KLINGER LAB
Polymer Colloids & Nanomaterials

Polymer Particles for (Bio-)materials:

Controlling Function through Chemistry, Morphology, and Shape

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www.klinger-lab.de

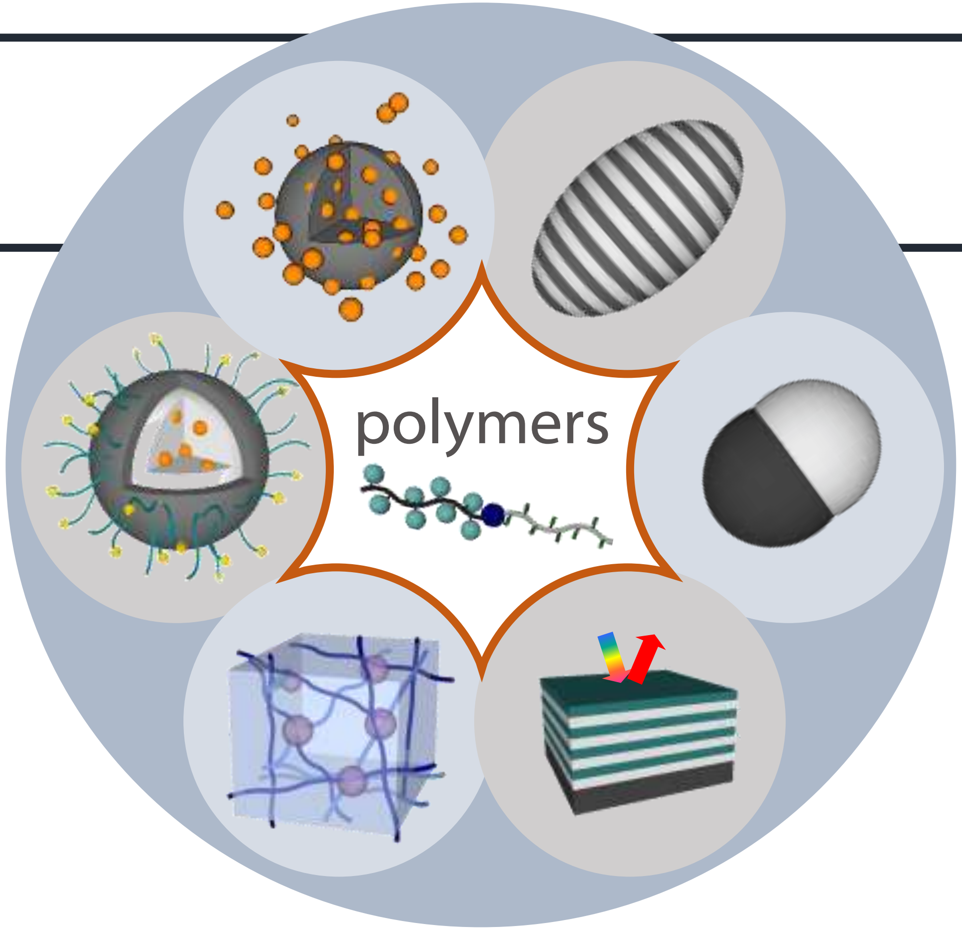
38th APS, Auckland, NZ

Freie Universität Berlin

Functional colloids and nanomaterials

stimuli-responsive
nanogels

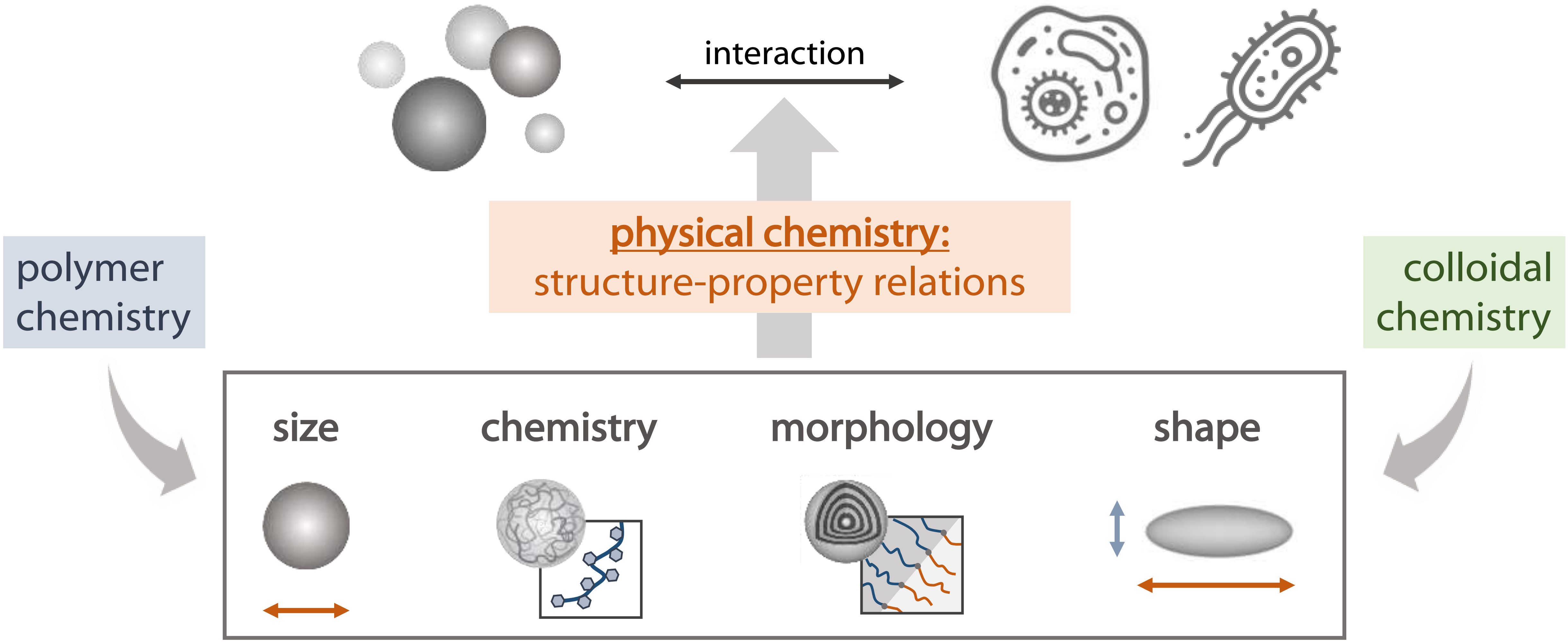
shape anisotropic
nanoparticles



stimuli-responsive
hydrogels

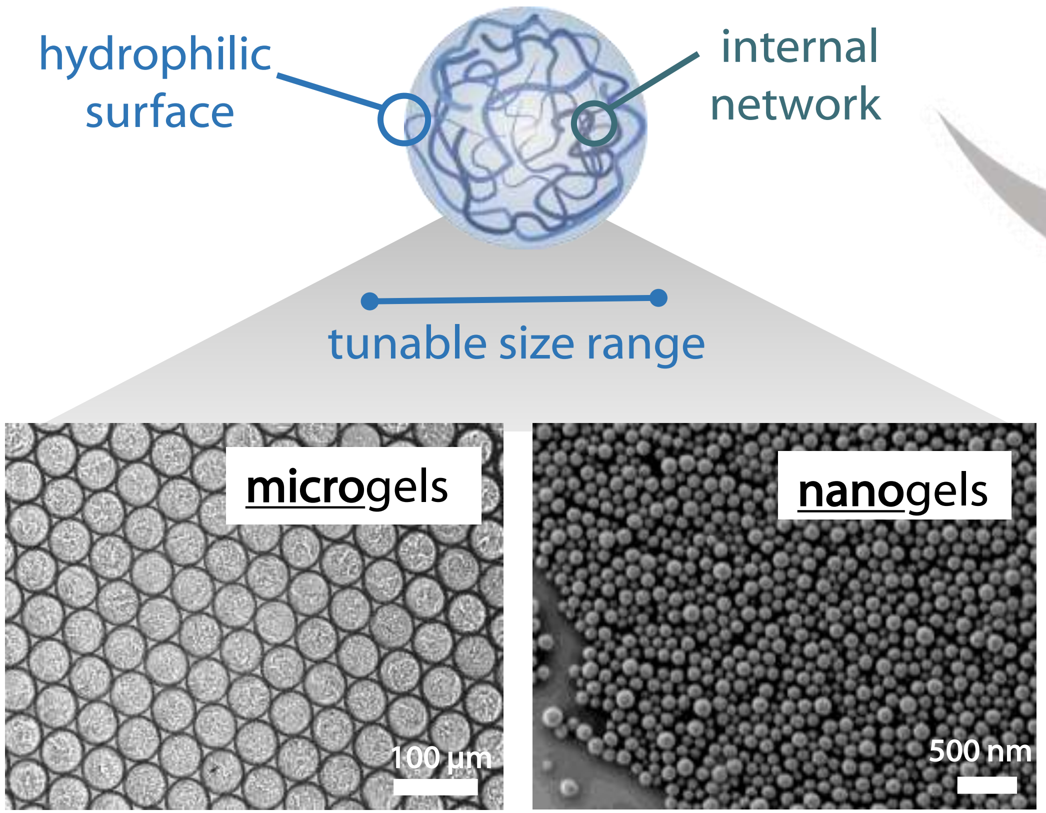
functional
surfaces & coatings

Functional polymer nanoparticles for applied (bio-)materials

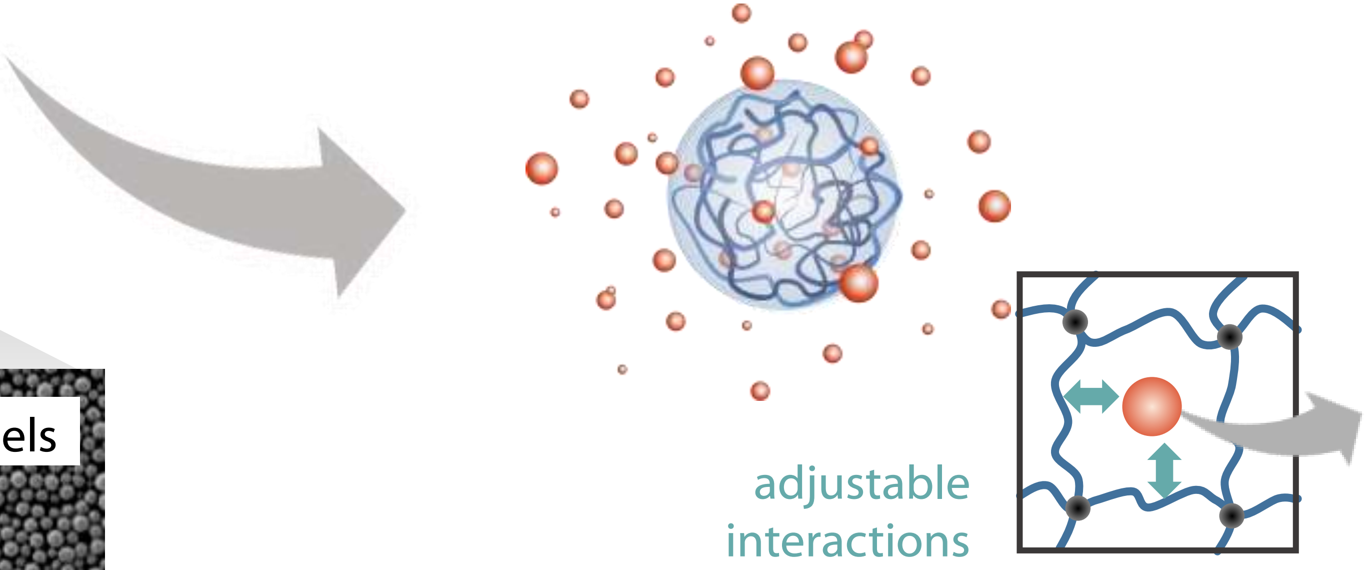


Micro-/Nanogels are polymeric hydrogel particles

biocompatible carriers in various sizes



tunable loading and release through responsive networks

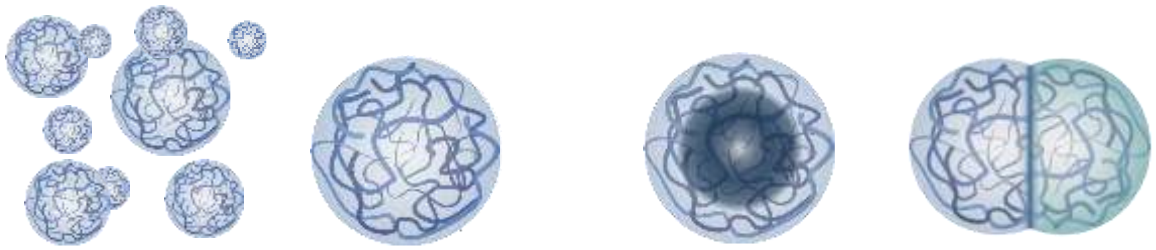


adjusting chemical functionality

Needed: Chemical variation <u>and</u> colloidal comparability

<u>state of the art</u>

tuning chemical functionality also
changes colloidal features

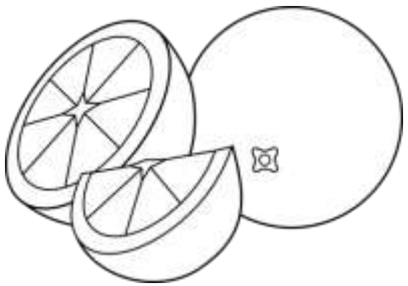


chemical network functionality

?

~~therapeutic potential,~~
~~structure-property relations~~

vs.



Needed: Chemical variation and colloidal comparability

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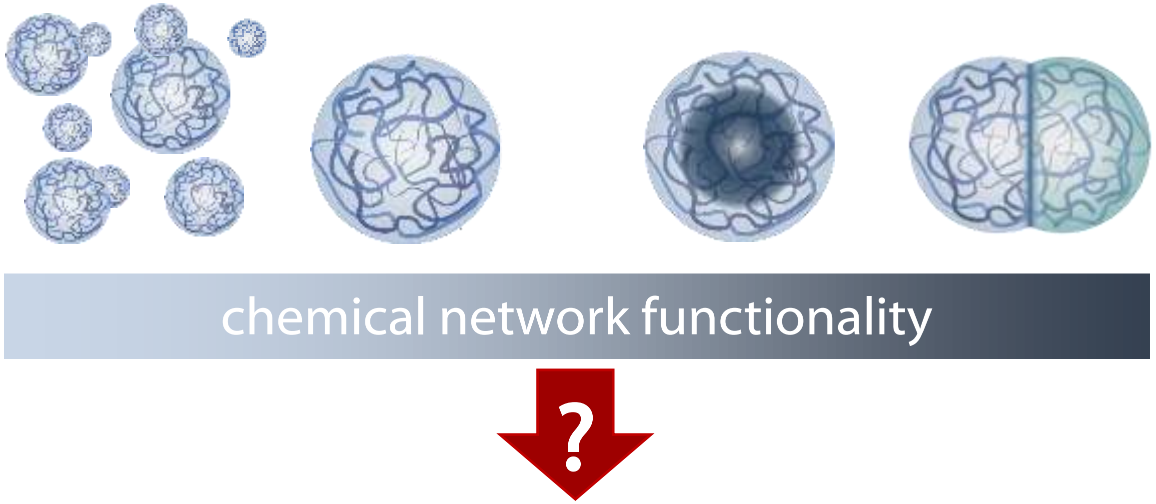
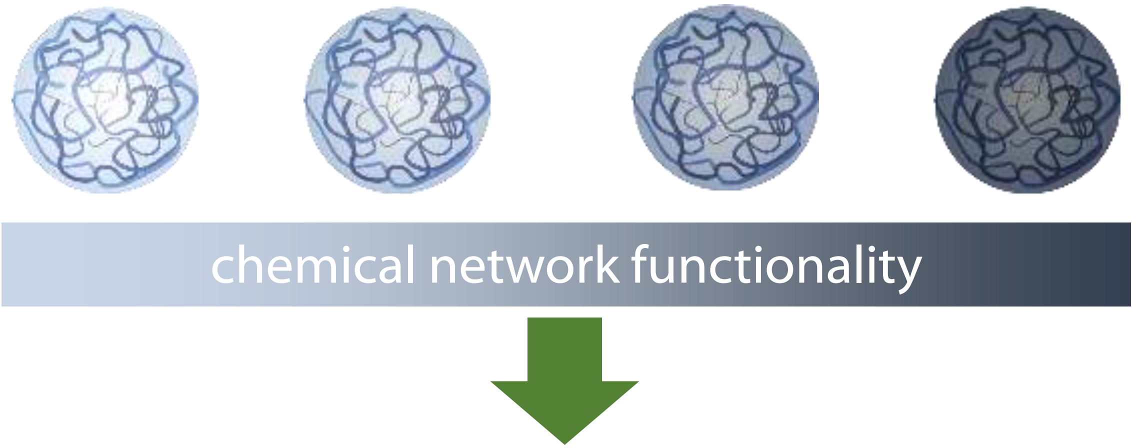


therapeutic potential, structure-property relations

our work

similar colloidal features allow systematic studies

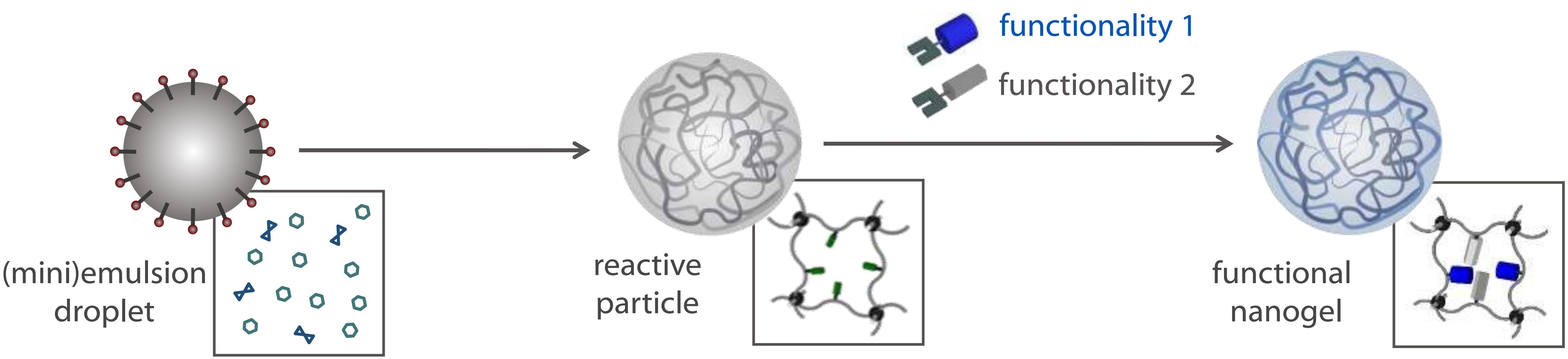


therapeutic potential, structure-property relations

Network functionalization after particle preparation

Step 1:
particle preparation

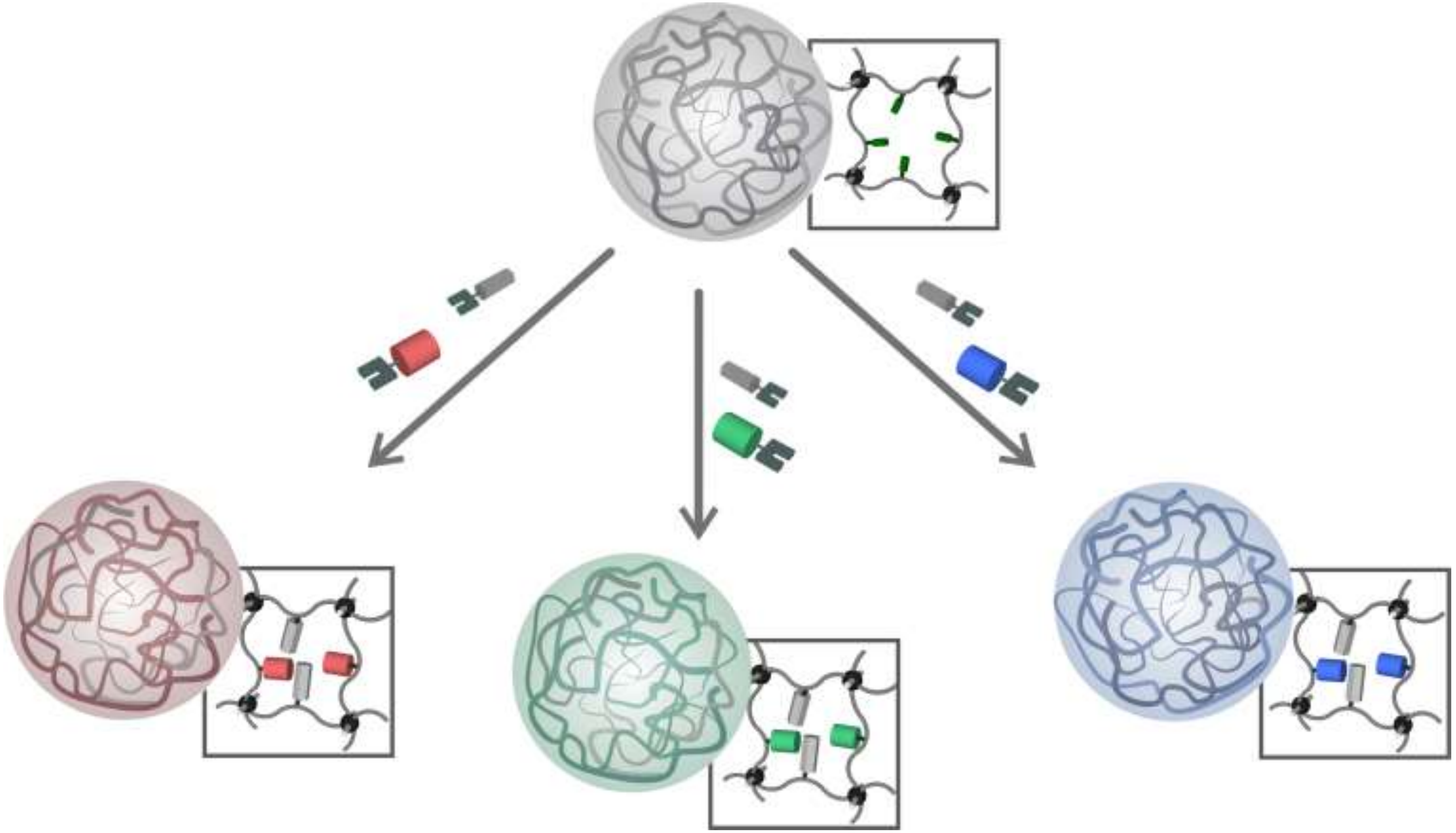
Step 2:
particle functionalization



Review:
Adv. Mater. Interf. 2020

A synthetic platform: All particles are created equal

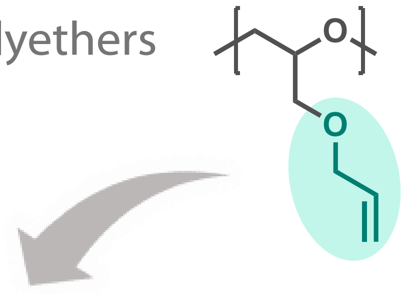
nanogel libraries with comparable colloidal features



