June 2008,HDR

Self-Assembling Nanostructures: A Materials Scientist Perspective

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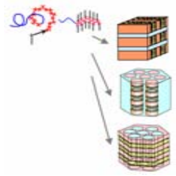
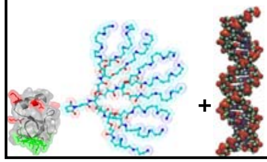
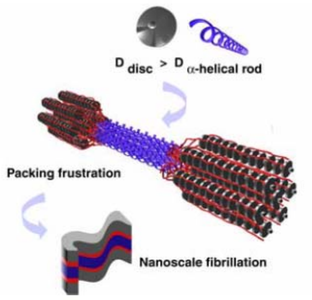


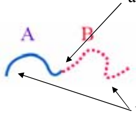
- Fundamental question:
  - Concepts for complex but still rational self-assembled hierarchies
  - On implications on functional properties
- Control of self-assembly
  - Micelles
  - Vesicles
  - Fibrils
  - External control
- Use of weak interactions

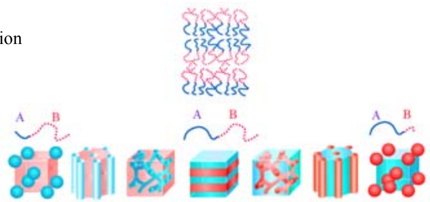




Self-assembly arises due to competing interactions

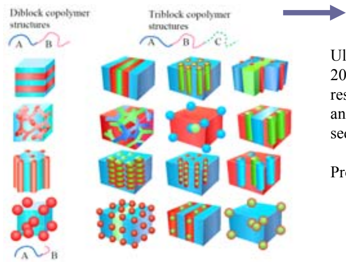
- Perhaps the simplest examples: diblock copolymers





- The structures controlled by the relative weight fractions of the blocks

Towards complex self-assembled structures of polymers



Ultimately:
20 types of residues and their sequencies:

Proteins

Competing repulsions and attractions

(covalent or physical forces)

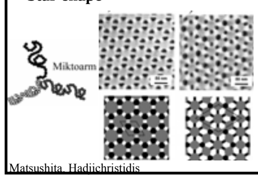
→ **self-assembly**

Complexity, specifity →

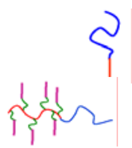
← "Ease of materials design"

Numerous ways to tune the architecture and self-assembly

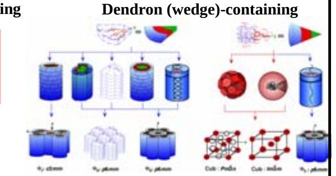
Star-shape | **Mesogen-containing** | **Dendron (wedge)-containing**



Matsushita, Hadjichristidis

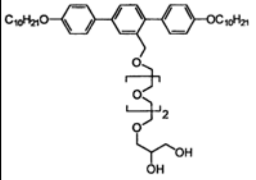


Ober, Thomas

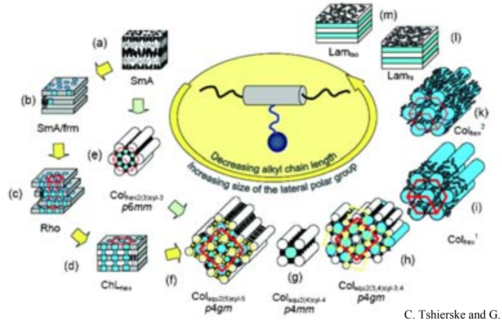


Percec

Related progress in liquid crystals

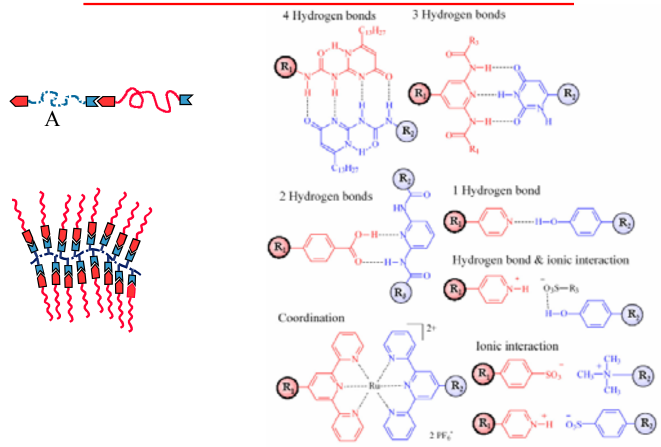


Competitions
- Aromatic rod
- Flexible alkyl
- Flexible polymer with ”sticky” hydrogen bonding



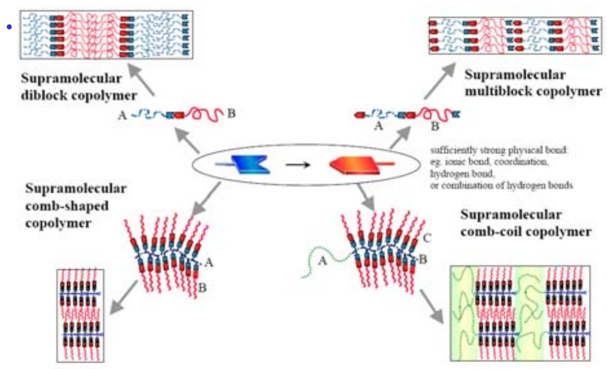
C. Tshierske and G. Ungar

Attractive covalent interactions can be replaced by sufficiently strong physical interactions: Must withstand the invariably present repulsive interactions



Complementary physical interactions to construct self-assembling polymer-like entities (supramolecular polymers)

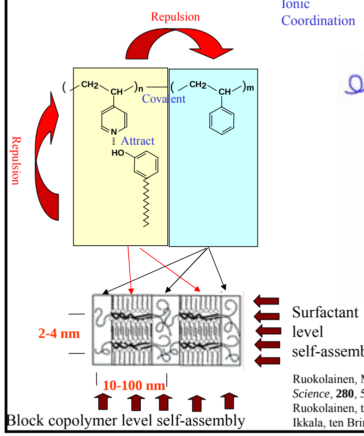
Hydrogen bonds, ionic bonds, coordination bonds

