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Novel nanosized delivery and diganostic polymeric particles : single chain nanoaprticles for 2-photon imaging and drug delivery

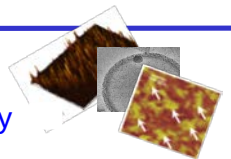
Wolfgang H. Binder with Justus Hoffmann/Thümmler and Senbin Chen

Collaboration with Prof. Jan Laufer, Physics department

Martin Luther University Halle-Wittenberg

Macromolecular Chemistry

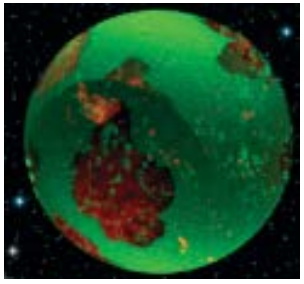
www.macrochem.uni-halle.de wolfgang.binder@chemie.uni-halle.de

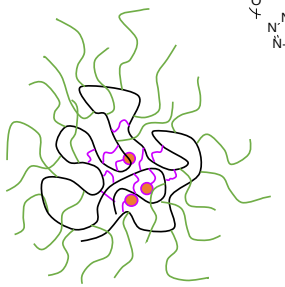


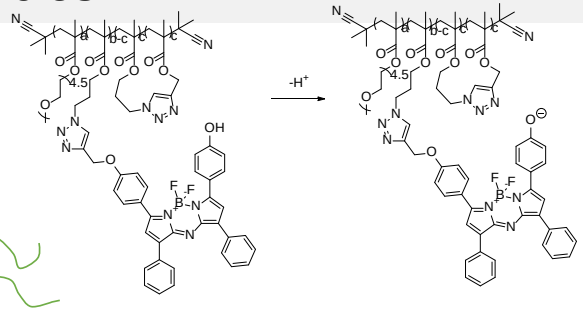
Bio-Material-Research @ AGBinder

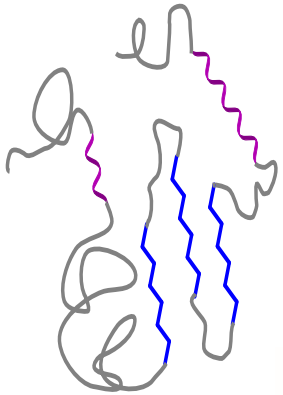
Martin Luther University Halle-Wittenberg

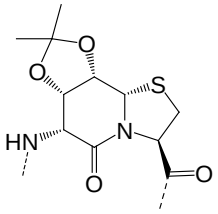
❑**Live 3D-Imaging**
- Single Chain Nanoparticles → photacoustics
❑**Drug Delivery**
- Polymer-Drug Conjugates / Micellelar Delivery
❑Polymeric and Lipid Vesicles

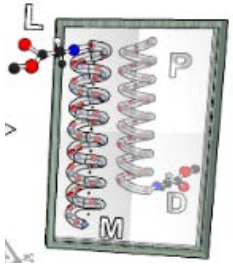


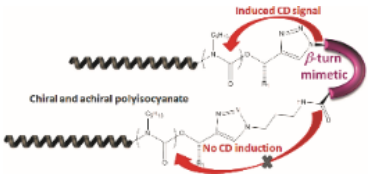










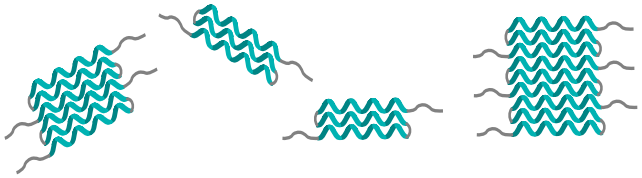


Polymer Synthesis

❑ Synthetic Design of functional Macromolecules via Living Polymerization Methods

❑ Homogeneous and Heterogeneous Catalysis

❑ Assembly and Degradation



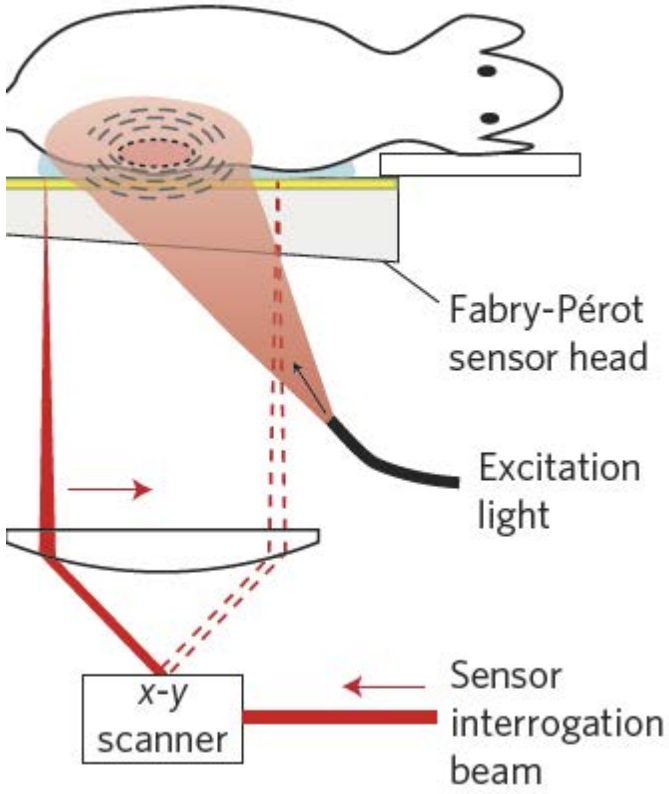
❑Fibrous Aggregation
- Artificial fibers for neuron regeneration
- Amyloid fibrillation

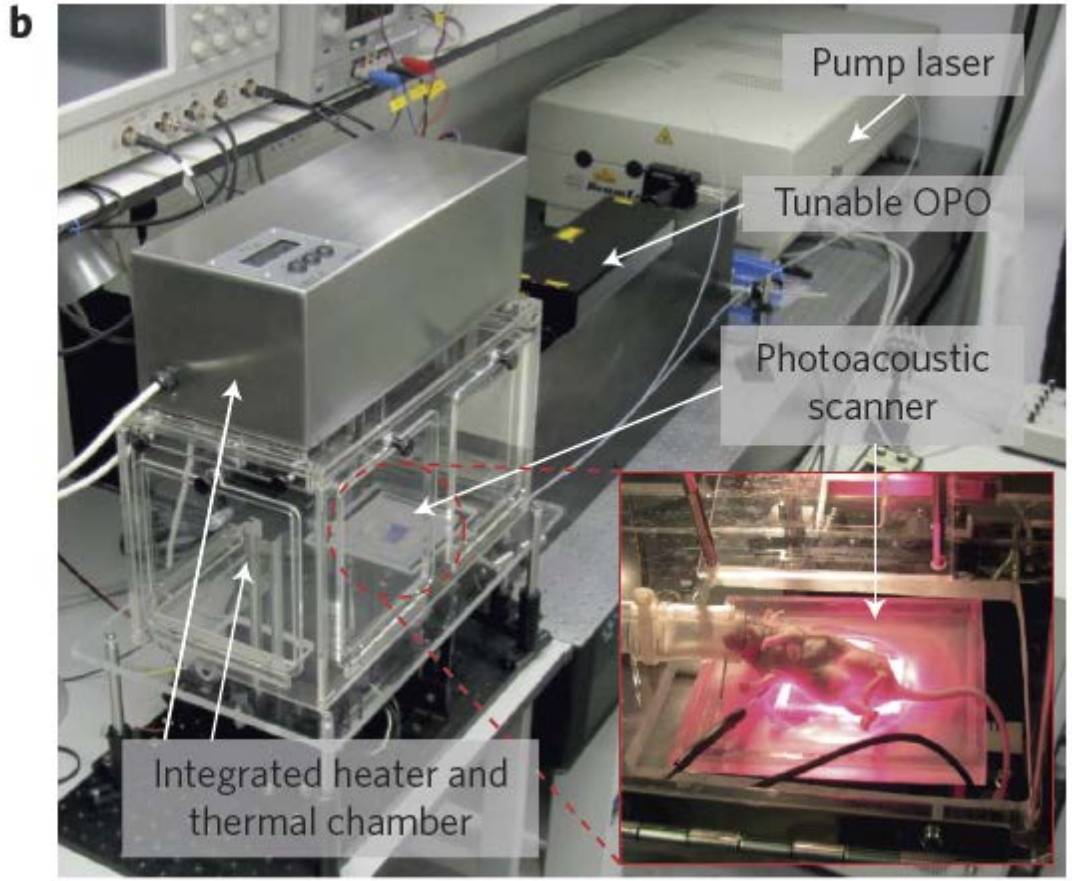
❑Biohybridpolymers
- PEG conjugates with proteins/peptides
- Artificial beta-turn mimetics