Review:
Adv. Mater. Interf. 2020

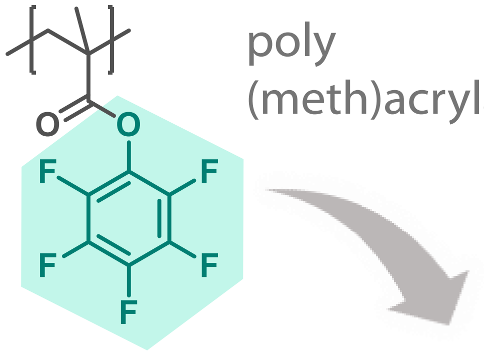
Two synthetic platforms based on different functionalization reactions

polyethers



thiol-ene
functionalization

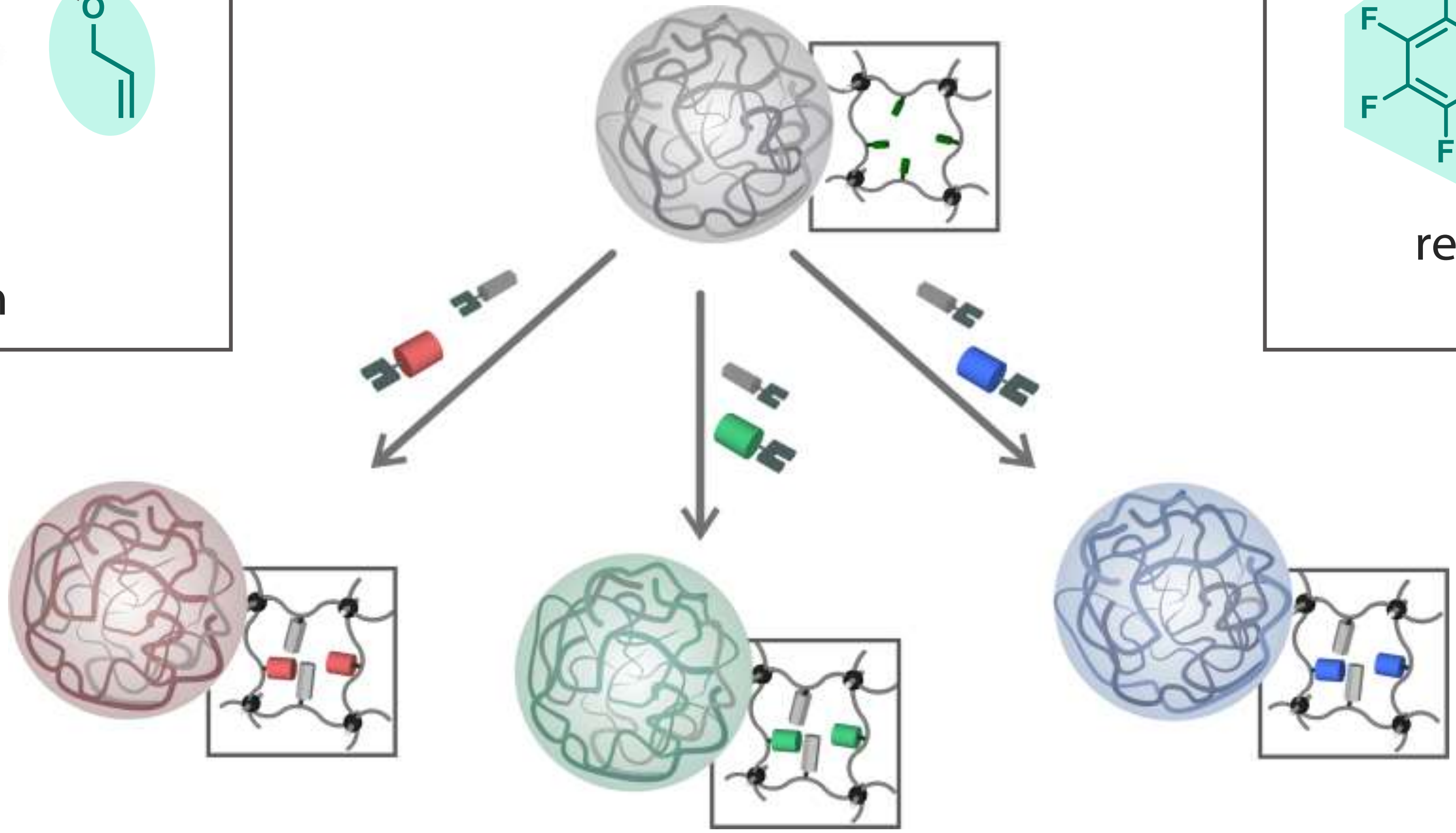
Polym .Chem. 2015



poly
(meth)acrylates

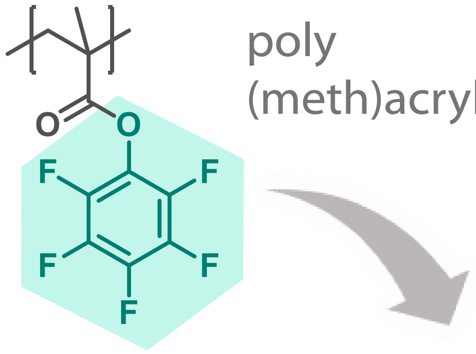
reactive ester-amine
functionalization

Polym .Chem. 2018



Review:
Adv. Mater. Interf. 2020

Well-defined precursor particles through emulsion polymerization



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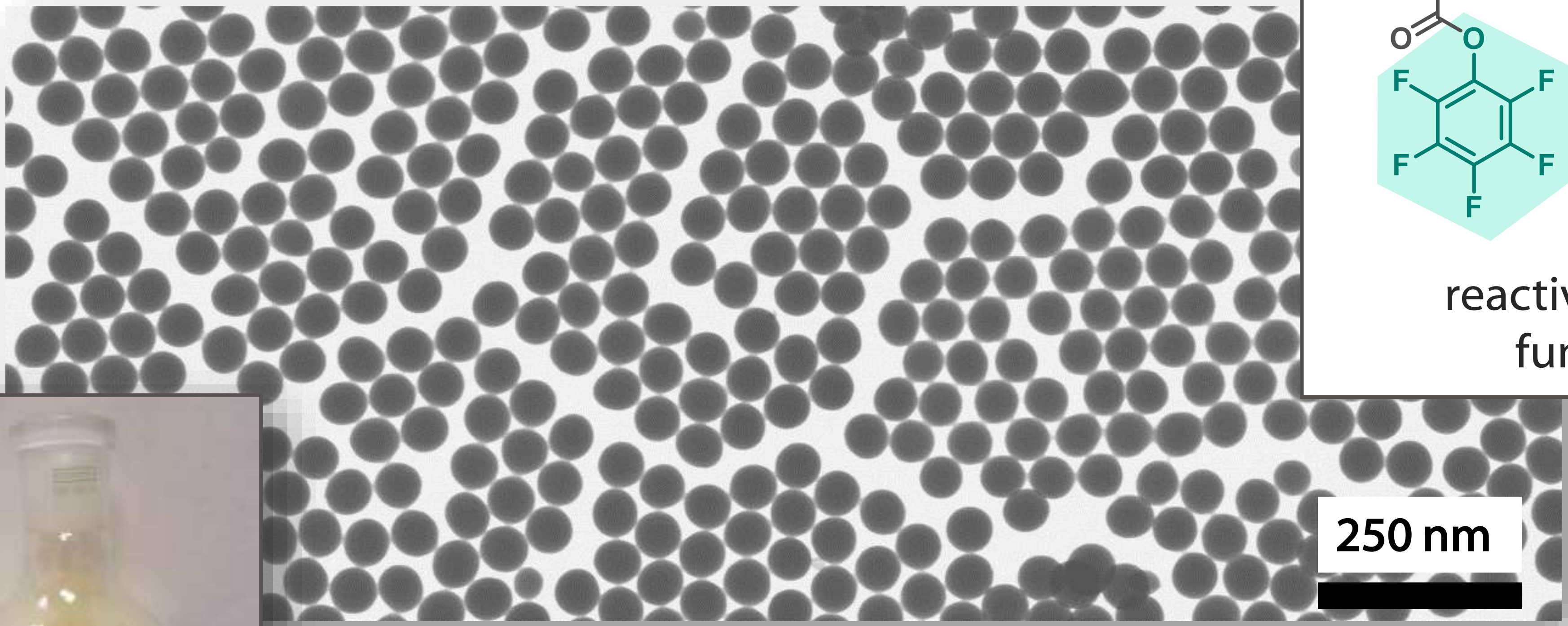


<u>Scalable synthesis</u>

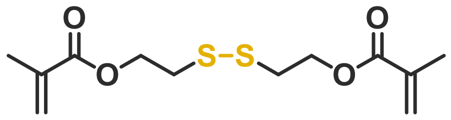
→ standard batch 10-20 g

→ stable storage as powder

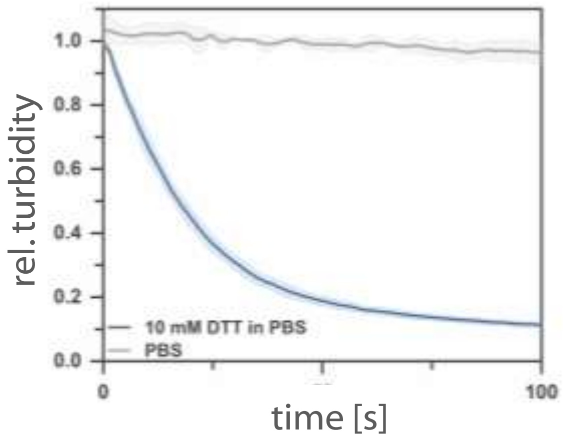
Towards a platform for personalized medicine

network degradability
polymer backbone vs. crosslinkers

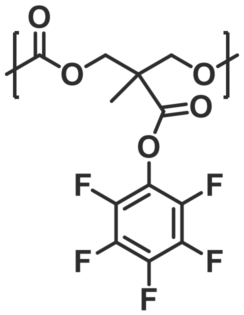
reduction-sensitive
disulfide crosslinker

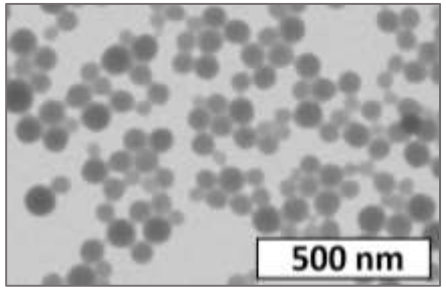


Soft Matter 2021

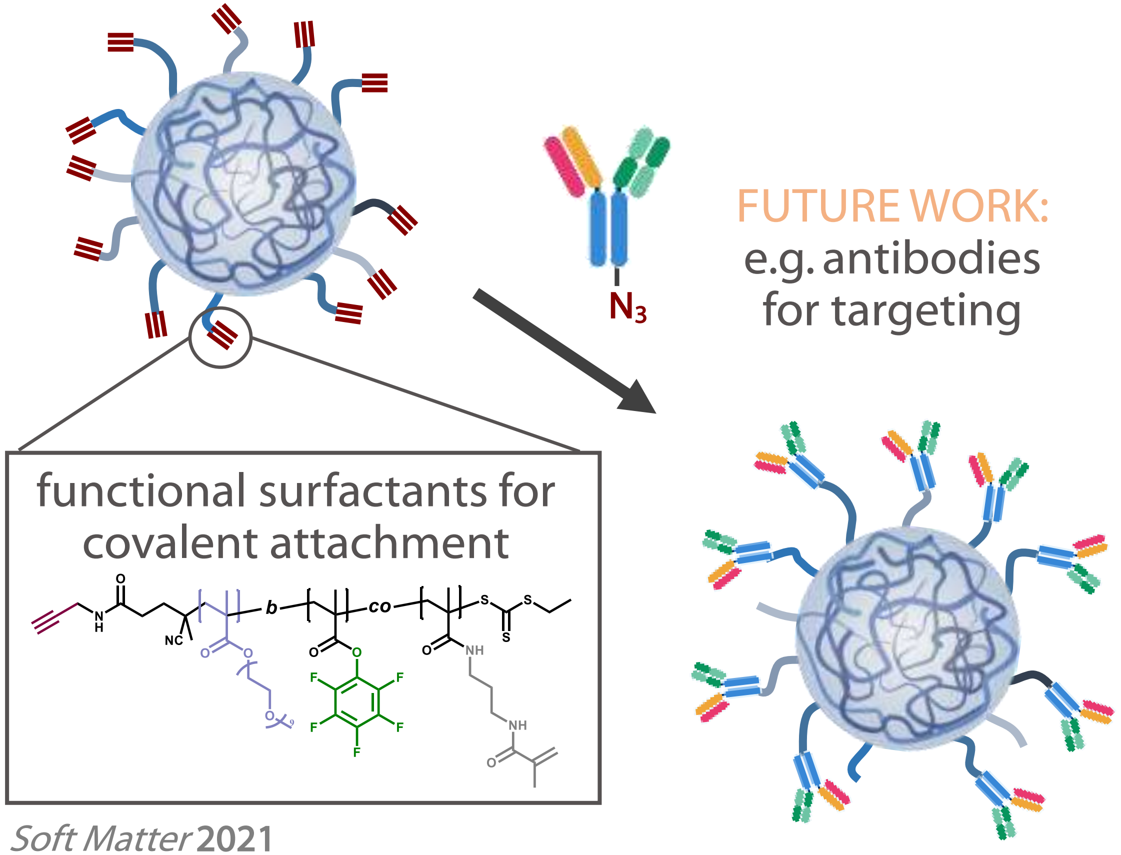


degradable
aliphatic
polycarbonates





orthogonal surface
"click" functionalization



Soft Matter 2021

Amphiphilic Nanogels for Drug Delivery

Hydrogel particles with hydrophobic domains

Hydrophobicity of drugs can result in low bioavailability

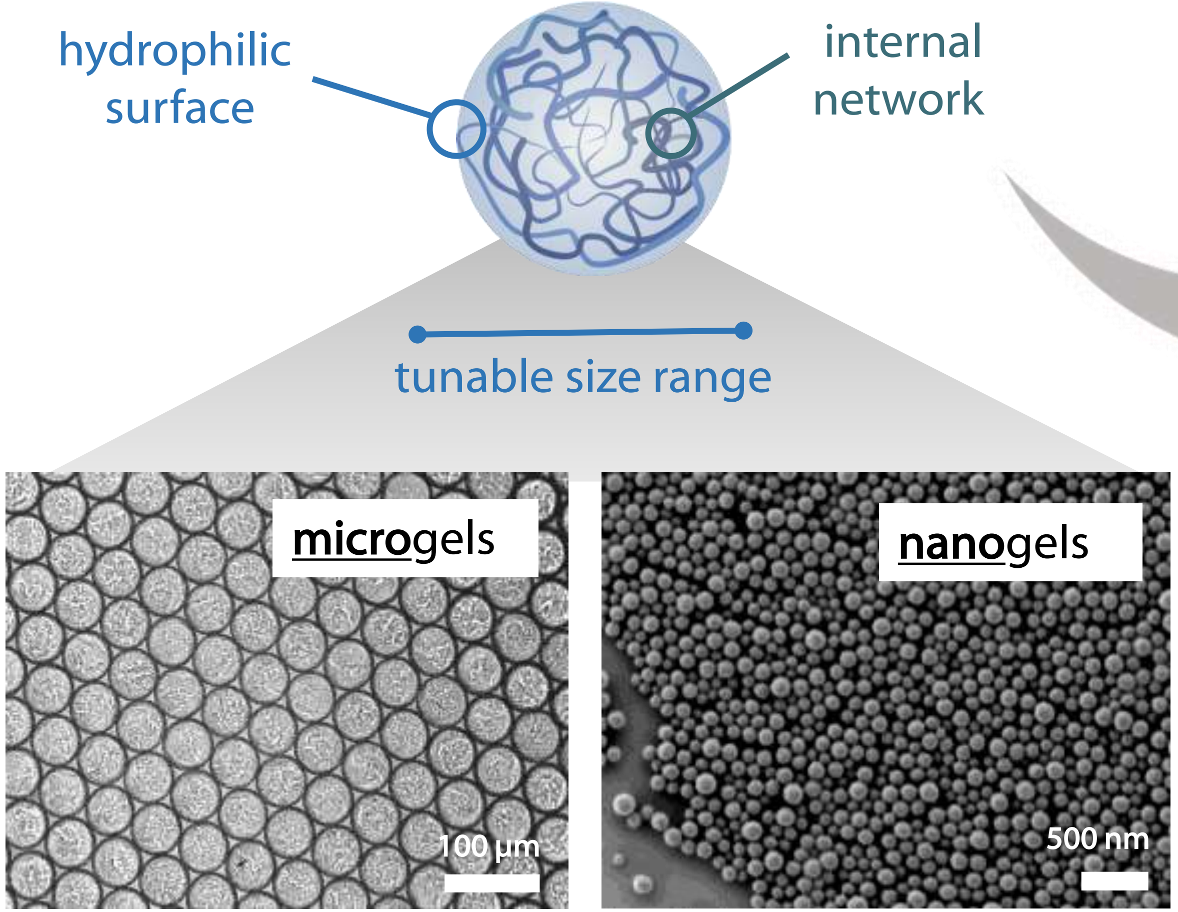
hydrophilic

hydrophobic

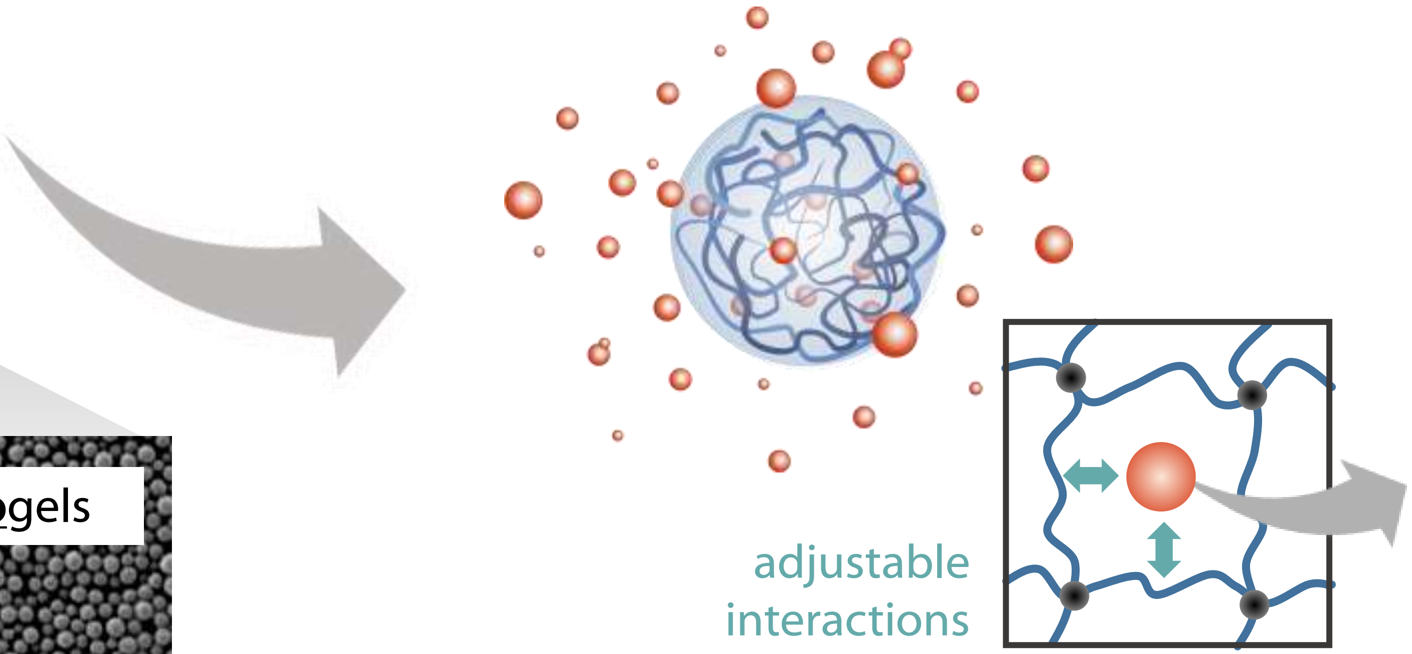
high bioavailability low

Micro-/Nanogels are polymeric hydrogel particles

biocompatible carriers in various sizes

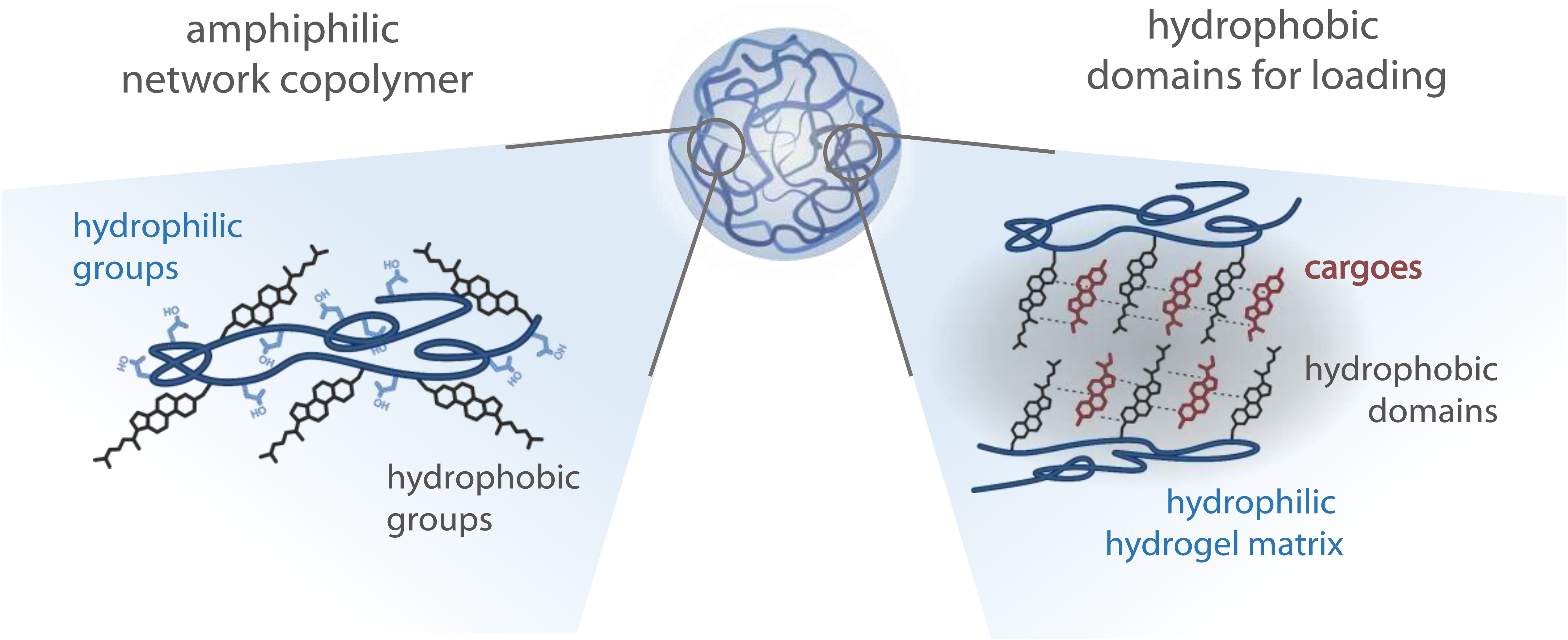


tunable loading and release through functional networks



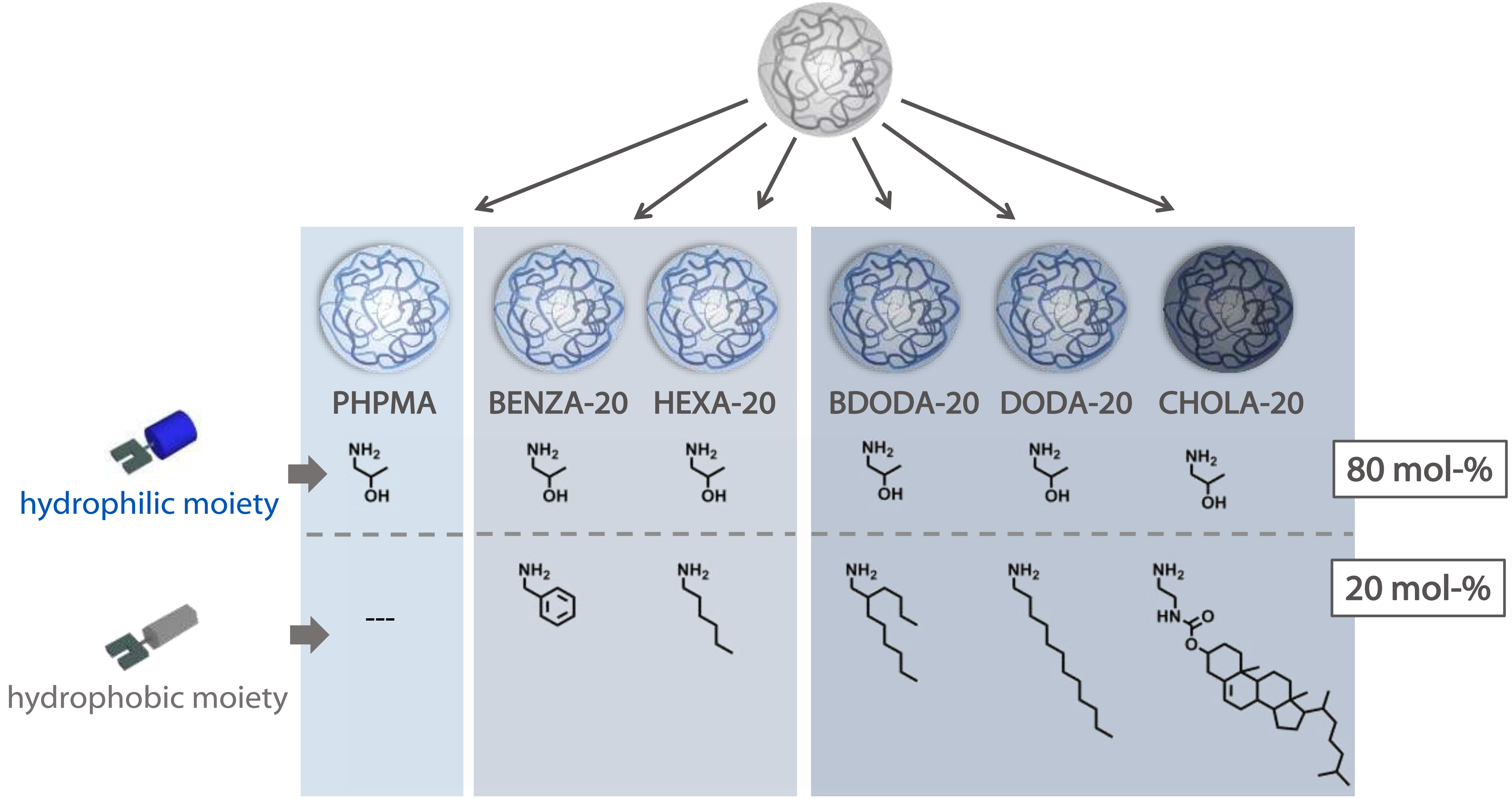
limited to hydrophilic drugs !

