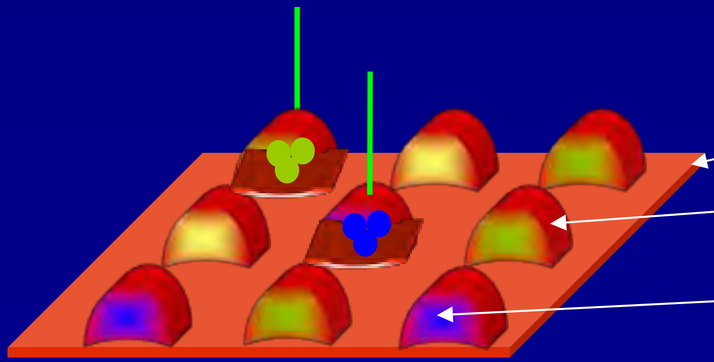
Microchamber made of 40 PSS/PAH bilayers – about 320nm thickness

Piercing the microchambers

Stress-deformation curves for high loading speeds

Maxim Kiryukhin et al. Soft Matter, 2011

Site-specific release-on-demand

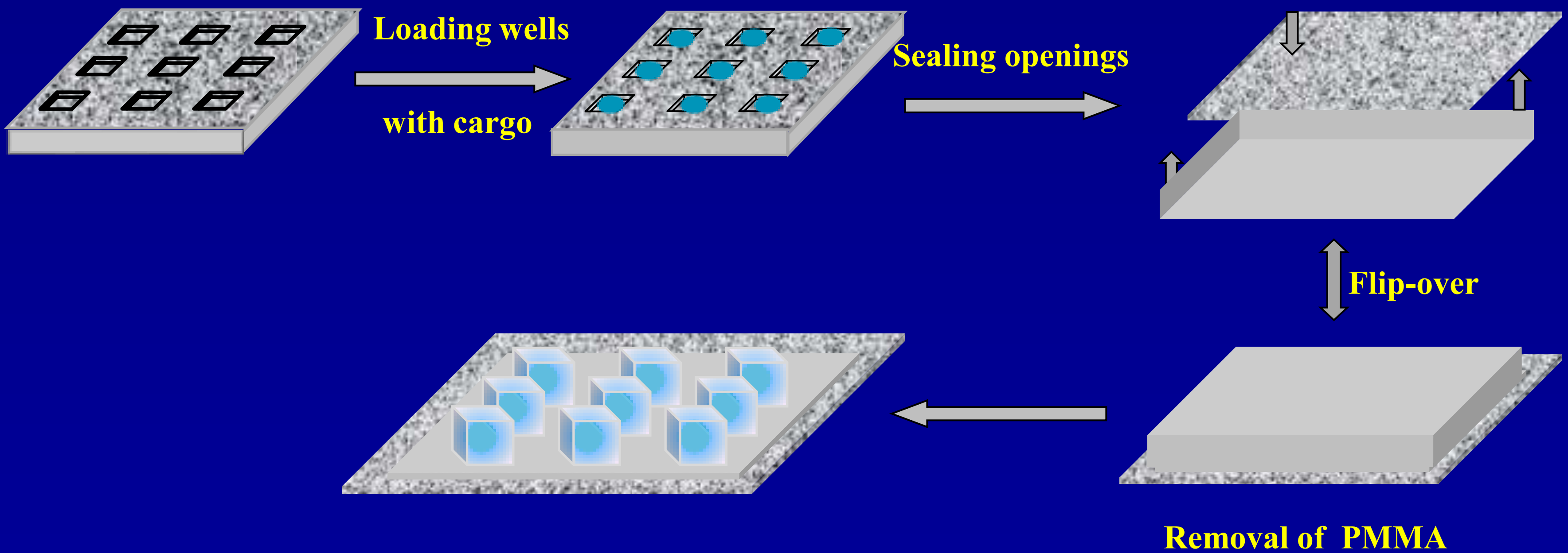


Polymer film with array of

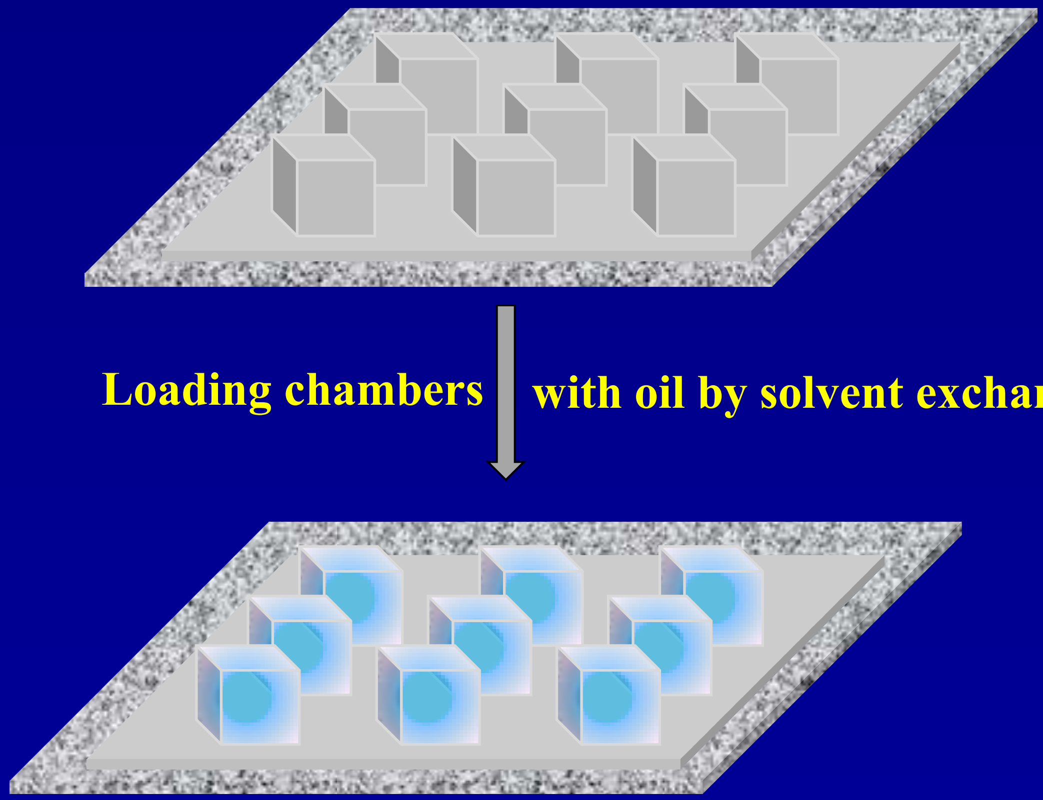
microchambers loaded with

active cargo

Loading the chambers with cargo



Loading the chambers with cargo

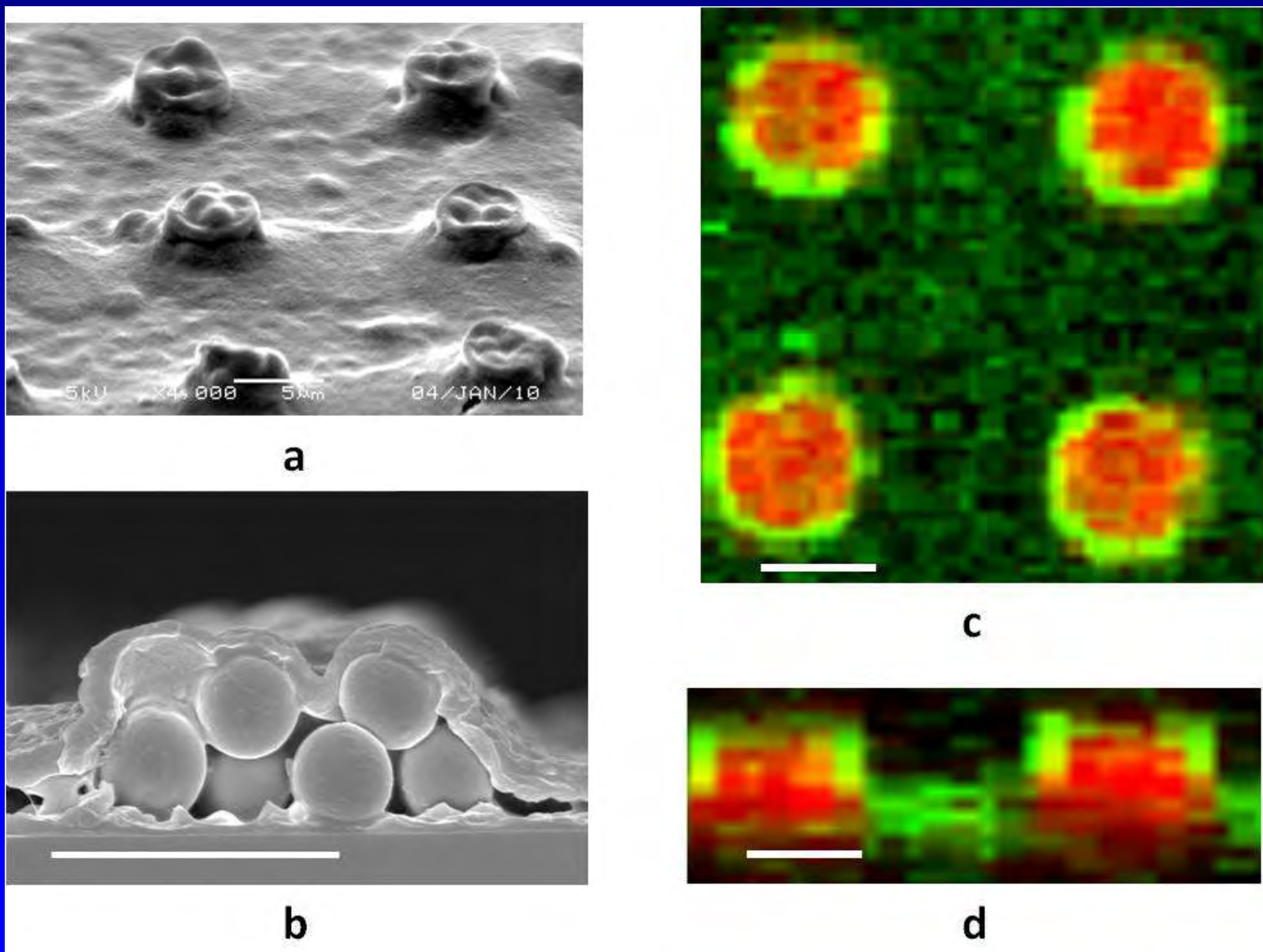


Loading chambers with oil by solvent exchange