❑Artificial Folding

❑Enzymatic Degradation

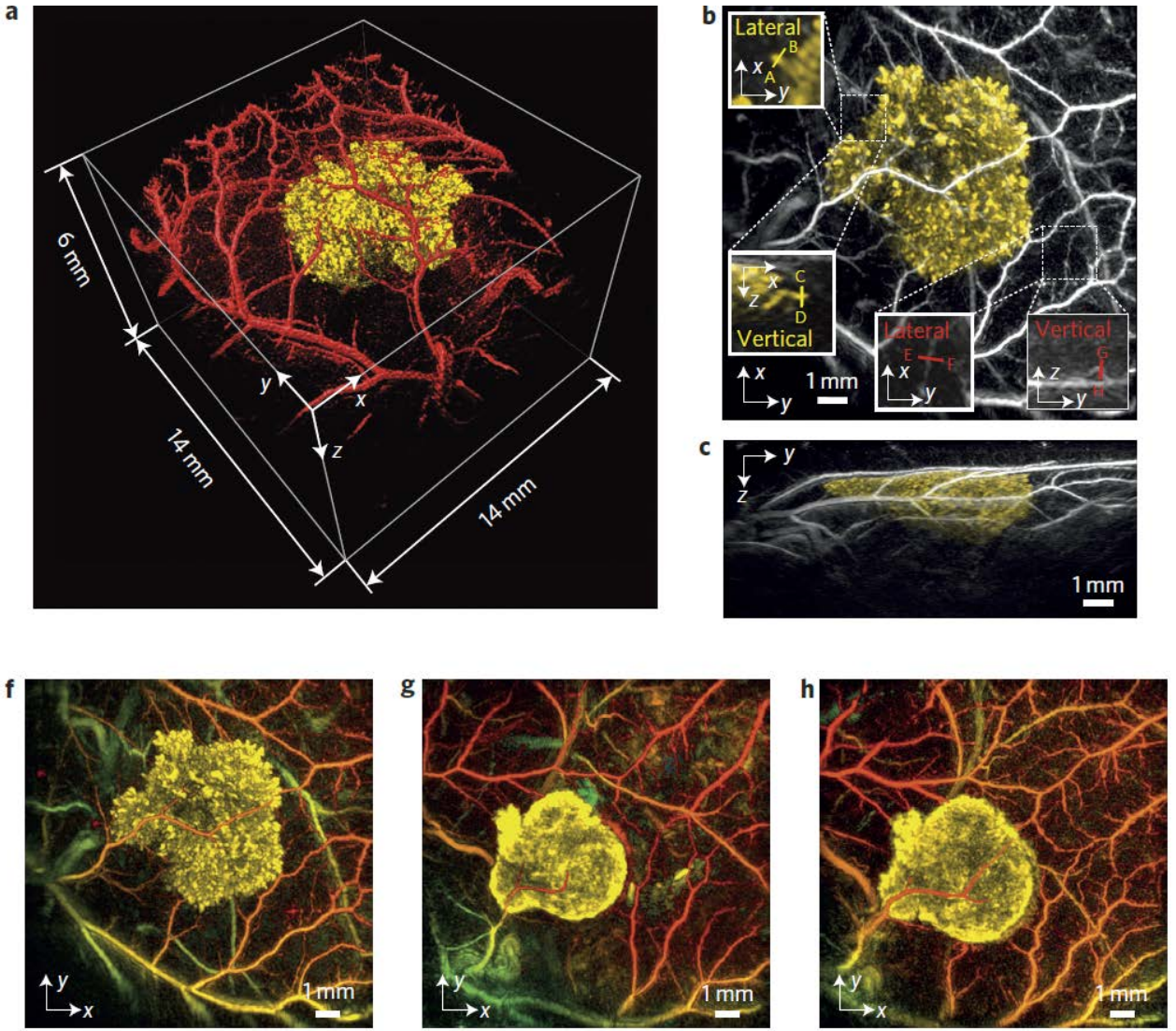
NIR Photoacoustic Imaging (with Prof. Laufer)





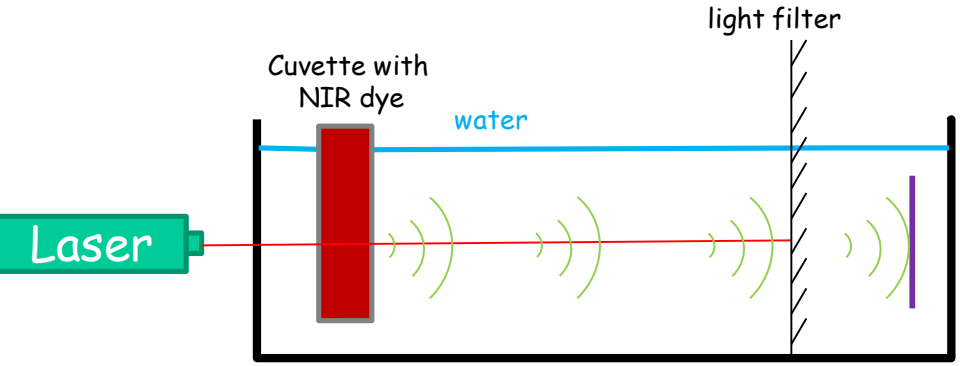
[7] *Chem. Rev.*, **2015**, 115, 10816-10906
[8] *Nano Res.*., **2015**, 8 (9), 3027-3034

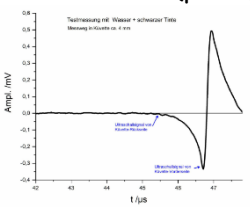
NIR Photoacoustic Imaging

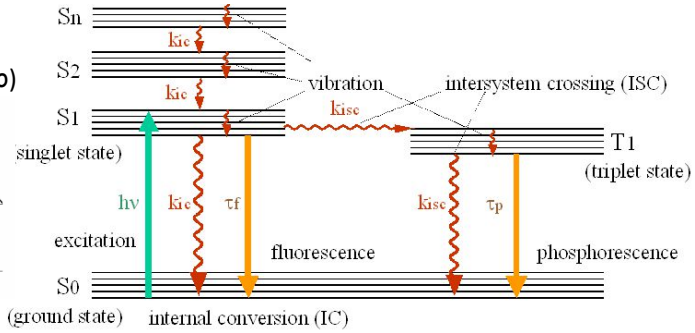


[7] *Chem. Rev.*, **2015**, 115, 10816-10906
[8] *Nano Res.*., **2015**, 8 (9), 3027-3034

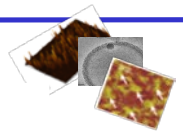
NIR Photoacoustic Imaging







- dye gets excited by laser pulse
- internal conversion of fluorescent dye heats up surrounding molecules
- pulsed excitation with > 20 kHz creates acoustic ultrasonic (US) waves -> waves can be detected
- Relaxation by internal conversion or pump-probe excitation

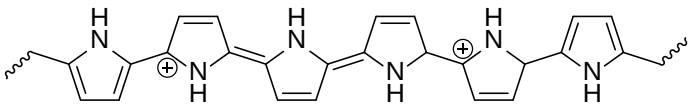


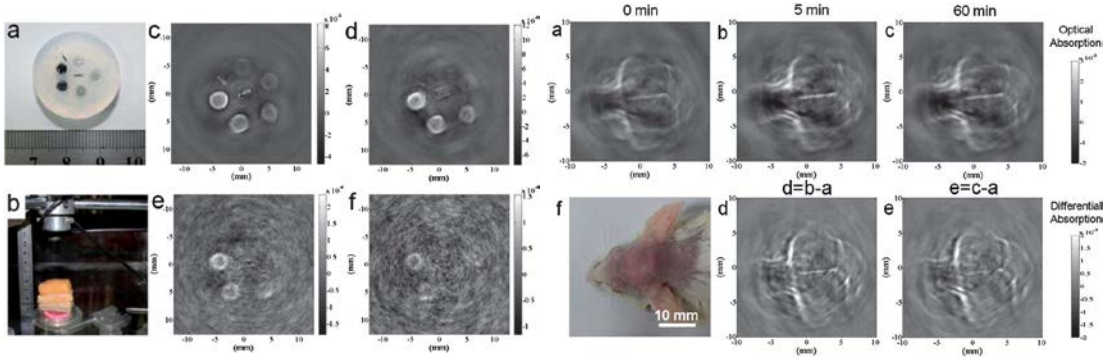
[7] *Chem. Rev.*, **2015**, 115, 10816-10906
[8] *Nano Res.*., **2015**, 8 (9), 3027-3034

NIR Dyes for Photoacoustic Imaging

Classic photoacoustic measurments

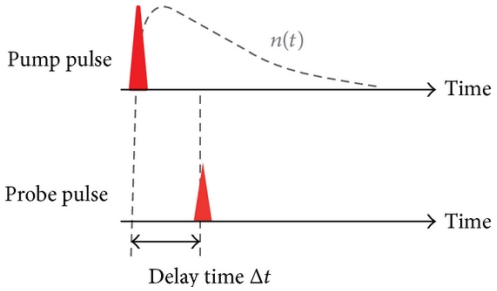
- heat by internal conversion
- Dyes with low Φ_{Fl}
- Metal nanoparticles
- Polypyrrole