Amphiphilic nanogels (ANG) are versatile new colloidal materials



Review:
J. Polym. Sci. 2021

A small library of particles with varying amphiphilicity



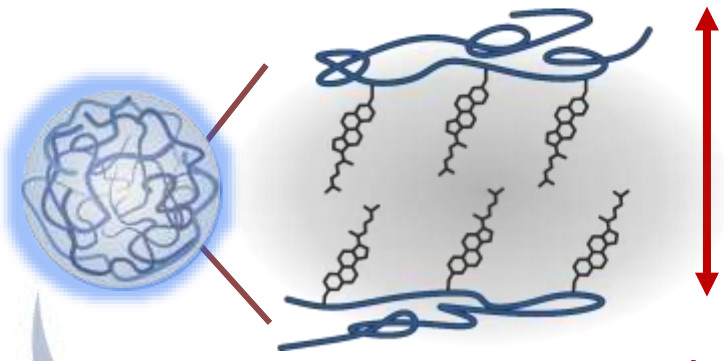
Polym. Chem. 2018

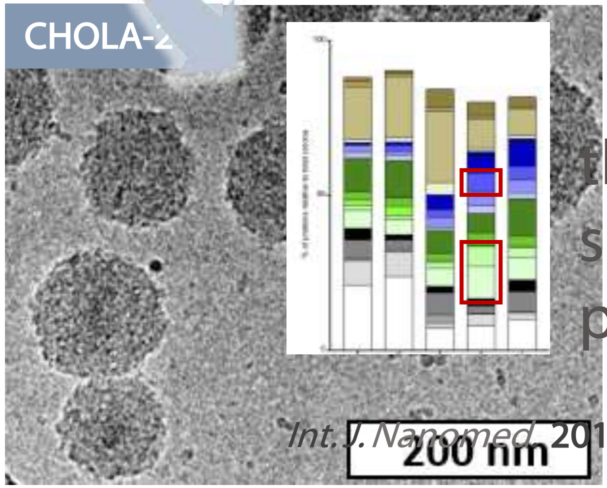
Amphiphilic network results in internal hydrophobic domains

AG Thünemann
BAM Berlin

internal hydrophobic domains

SAXS



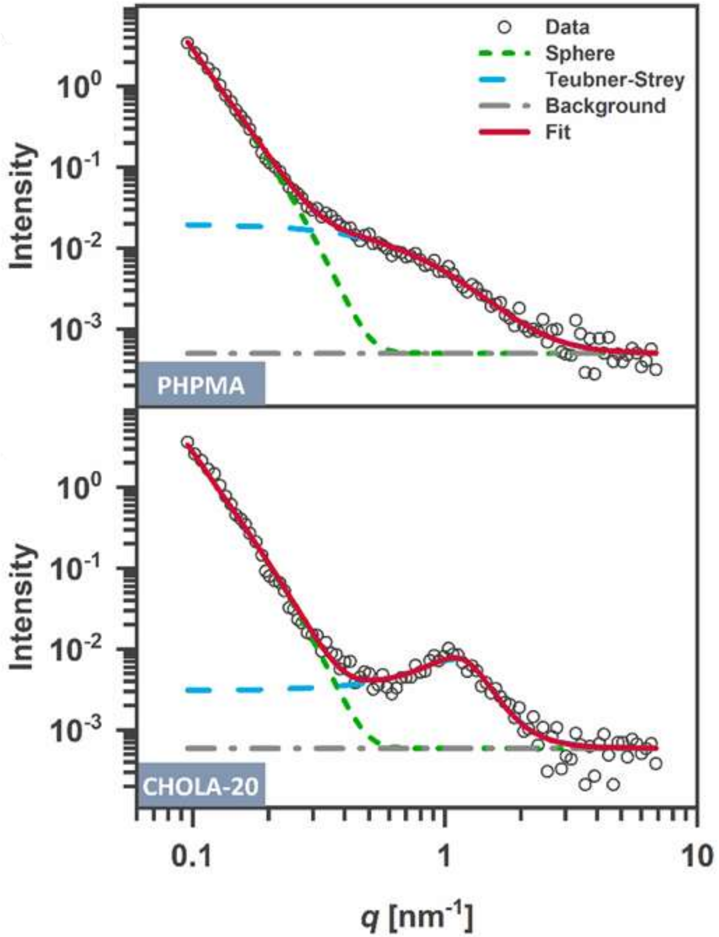


thin fuzzy surface governs protein corona

cryo-TEM shows nanoscopic homogeneity

Int. J. Nanomed. 2019

Polym. Chem. 2018



hydrophilic

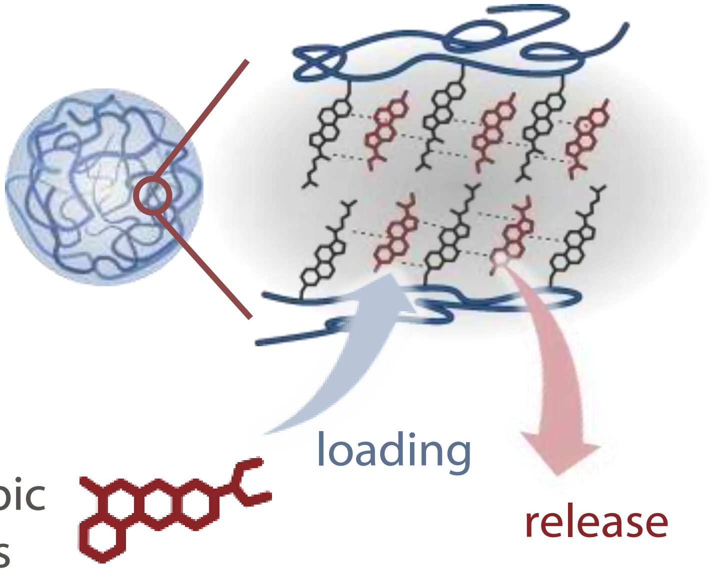
amphiphilic

Langmuir 2020

Different compartments are loaded with hydrophobic compounds

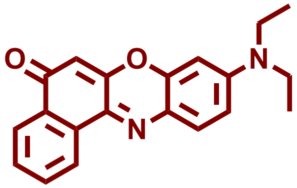
AG Resch-Genger
BAM Berlin

interaction of network with cargoes



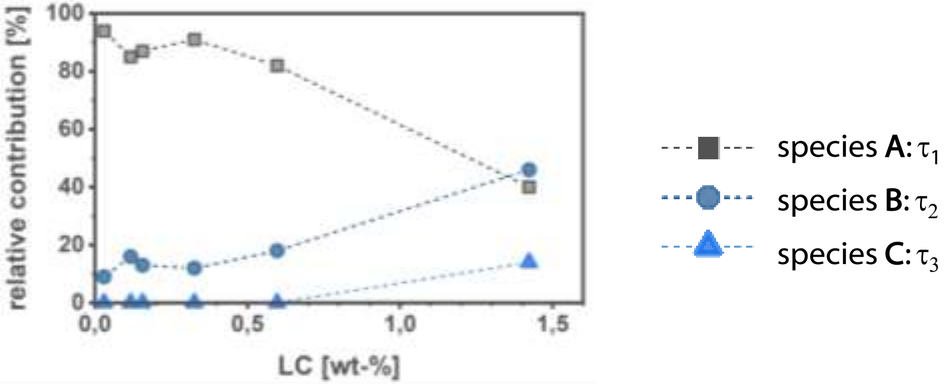
hydrophobic
drugs/dyes

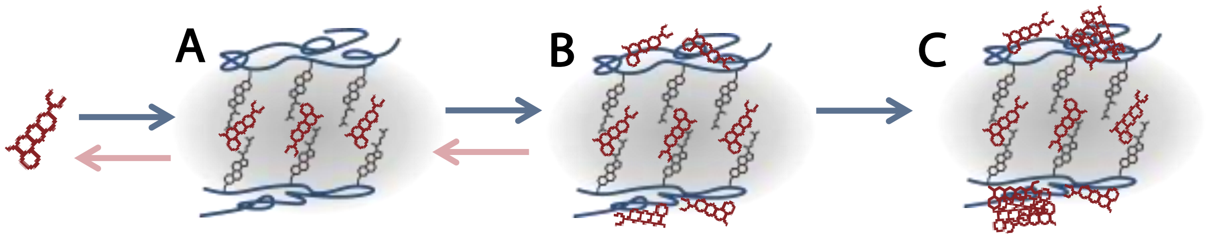
solvatochromic
Nile red



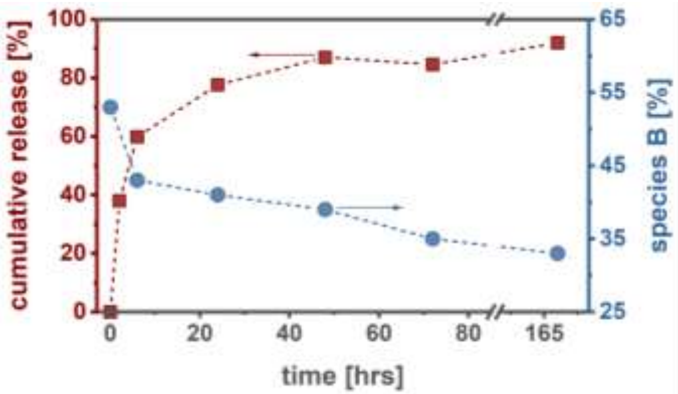
fluorescence lifetime

loading



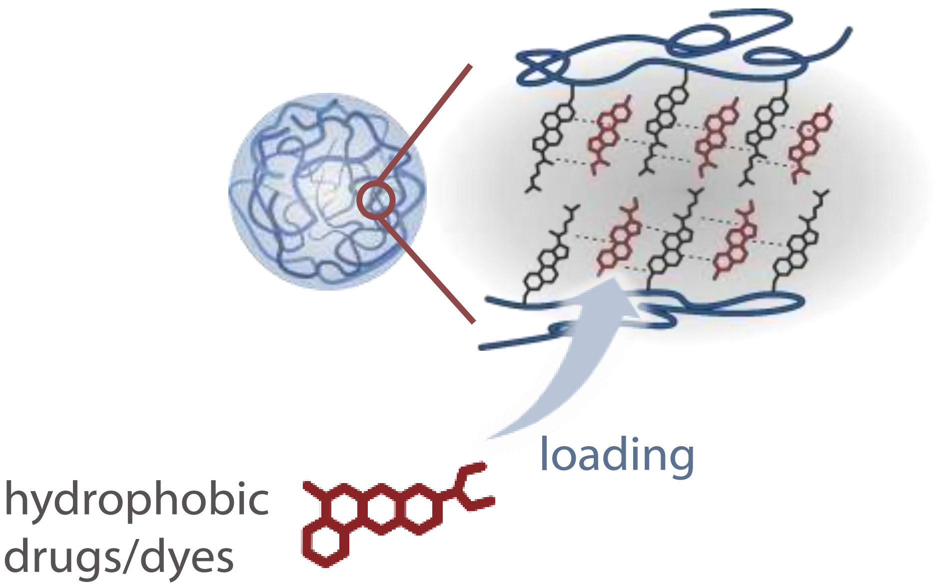


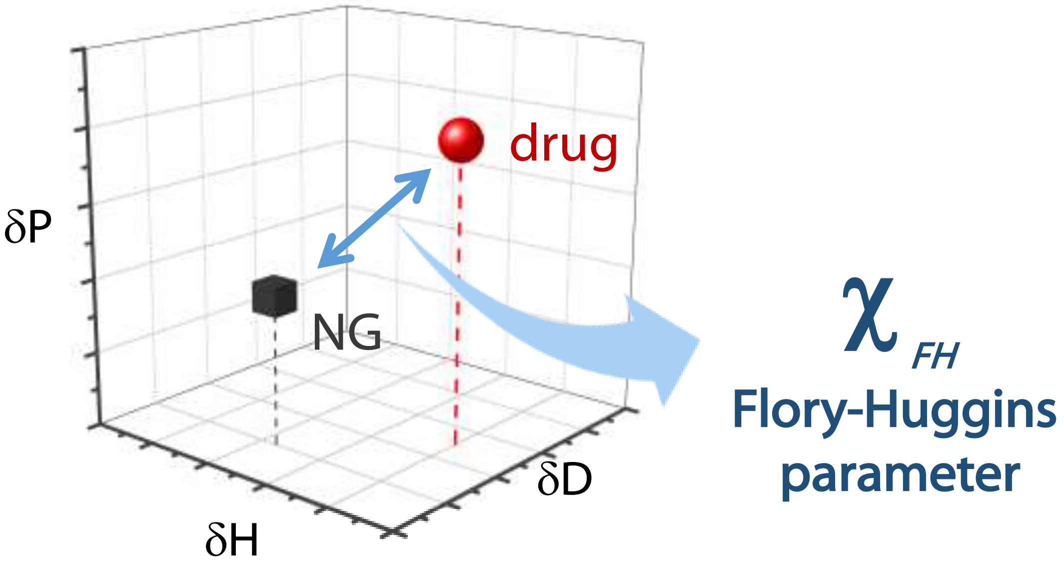
release



Predicting LC with Flory-Huggins parameters?

interaction of network with cargoes → numerical values



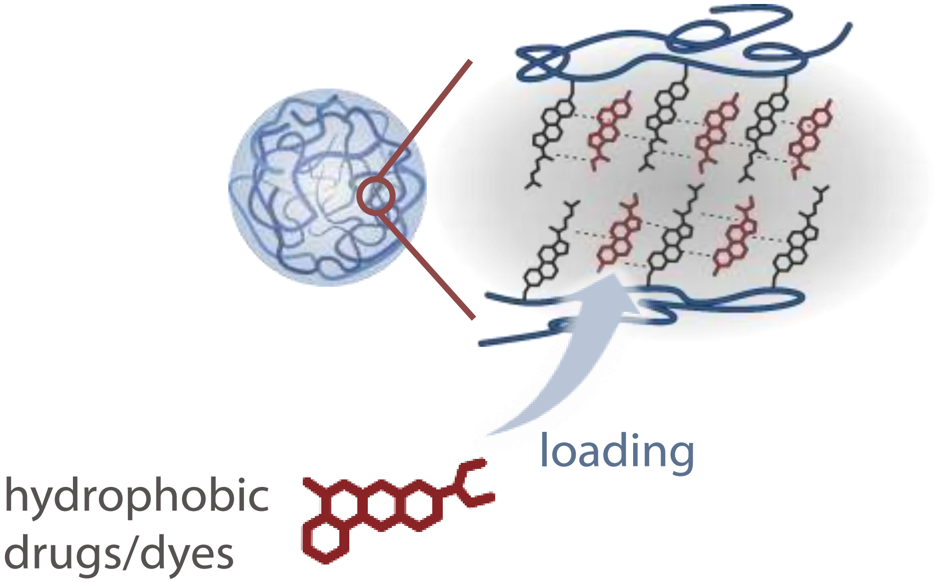


library

BERB:	berberine	**MLX:**	meloxicam
CUM:	coumarine	**PTX:**	paclitaxel
CUR:	curcumine	**TMS:**	telmisartan
DEX:	dexamethasone	**NILE:**	nile red
EFV:	efavirenz	**SUD I:**	sudan I
LOT:	loteprednol	**IND:**	indigo

Good correlation when combining one drug with different NGs

interaction of network with cargoes



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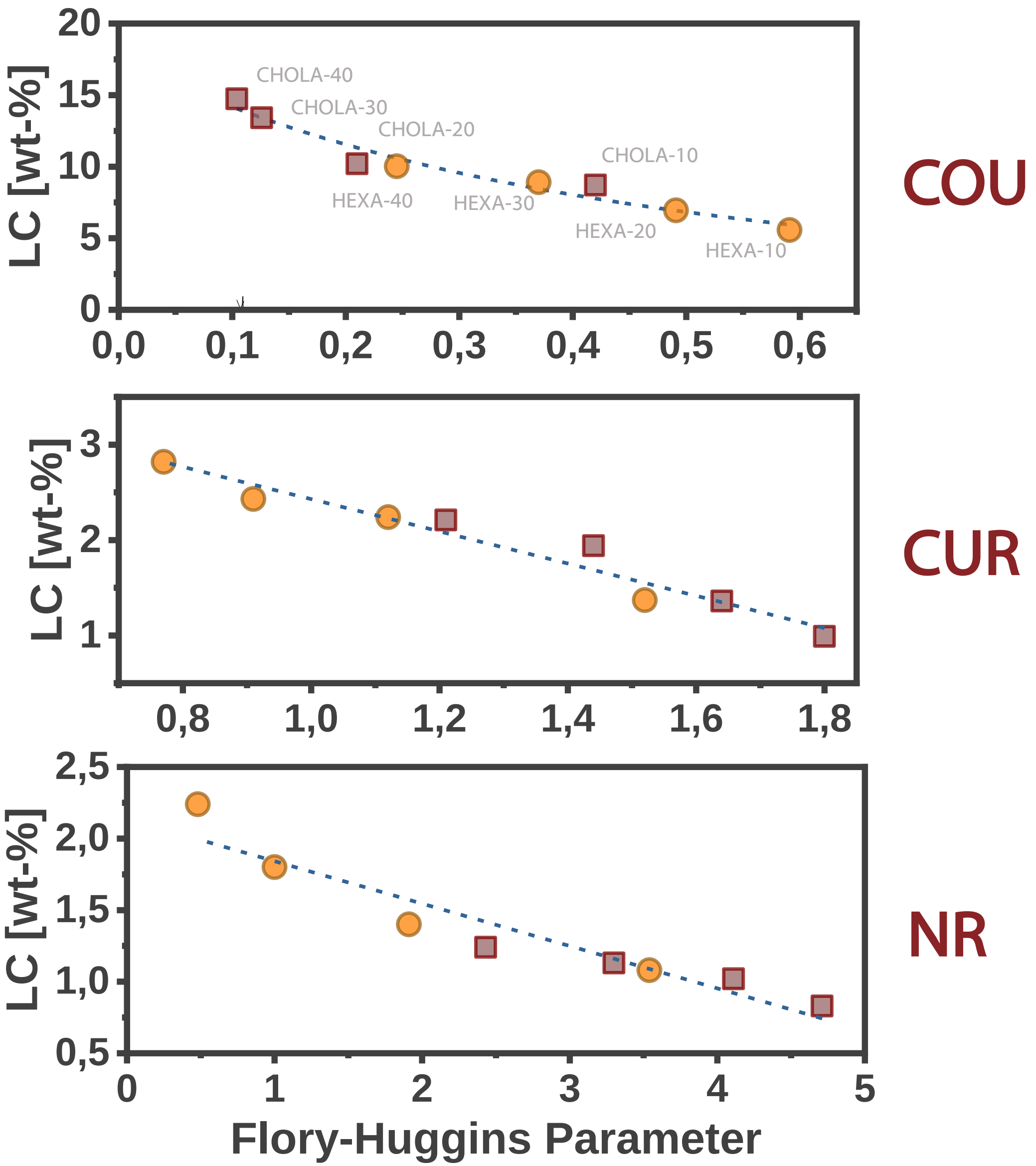
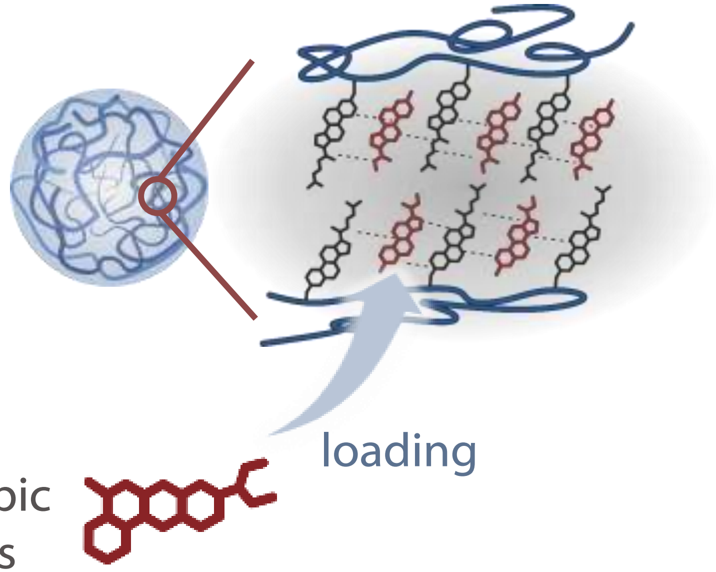
same drug – different nanogels



Selection of the best nanogel for a given drug is possible

interaction of network with cargoes



hydrophobic drugs/dyes

library

BERB:	berberine	MLX:	meloxicam
COU:	coumarine	PTX:	paclitaxel
CUR:	curcumine	TMS:	telmisartan
DEX:	dexamethasone	NILE:	nile red
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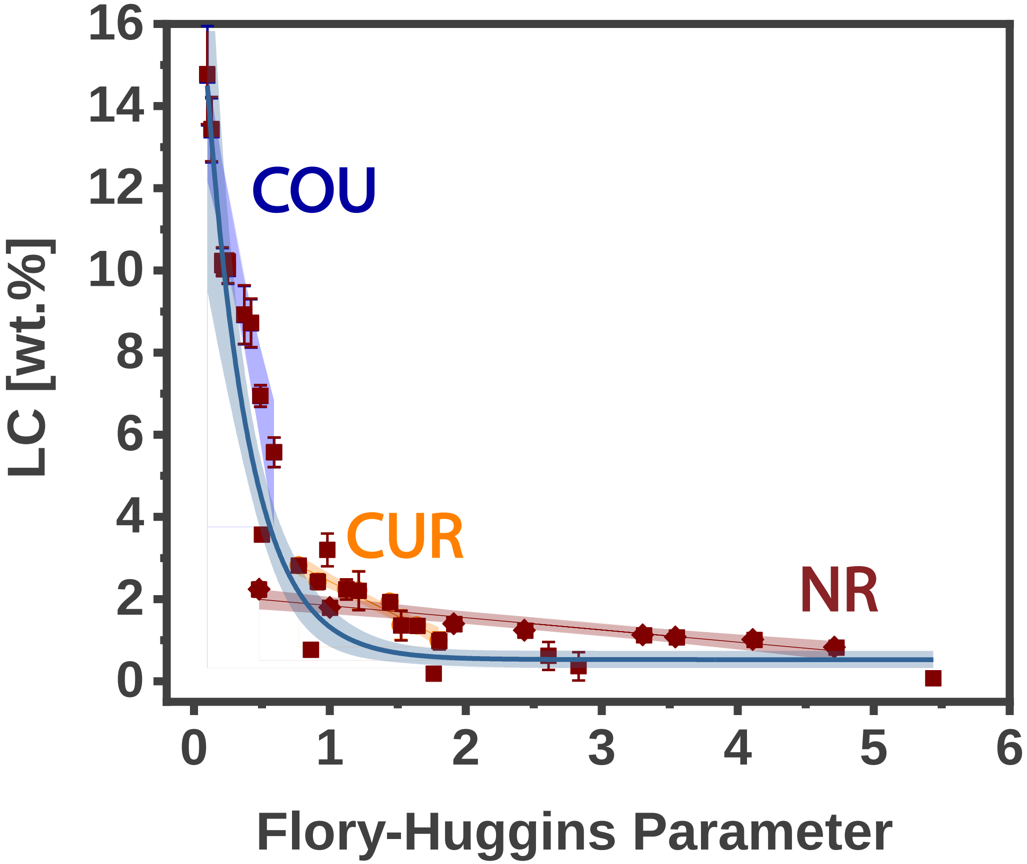
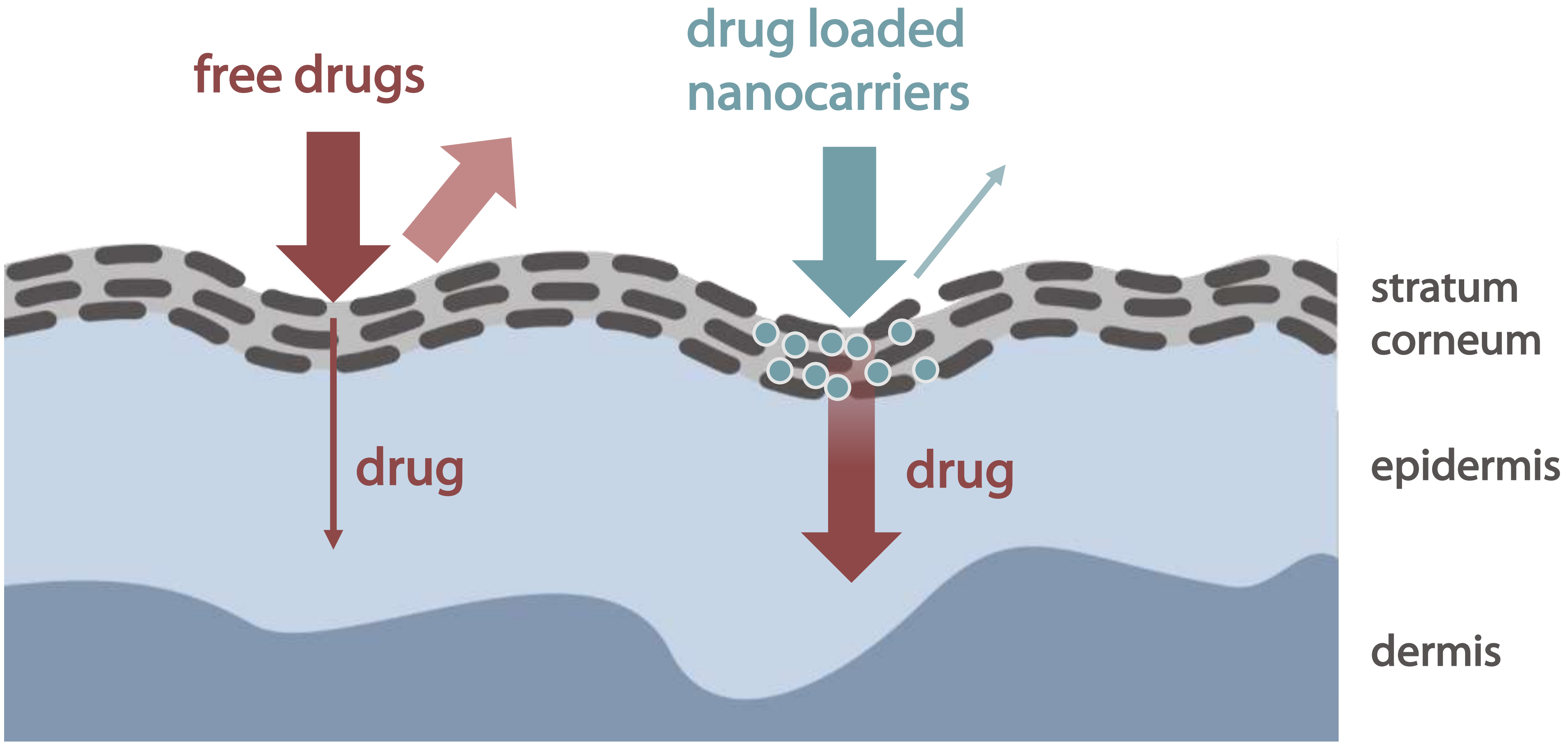