Sealed and filled Microchamber arrays

Chamber filled with 1.2mkm particles

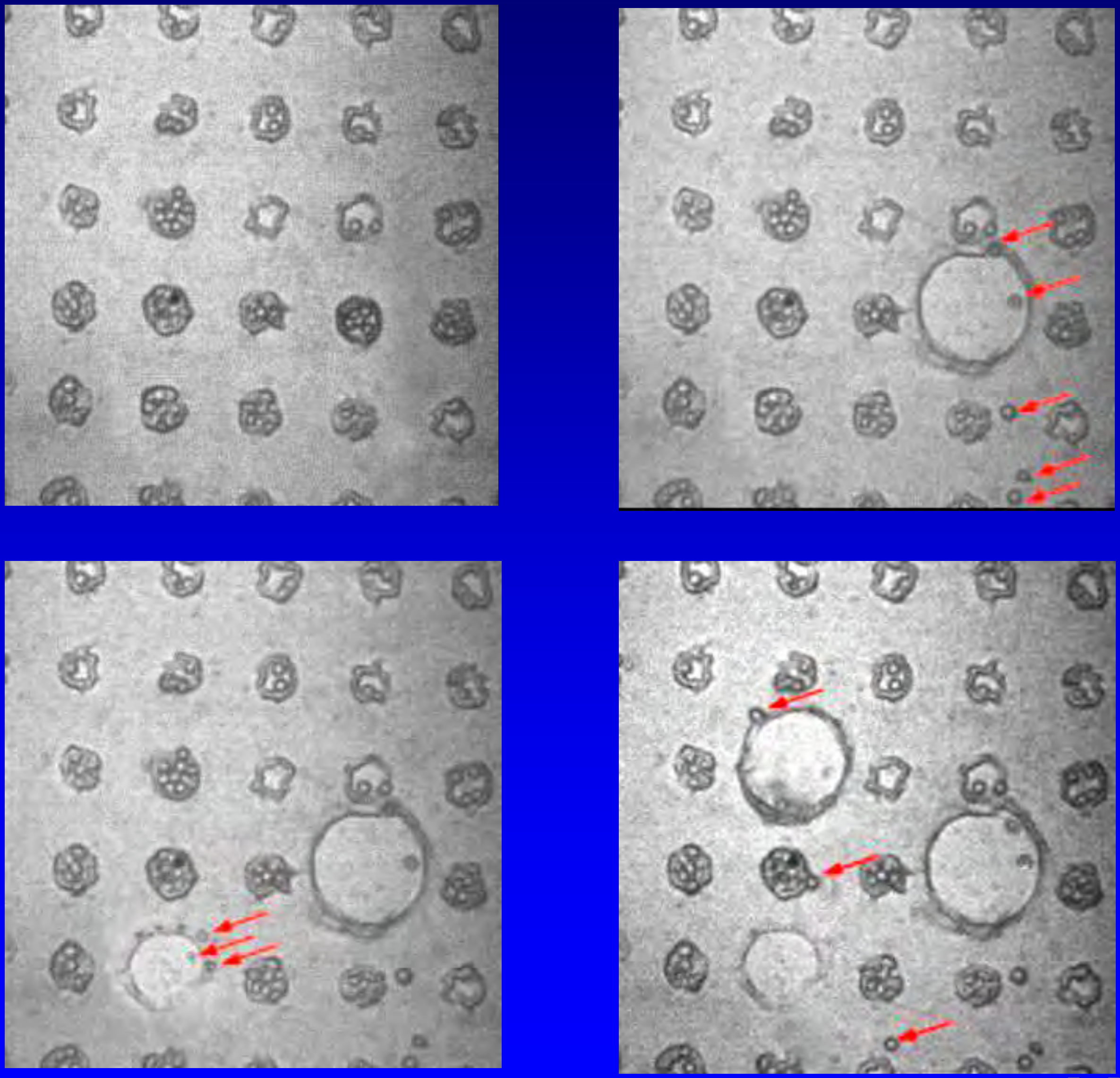
Chamber filled with Sunflower oil



Raman Microscopy
Chemical Imaging
Red – oil
Green - polymers

Laser-induced “kicking-off” of microparticles

Gold nanoparticles in multilayers



Maxim Kiryukhin

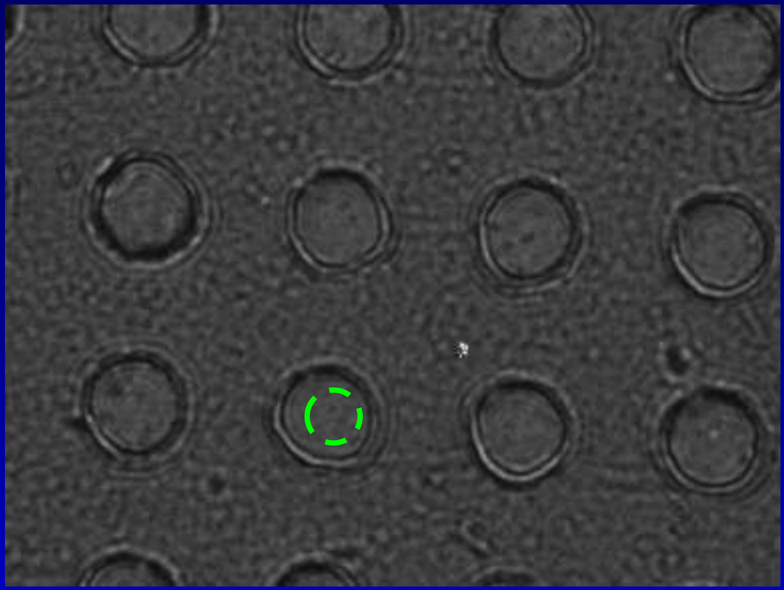
Laser opening of chambers filled with sun-flower oil, Fluorescence microscope study.

Laser: pulse, 532 nm,

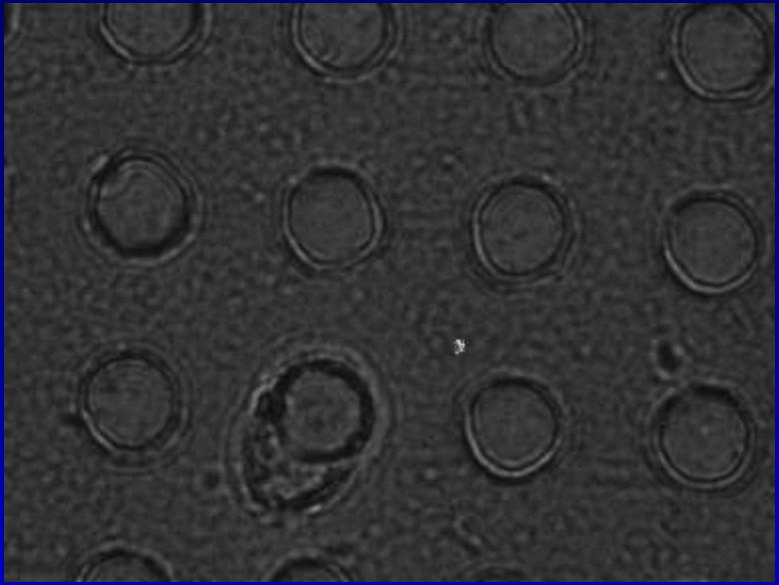
Sunflower oil colored with fluorescent dye.