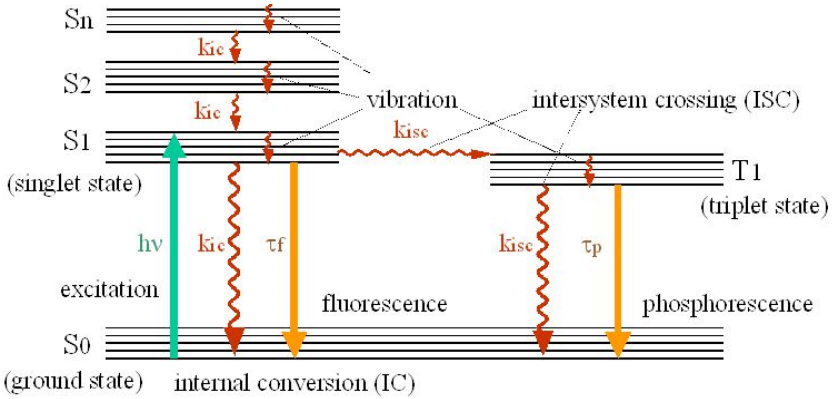


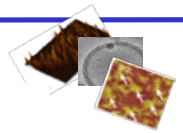


Pump-probe photoacoustiv measurments

- heat by excitation and forced relaxation
  -> vibratonal relaxation
- Dyes with high Φ_{Fl} and τ_{Fl}
- advantage: fluorophore specific contrast



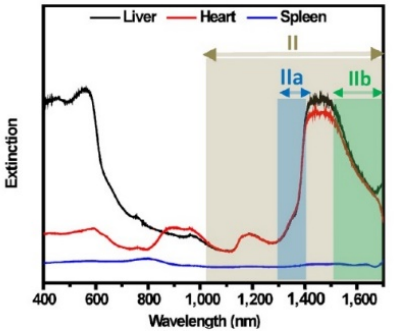




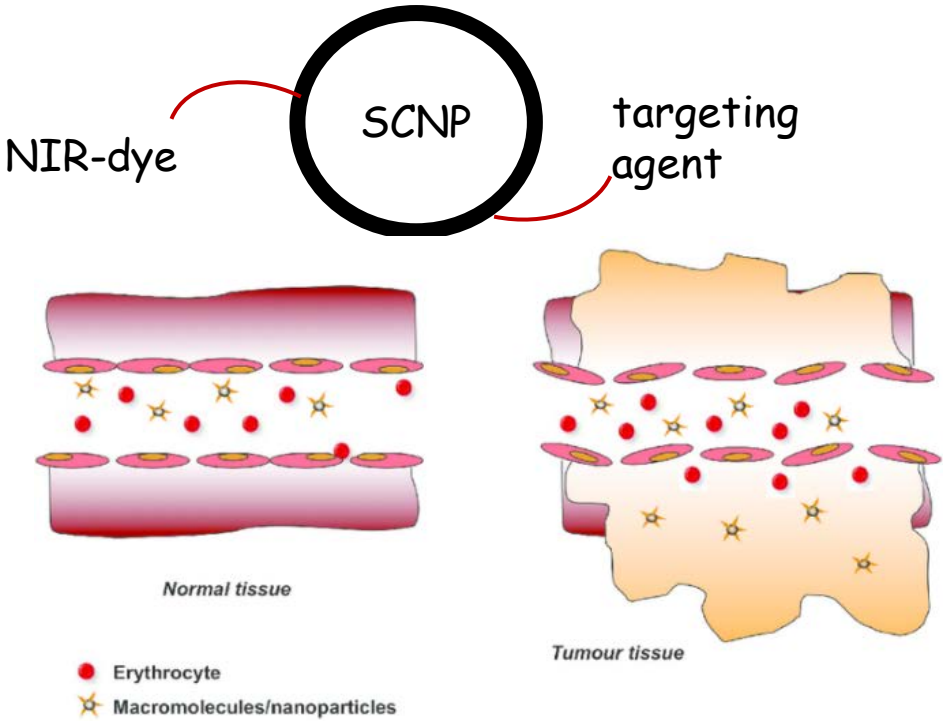
[9] *Nanoscale.*, **2013**, 5, 4462-4467

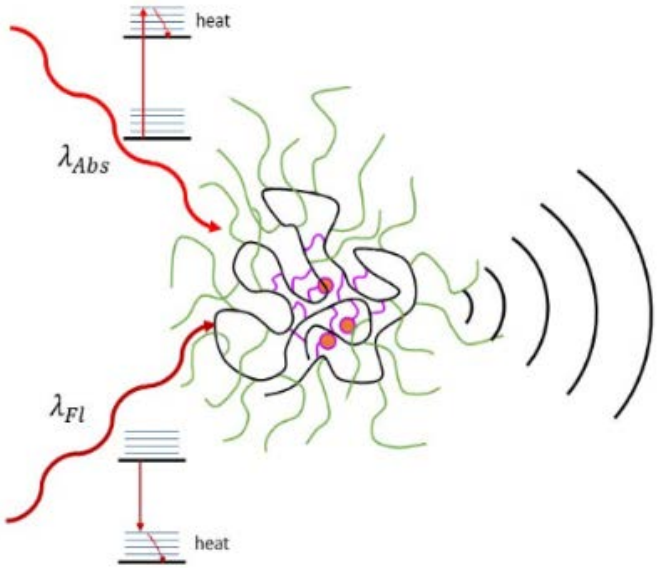
NIR-active Single Chain Nanoparticles (with Prof. Laufer, MLU)

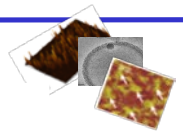
- **Biomedical imaging via NIR photoacoustic measurments (cooperation with Prof. Laufer)**
- **single chain nanoparticles with NIR-fluorescent dyes (and targeting agent)**
- **particles should be: biocompatible, water dispersable, small (<20 nm)**



[6] *Biomacromolecules.*, **2016**, 17, 3213-3221
[7] *Chem. Soc. Rev.*, **2014**, 43, 6570-6597
[8] *Rev. Sci. Instrum.*, **2006**, 77, 041101



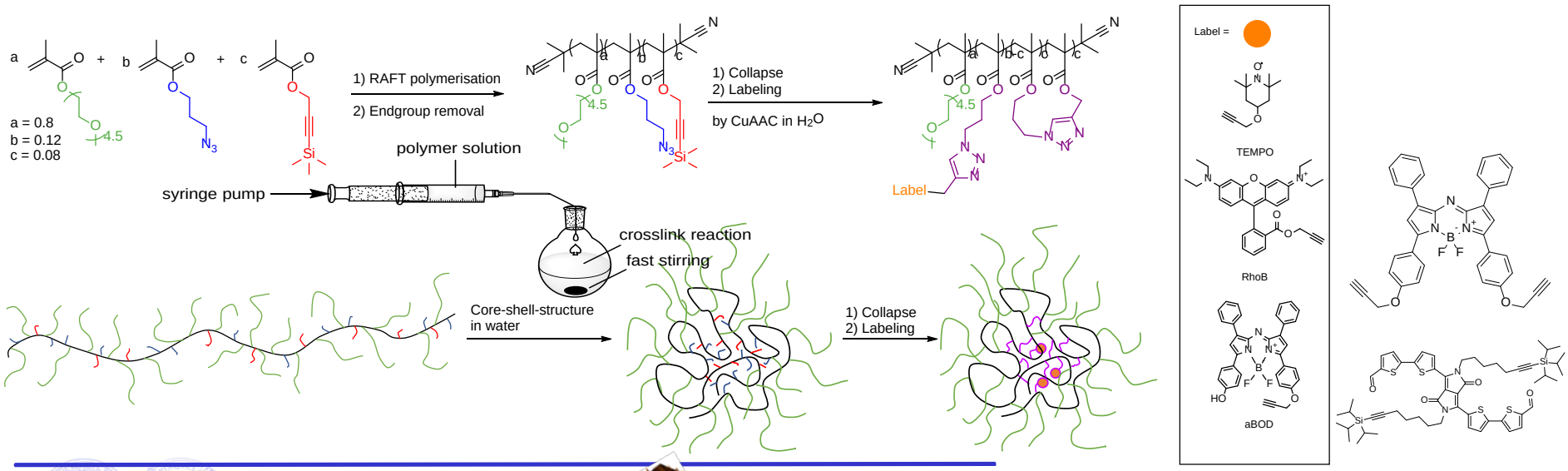




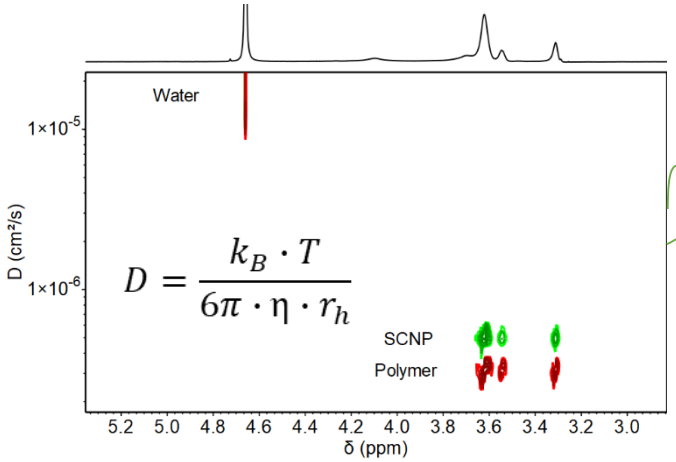
Hoffmann, Binder *Angew. Chem. Int. Ed.* 2021, 60,7820 –7827