submitted

Nanocarriers for passive dermal delivery of hydrophobic drugs

Formation of depots in the stratum corneum



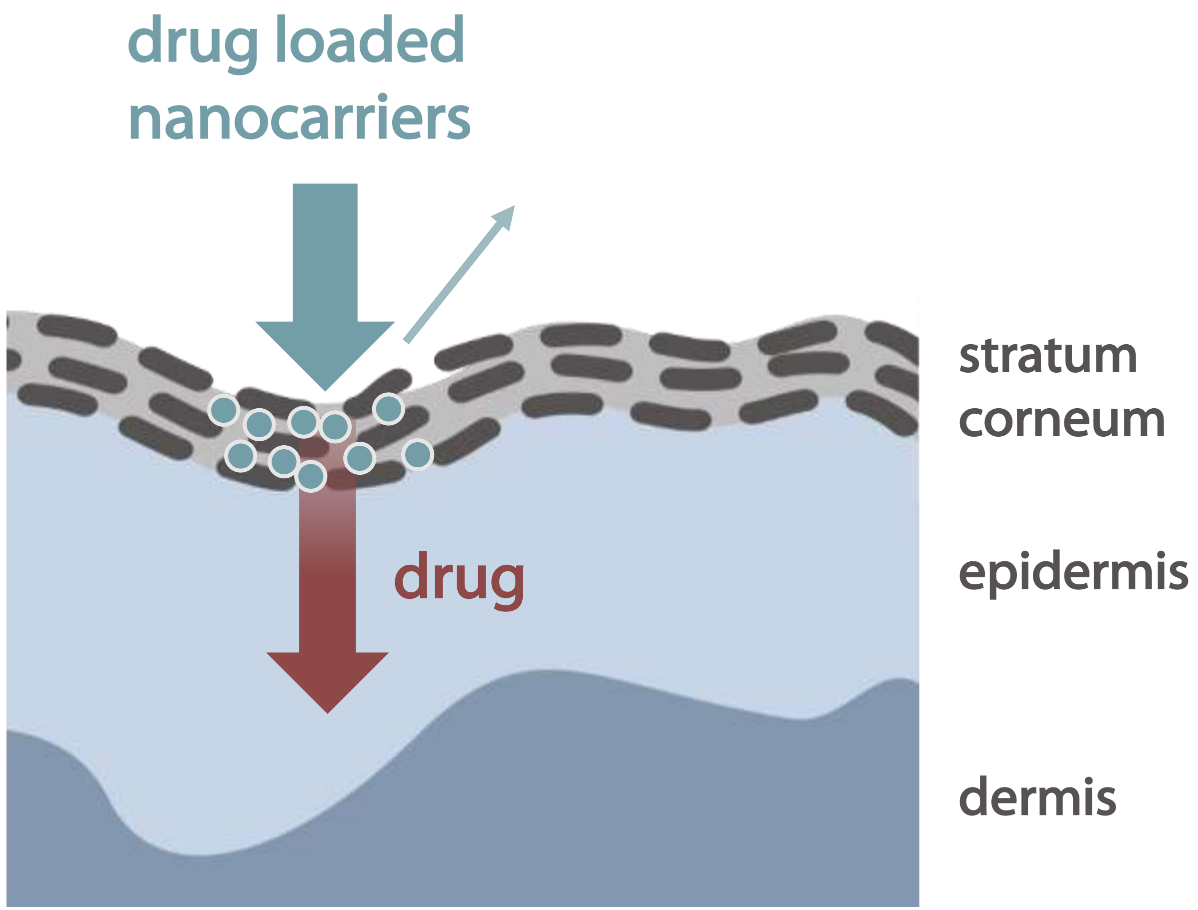
Nanocarriers for passive dermal delivery of hydrophobic drugs

Formation of depots in the stratum corneum

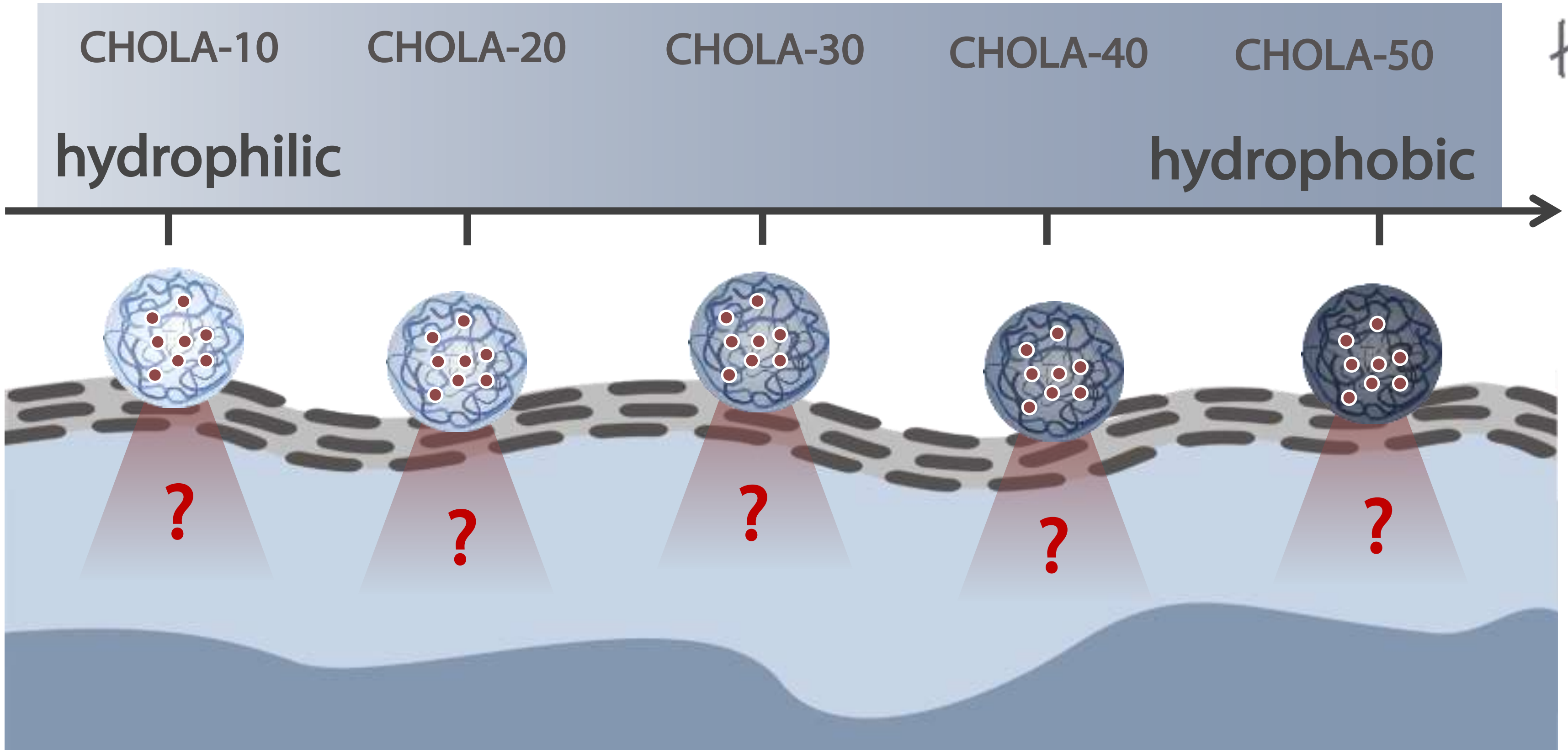
Influencing factors:

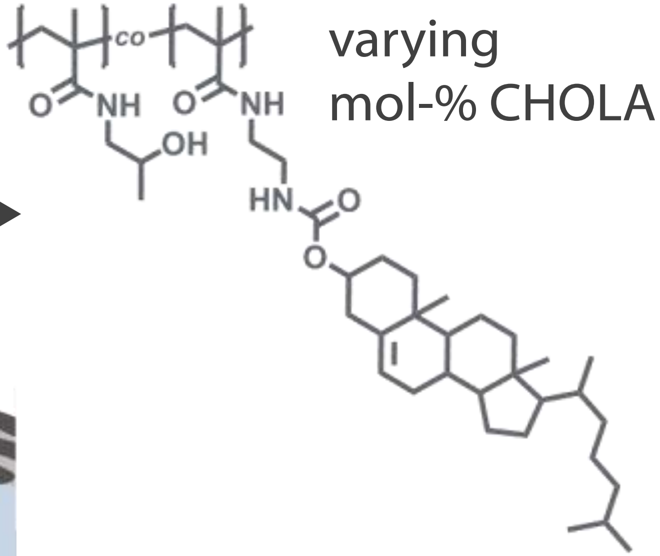
- Barrier hydration
- Carrier anchoring
- Drug release

nanogel amphiphilicity



Dermal delivery: influence of nanogel hydrophobicity on skin interaction



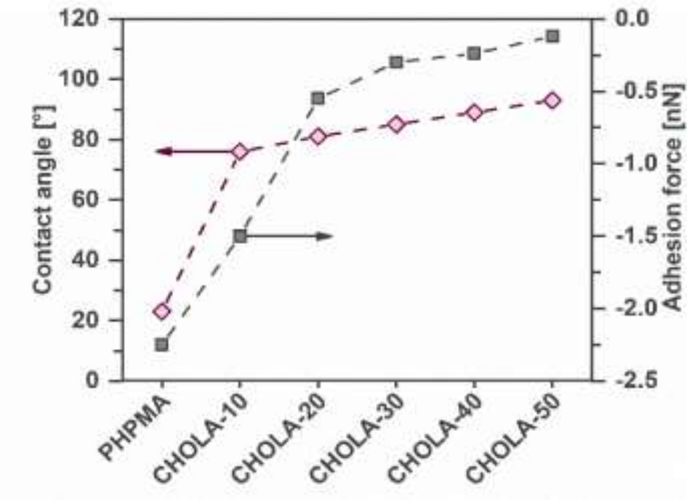


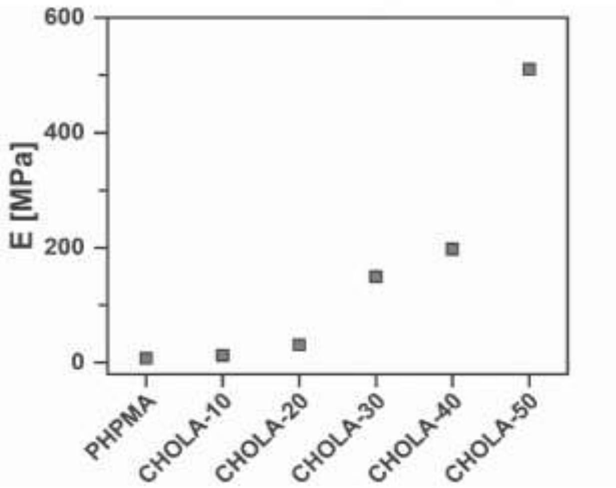
varying mol-% CHOLA

Influence of CHOLA content on dermal delivery?

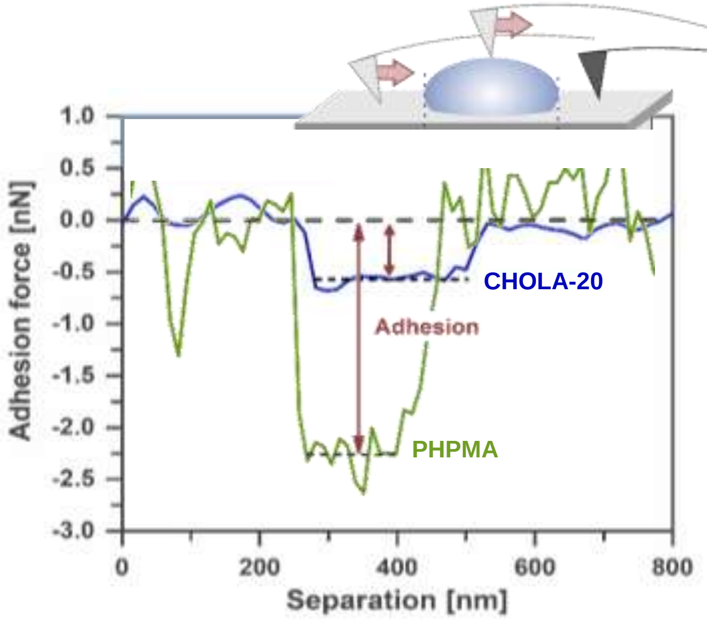
Balancing surface hydrophobicity and network rigidity for efficient delivery

surface hydrophobicity

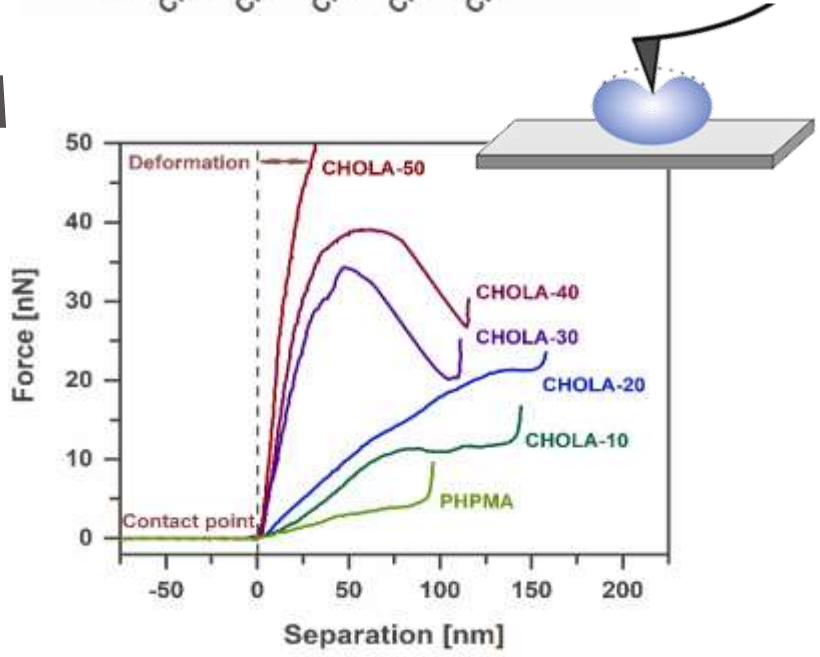




internal network rigidity



AFM

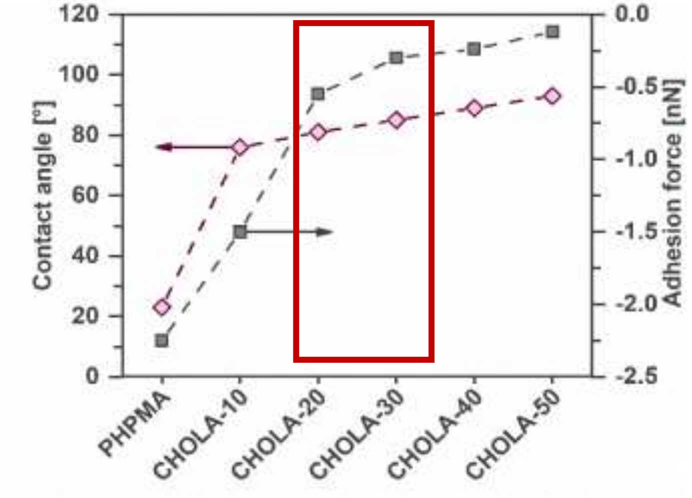


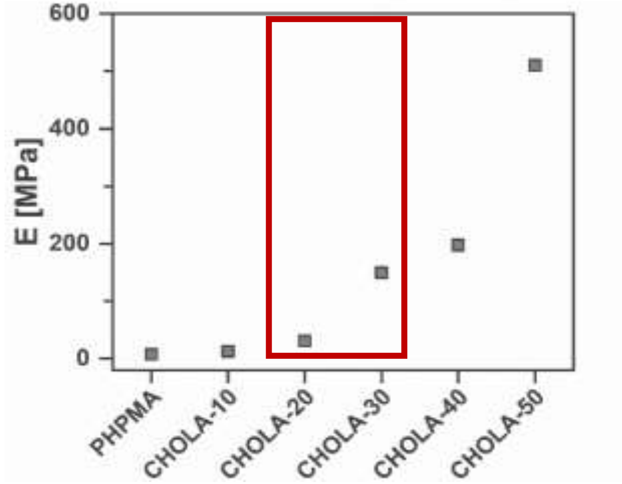
Biomacromolecules 2021

Balancing surface hydrophobicity and network rigidity for efficient delivery

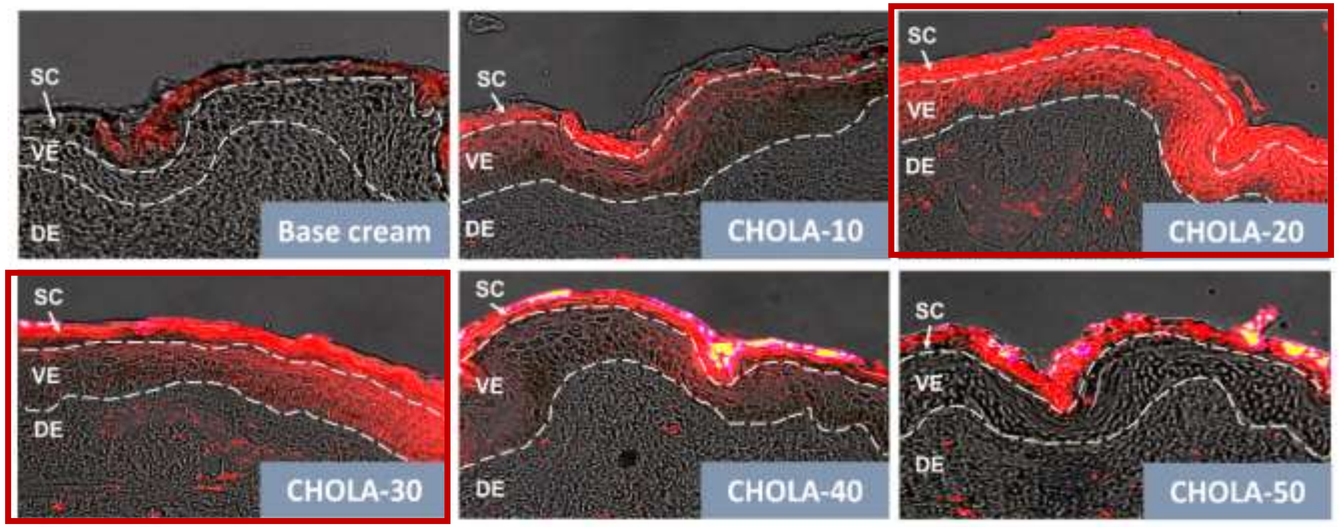
AG Hedtrich
FU Berlin

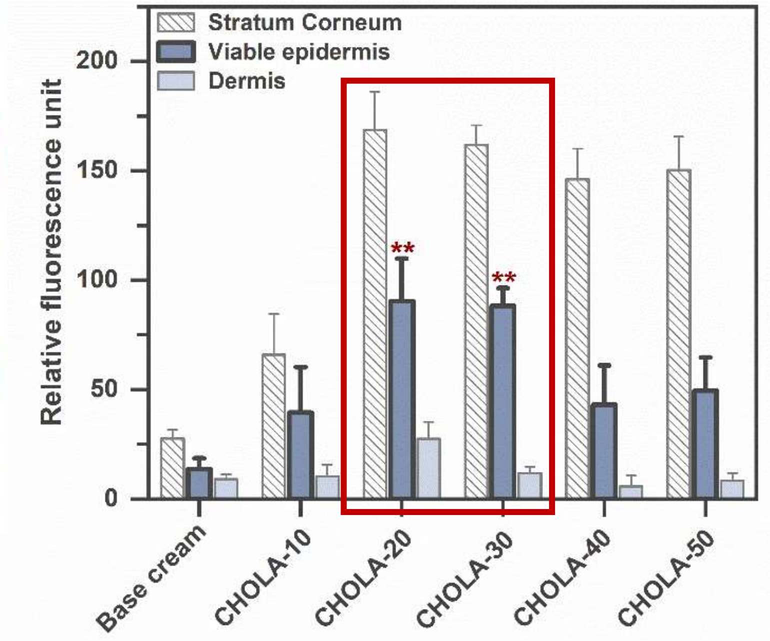
surface
hydrophobicity



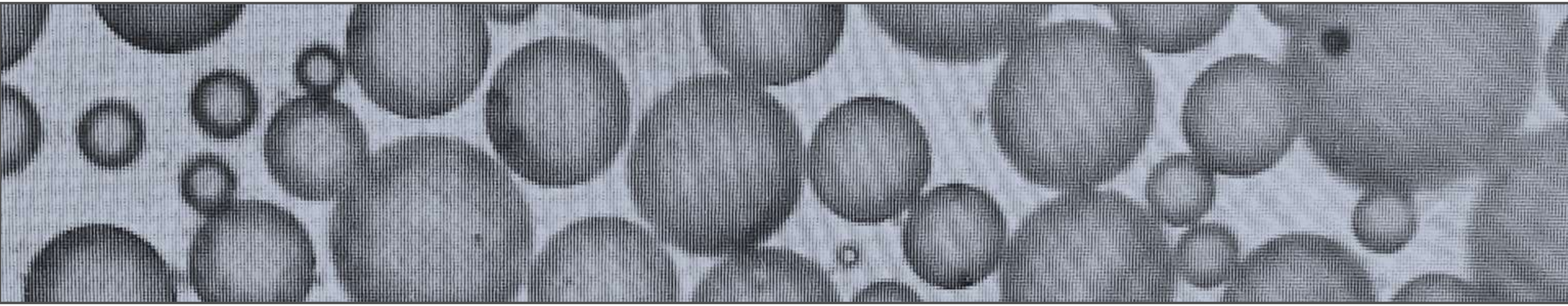


network
rigidity





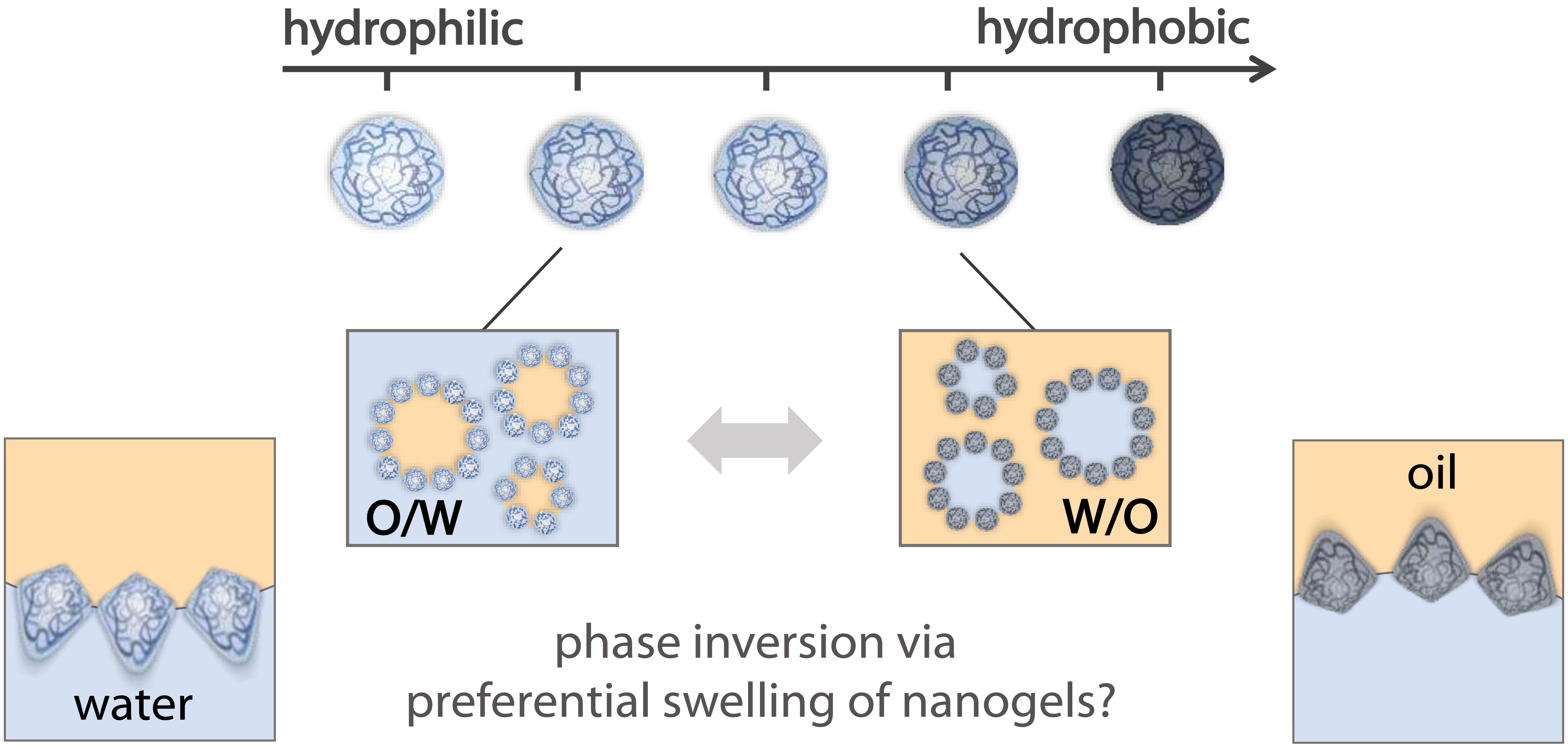
Biomacromolecules 2021



Amphiphilic Nanogels at Liquid Interfaces:

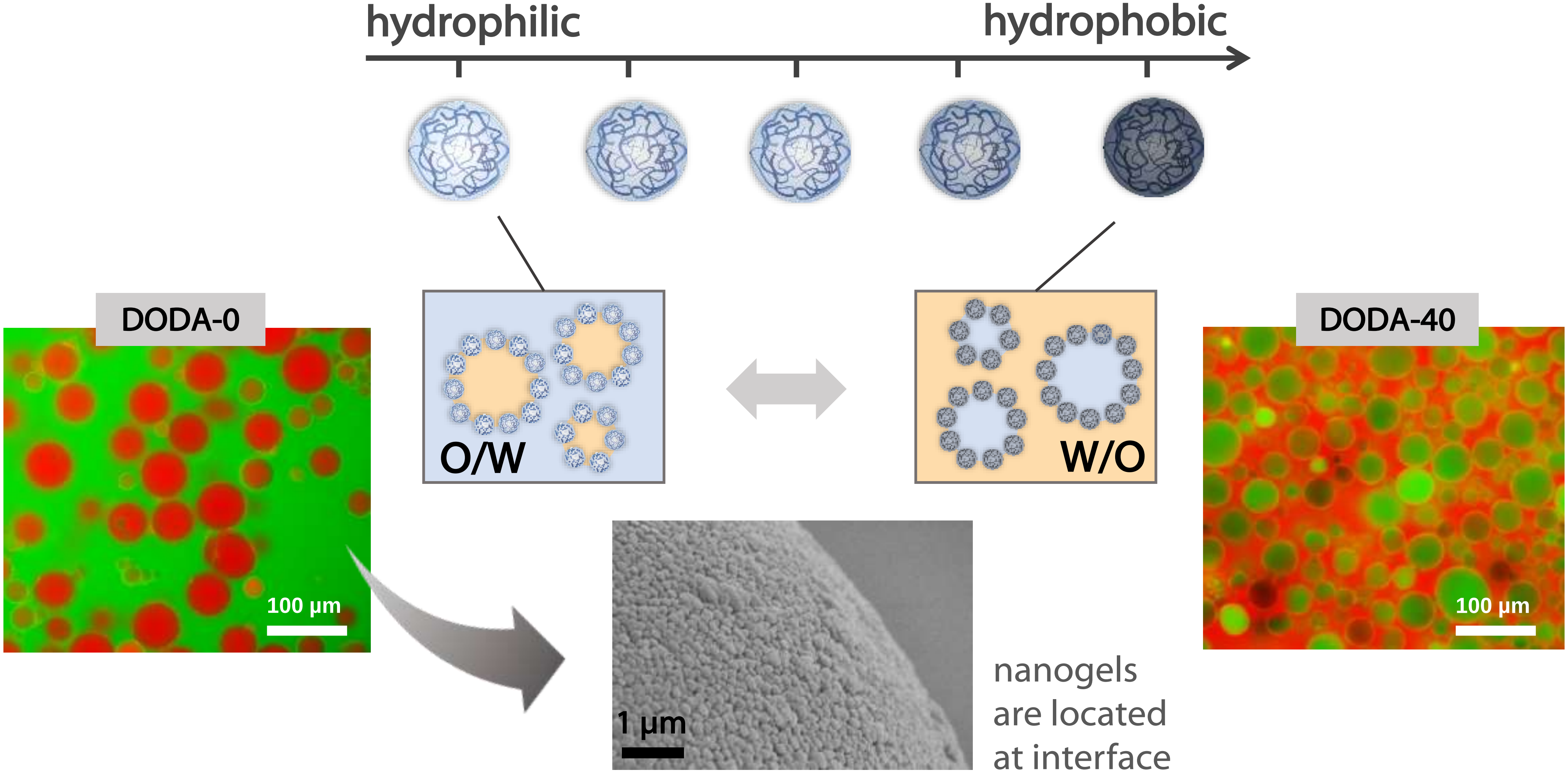
Versatile Pickering Emulsions

How does network hydrophilicity determine emulsion type?



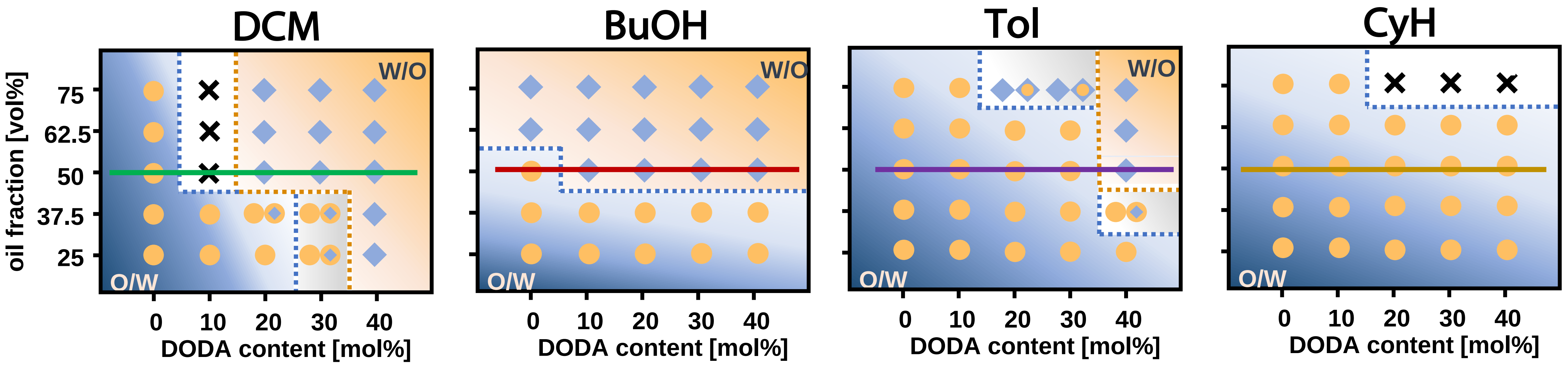
phase inversion via
preferential swelling of nanogels?

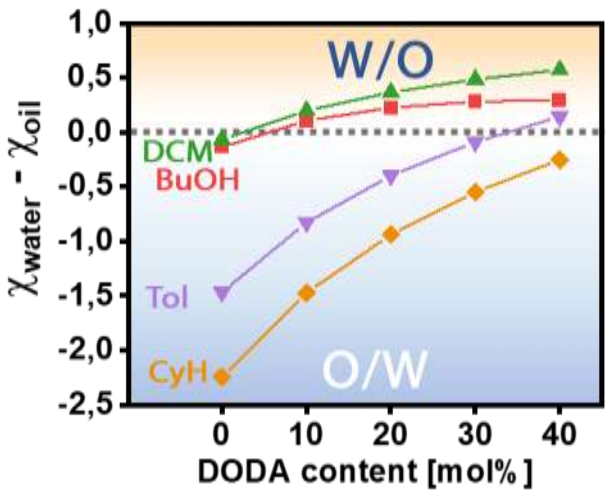
Toluene/water system: Phase inversion due to changing DODA content



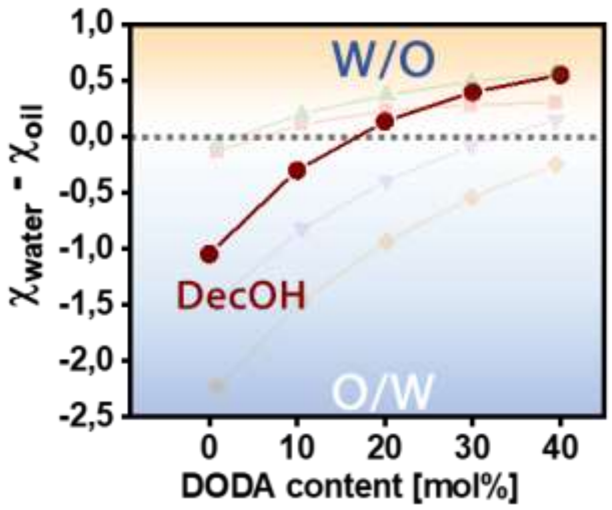
nanogels
are located
at interface

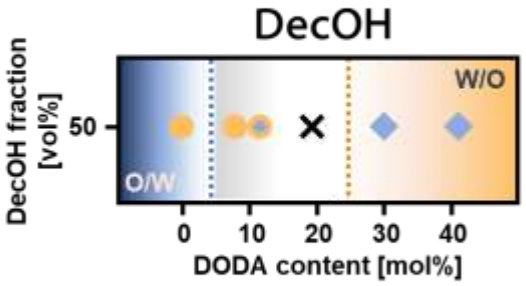
Variation of phase inversion point due to different swelling in oil





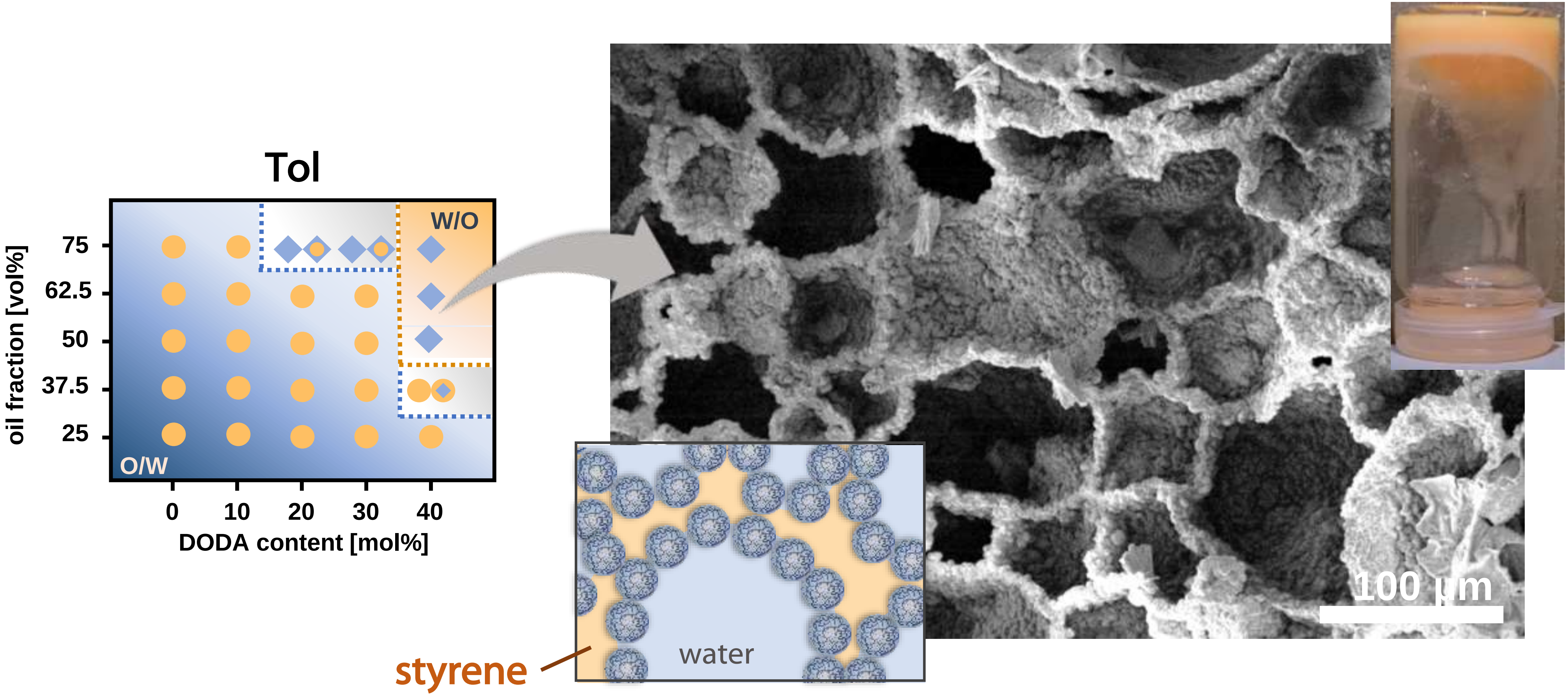
prediction





submitted

Water-in-oil high internal phase emulsions (HIPEs) are accessible



Addressing current threats:

Responsive nanogels to fight resistant bacteria

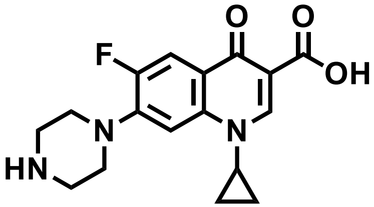
Major killers: β-Lactam resistant bacteria

- Resistance due to **excessive and inefficient use** of first line β-lactam antibiotics
- **Life-threatening** infections
- Origin of **multi-resistance**

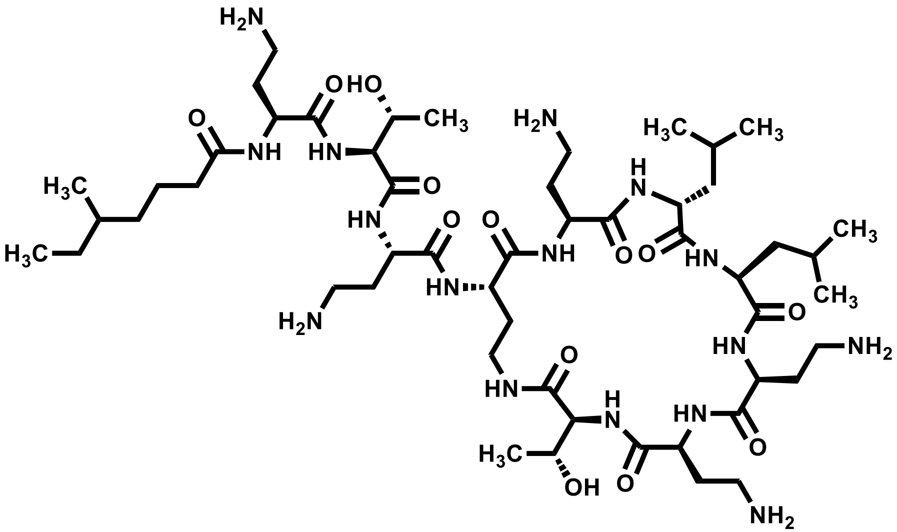
picture source: Center for Disease Control; www.avalonpharmacy.com; www.gelbe-liste.de

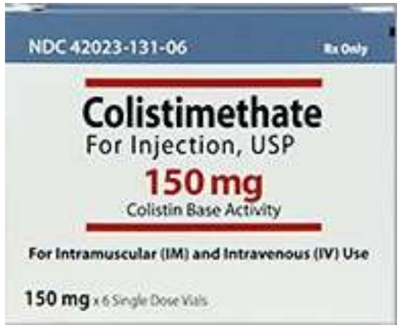
Can we improve "old" antibiotics?