Maxim Kiryukhin, Sergey Gorelik

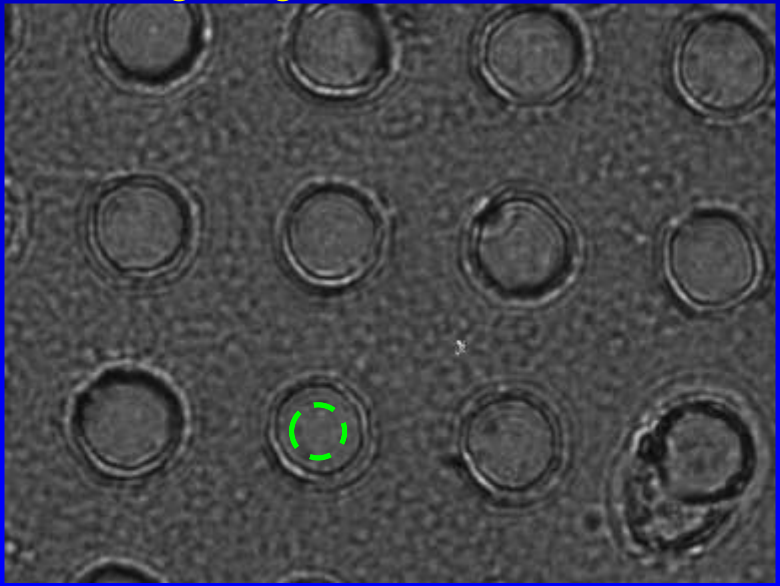
Transmission mode



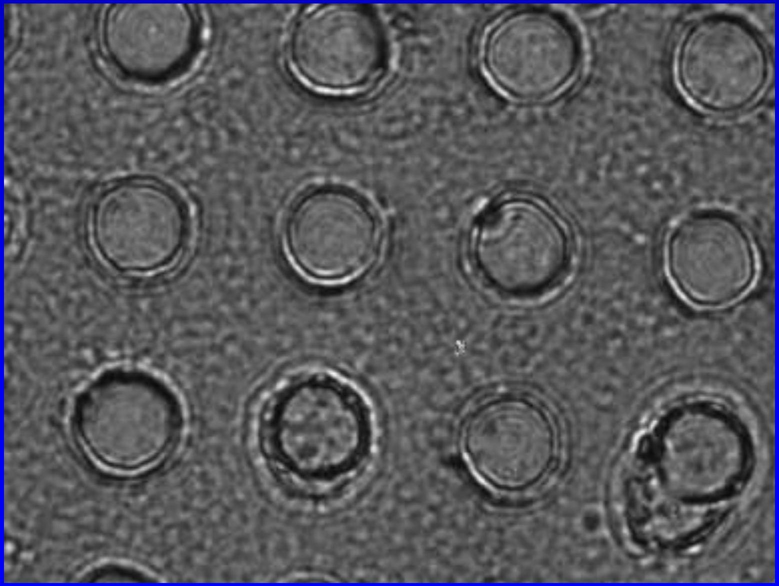
Targeting first chamber



1st chamber burned

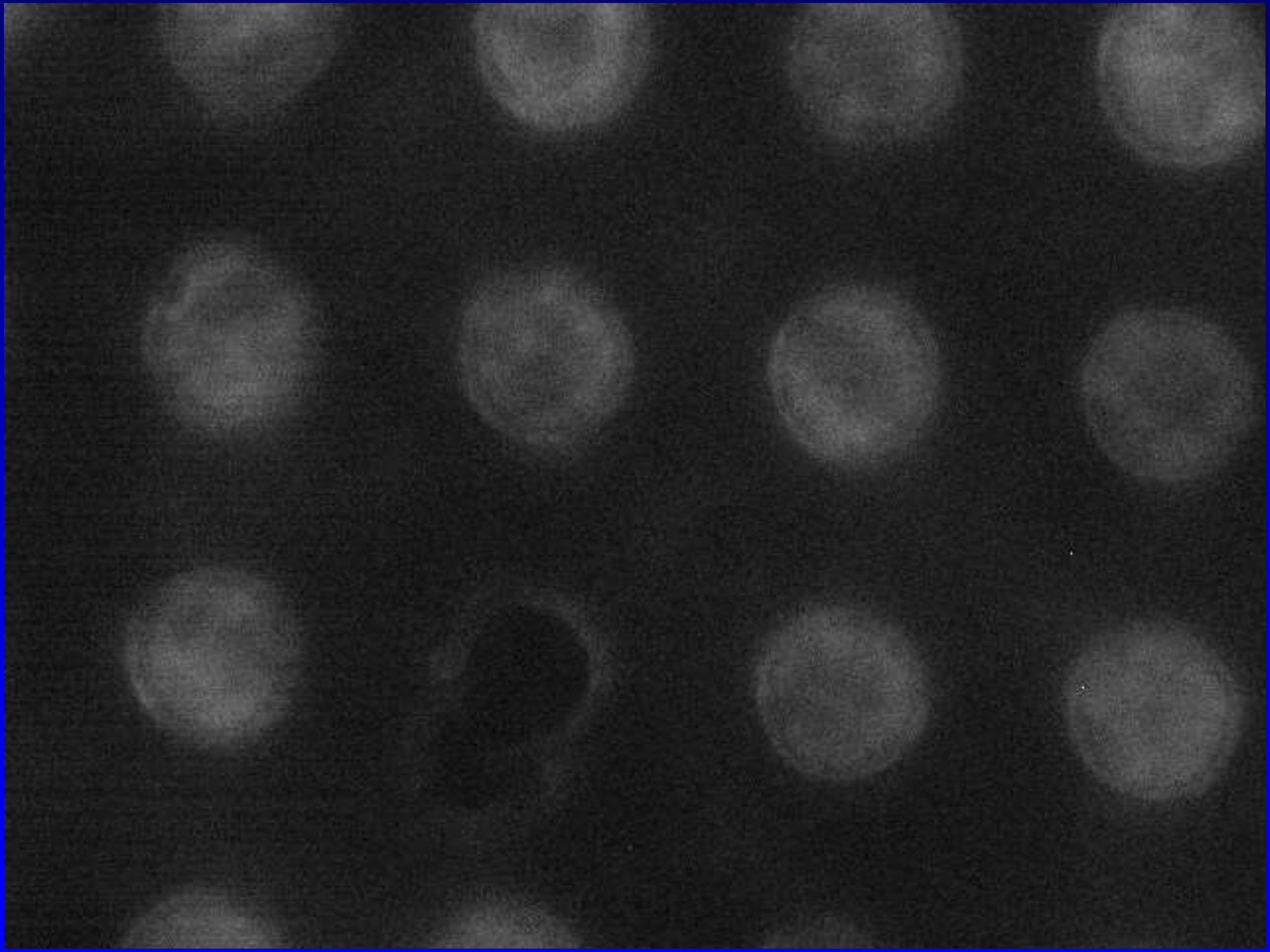


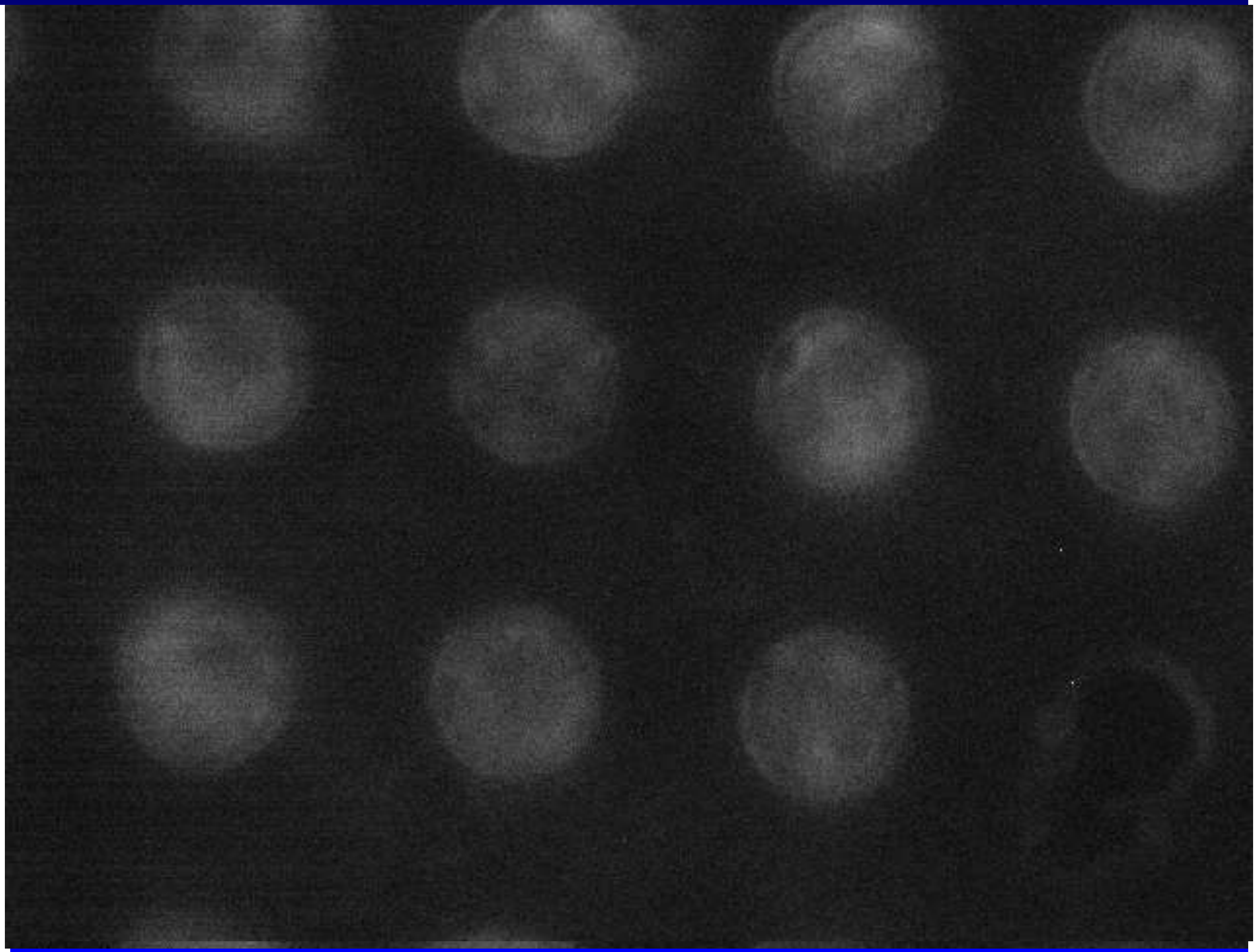
