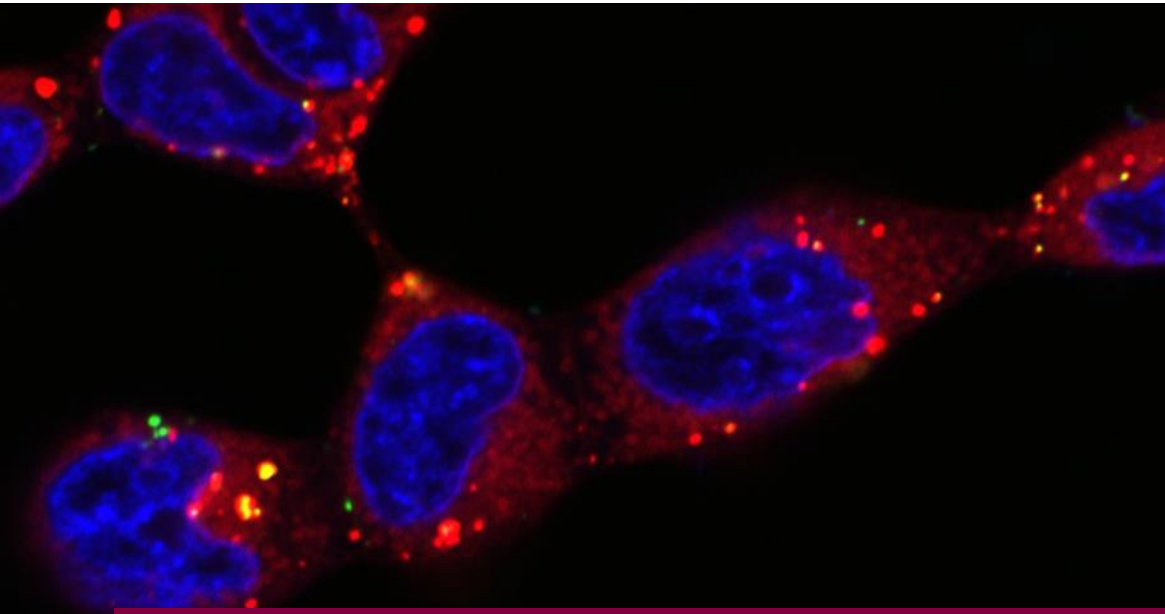
FRIEDRICH-SCHILLER-
UNIVERSITÄT
JENA

Collaborative Research Center 1278
PolyTarget



SYMPOSIUM ON INNOVATIVE POLYMERS FOR THE NANOMEDICINE OF THE 21ST CENTURY

Scientific Program

15 - 17 July 2019 | Jena (Germany)

TABLE OF CONTENTS

WELCOME NOTE

Dear friends and colleagues,

it is my great pleasure to welcome you to the Symposium on Innovative Polymers for the Nanomedicine of the 21st Century!

I am looking forward to three days of excellent scientific exchange and networking with international experts from science, research, politics, administration and industry to exchange knowledge and experience on the latest developments in the field of pharmapolymers with particular emphasis on:

- Living polymerization methods and multicomponent reactions for the synthesis of pharmapolymers and hybrid materials.
- Progress in application of polymer classes, e.g. poly(oxazolines), polysaccharides, cationic polymers, polyesters.
- Novel polymer architectures:, e.g. sequence defined macromolecules, polymers with hyperbranched segments.
- Self-assembeld nanosystems, responsive hydrogels, composite polymer colloids, polymersomes and nanoparticles.
- Targeting strategies for nanostructures and barrier interactions.
- Preclinical test strategies.
- Advances in characterization methods: Electron microscopy, ultra centrifugation, Raman spectroscopic imaging, light microscopy.
- In silico design of polymer nanocarriers.

After two and a half days of oral and poster presentations that will be opened by one of the pioneers of application of nanoparticles in the biomedical field, Prof. Dr. Kazunori Kataoka, the conference program will be rounded off on Wednesday by hands-on workshops.