Ciprofloxacin
→ a fluoroquinolone



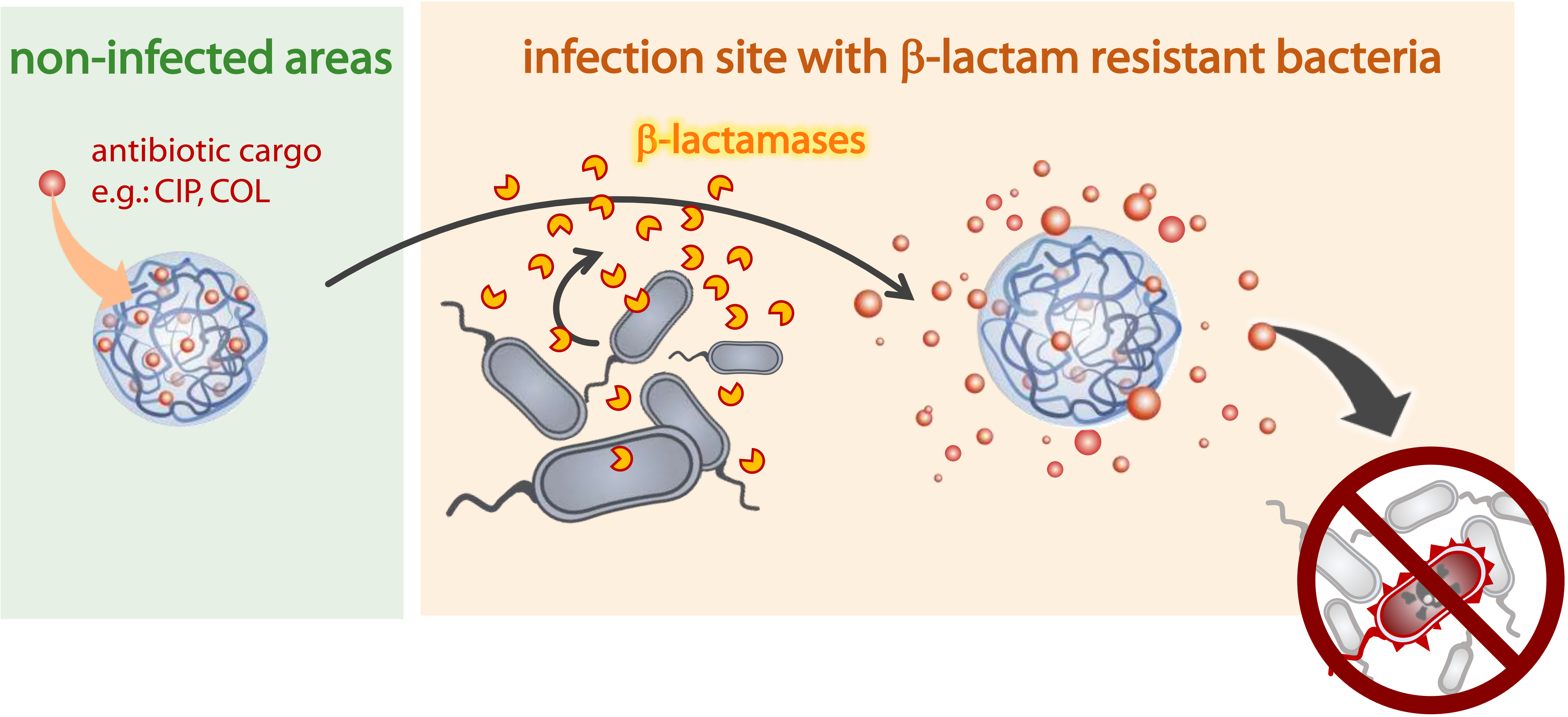
Colistin
→ a polymyxin





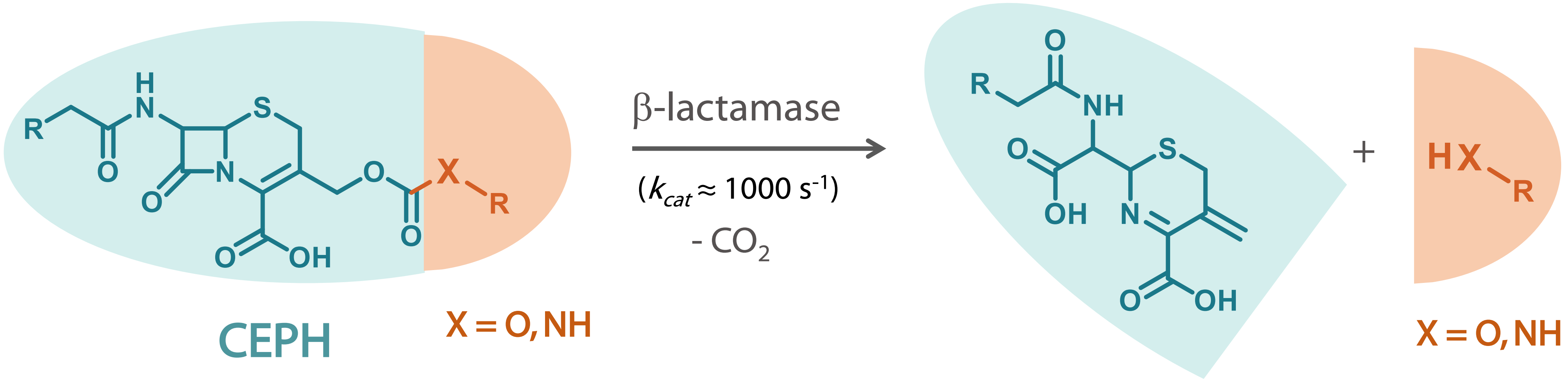
effective but severe side-effects

Turning the bacteria's defense against themselves: β-lactamases as triggers



The Design: Cephalosporins (CEPH) as β-lactamase cleavable linkers

Highly selective and efficient **fragmentation** of cephalosporins

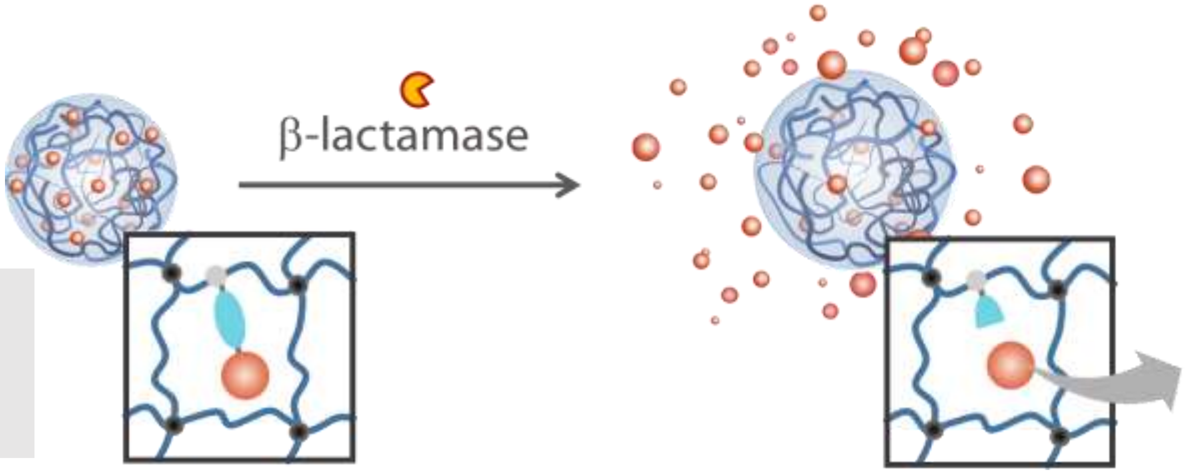


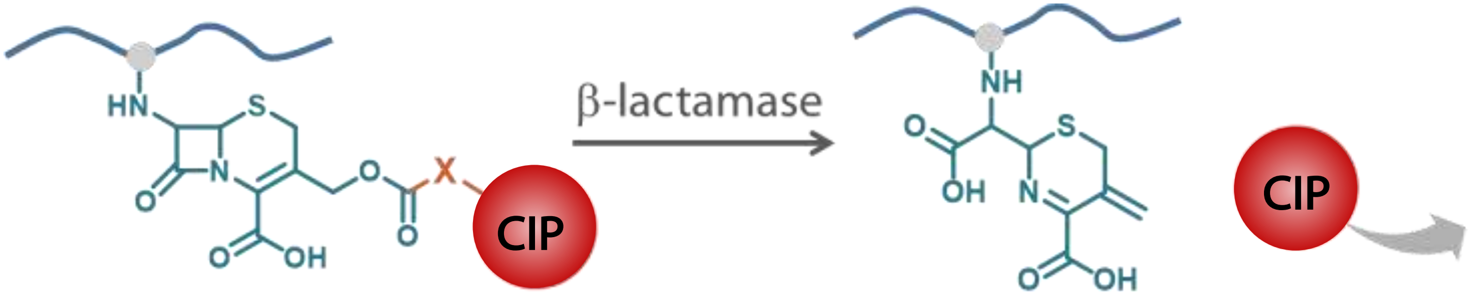
X = O, NH

X = O, NH

Nanogels for delivery of ciprofloxacin

labile linkers:
drug-network



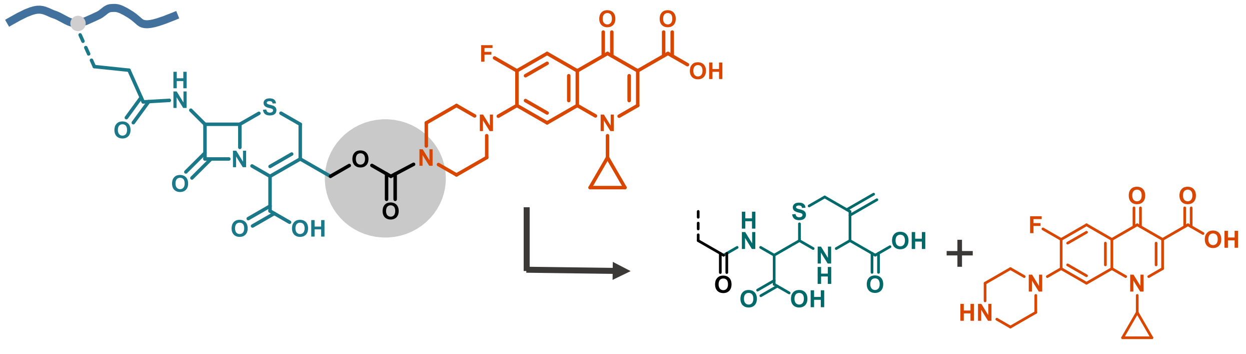


free
antibiotic

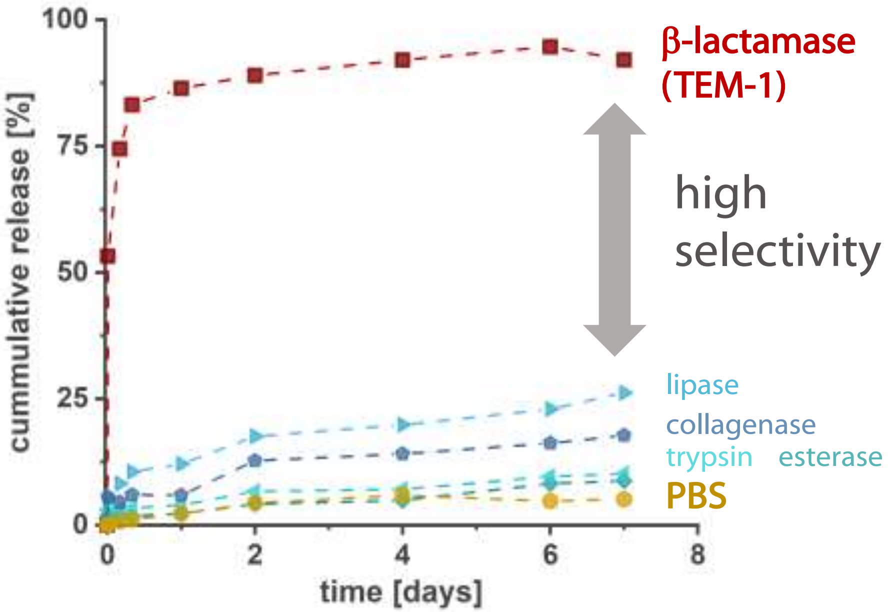
CEPH antibiotics as linker
to liberate alternative antibiotics

Incubation with β-lactamase: linker structure controls release kinetics

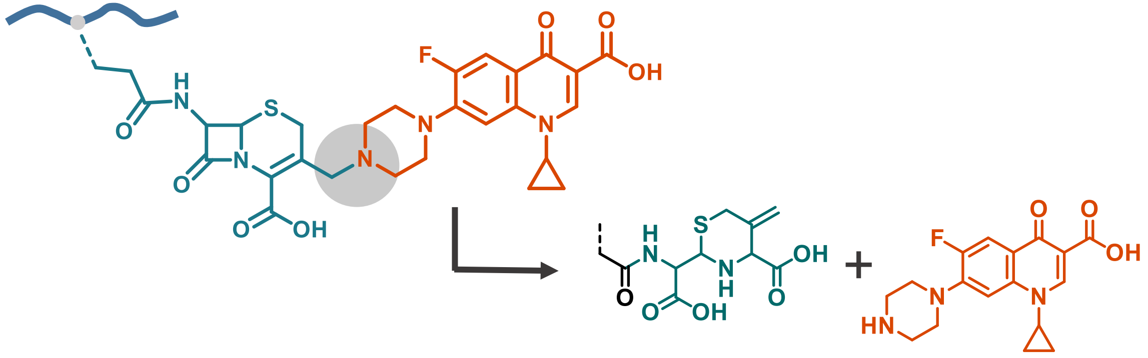
PDC-CA



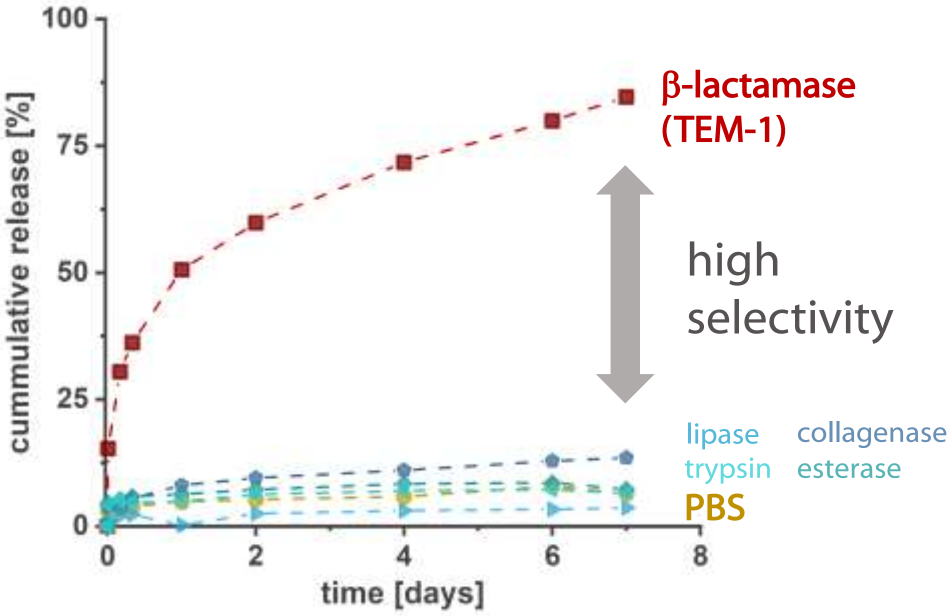
immediate



PDC-AM



sustained



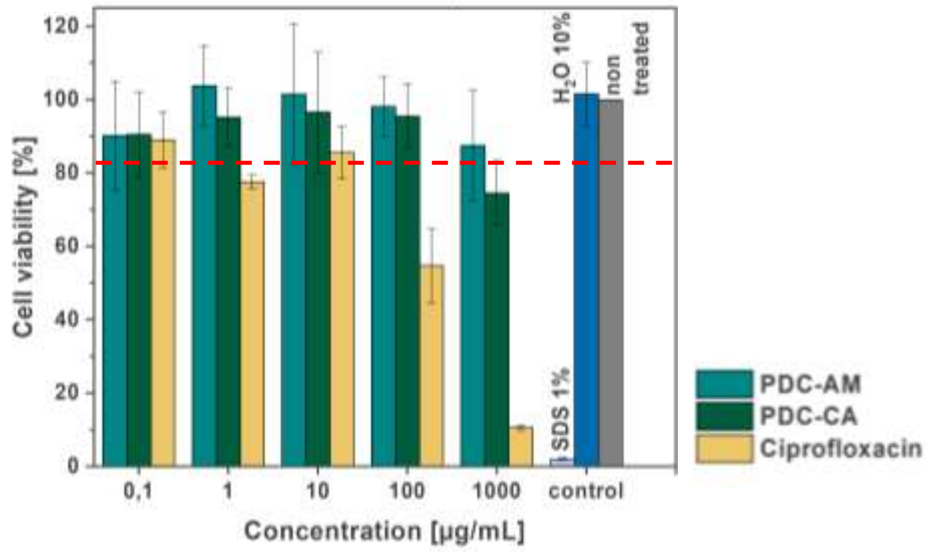
Triggered cipro release selectively inhibits growth of resistant bacteria

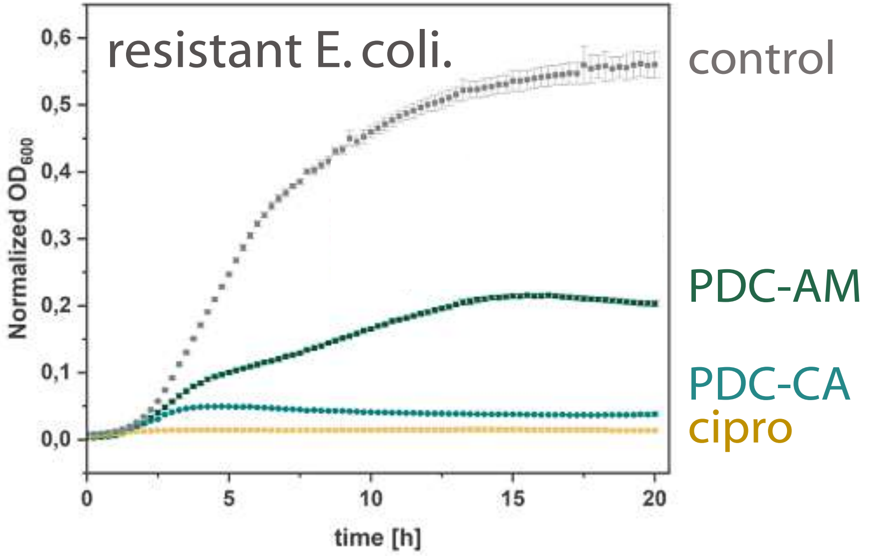
+ antibiotic activity   − no effect

activation of antibiotic activity **only** in the presence of resistant bacteria

Triggered cipro release selectively inhibits growth of resistant bacteria

keratinocytes (HaCat)





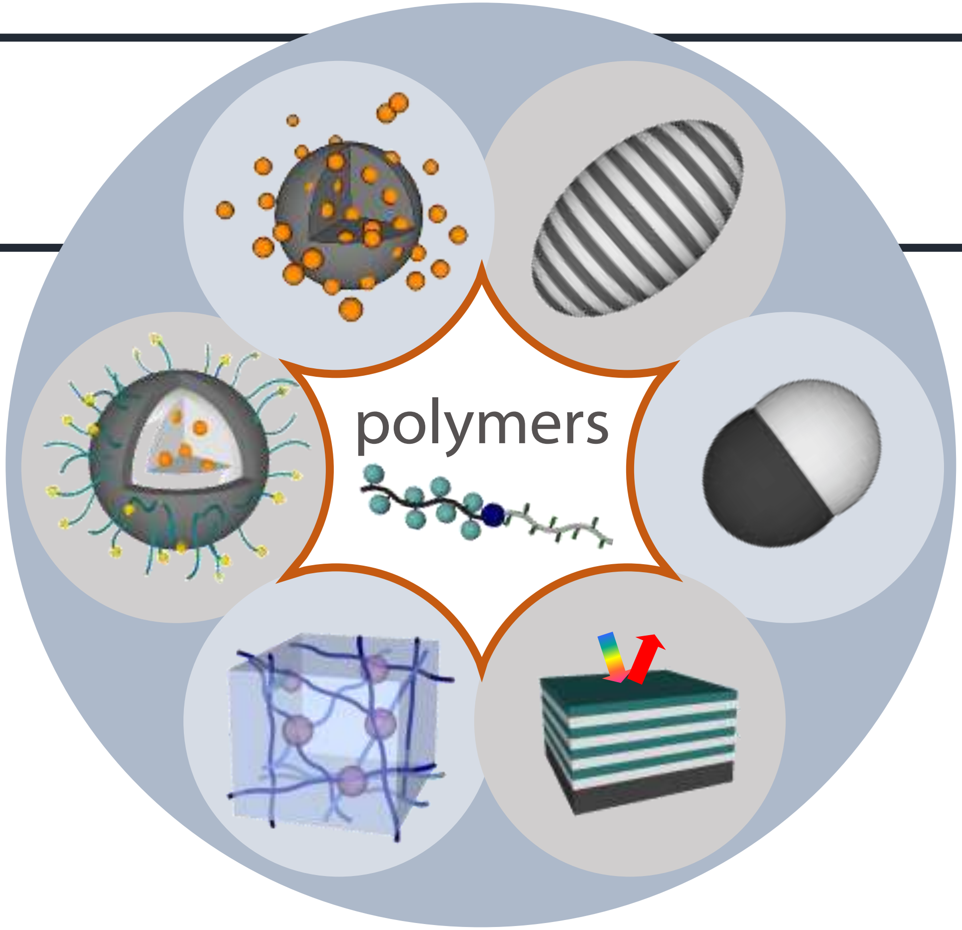
- selective
- effective
- less toxic

in preparation

Functional colloids and nanomaterials

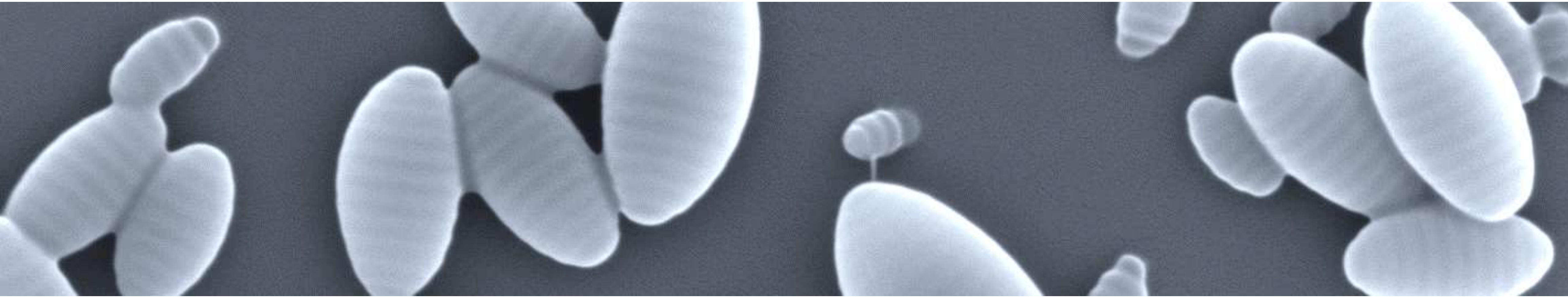
stimuli-responsive
nanogels

shape anisotropic
nanoparticles



stimuli-responsive
hydrogels

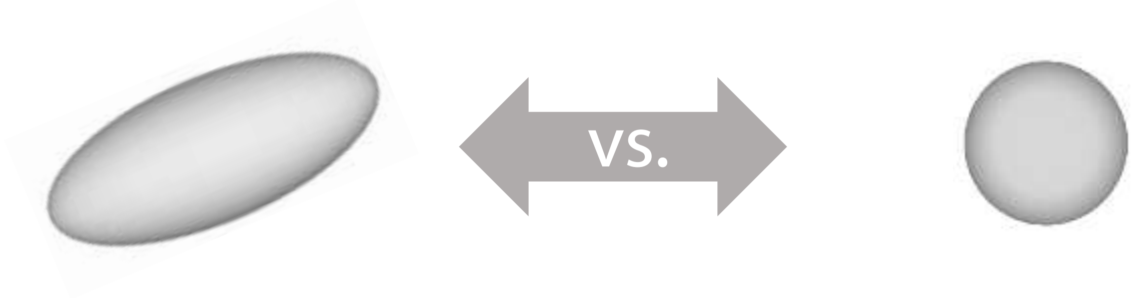
functional
surfaces & coatings



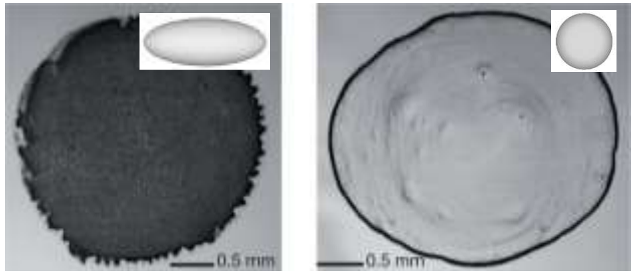
Striped ellipsoidal nanoparticles

Stimuli-responsive shape change for new materials

Ellipsoidal particles as building blocks for new materials

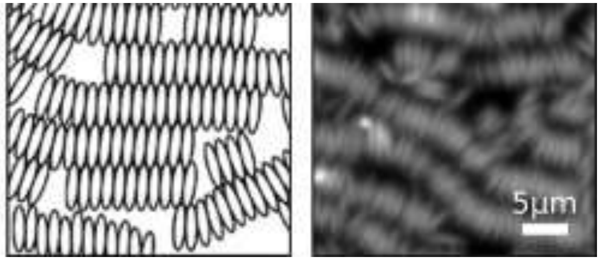


capillary interactions



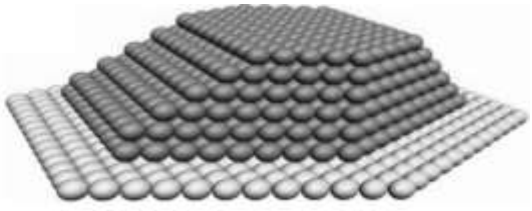
P. Yunker et al.
Nature **2011**, *476*, 308

packing at interfaces



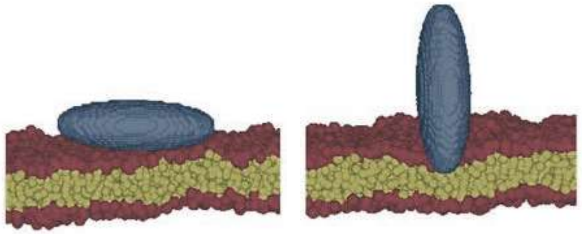
A.M. Luo et al.
J. Colloid Interface Sci. **2019**, *534*, 205

packing in 3D



T. Ding et al.
Adv. Mater. **2009**, *21*, 1936

cellular uptake

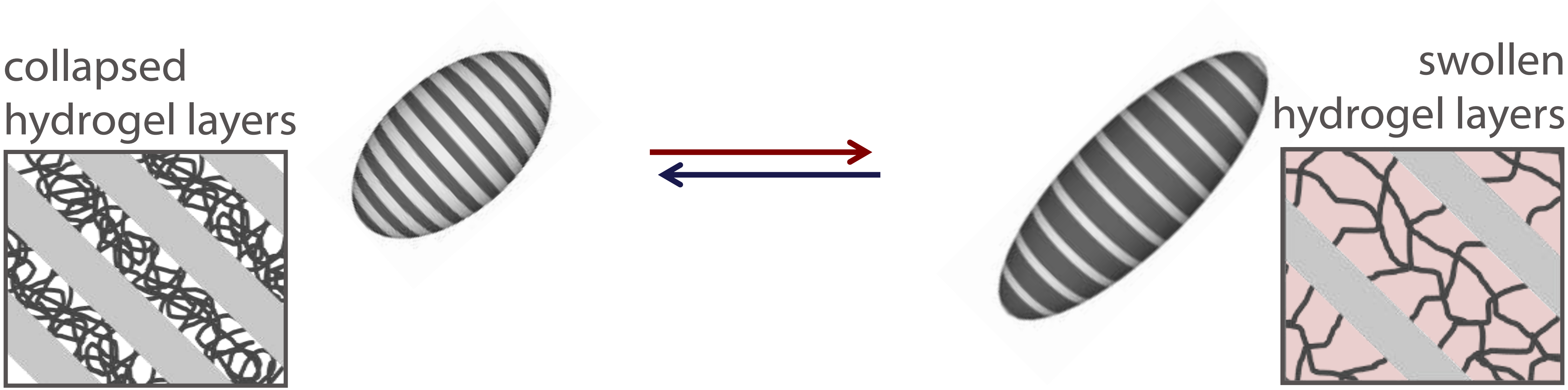


K. Yang et al.
Nat. Nanotech. **2010**, *5*, 579

anisotropic shape change

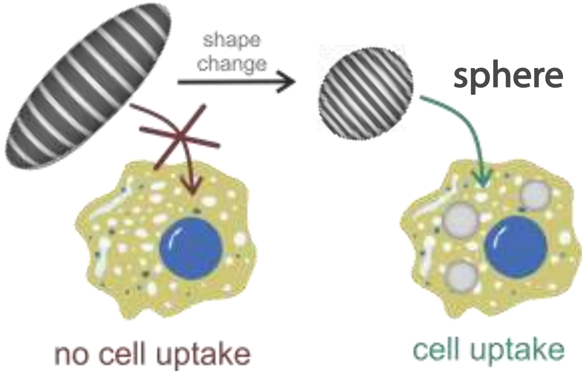
NEW DYNAMIC MATERIALS

Swelling of striped particles to induce shape change

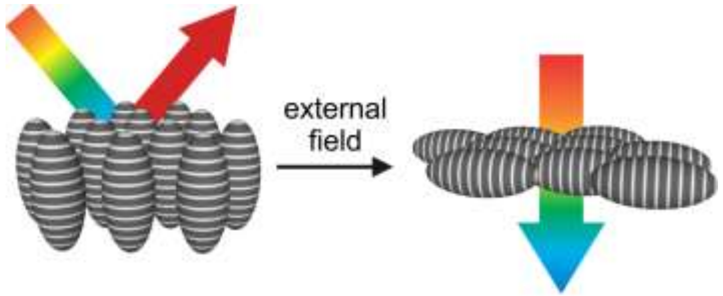


towards new materials

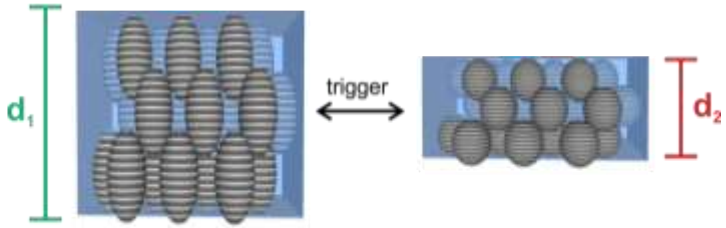
Targeting?



Photonics?