Targeting next one



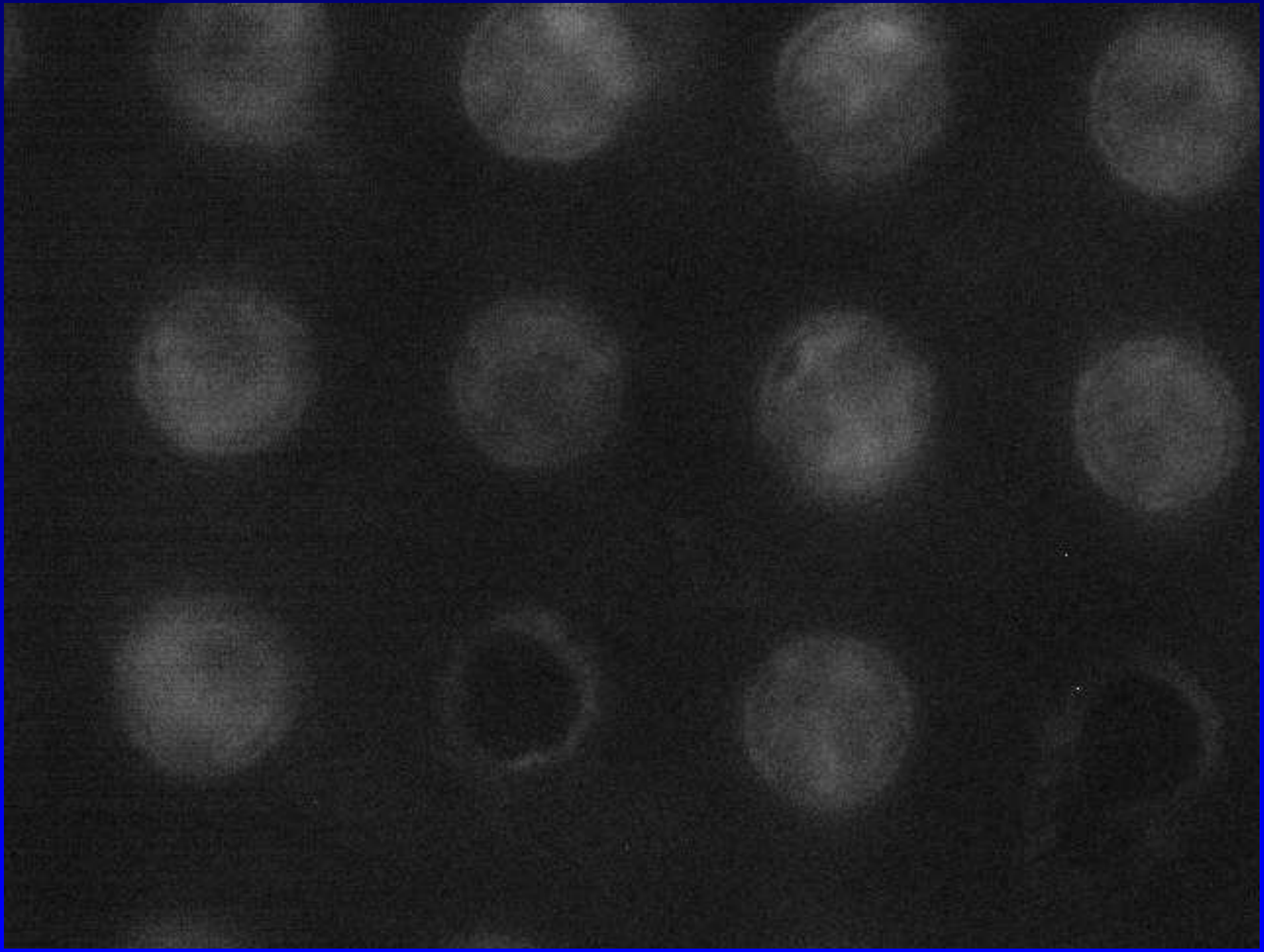
2nd chamber burned

Fluorescence mode, video of the 1^{st} shot



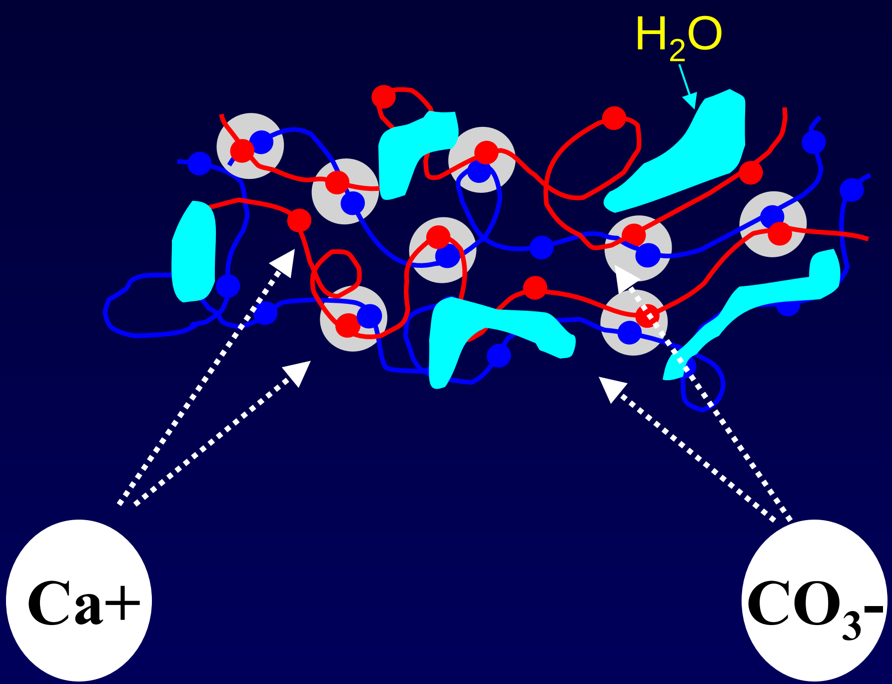


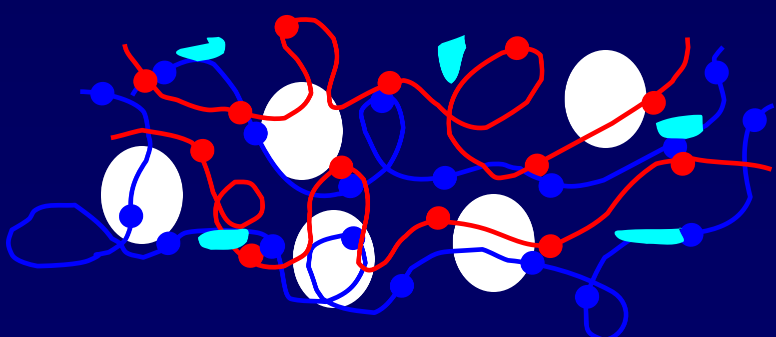
Fluorescence mode, video of the 2nd shot