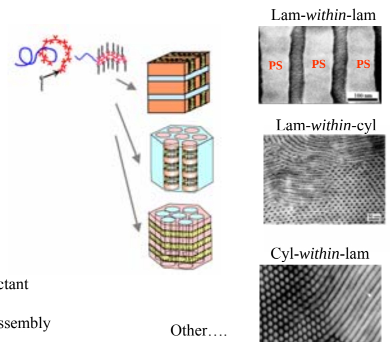


Towards dynamic self-assembly with two length scales

Tune the competing attractive and repulsive interactions

attractive	repulsive
Covalent (permanent)	Polar/nonpolar
Hydrogen bonding	Polymer immiscibility
Ionic	etc
Coordination	

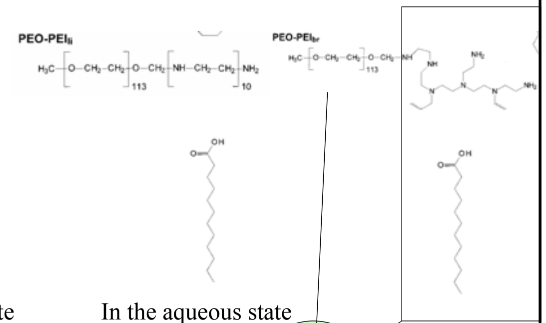




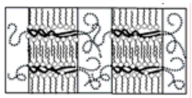
Ruokolainen, Mäkinen, Torkkeli, Mäkelä, Serimaa, ten Brinke, Ikkala, *Science*, **280**, 557 (1998)
Ruokolainen, ten Brinke, Ikkala, *Adv Mat*, **11**, 777 (1999)
Ikkala, ten Brinke *Science* 2002, 295, 2407

Towards aqueous solutions and drug release

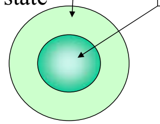
- PEO-*b*-PEI double-hydrophilic block copolymer
- But surfactant complexes become hydrophobic
- This amphiphilicity created
- Formation of micelles
  - Drug encapsulation



In the solid state

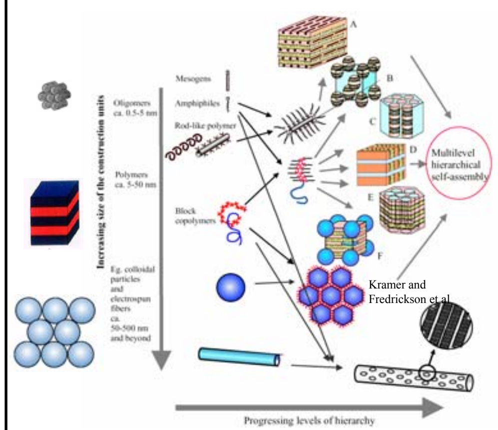


In the aqueous state



General & Thuenemann, Macromolecules 2001, 34, 6978 (Schering)

Generalizing: Facile selection of the length scales for hierarchical self-assembly



Ruokolainen, Mäkinen, Torkkeli, Mäkelä, Serimaa, ten Brinke, O. Ikkala, ***Science*, 280, 557 (1998).**

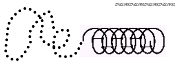
Ikkala & ten Brinke
Science 2002, 295, 2407.

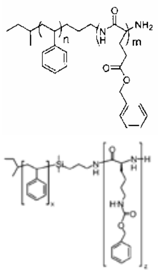
Mezzenga, Ruokolainen, Fredrickson, Kramer, Moses, Heeger, Ikkala, ***Science*, 299, 1872 (2003).**

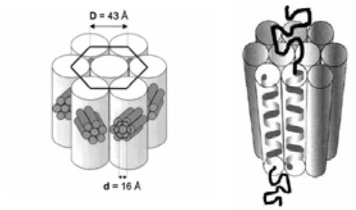
Ikkala & ten Brinke
***Chem Comm* 2004, 2131**

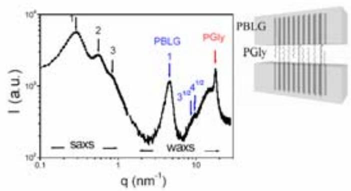
Valkama, Kosonen, Ruokolainen, Haatainen, Torkkeli, Serimaa, ten Brinke, and Ikkala, ***Nature Materials*, 2004, 3, 872**

Block colypeptides show more rich self-assembly due to secondary structures than the synthetic ones



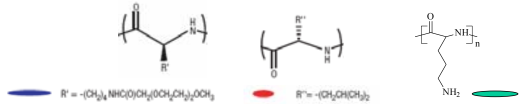






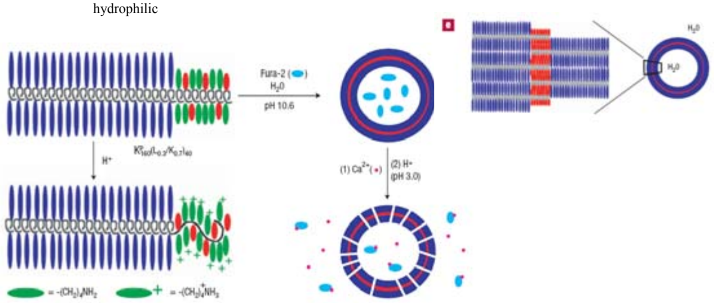
- New structures and hierarchies
- Deming, Pochan, Schlaad, Gallot, Antonietti, Klok, Gnanou, Lecommandeux, Hadjichristidis,..