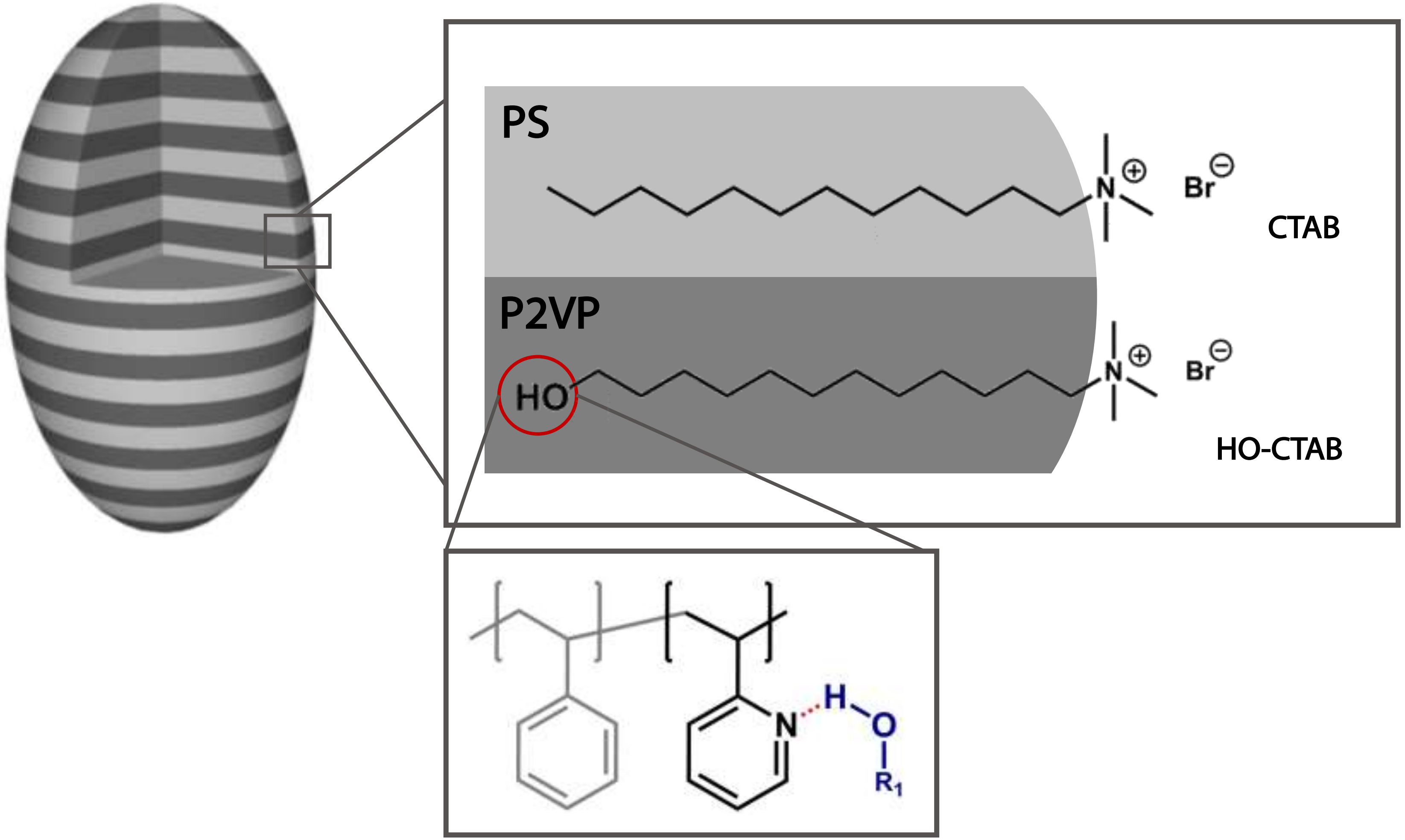


Actuation ?



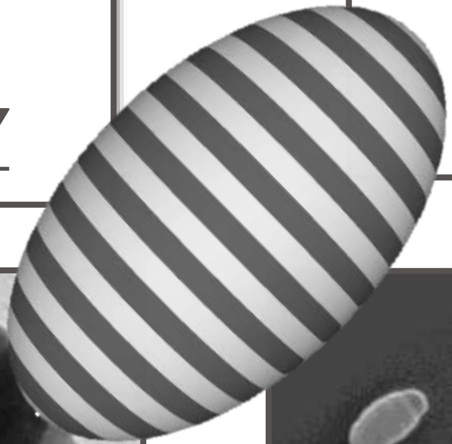
Mixed surfactants control the morphology of PS-*b*-P2VP particles

Morphology is governed by the particle/water interface

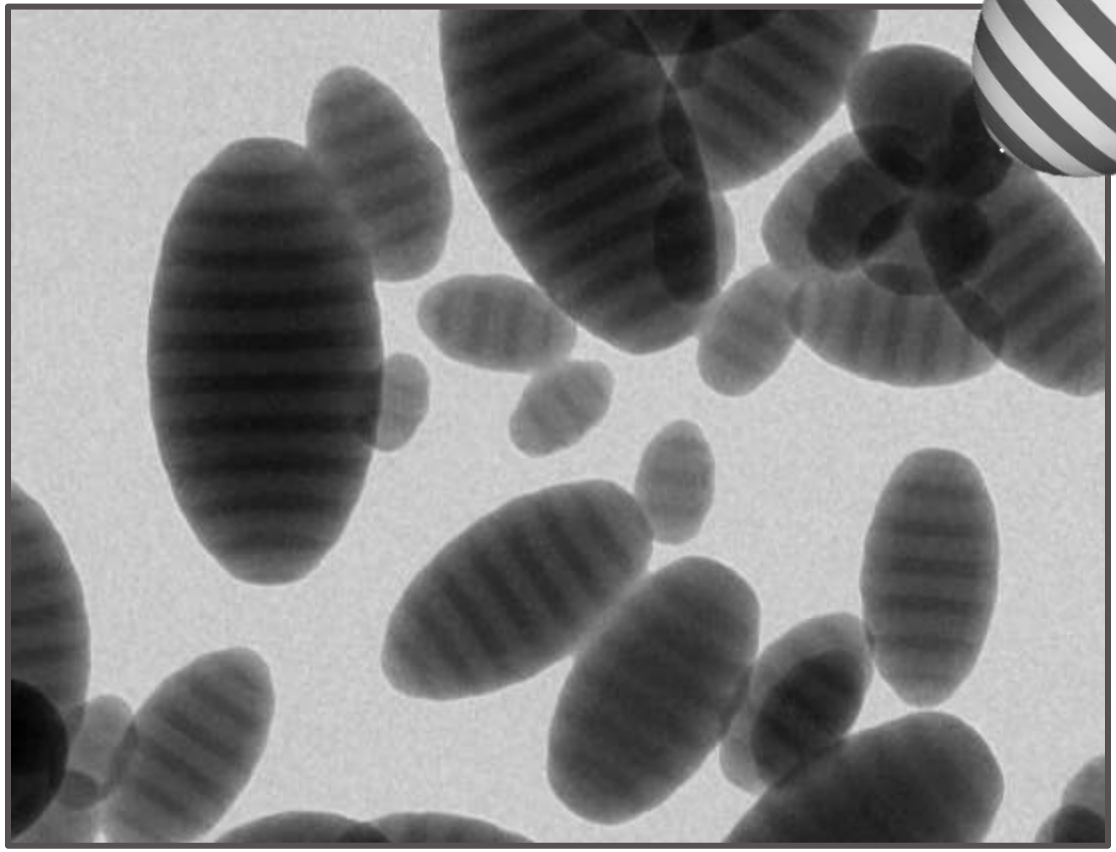


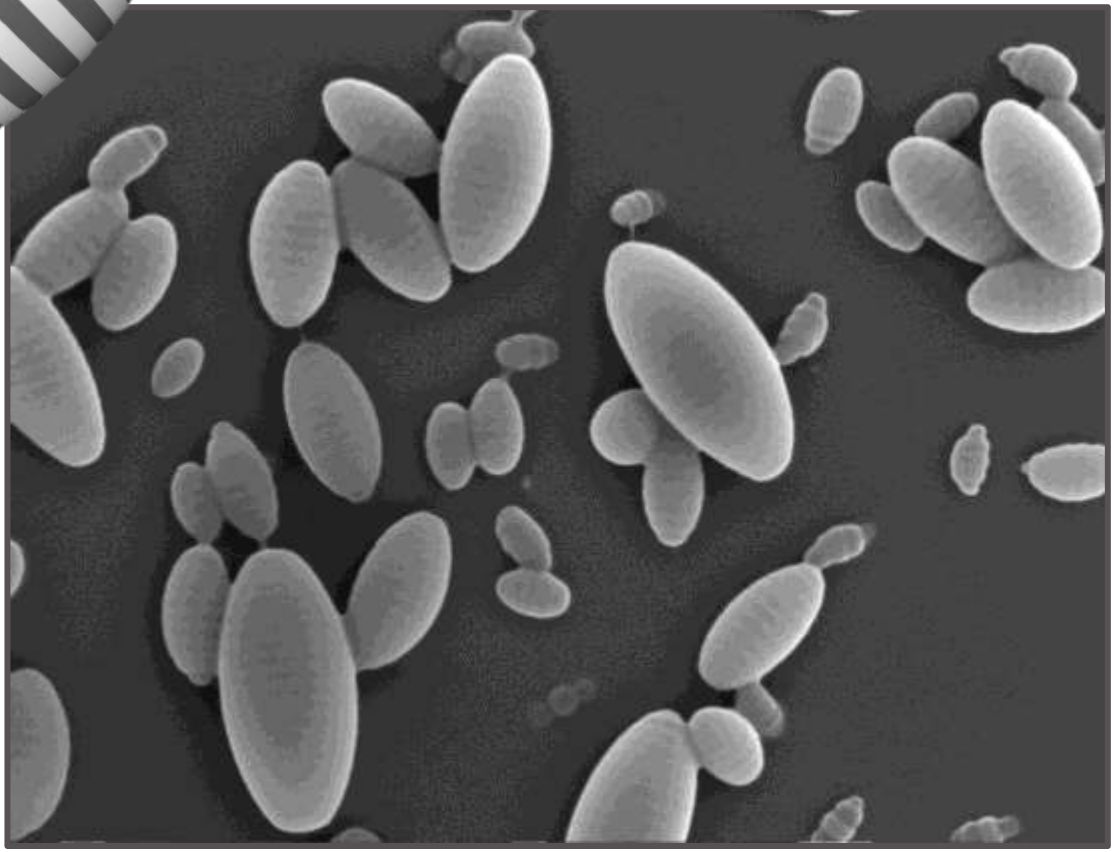
Hierarchical structures: striped lamellar ellipsoids

LAMELLAR
MORPHOLOGY

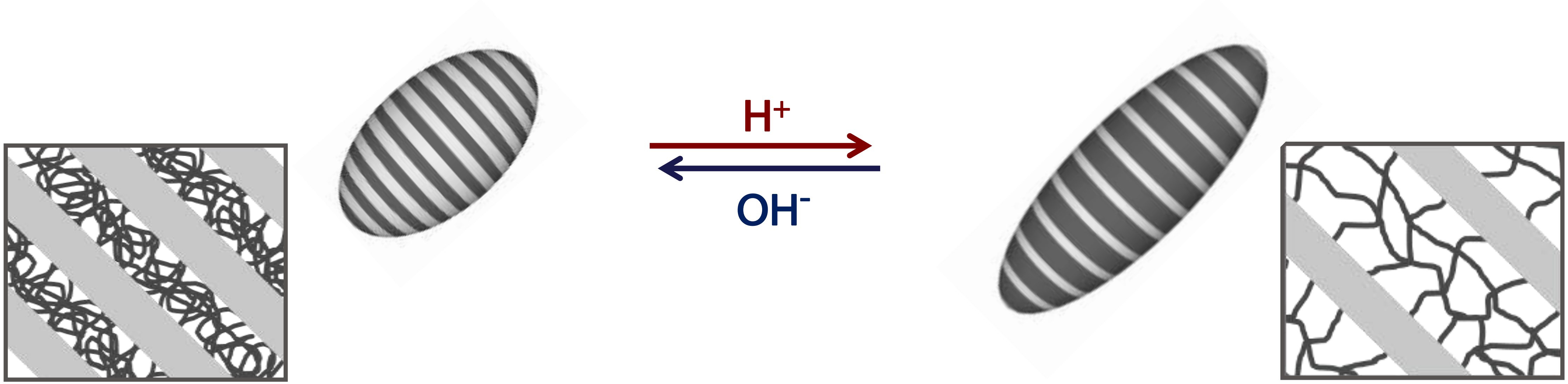


ELLIPSOIDAL
SHAPE

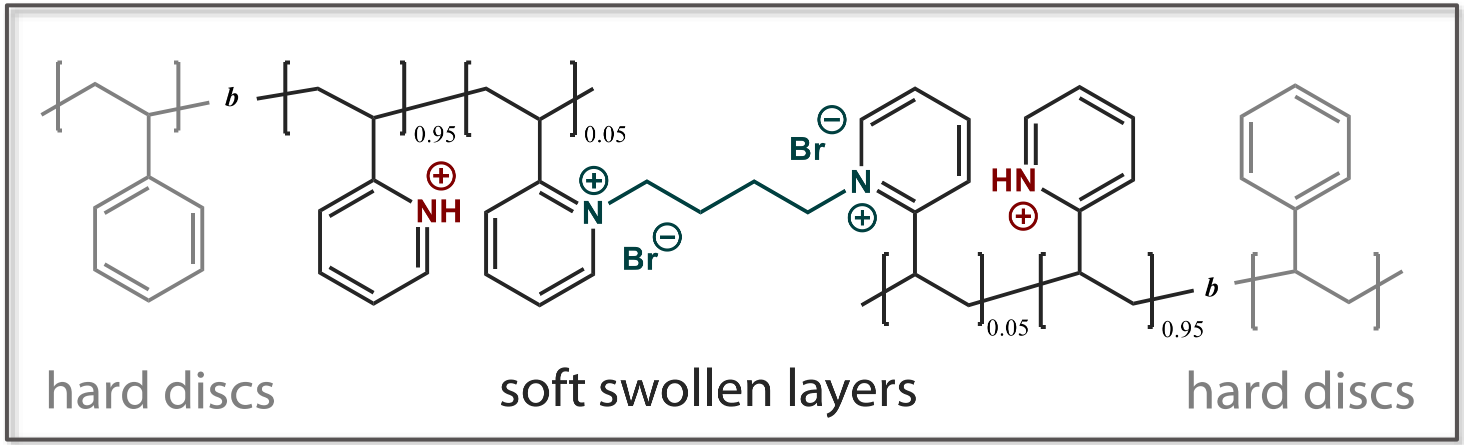




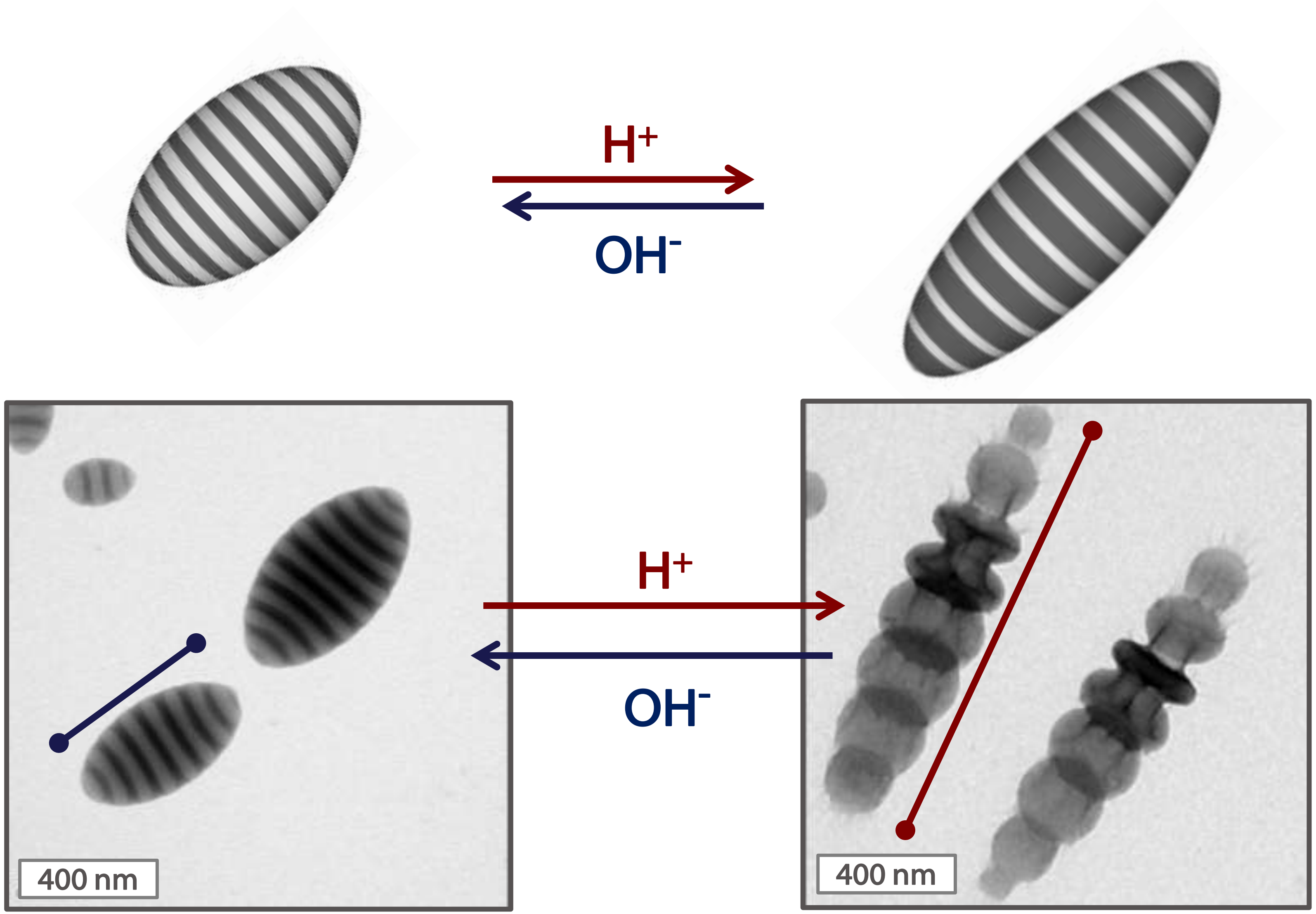
Swelling of striped particles to induce shape change



crosslinking of P2VP domains to prepare hydrogel layers



Selective domain swelling: pH-triggered shape change

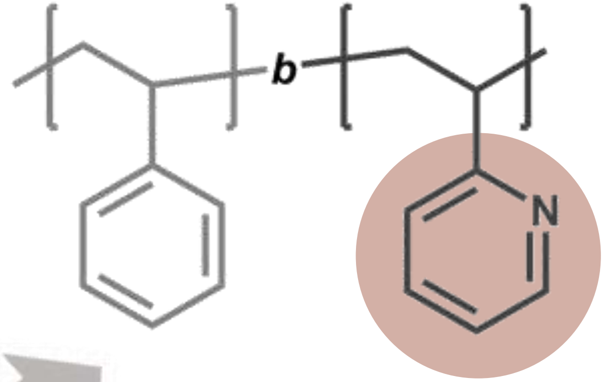


Angew. Chem. Int. Ed. 2014

How to include more chemical functionality?

additional functionality in specific domains?

chemical functionality

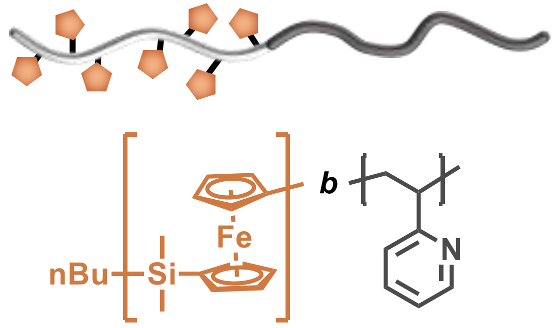


pH-responsive

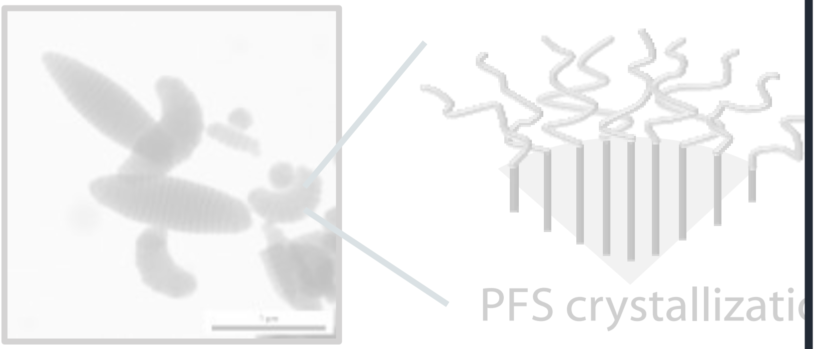
Chem. Mater. 2017

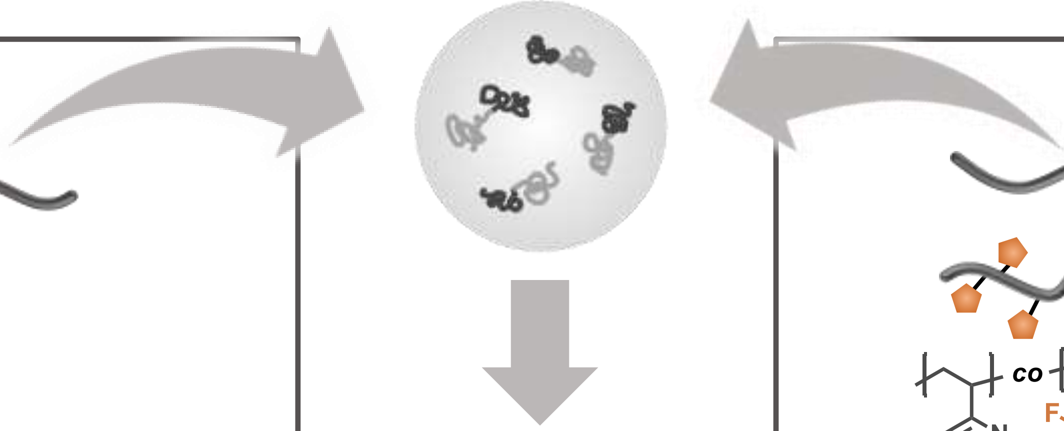
Introducing chemical function during particle preparation is challenging