Sincerely yours

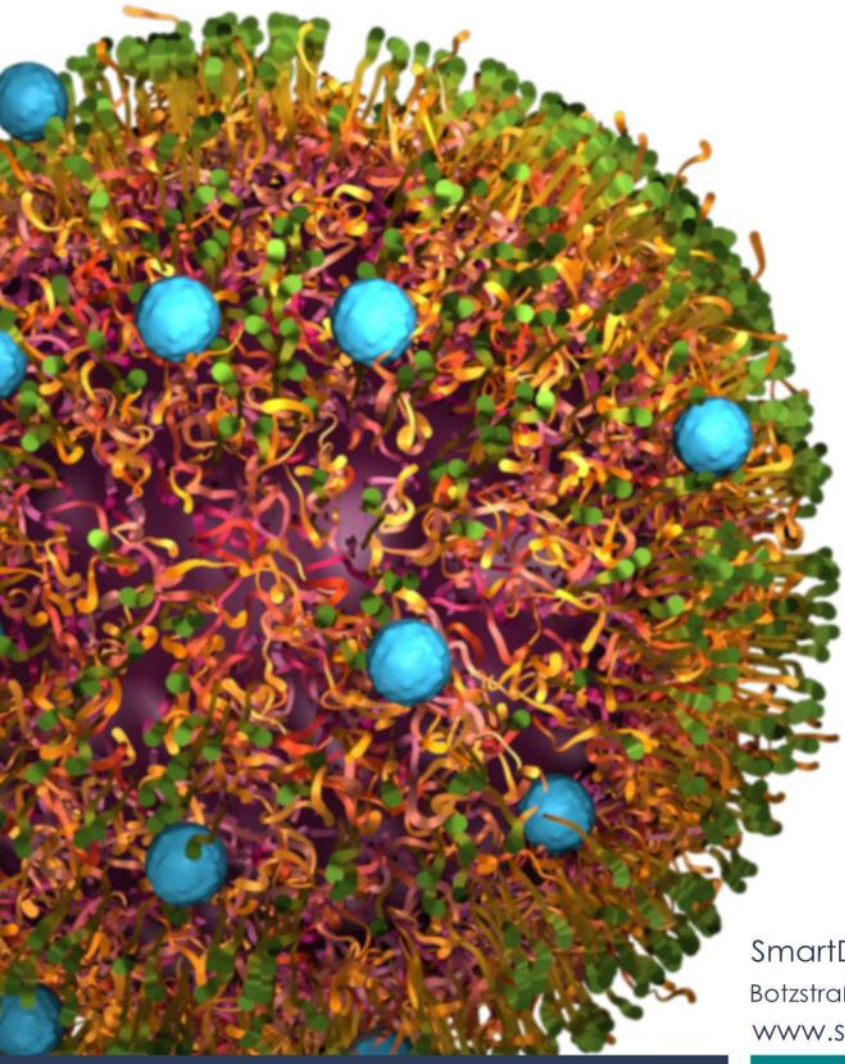
Ulrich Schubert

Prof. Dr. Ulrich S. Schubert

SmartDyeLivery

Clever nano transport

Targeted Drug Delivery by Nanoparticles



SmartDyeLivery GmbH
Botzstraße 5 • D-07743 Jena
www.smartdyelivery.de

GENERAL INFORMATION

Date
15 - 17 July 2019

Venue
Friedrich Schiller University Jena
Jena Center for Soft Matter (JCSM)
Philosophenweg 7
07743 Jena
Germany

Unless otherwise indicated, the sessions will take place in the lecture hall of the
Center for Applied Research (ZAF)
Philosophenweg 7
07743
Jena, Germany.