Sample moved to target nest chamber

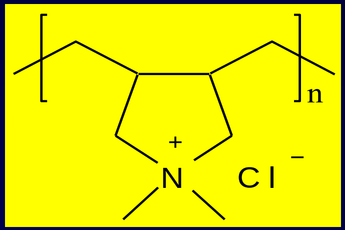
Chemical infiltration in Polyelectrolyte Multilayer Films



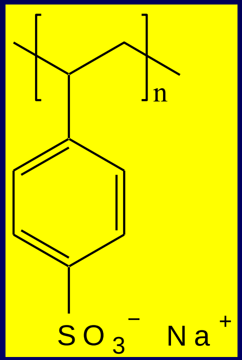


Growing $CaCO_3$ particles

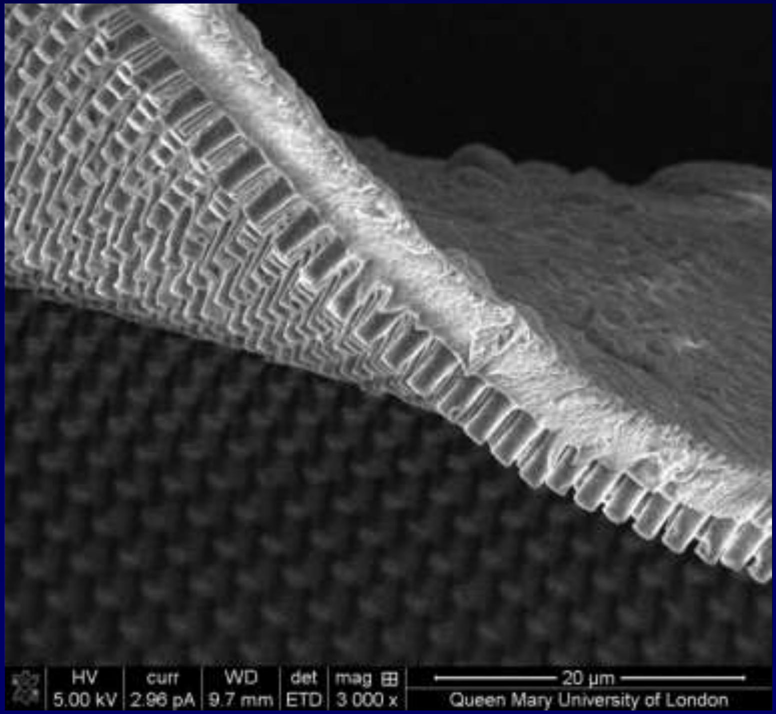
PDADMAC

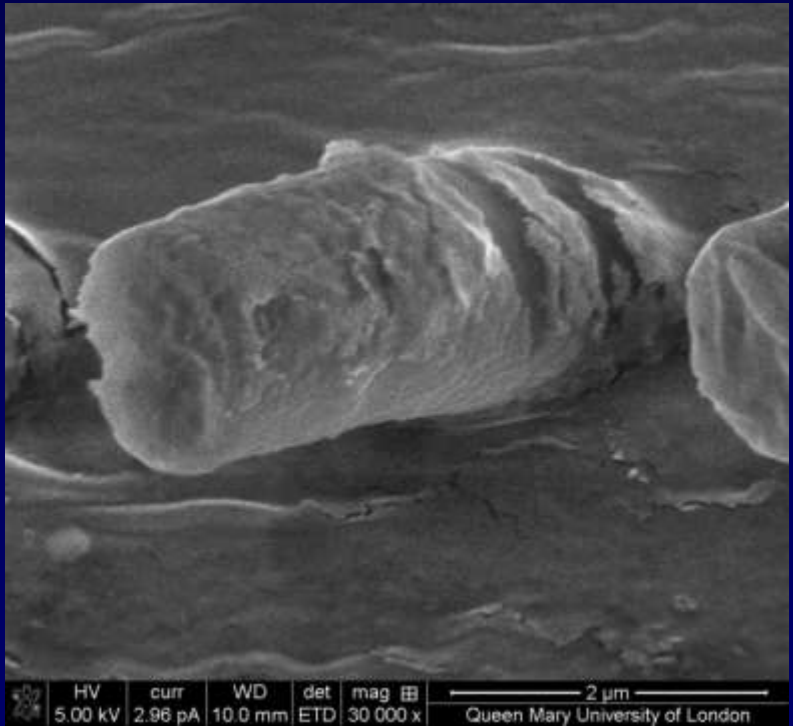


PSS

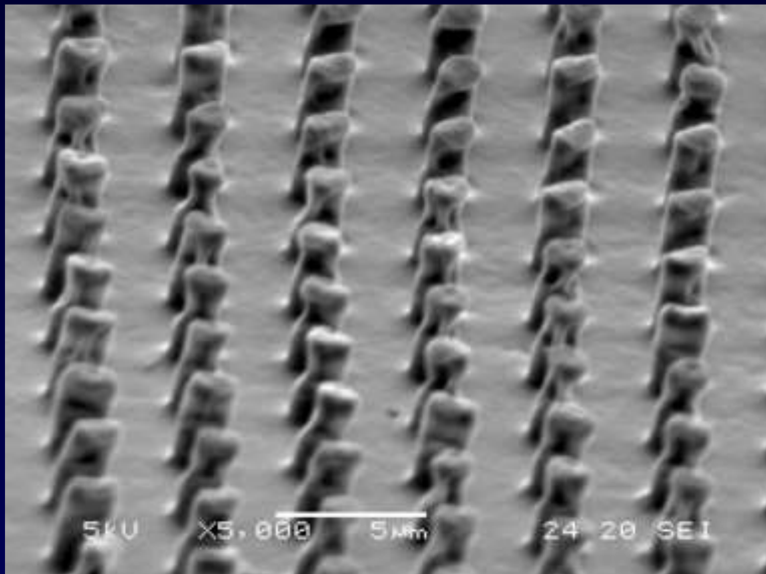


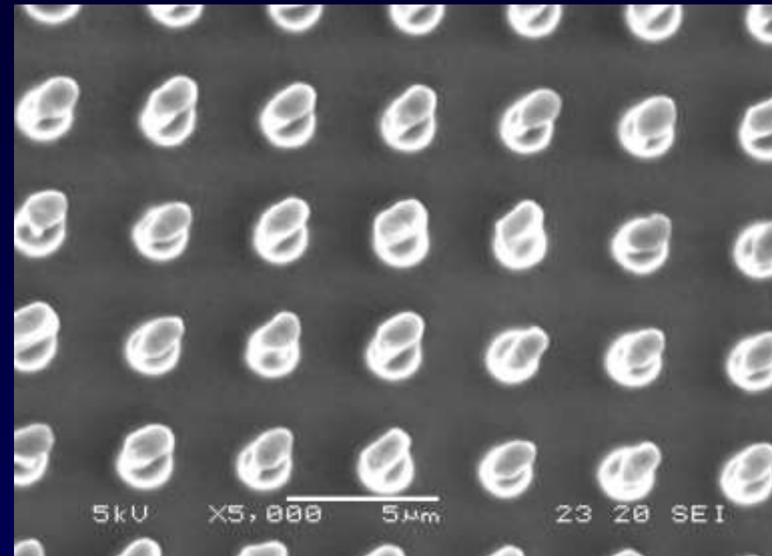
Chemical infiltration in Microchamber Arrays Made of Layer-by-Layer Assembly