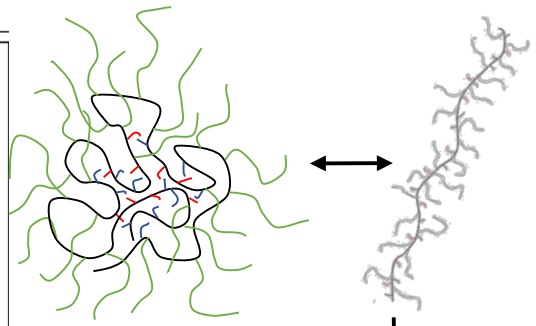
Folding of Single Polymer Chains : NIR- and Catalytically Active Single Chain Nanoparticles

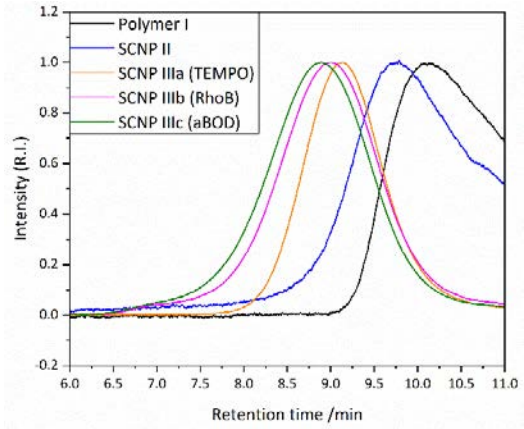
- poly(ethylene glycol) methyl ether methacrylate (PEGMA) as main part of the polymer
- biocompatibile, water soluble and other effects (LCST, stealth effect)
- azide and alkyne functionalized methacrylates as crosslinking groups (CuAAC)
- excess of azide to attach NIR fluorescent dye by additional CuAAC
- drug delivery system for a contrast agent for pump-probe photoacoustic imaging
- dye is hidden in the particles core -> no fluorescence quenching by water



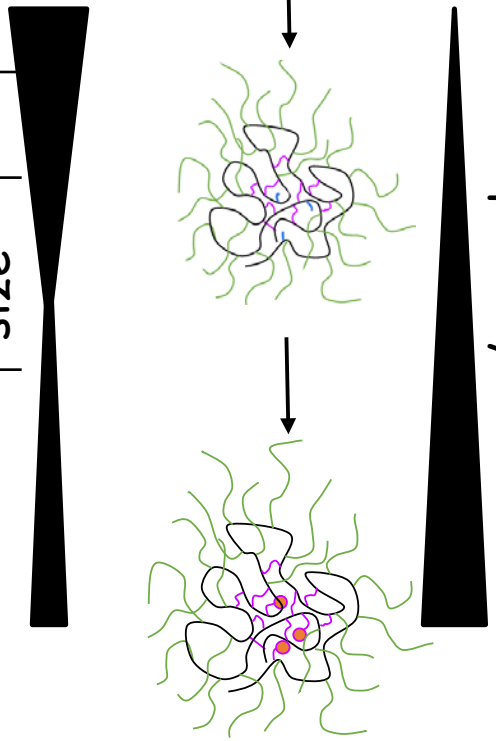
SCNP - Particle Size and Polarity

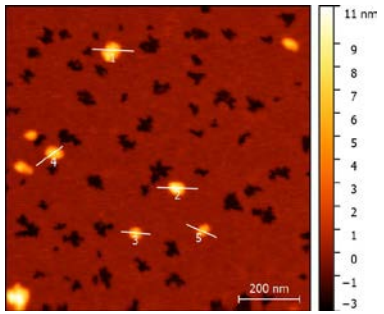


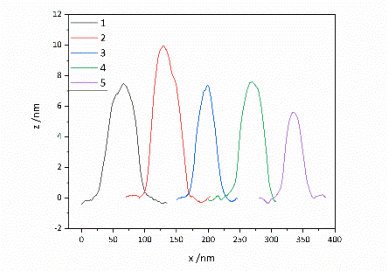


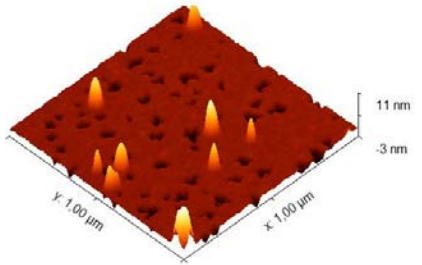


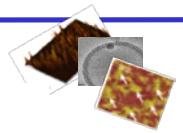
	$r_{h,DOSY}$ /nm	$r_{h,DLS}$ /nm
Polymer I	5.3	5.2
SCNP II	3.6	4.2
SCNP IIIa (TEMPO)	5.2	4.9
SCNP IIIb (RhoB)	5.2	4.5
SCNP IIIc (aBOD)	4.7	4.6







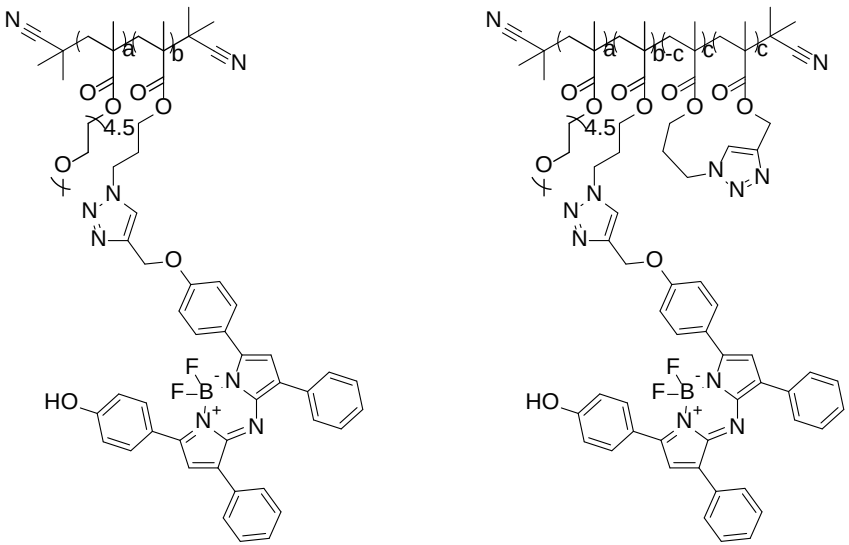




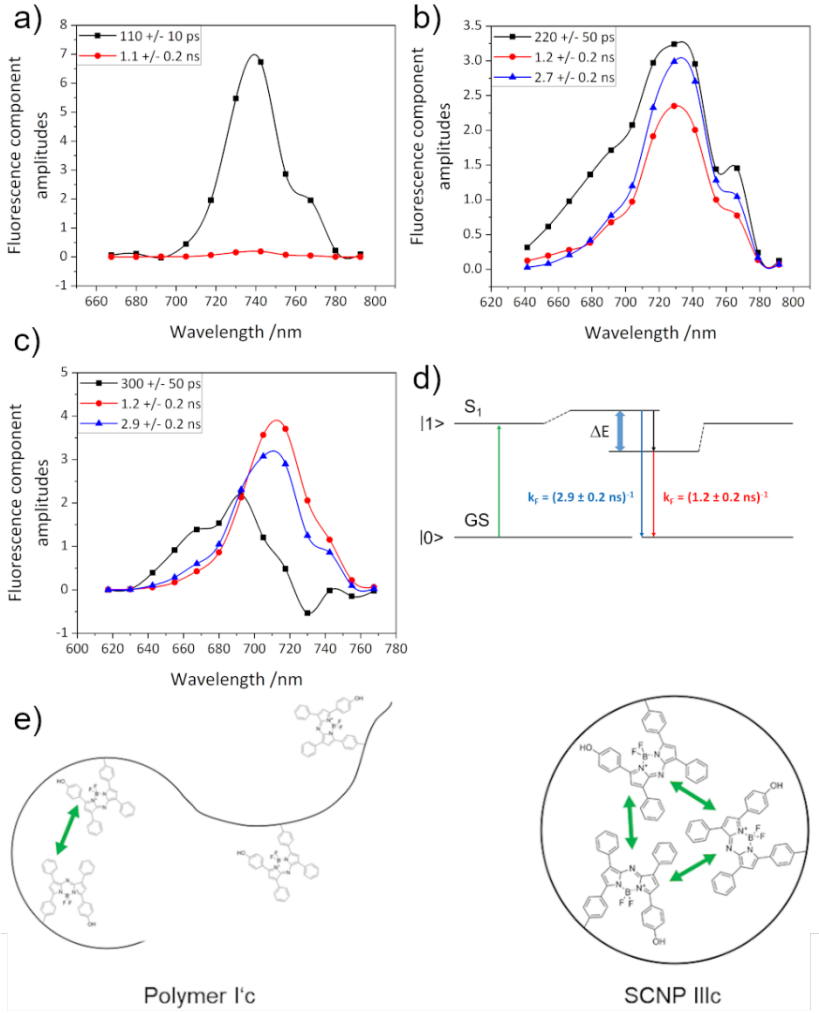
Hoffmann, Binder *Angew. Chem. Int. Ed.* 2021, 60,7820 –7827