Example 1: pH dependent release of model dye from block copolypeptide vesicles



KP = poly(Nε-2-(2-(2-methoxyethoxy) ethoxy)acetyl-L-lysine
hydrophilic

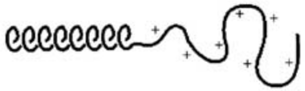
L = poly(L-leucine)
hydrophobic

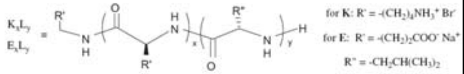


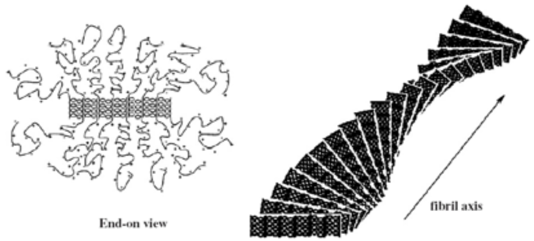
Deming et al, *Nature Materials* 2004 **3** 244

Hydrogel scaffolds

- Hydrated networks, mimic extracellular matrix
- Block copolypeptides
  - Helical ”rod-like” blocl
  - Charged block



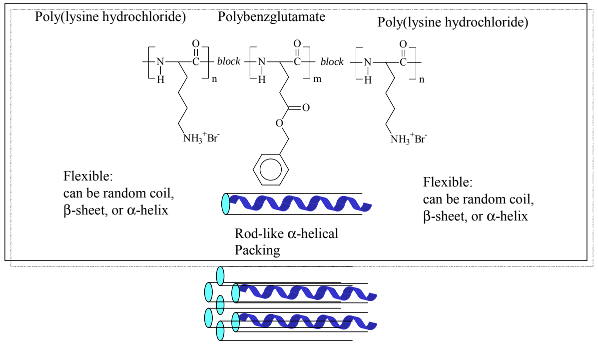




Timothy J. Deming Prog. Polym. Sci. 32 (2007) 858–875

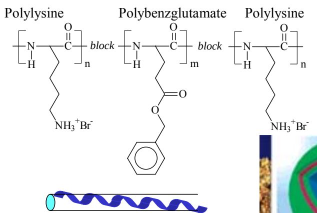
Example 2: Self-Assembling Block Copolypeptides to Lead Responsive Vesicles

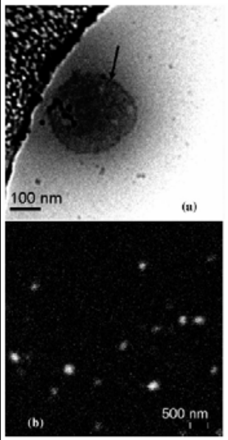
- Poly(lysine hydrochloride)-*block*-polybenzglutamate-*block*-poly(lysine hydrochloride)
  - PLL-*b*-PBLG-*b*-PLL
- Ring-opening polymerization with initiator diaminohexane under high vacuum
- Narrow molecular weight distribution



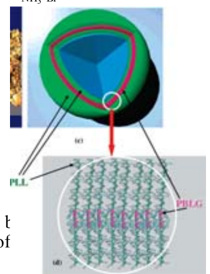
Iatrou, Frielinghaus, Hanski, Ferderigos, Ruokolainen, Ikkala, Richter, Mays, Hadjichristidis, *Biomacromolecules*, **8**, 2173 (2007).

Cryo-TEM: Forms vesicles (Also light scattering and neutron scattering)



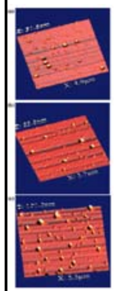


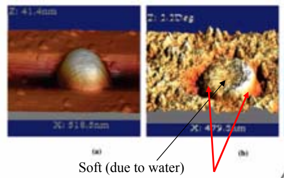
- pH 7.4
- ca. 250 nm vesicles, t a large distribution of sizes

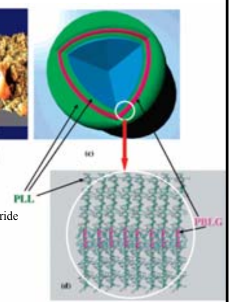


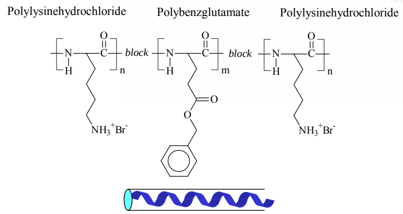
Vesicles: Atomic Force Microscopy

- Surface thickness
  - ca 10-30 nm
- Vesicle diameter
  - 250 nm



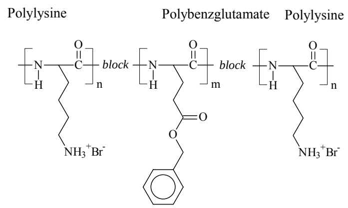






Iatrou, Frielinghaus, Hanski, Ferderigos, Ruokolainen, Ikkala, Richter, Mays, Hadjichristidis, *Biomacromolecules*, **8**, 2173 (2007).

PLL secondary structure depends on pH and temperature: Source for responsive behavior



Polylysine adopts different secondary structures, see eg.

Random coil

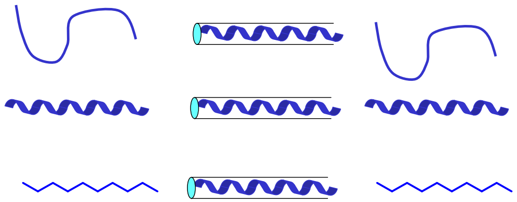
pH=7.4

α-helix

pH=11.5

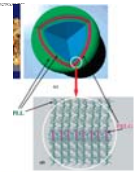
β-sheet

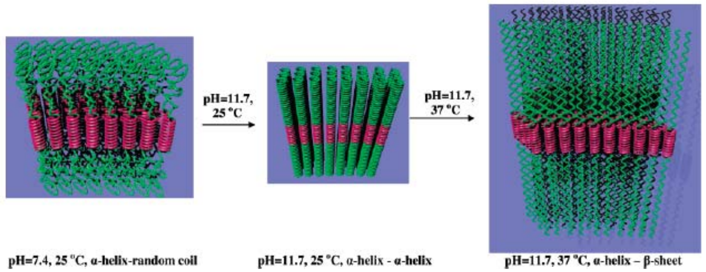
pH=11.5
& elevated temp



Vesicle surface can be controlled externally

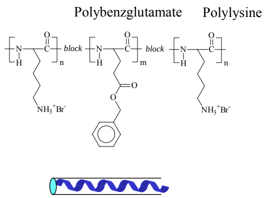
- Circular Dichroism Spectra reveals that the secondar structure of polylysine depends on pH and T

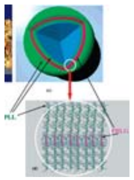




Iatrou, Frielinghaus, Hanski, Ferderigos, Ruokolainen, Ikkala, Richter, Mays, Hadjichristidis, *Biomacromolecules*, **8**, 2173 (2007).