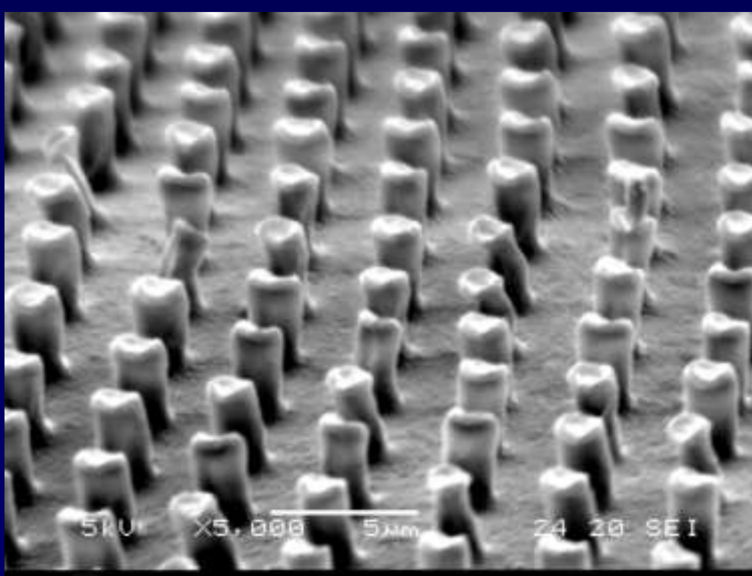


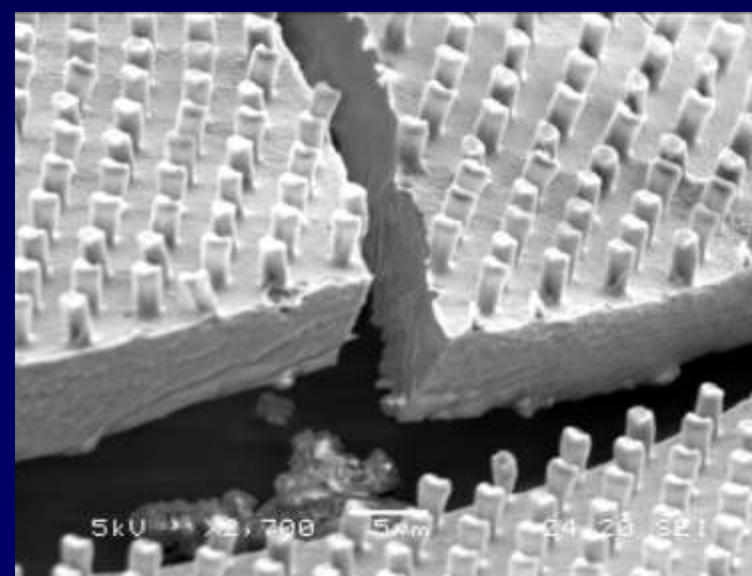
PMMA (PSS/PDADMAC) 20





PMMA (PSS/PDADMAC)CaCO3-20





Acknowledgements

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Arthritis Research UK

BBSRC bioscience for the future

EPSRC Engineering and Physical Sciences Research Council

Institute of Materials Research&Engineering, Singapore
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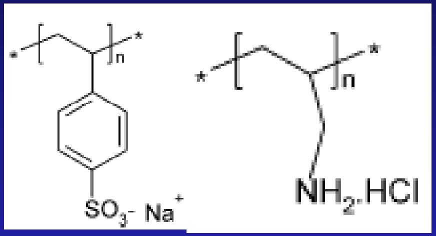
University of Leeds *Prof. Dongsheng Wen*

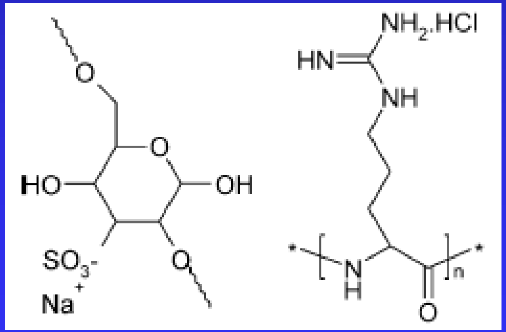
Intracellular Degradation of polyelectrolyte capsules