Folding of Single Polymer Chains :

Nanocompartments in Single Chain Nanoparticles

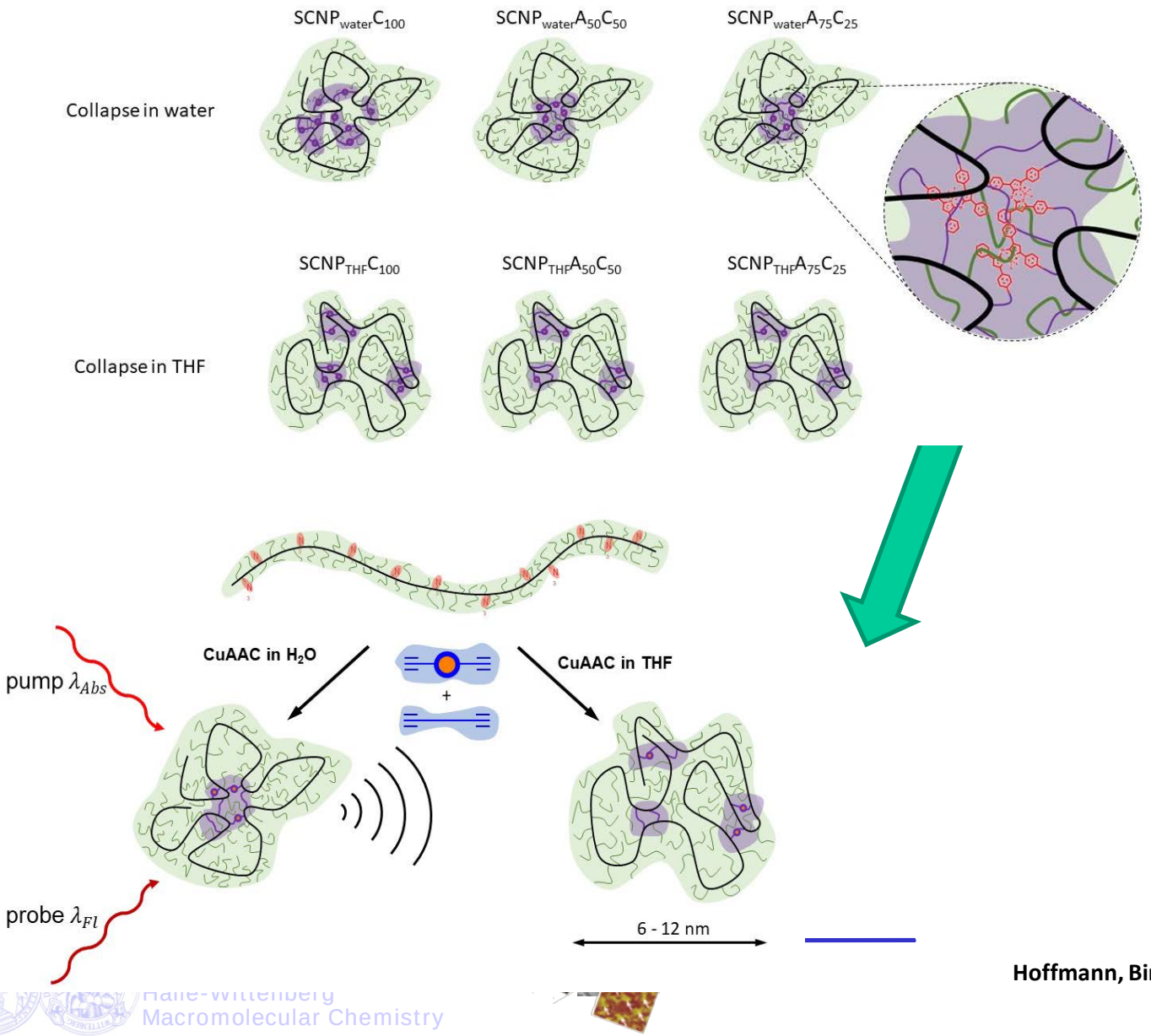


- strong excitonic splitting in collapsed SCNP
- only weak interaction in linear polymer
- excitonic splitting leads to longer τ_{fl}



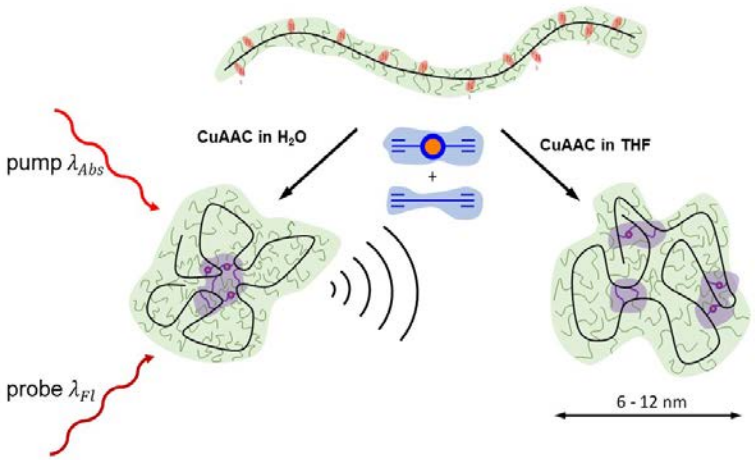
Hoffmann, Binder *Angew. Chem. Int. Ed.* 2021, 60,7820 –7827

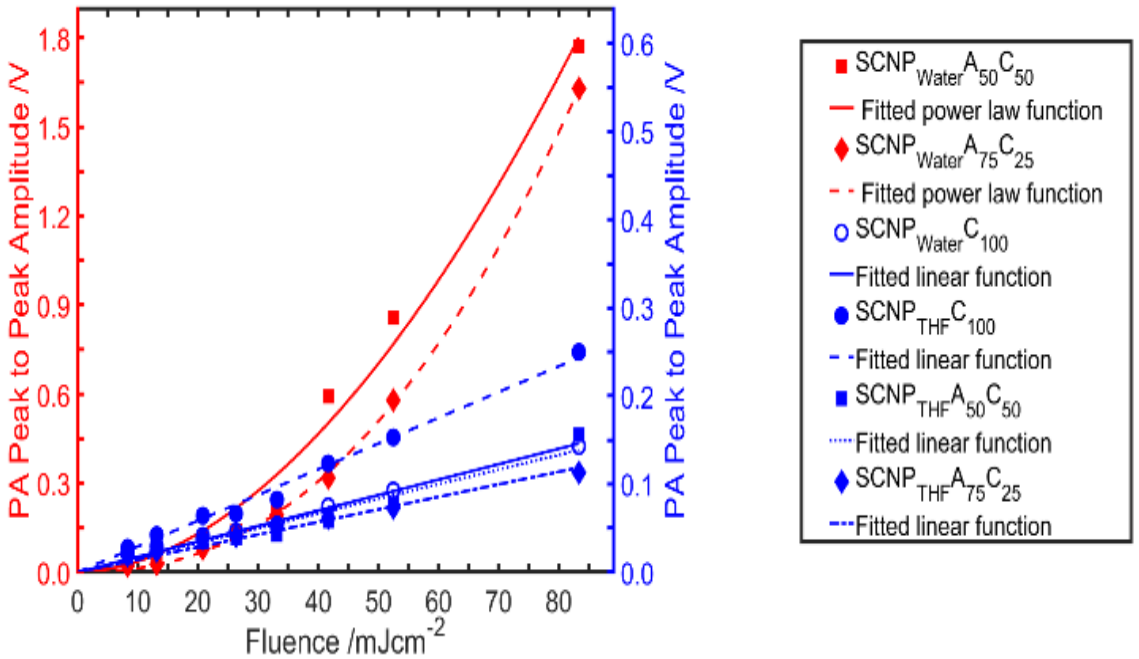
SCNP - Particle Size and Polarity – Strong Effect on PA (cooperation Prof. Laufer, MLU)

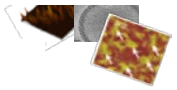


Hoffmann, Binder, Laufer, ***submitted***

SCNP - Particle Size and Polarity – Strong Effect on PA (cooperation Prof. Laufer, MLU)







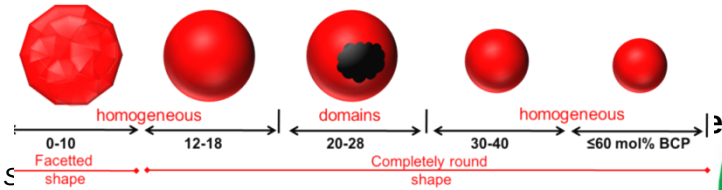
Hoffmann, Binder, Laufer, ***submitted***