Encapsulation of DNA within the vesicle

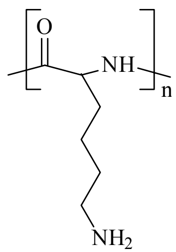




- Aqueous DNA solution
- PLL-*b*-PBLG-*b*-PLL in DMSO
- Add the DNA solution to the polymer solution
- Rinse

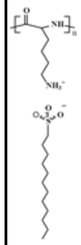
- So far, encapsulation of DNA can be detected by UV

It is helpful to observe self-assembled structures of homopolymeric Poly(L-lysine)/anionic surfactants



Polylysine/*n*-alkylsulfonic acid salts
Linear alkyl tail

From water

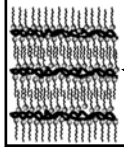


Surfactant tail length:

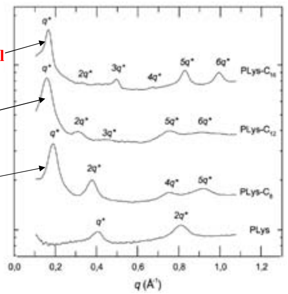
Hexadecyl

Dodecyl

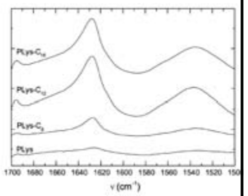
Octyl



SAXS



FTIR

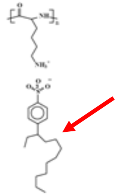


- 1628 and 1536 cm^{-1}
- lamellae
- β-sheets

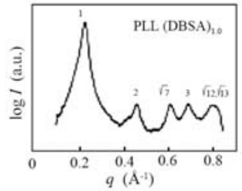
Ponomarenko, Tirrel, MacKnight 1996
Junnila, Hanski unpublished

- Problem: Brittle solid, PLL chains interlocked by *β*-sheet hydrogen bonds
- No fluid-like liquid crystallinity
- Use more disordered side chains

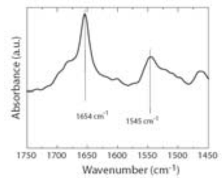
β-sheets can be broken by more disordered side chains: Polylysine/branched dodecylbenzenesulfonic acid PLL(DBSA)

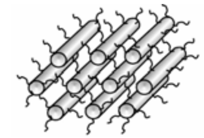


Small Angle X-ray Scattering

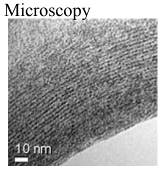


FTIR





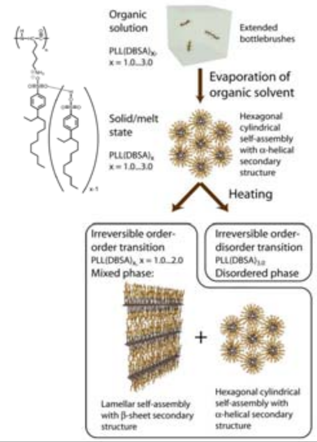
Transmission Electron Microscopy



- Re-cast from chloroform (+ some trifuoroacetic acid)
- 1654 and 1549 cm^{-1}
- α-helix
- Can become plasticized to allow flow: Liquid crystal

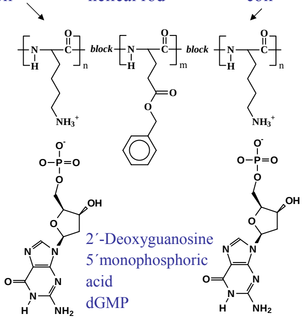
Hanski, Junnila, Almásy, Ruokolainen, Ikkala, *Macromolecules* 2008, 41, 866

Polylysine/dodecylbenzenene sulphonic acid complexes

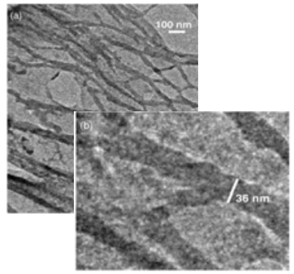


x-level hierarchical self-assembly to control supramolecular fibrillation and functionality

Polylysine coil | Polybenzglutamate "helical rod" | Polylysine coil



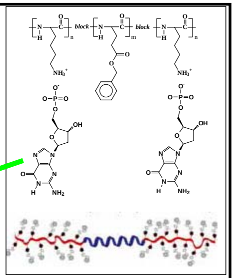
2´-Deoxyguanosine 5´monophosphoric acid dGMP



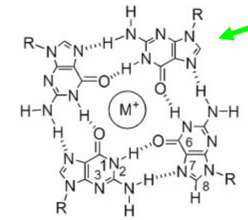
Instructive to follow step by step:

Houbenov, Nykänen, Iatrou, Hadjichristidis, Ruokolainen, Faul, Ikkala, Adv Funct Mat, in press

Stage 1



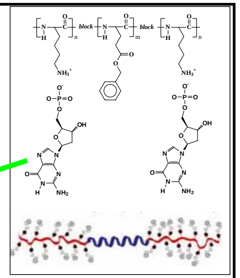
Four guanosine groups make 8 hydrogen bonds to assemble as **guanosine quartets** i.e. **G-quartets as disc-like supramolecular mesogen**