functional BCP phase-separation



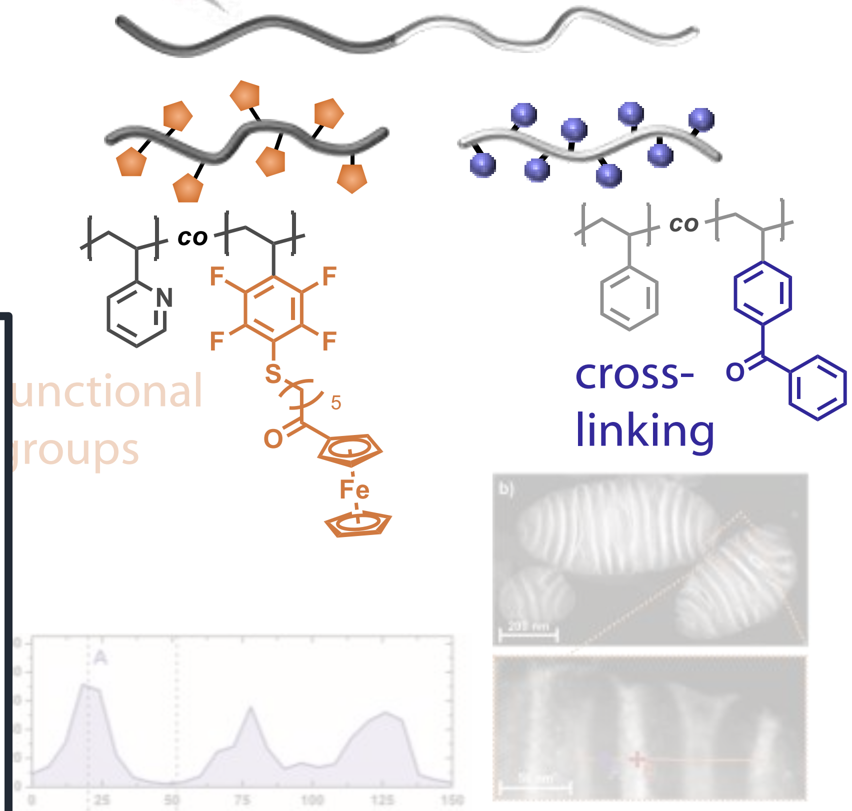
PFS-*b*-P2VP





polymer functionality can disturb phase separation

homopolymer/ BCP blends

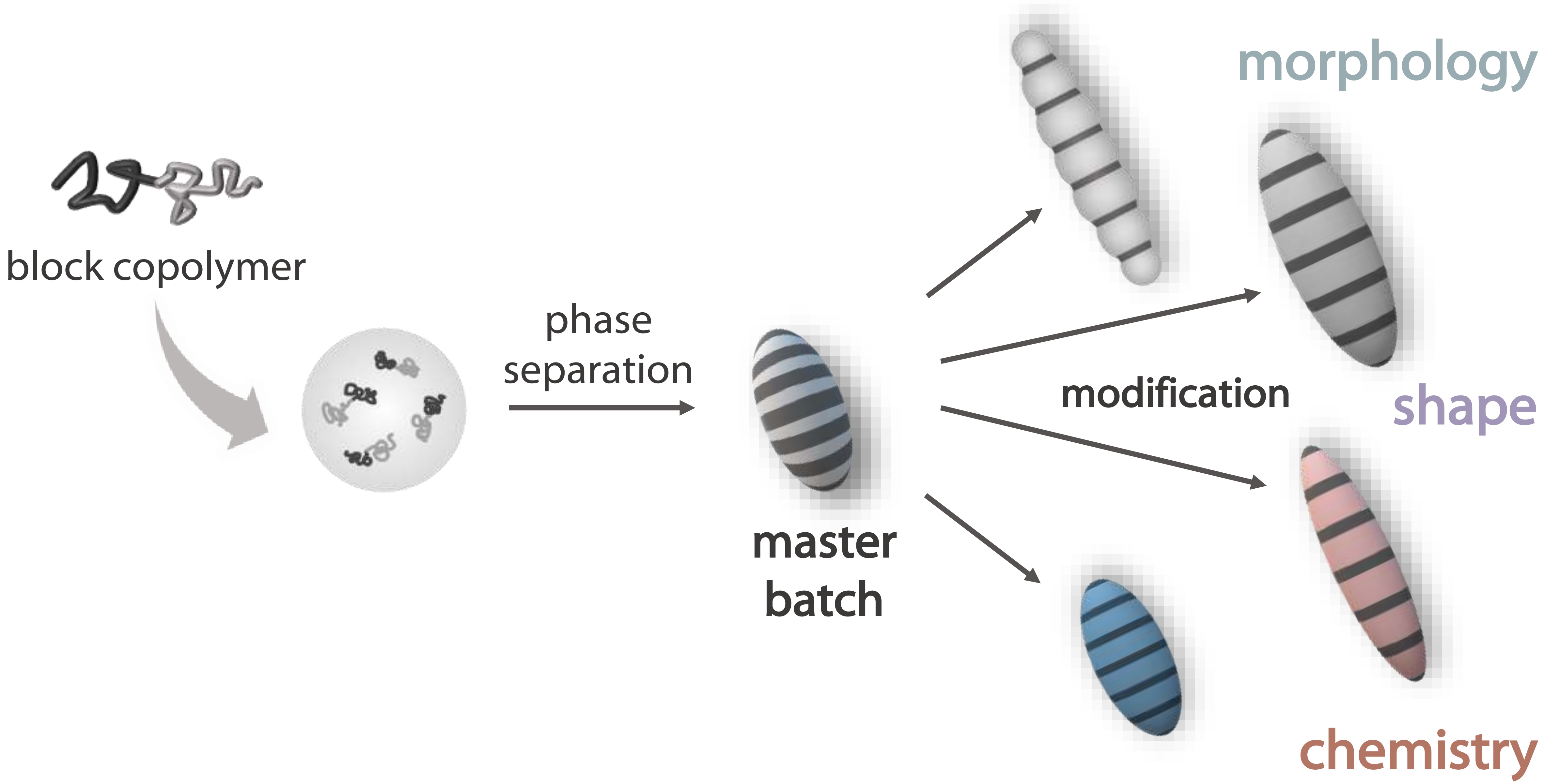


ACS *Macro Lett.* **2015,** *4,* 731

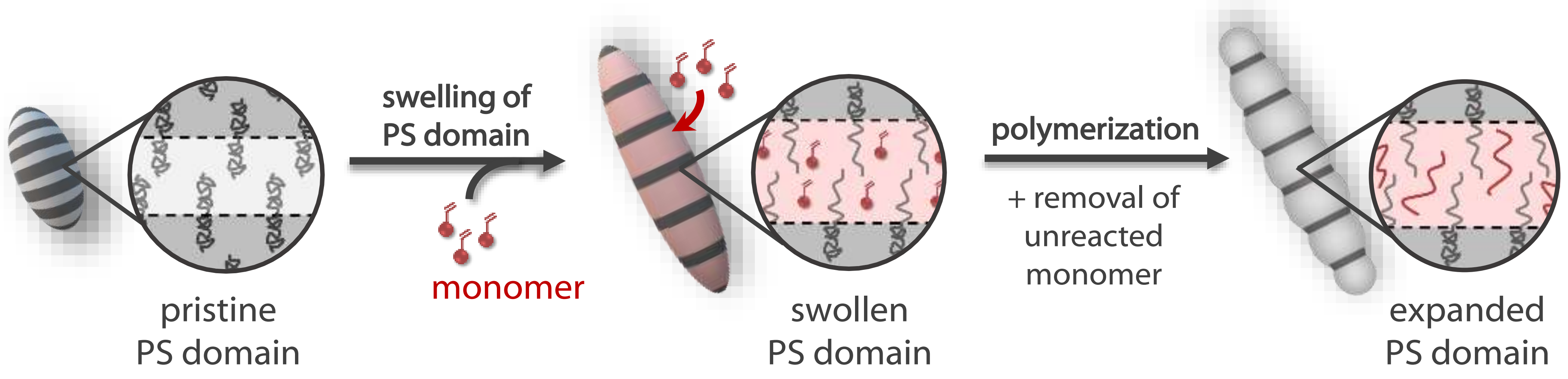
Polym. Chem. **2018,** *9,* 1638

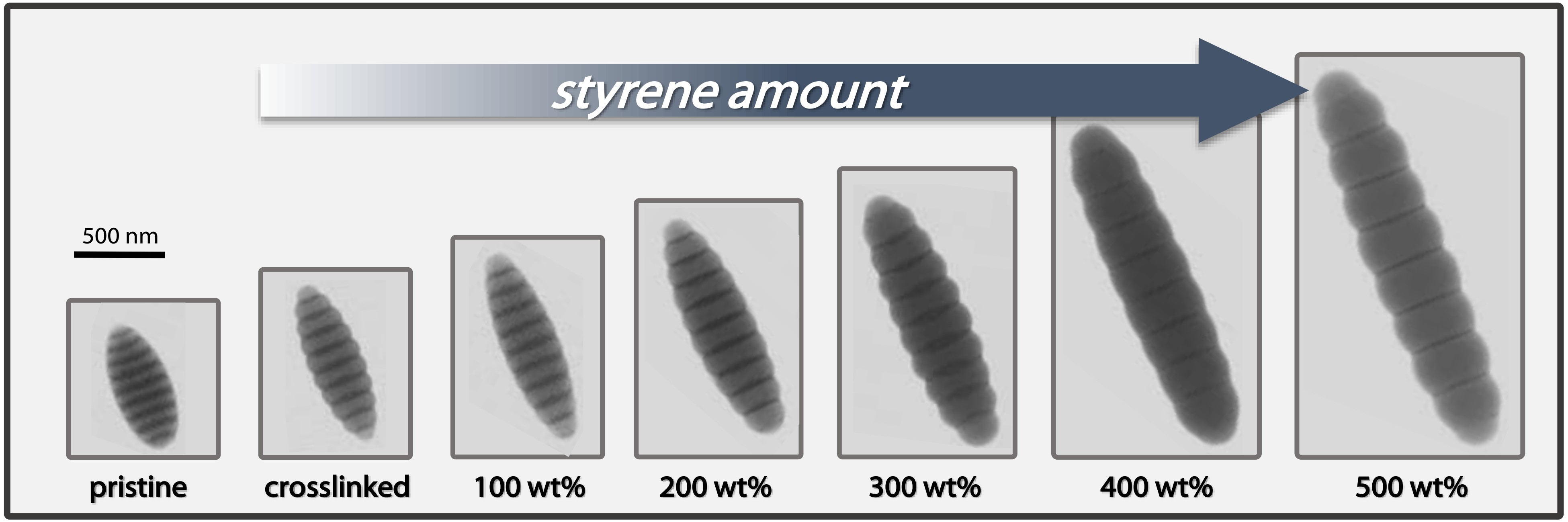
with M. Gallei
Uni Saarland

Post-assembly modifications as versatile approach



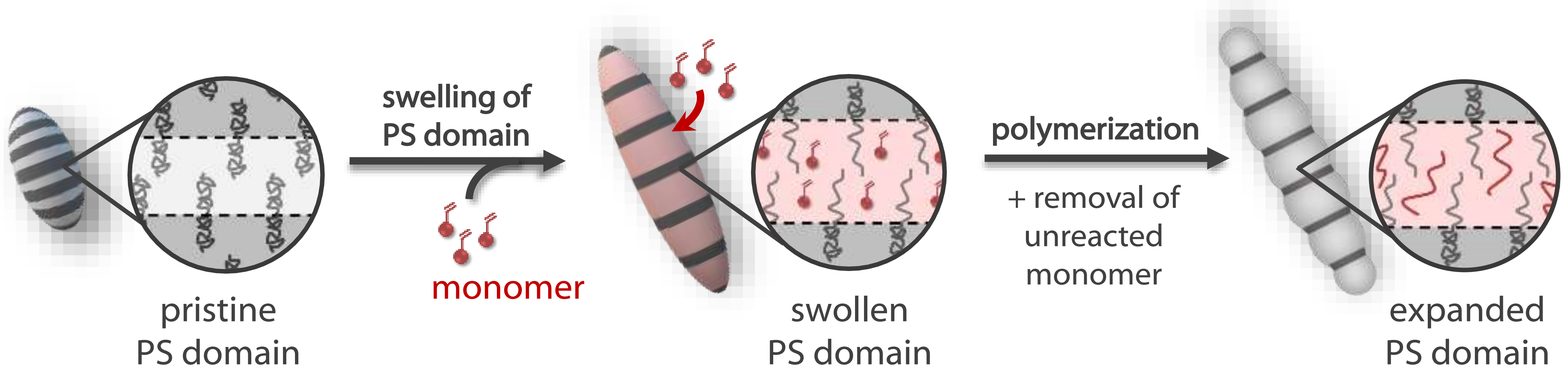
Domain-selective seeded polymerizations for highly asymmetric lamellae



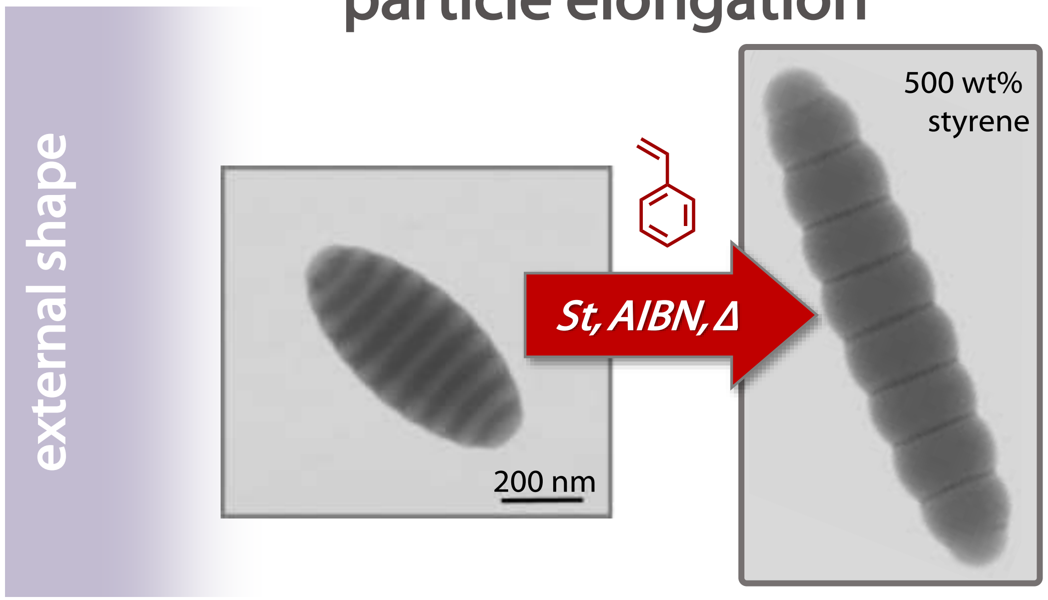


ACS Macro Lett. 2022, *Angew. Chem.* 2022

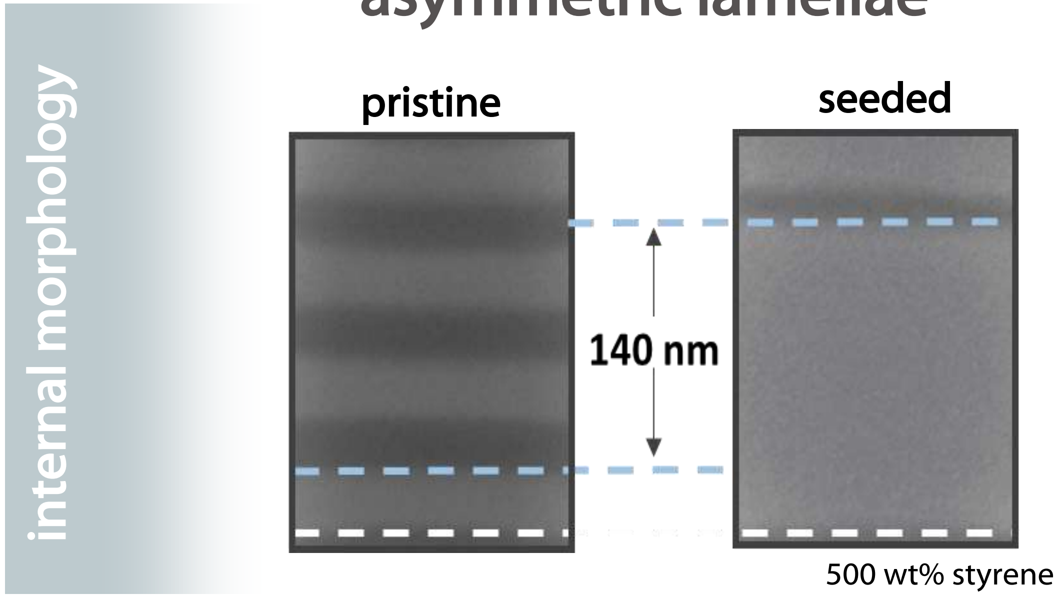
Domain-selective seeded polymerizations for highly asymmetric lamellae



particle elongation

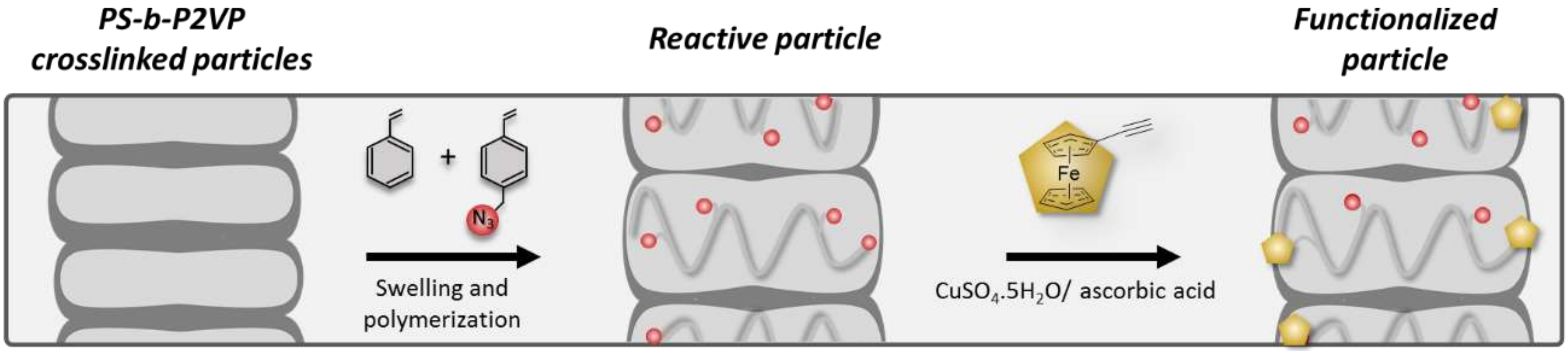


asymmetric lamellae

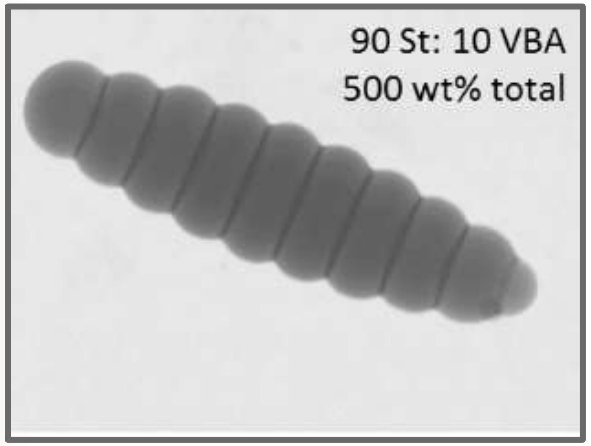


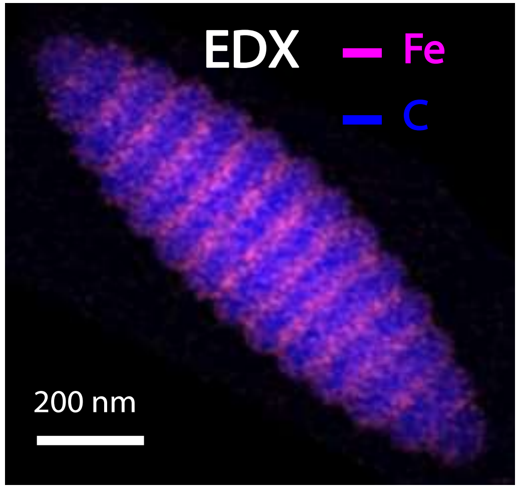
ACS Macro Lett. **2022**, *Angew. Chem.* **2022**

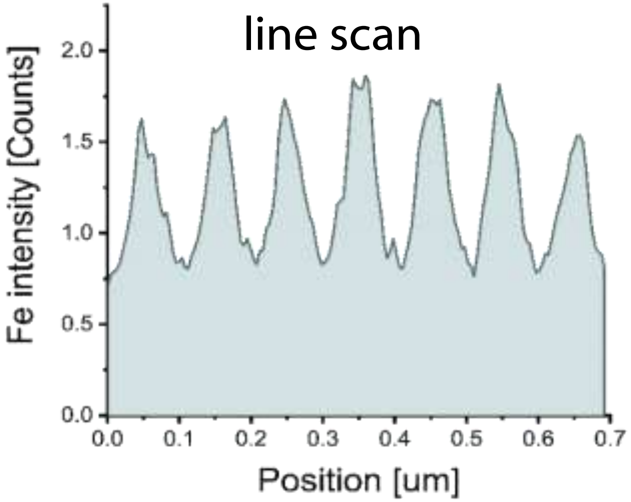
Seeded polymerization with functional monomers



chemical functionality



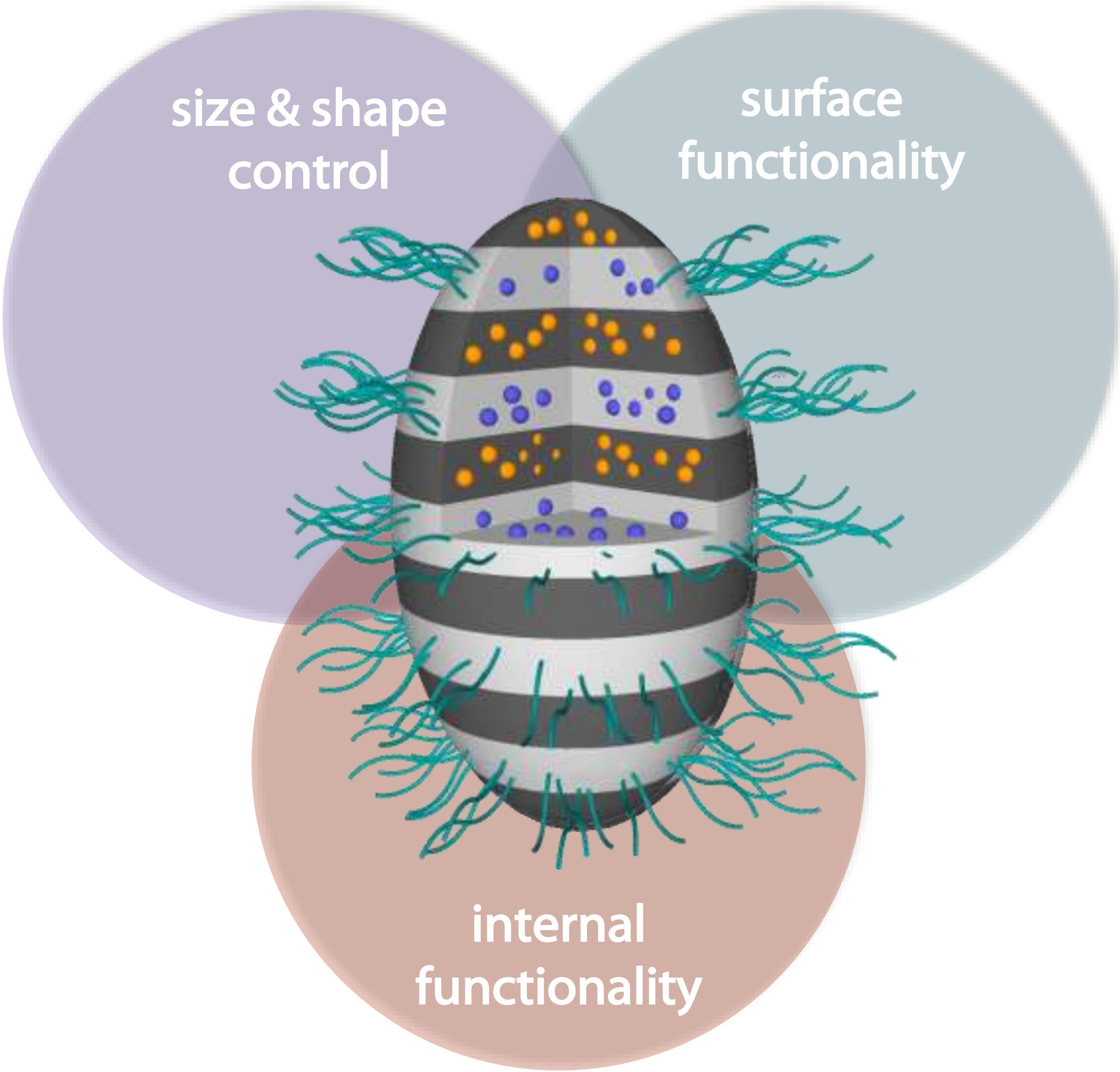




periodic distribution of ferrocene

ACS Macro Lett. **2022**, *Angew. Chem.* **2022**

Our aim: Hierarchically structured multifunctional particles

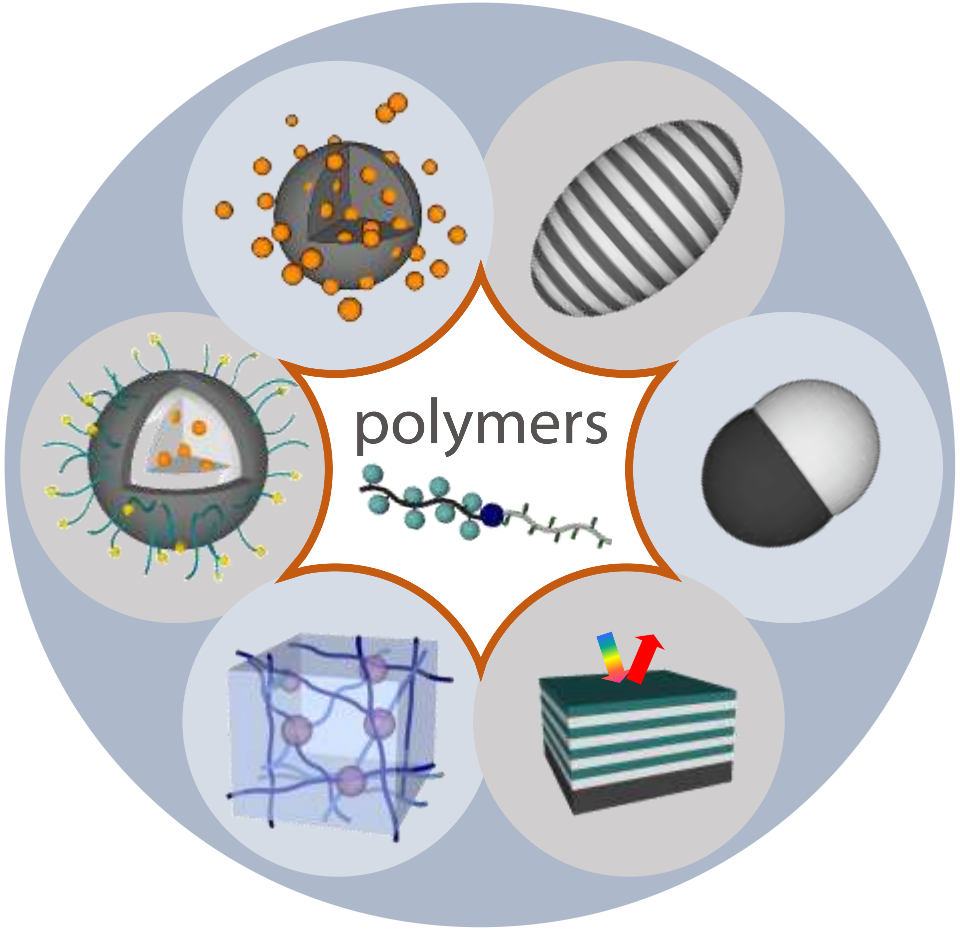


Highlights:
JACS 2013; *Angew. Chem.* 2014; *ACS Macro Lett.* 2015; *Chem. Mater.* 2017; *Macromolecules* 2017; *Polym. Chem.* 2018; *Nat. Mater.* 2019; *ACS Macro Lett.* 2022; *Angew. Chem.* 2022

Functional colloids and nanomaterials

stimuli-responsive
nanogels

shape anisotropic
nanoparticles



stimuli-responsive
hydrogels

functional
surfaces & coatings

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N. Vogel
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FCI FONDS DER CHEMISCHEN INDUSTRIE
DFG Deutsche Forschungsgemeinschaft
CHINA SCHOLARSHIP COUNCIL

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