Nanocompartments in vesicular membranes

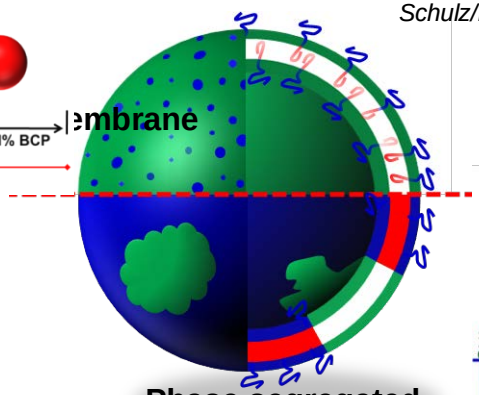
Control of phase segregation/ lateral membrane morphology is possible by composition and temperature (below T_m DPPC)

Assignment of polymer-rich phase by fluorescent labeled BCPs and by antibody interactions

GUV morphologies visualized by Rh-DHPE or diBCP-488

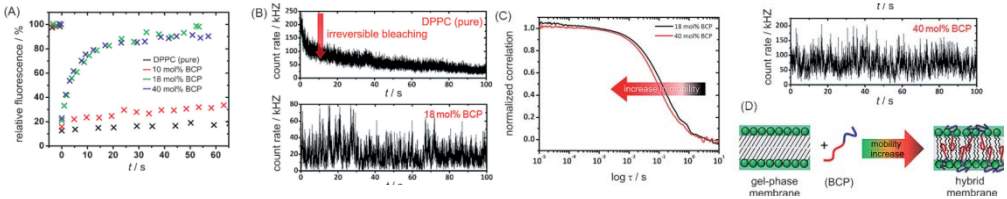


Schulz/Binder Soft Matter **2011**, 7, 8100-8110.



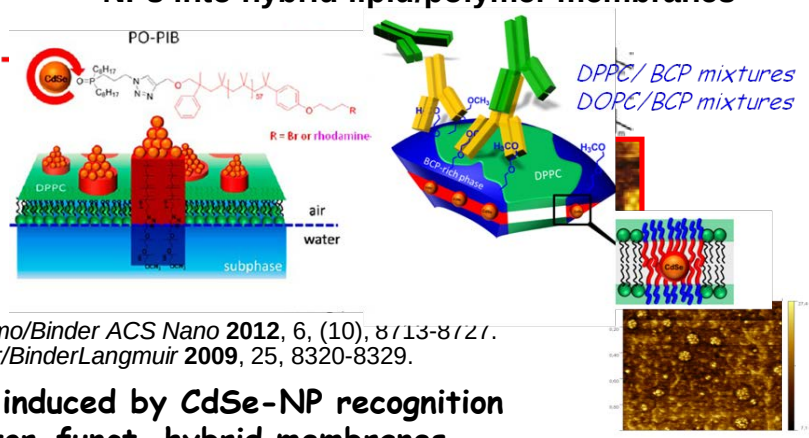
Phase segregated membrane

Distinct effects of incorporated BCPs on lipid bilayer organization (FRAP and FCS studies)



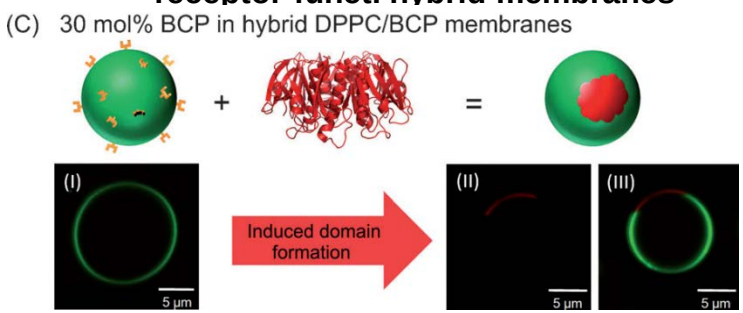
Schulz/Binder Angew. Chem. Int. Ed. **2013**, 52, 1829-1833.

Selective incorporation of polymer-funct. CdSe-NPs into hybrid lipid/polymer membranes



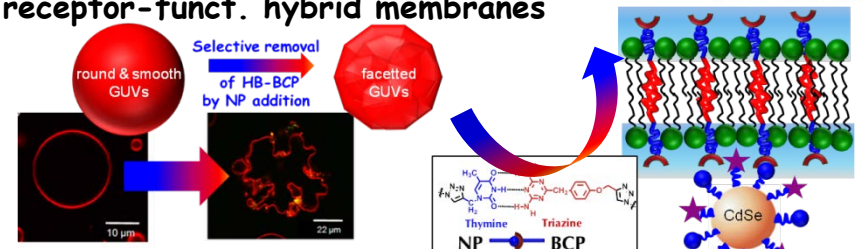
Olobummo/Binder ACS Nano **2012**, 6, (10), 8713-8727.
Kressler/BinderLangmuir **2009**, 25, 8320-8329.

Control of recognition behavior of protein with receptor-funct. hybrid membranes



Schulz/Binder Angew. Chem. Int. Ed. **2013**, 52, 1829-1833.

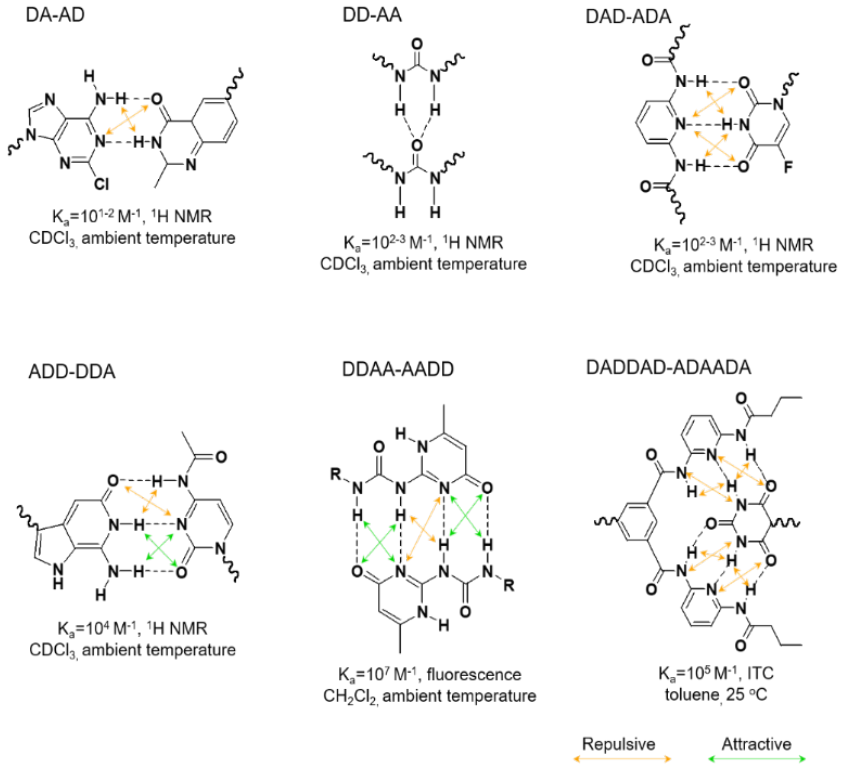
Phase changes induced by CdSe-NP recognition with receptor-funct. hybrid membranes

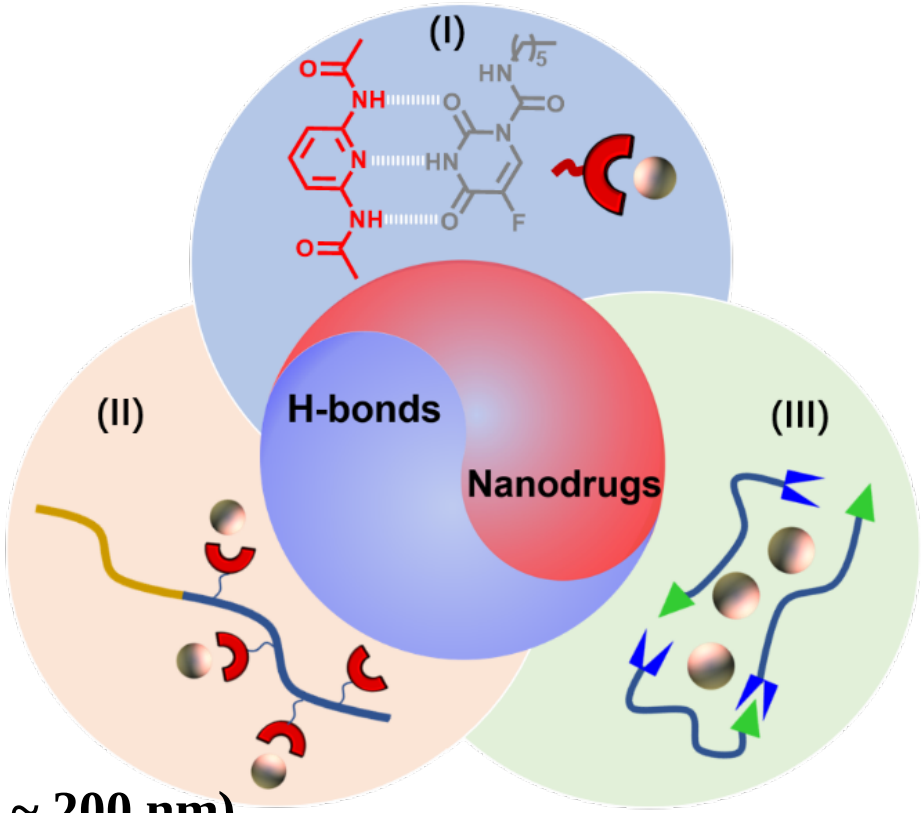


Olobummo/BinderLangmuir **2014**, 30, 259-267.