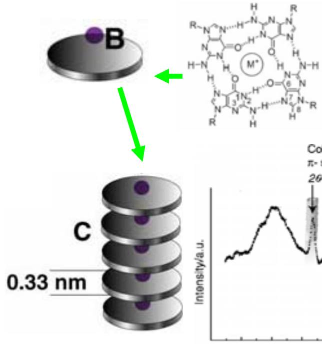
- Need metal cation B for stabilization
  - Na+, K+, ...
  - Allows tuning and functions

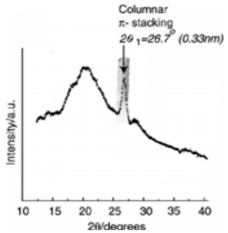
J. T. Davis, Angew. Chem. Int. Ed. 2004, 43, 668

Stage 2



Supramolecular **G-quartet disks stack into columns**



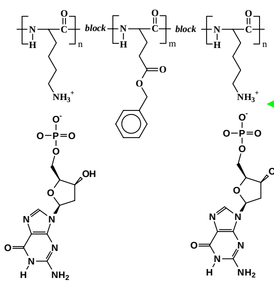


- Need metal cation B for stabilization
  - Na+, K+, ...
  - Allows tuning and functions

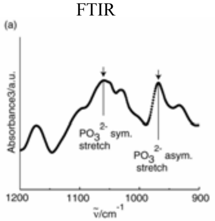
Houbenov, Nykänen, Iatrou, Hadjichristidis, Ruokolainen, Faul, Ikkala, Adv Funct Mat, in press

Stage 3

2´-Deoxyguanosine 5´monophosphoric acid (dGMP) ionically complexes to Polylysine



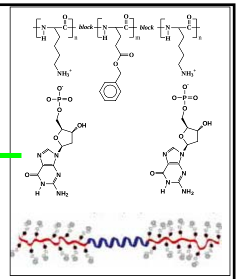
FTIR



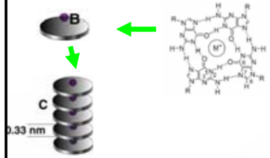
see later also SAXS

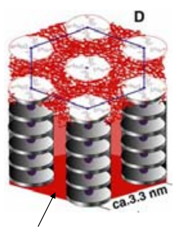
Houbenov, Nykänen, Iatrou, Hadjichristidis, Ruokolainen, Faul, Ikkala, Adv Funct Mat, in press

Stage 4

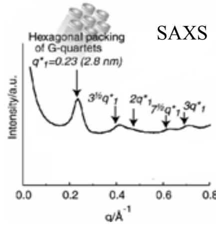


Hexagonal cylindrical self-assembly of G-quartet columns within polylysine





SAXS



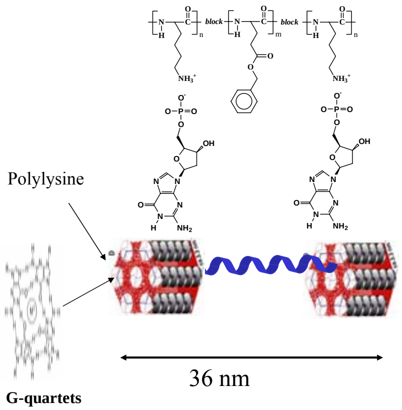
- Also indirectly shows ionic complex

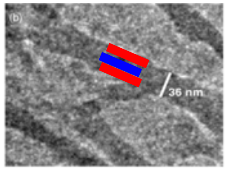
Polylysine

Houbenov, Nykänen, Iatrou, Hadjichristidis, Ruokolainen, Faul, Ikkala, Adv Funct Mat, in press

Stage 5

Discotic LC motif and helical rod-like (calamitic) LC motif leads to microphase separation





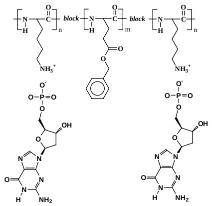
Cannot be resolved in SAXS

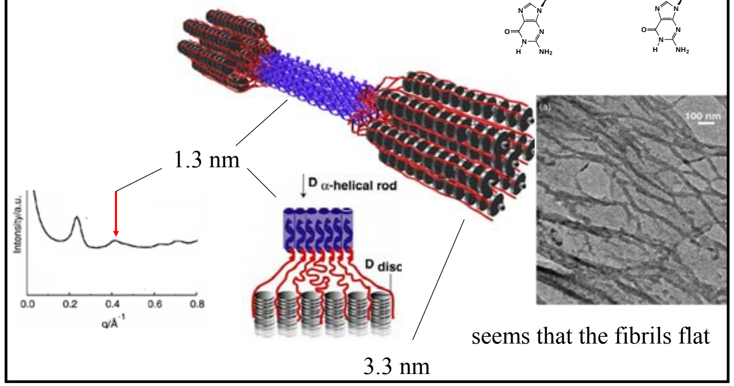
- Only 2 layers within a fibril

The internal layered structure does not become resolved in TEM, even with staining

Stage 6

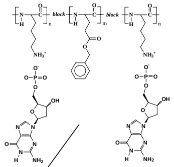
Both discotic LC motif (G4/PLL) and helical rod-like (calamitic) LC (PBGL) motif undergo cylindrical hexagonal self-assembly but different periodicity leading to packing frustration and limit width

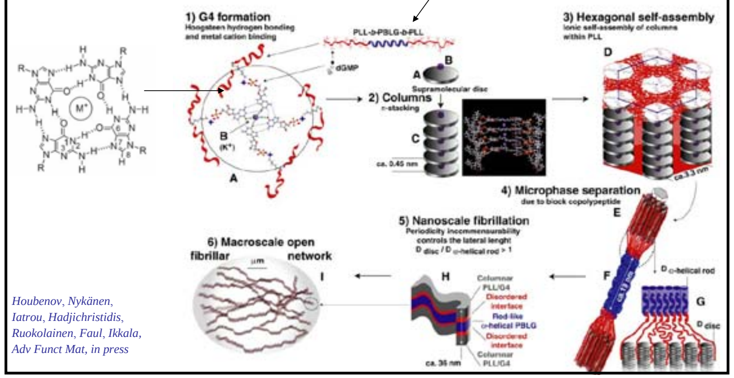




Combine

- Guanosine quartets (DNA-like interactions)
- Rod-coil block copolymers
- Packing frustrations
- Rod-like and disc-like liquid crystallinity
- **Towards Multifunctional gels and scaffolds**