VERO-1 cells, 60h incubation



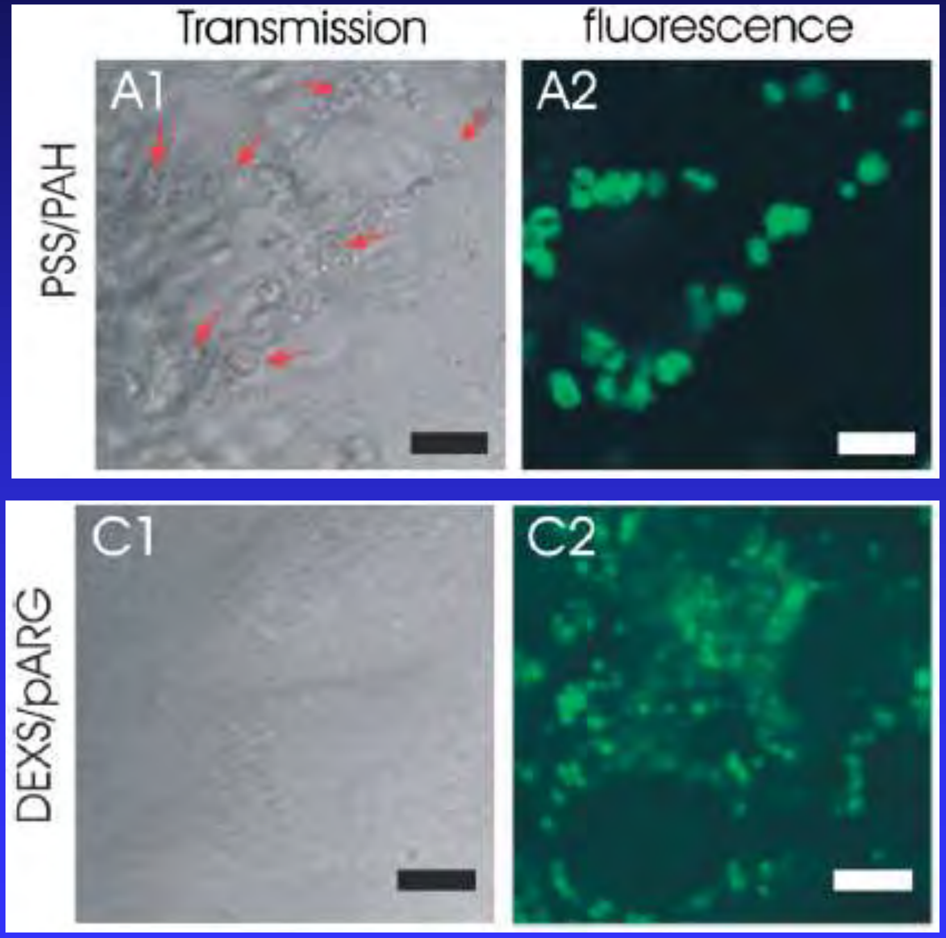
Synthetic PSS/PAH

No degradation



Dextran sulfate/ polyArginine

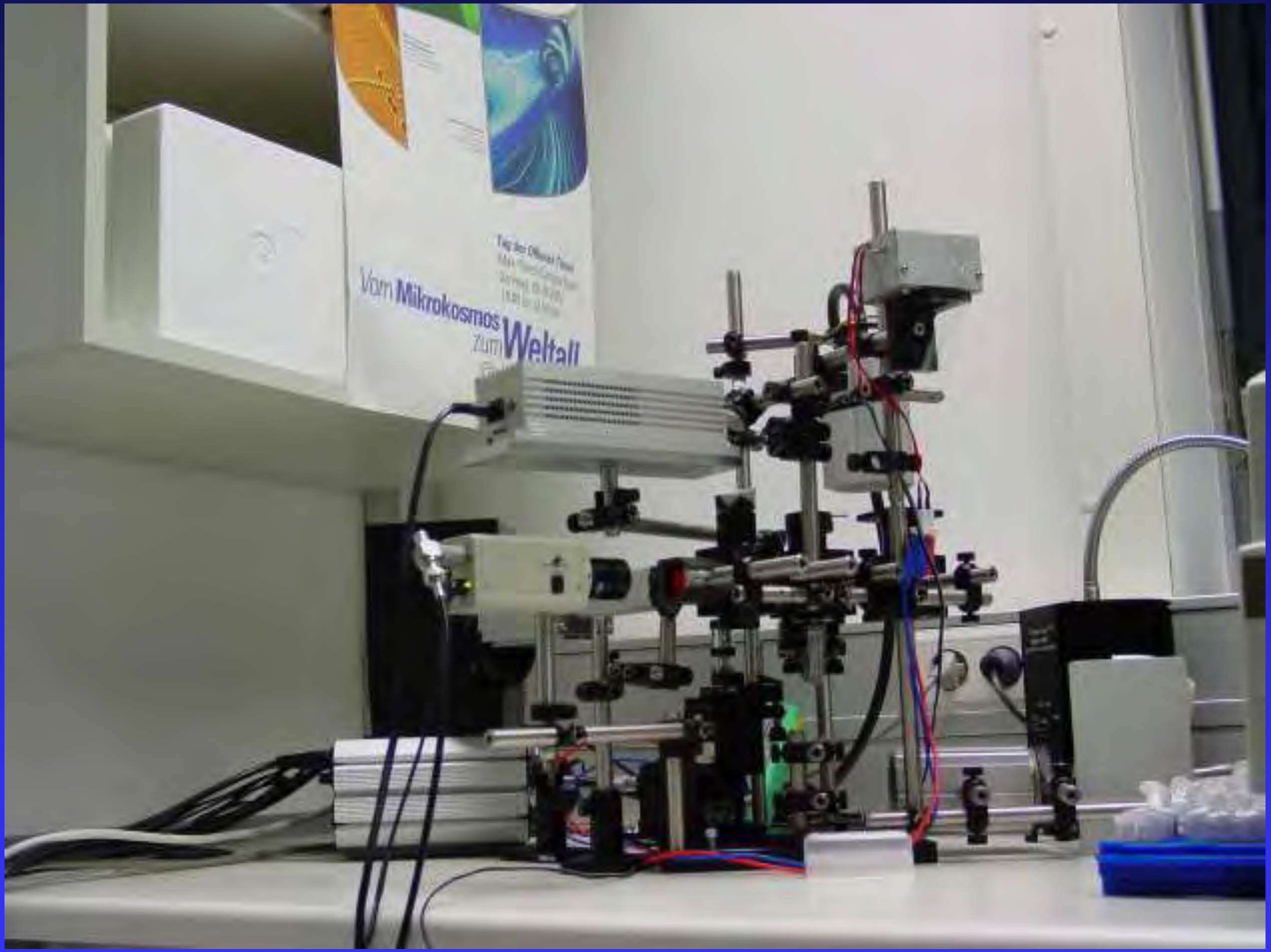
Degradation, Release of FITC-dextran



De Geest, B.G.,. et al (2006), *Advanced Materials*, 18, 1005

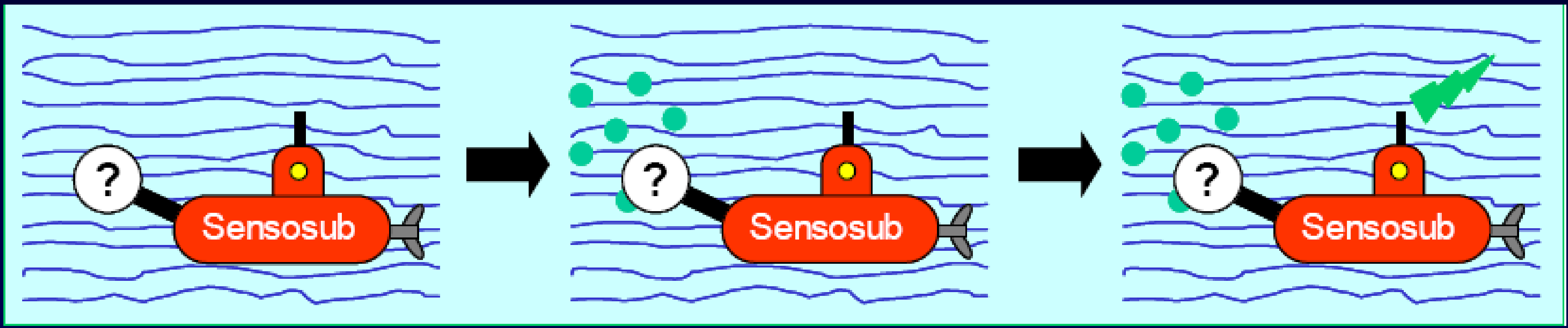
In-house developed optical setup for remote release experiments

Andre Skirtach

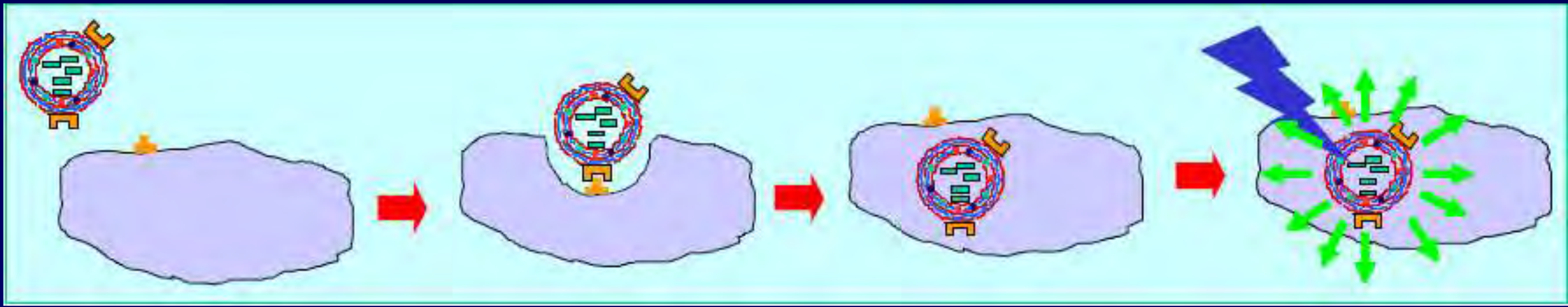


Various sources, CCD, real-time imaging, portable, easy tranferable to new location