Binder Angew. Chem., Int. Ed. **2008**, 47, 3092.
Binder Angew. Chem., Int. Ed. **2003**, 42, 5802.
Schulz/Binder Soft Matter ***2012***, *8, (18), 4849.*

Drug Delivery by NIR-triggered thermal release

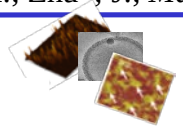




- **Fabricate Polymer Micelles (sized ~ ~ 200 nm)**
- **Equip with additional Hydrogen bonds to favor slow release**
- **Increase Cargo of Drugs**
- **Triggered thermal release by NIR-irradiation.**

Hydrogen-Bonds Mediated Nanomedicine: Design, Synthesis and Applications

Chen, S.; Wu, Y.; Lortie, F.; Bernard, J.; Binder, W. H.; Zhu*, J.; *Macromolecular Rapid Communications*, *2022*, ASAP, https://doi.org/10.1002/marc.202200168



Drug Delivery by photo-thermal release

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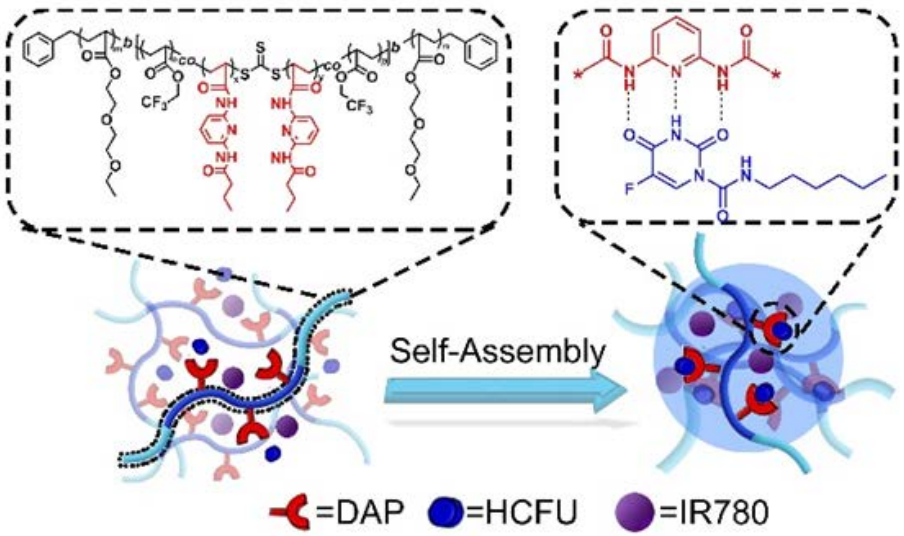
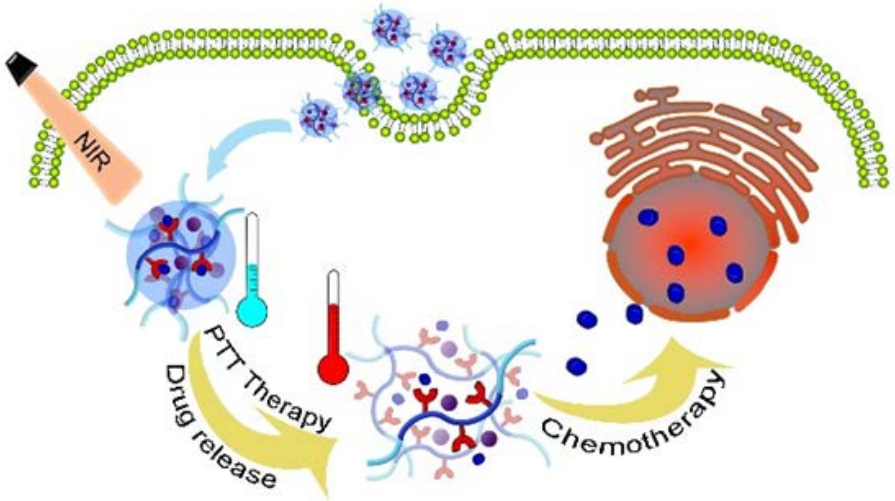
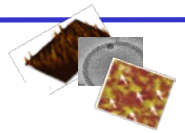




- **PEG/Acrylate Blockcopolymeric Micelles**
- **Load with HCFU via H-bonds**
- **Triggered Release by NIR-irradiation (808 nm)**
- **Enhanced and triggered Availability of the HCFU Drug upon Irradiation**
- **Reduction of Cell Viability by released HCFU**



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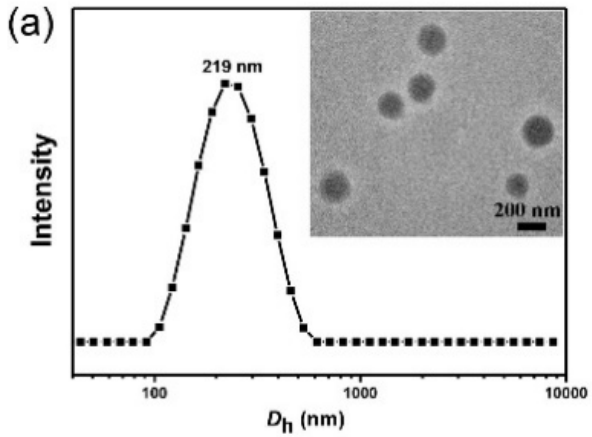
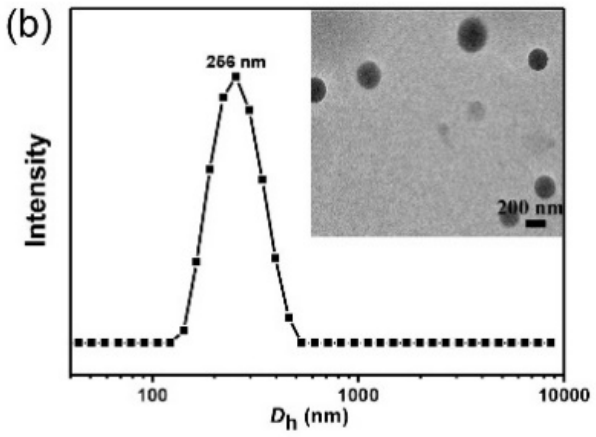
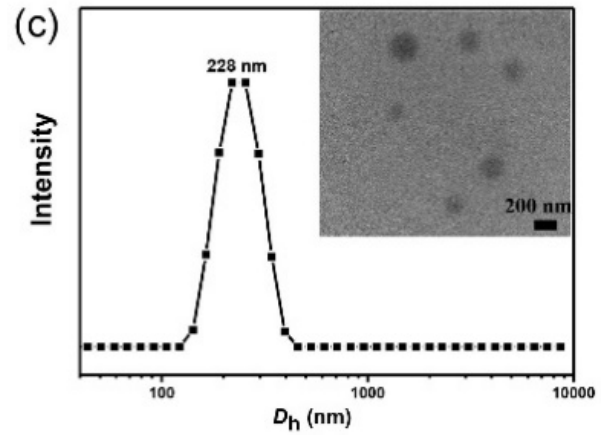
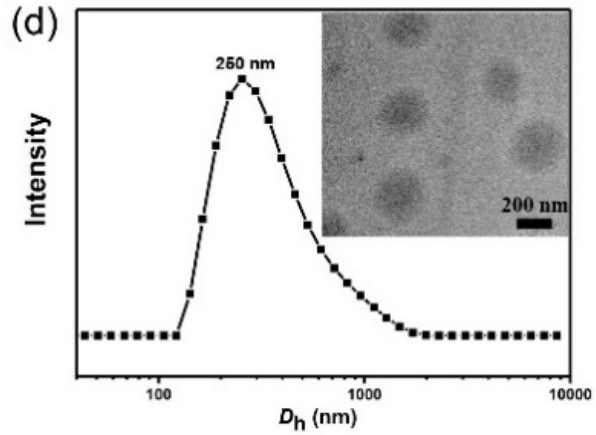
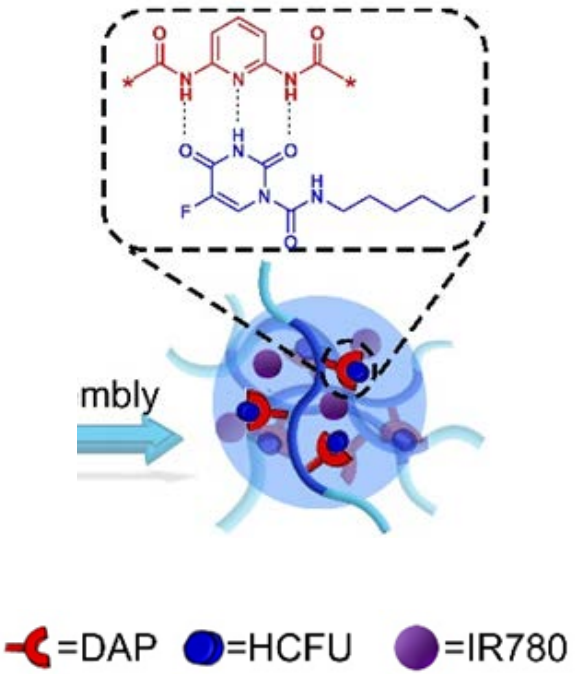
- **Polymeric Micelles sized ~ 200 nm**
- **Bound HCFU via H-bonds inside the micelles**