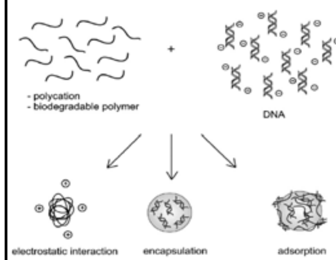


Houbenov, Nykänen, Iatrou, Hadjichristidis, Ruokolainen, Faul, Ikkala, Adv Funct Mat, in press

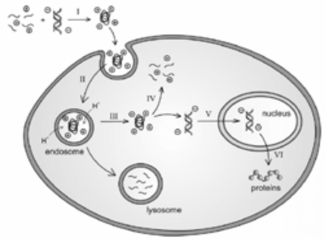
Towards gene delivery

Common methods for gene packaging

Barriers to be crossed

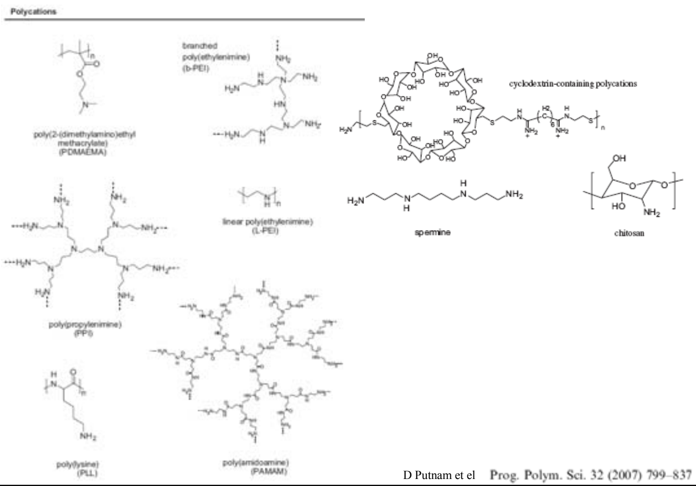


biodegradable nano- or microspheres



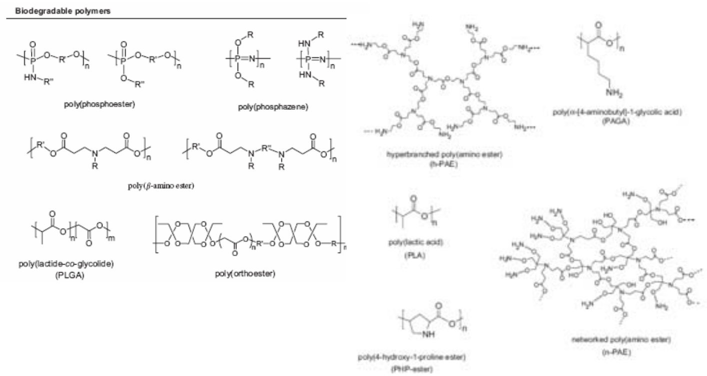
D Putnam et el Prog. Polym. Sci. 32 (2007) 799–837

Cationic vectors, examples



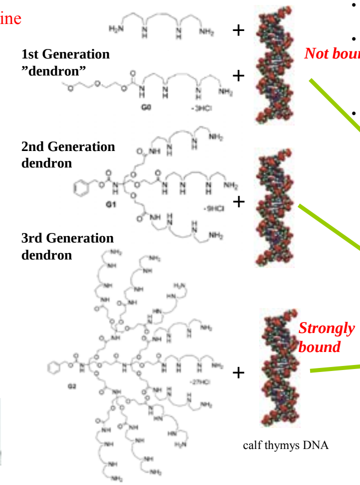
D Putnam et el Prog. Polym. Sci. 32 (2007) 799–837

Biodegradable vectors



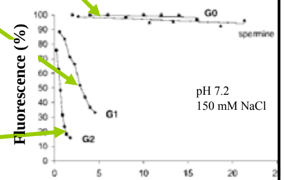
D Putnam et el Prog. Polym. Sci. 32 (2007) 799–837

Amplification of weak interactions to bind DNA: *Multivalency*



- Interaction between protonated amine and DNA phosphate is weak
- Combine amines
  - Dendrons
  - Divergent synthesis
- Investigate whether spermine derivatives can liberate Ethidium bromide
  - Fluorescence of free ethidium bromide quenched

DNA/ethidium bromide assay

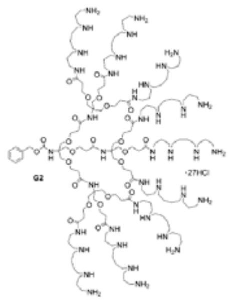


Relative amount of spermine derivative
(units by Charge Excess,
i.e. # spermine amines vs # DNA phosphates)

Kostiainen, Hardy, Smith, *Angew Chem* 2005, **44**, 2556

Towards tailoring the vector

- Taíloring of the release
- Tailoring of the dendron apex
  - Amphiphilicity promotes self-assembly with DNA
  - Proteinic functionality is the apex?
  - Possibility of detailed tailoring by protein engineering?