Sensing/Delivering Submarine

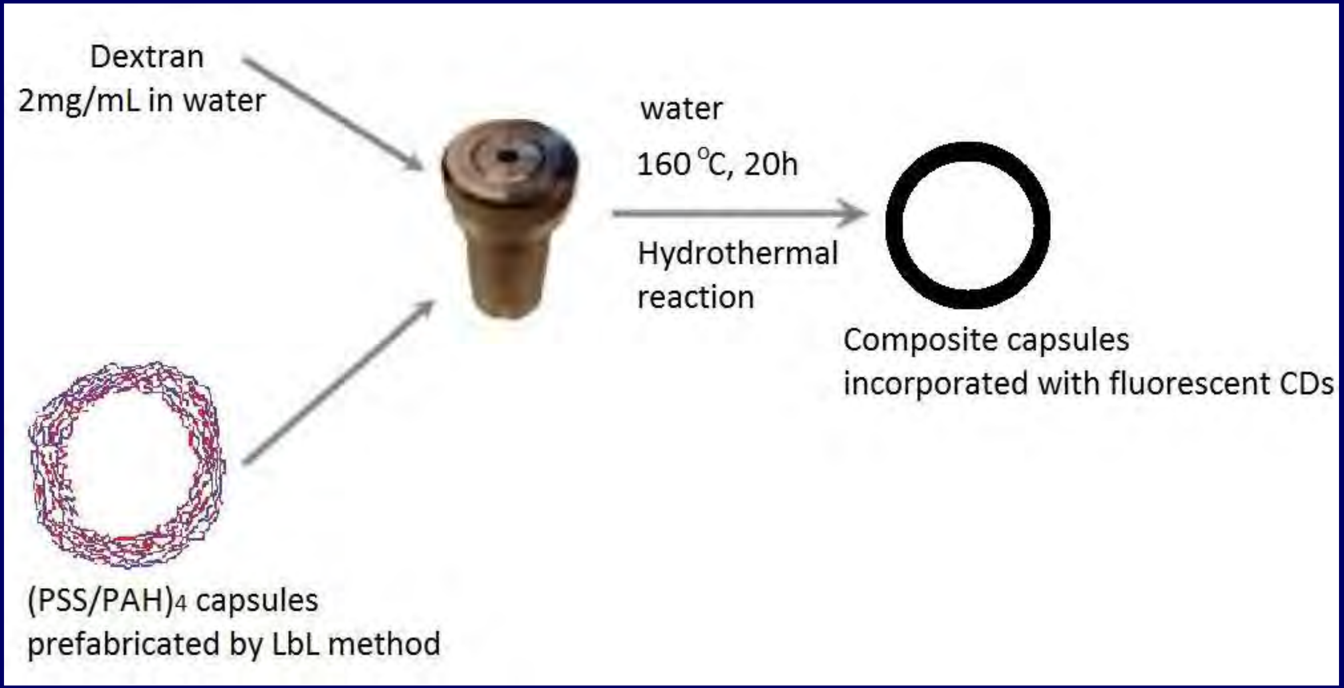


Floating in body Submarine



External triggering / reporting inside cells/tissues

Carbonization at LbL capsules

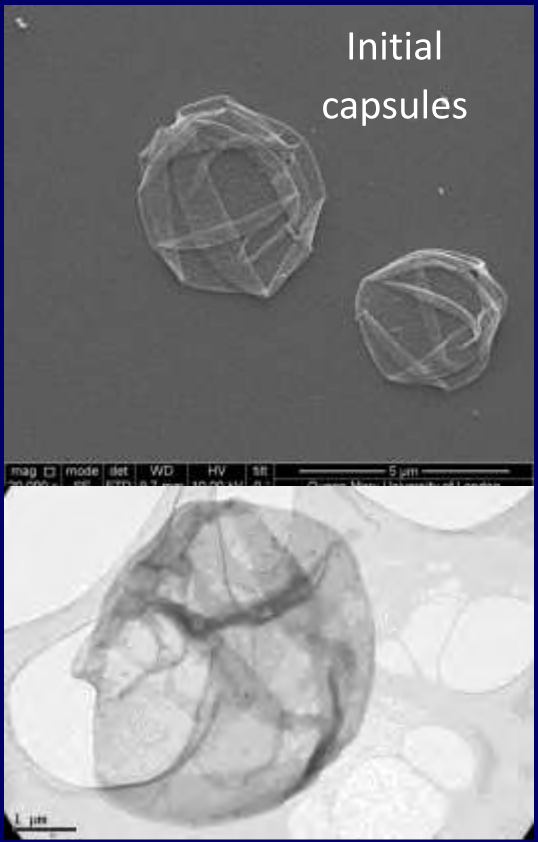


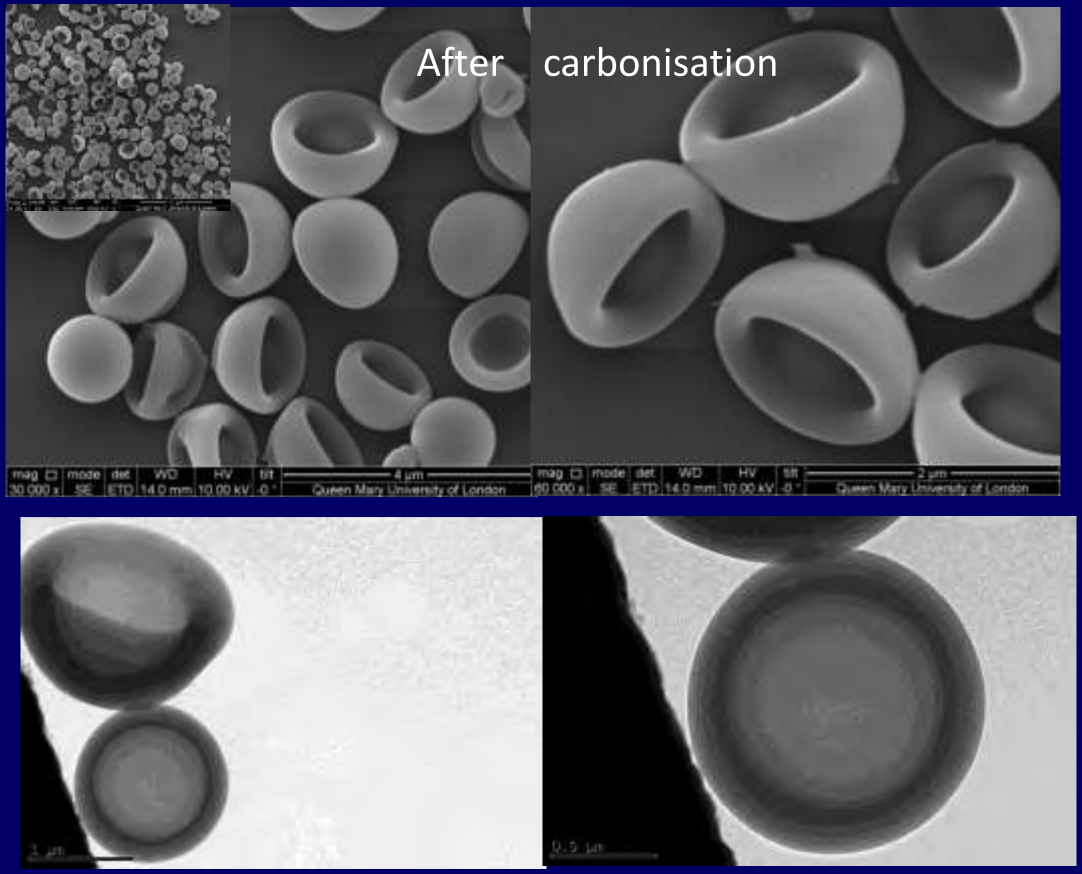
1. Photoluminescent carbon dots (CDs) that can be synthesized by hydrothermal method

2. One-step synthesis and incorporation of CDs into the pre-fabricated PEs by hydrothermal carbonization of dextran at 160°C to modify fluorescent, mechanical and permeability properties in one step

Y. Yang, J. Cui, et al. Chem. Commun., 48 (2012)380–382
B. Hu,....MM. Titirici, et al Advanced Materials, 22 (2010) 813–827

Morphology and Structure Analysis – SEM, TEM

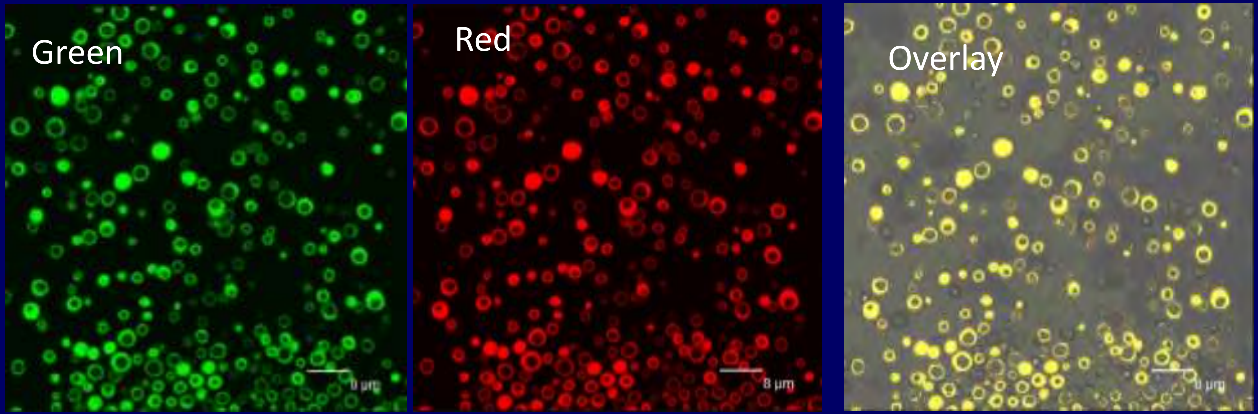


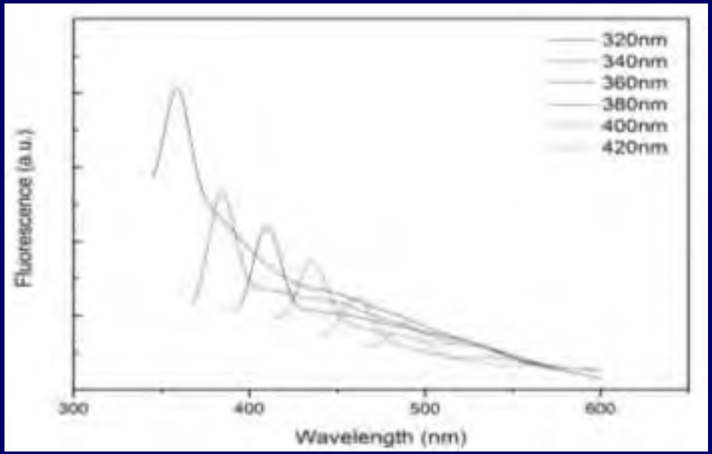


Size Thickness

Treatment condition: (PSS/PAH)$_4$ capsules were heated in dextran solution (2mg/ml) at 160^{o}C for 20h,and finally washed with water

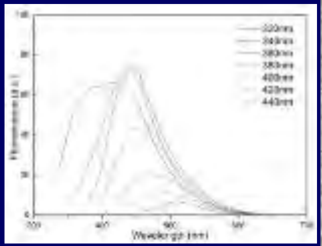
Fluorescent property of carbonized LbL capsules





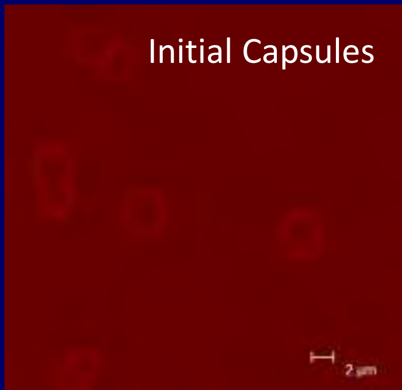
CLSM images and fluorescence spectrums of carbonized composite capsules

TEM image and fluorescence spectrum of carbon quantum dots obtained from dextran solution (2mg/ml) heated at 160 °C for 20h (no capsules)

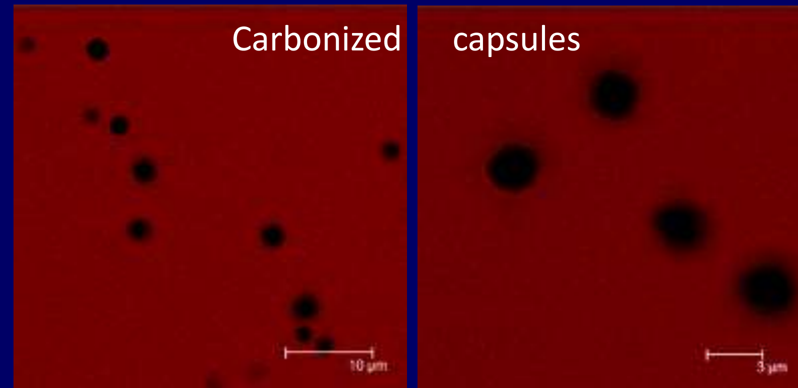


Emission depends on excitation wavelength for carbon QDs and carbonized capsules

Reduced Permeability of Carbonized capsules



Rhodamin B is not permeable after carbonisation



Laser (840 nm) burning holes in carbonized capsules