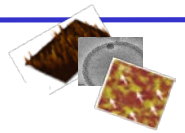












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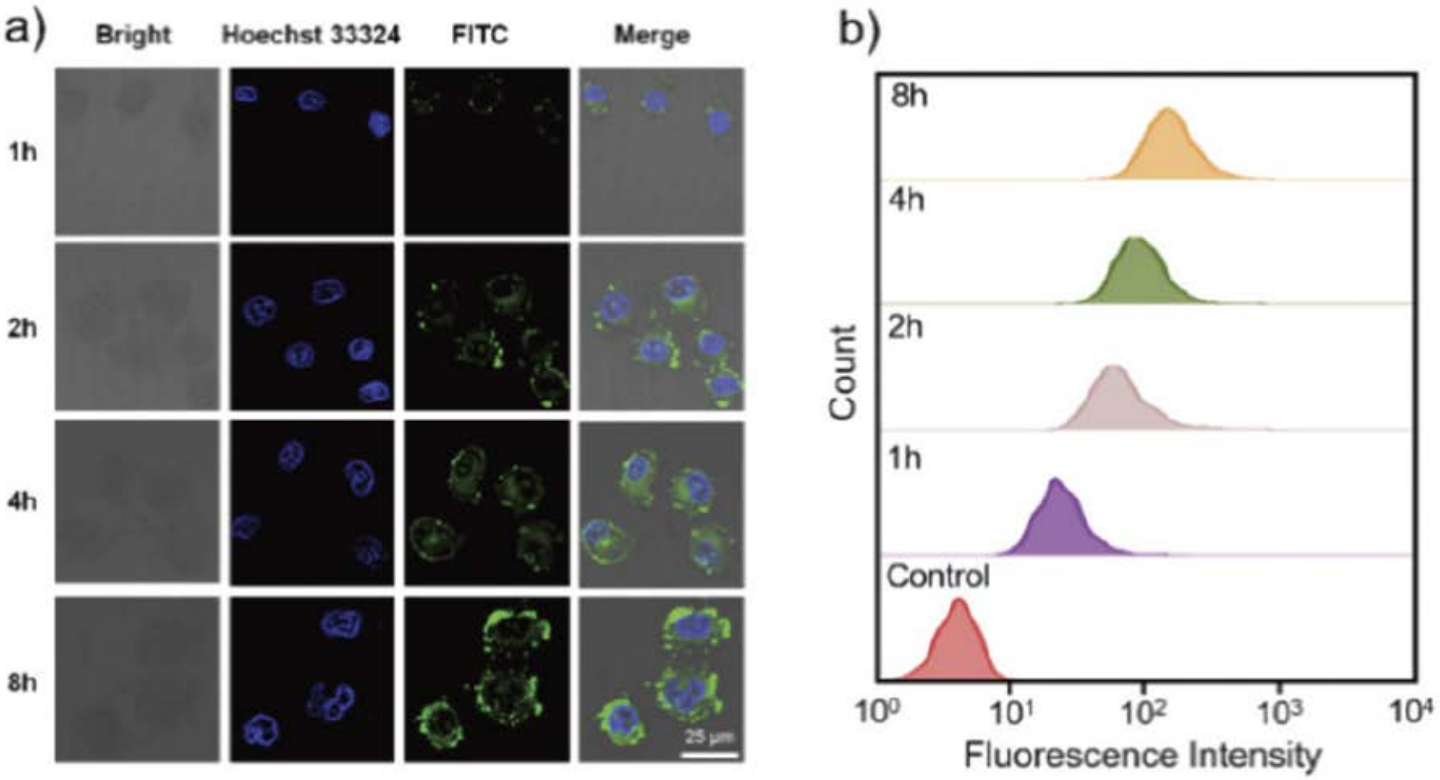
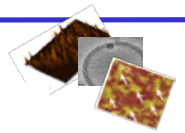
- **CLSM micrographs : Excellent cellular uptake**



CLSM images of the time-dependent cellular uptake of H-bonded supramolecular polymeric micelles (a), and the fluorescence signal intensity extracted from CLSM.



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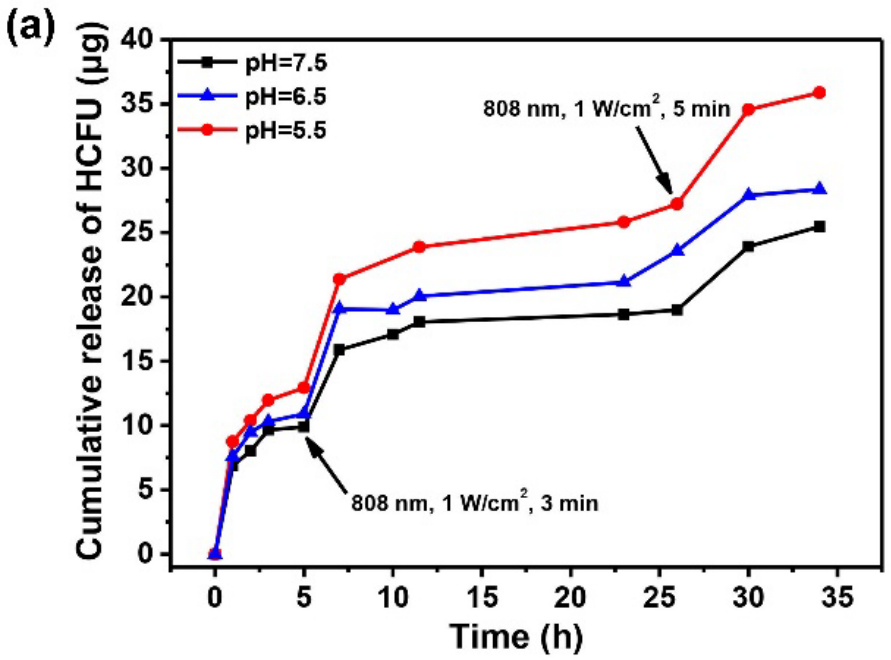
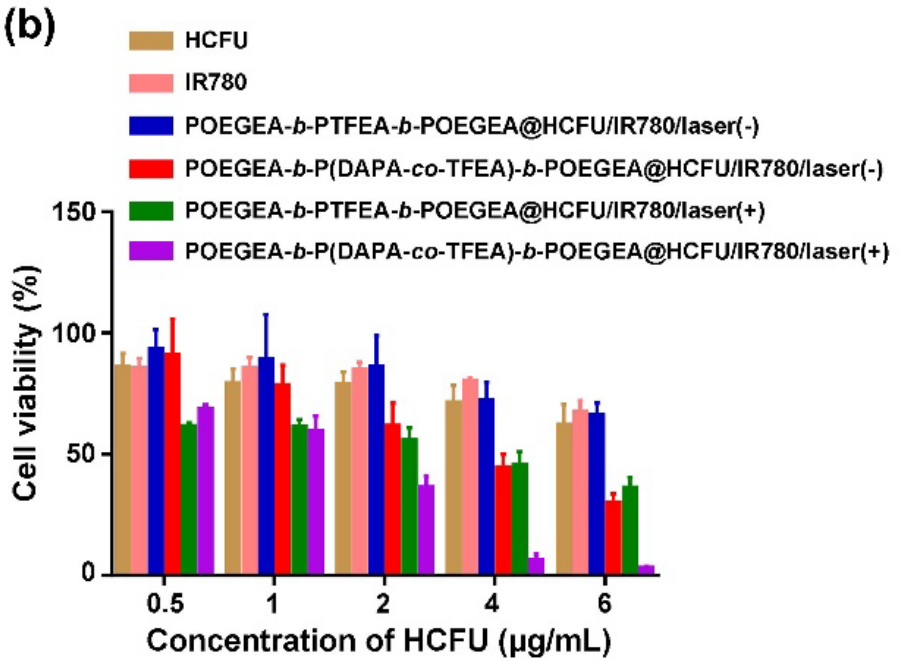
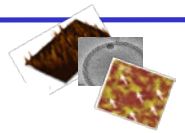
- **Release of HCFU by NIR-irradiation**
- **Reduction of Cell Viability by released HCFU**





In vitro drug release-time profiles for POEGEA-*b*-P(DAPA-*co*-TFEA)-*b*-POEGEA @HCFU/IR780 in PBS buffer at pH 7.5, 6.5 and 5.5 with/without NIR laser irradiation.



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