Hydrophobins

Annu. Rev. Microbiol. 2001. 55:625–46
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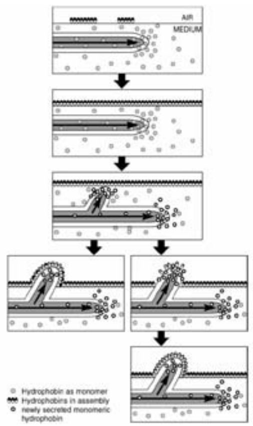
HYDROPHOBINS: Multipurpose Proteins

Han A. B. Wösten*

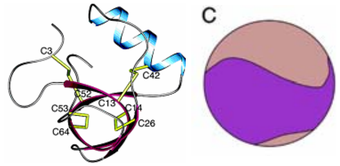
■ **Abstract** Class I and class II hydrophobins are small secreted fungal proteins that play a role in a broad range of processes in the growth and development of filamentous fungi. For instance, they are involved in the formation of aerial structures and in the attachment of hyphae to hydrophobic surfaces. The mechanisms by which hydrophobins fulfill these functions are based on their property to self-assemble at hydrophilic-hydrophobic interfaces into a 10 nm-thin highly amphipathic film. Complementation studies have shown that class I hydrophobins belong to a closely related group of morphogenetic proteins, but that they have evolved to function at specific interfaces. Recent evidence indicates that hydrophobins do not only function by self-assembly. Monomeric hydrophobin has been implicated in cell-wall assembly, but the underlying mechanism is not yet clear. In addition, hydrophobin monomers could act as toxins and elicitors.

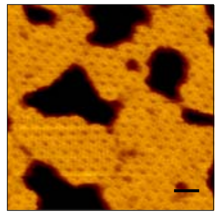


Hydrophobins are strong mesoscopic surfactants

- Chandler (*Nature* 2005 437 640)
  - Mesocscopic surfactants (1 nm) behave "synergistically"
- Janus type micelles could be interesting
- Hydrophobins are mesoscopic surfactants
- Produced in *Tricoderma Reesei*
- Hydrophobin HFBI: shape persistence due 4 internal disulfide bridges
- Hydrophobins perhaps the strongest known biological surfactants

Thin films
Structures
Self-assembly





Hakanpää, J.; Paananen, A.; Askolin, S.; Nakari-Setälä, T.; Parkkinen, T.; Penttilä, M.; Linder, M. B.; Rouvinen, J. *J. Mol. Biol.* **2004**, *279*, 534
Linder et al FEMS Microbiol Reviews 2005 29 877

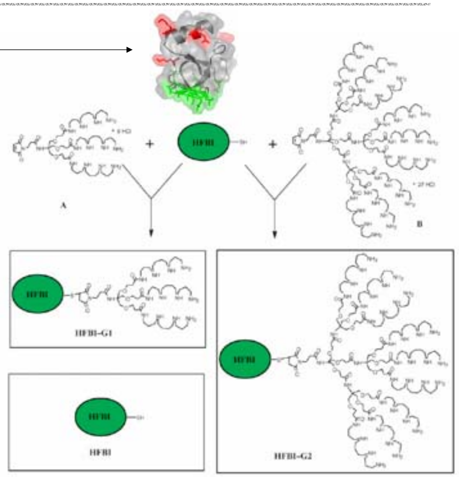
Biochemistry **2003**, *42*, 5253–5258

Structural Hierarchy in Molecular Films of Two Class II Hydrophobins

Arja Paananen, Elina Vuorimaa, Mika Torkkeli, Merja Penttilä, Martti Kauranen, Olli Ikkala, Helge Lemmetyinen, Ritva Serimaa, and Markus B. Linder

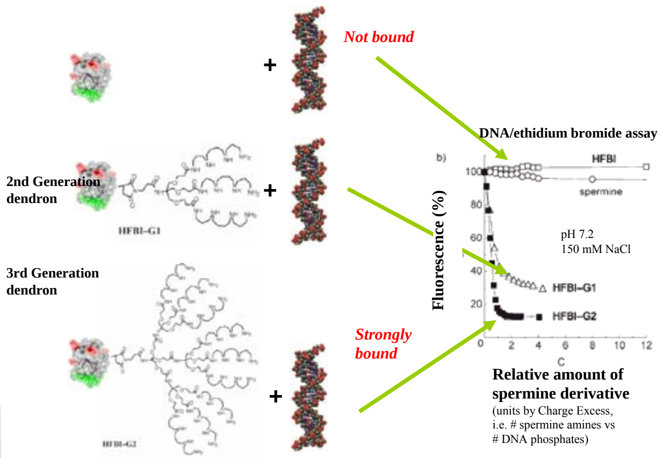
Towards block copolymers with proteinic functional blocks as gene vectors

- Very surface active protein: hydrophobin Class II
  - Linder arl /VTT
- Protein engineering
  - New sulfhydryl groups engineered
  - Produced in *Tricoderma reesei*
  - HFB dimers reduced to HFB monomers by dithiothreitol
- Endlinking to spermine dendron maleimides



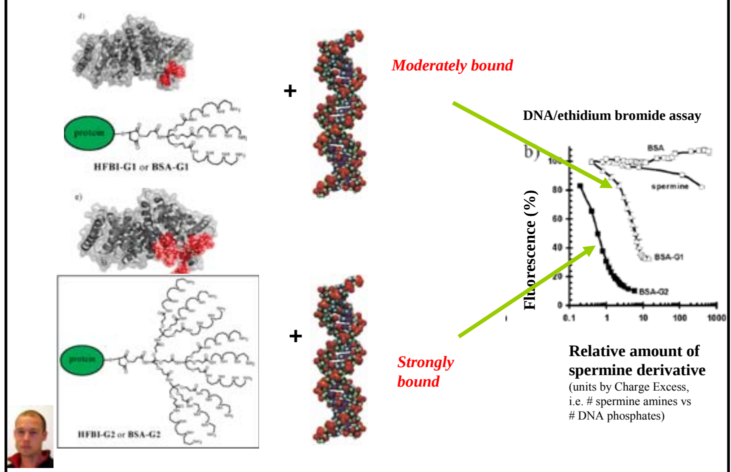
Kostiainen, Szilvay, Smith, Linder, Ikkala, *Angewandte Chemistry*, **45**, 3538 (2006).

Towards block copolymers with proteinic functional blocks as gene vectors



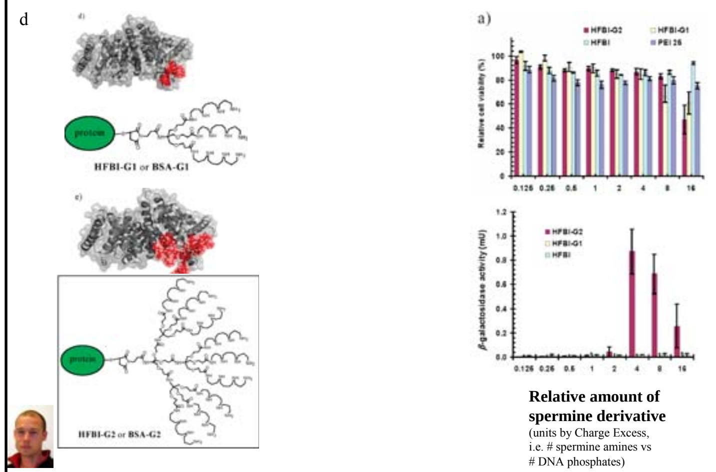
Kostiainen, Szilvay, Smith, Linder, Ikkala, *Angewandte Chemistry*, **45**, 3538 (2006).

Also other proteins: Bovine Serum Albumin (BSA)



Kostiainen, Szilvay, Lehtinen, Smith, Linder, Urtti, Ikkala, *ACS Nano*, **1**, 103 (2007).

Cytotoxicity and cellular uptake



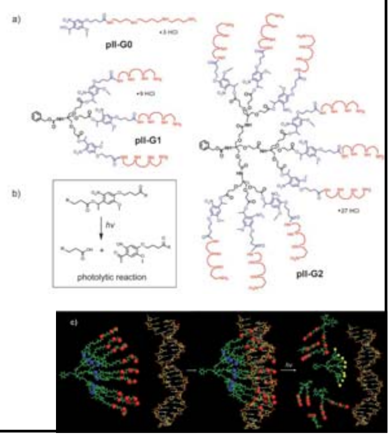
Kostiainen, Szilvay, Lehtinen, Smith, Linder, Urtti, Ikkala, *ACS Nano*, **1**, 103 (2007).

Optically Triggered Release of DNA from Multivalent Dendrons by Degrading and Charge-Switching Multivalency**

Mauri A. Kostiainen, David K. Smith,* and Olli Ikkala*

Angew. Chem. Int. Ed. **2007**, *46*, 1–6

- The pristine dendron contains cationic spermine side groups
  - Spermines cationic, can bind electrostatically the anionic DNA chains
  - Binding multivalent: more efficient binding as there is a dense set of cationic side groups
- The spermine groups are linked to the apex using a photolabile nitrobenzyl groups
  - Exposure of UV light (350 nm) attacks the photolobile groups
  - The spermines "exploded" off
  - The density of the cationic groups drastically reduced
  - In addition, the UV degradation leaves negative charge at the apex instead of positive spermines
  - Charge repulsion
  - Optically triggered DNA release



Molecular materials lab of Helsinki University of Technology available facilities (big devices via *Center of New Materials*)

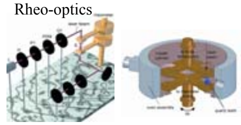
New nanoscience center *Nanopoli*
Special construction

Multidisciplinary research team
prof Olli Ikkala
prof Janne Ruokolainen
adjunct prof Robin Ras

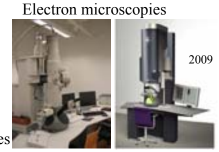
Small and medium angle scattering

Sample robotics

Rheo-optics

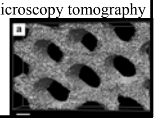


Electron microscopies

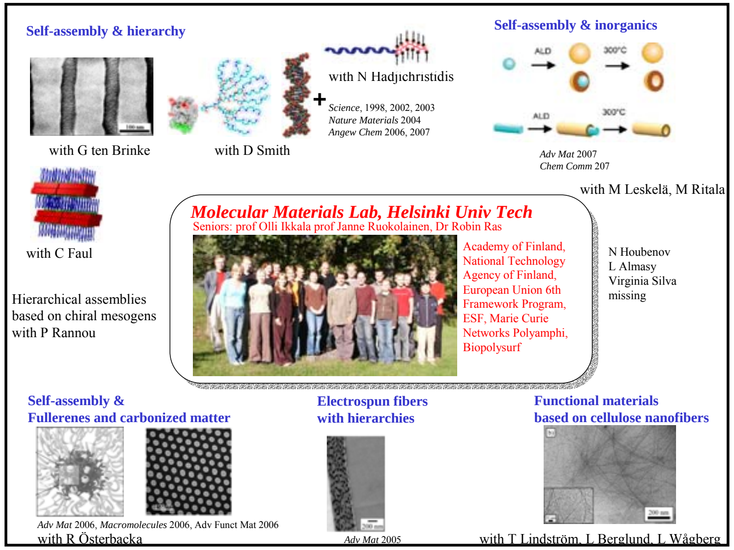


with
Cyo-facilities

Electron microscopy tomography



Next to our lab
- Production and research of carbon nanotubes
- Quantum transport and devices
- Photonics and optics
- Energy


Self-assembly & hierarchy
with G ten Brinke
with D Smith
with N Hadjichristidis
Science, 1998, 2002, 2003
Nature Materials 2004
Angew Chem 2006, 2007
Self-assembly & inorganics
ALD
300°C
ALD
300°C
Adv Mat 2007
Chem Comm 207
with M Leskelä, M Ritala
with C Faul
Molecular Materials Lab, Helsinki Univ Tech
Seniors: prof Olli Ikkala prof Janne Ruokolainen, Dr Robin Ras
Academy of Finland, National Technology Agency of Finland, European Union 6th Framework Program, ESF, Marie Curie Networks Polyamphi, Biopolysurf
N Houbenov
L Almasy
Virginia Silva
missing
Hierarchical assemblies based on chiral mesogens with P Rannou
Self-assembly & Fullerenes and carbonized matter
Electrospun fibers with hierarchies
Functional materials based on cellulose nanofibers
Adv Mat 2006, Macromolecules 2006, Adv Funct Mat 2006
with R Österbacka
Adv Mat 2005
with T Lindström, L Berglund, L Wågberg