Organizers

PolyTarget SFB 1278

JCSM Jena Center for Soft Matter

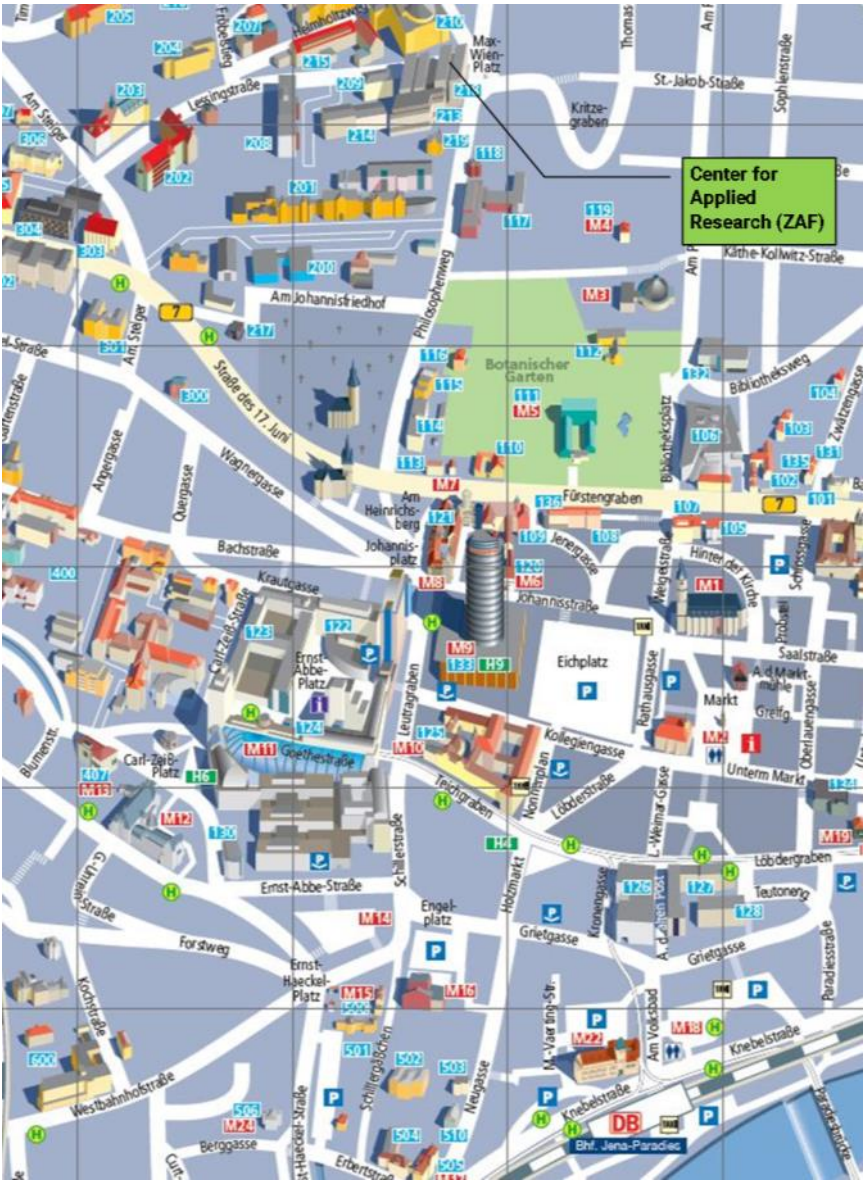
Supported by

DFG Deutsche Forschungsgemeinschaft German Research Foundation

Gold sponsor

SmartDyeLivery
Clever nano transport

MAP OF THE CONFERENCE VENUE



PROGRAM OVERVIEW (MORNINGS)

Lectures
Lab tours
Workshops
Poster session
Breaks and social events

	15 July 2019	16 July 2019	17 July 2019
09:00 am	Registration	Lab tours	Lab tours
09:15 am			
09:30 am			
09:45 am			
10:00 am	Conference opening		
10:15 am			
10:30 am	L01: K. Kataoka	L12: J. M. Asua	L21: D. Haddleton
10:45 am			
11:00 am			
11:15 am		L13: S. Schubert	L22: I. Nischang
11:30 am	L02: R. Becer		
11:45 am		L14: R. Heintzmann	L23: M. Barz
12:00 pm			
12:15 pm	L03: R. Hoogenboom	L15: A. Ramoji / A. Press	L24: S. Lecommandoux
12:30 pm			
12:45 pm		Lunch break	
01:00 pm	Lunch break		Farewell
01:15 pm			Lunch break

PROGRAM OVERVIEW (AFTERNOONS)

	15 July 2019	16 July 2019	17 July 2019
01:30 pm			
01:45 pm		L16: F. Wiesbrock	
02:00 pm	L04: M. Meier		
02:15 pm			Workshops
02:30 pm		L17: C. Höppener	
02:45 pm	L05: D. Fischer		
03:00 pm		L18: B. Iván	
03:15 pm	L06: S. Höppener		
03:30 pm			
03:45 pm	L07: M. Gericke	Coffee break	
04:00 pm			
04:15 pm	Coffee break	L19: M. Sierka	
04:30 pm			
04:45 pm	L08: I. Potemkin	L20: A. Dworak	
05:00 pm			
05:15 pm			
05:30 pm	L09: V. Deckert	Poster session	
05:45 pm			
06:00 pm	L10: A. Träger		
06:15 pm			
06:30 pm	L11: J.-F. Gohy		
06:45 pm			
07:00 pm		Barbecue	
07:15 pm			
07:30 pm			
07:45 pm			
08:00 pm	Conference dinner		
08:15 pm	(open end)		
08:30 pm			
08:45 pm			

SCIENTIFIC PROGRAM

Monday, 15 July 2019

09:00 am — REGISTRATION

10:00 am — CONFERENCE OPENING

Welcome notes
Prof. Dr. Ulrich S. Schubert
Chairman, Friedrich Schiller University Jena, Jena (DE)

Prof. Dr. Iris Winkler
Vice-President for Learning and Teaching of the Friedrich Schiller University Jena, Jena (DE)

SESSION 1
Session Chair: Prof. Dr. Ulrich S. Schubert

10:30 am — L01: PLENARY LECTURE

Self-assembled supramolecular nanosystems for smart diagnosis and targeted therapy of intractable diseases
Prof. Dr. Kazunori Kataoka
The University of Tokyo, Tokyo / Innovation Center of NanoMedicine, Kawasaki City (JP)

11:30 am — L02: INVITED LECTURE

Glycopolymer code: towards selective lectin recognition tuned by sequence and folding in macromolecules
Dr. Remzi Becer
University of Warwick, Warwick (UK)

12:15 pm — L03: INVITED LECTURE

Poly(2-oxazoline)s as drug delivery vehicles
Prof. Dr. Richard Hoogenboom
Ghent University, Ghent (BE)

01:00 pm — LUNCH BREAK

SCIENTIFIC PROGRAM

SESSION 2
Session Chair: Prof. Dr. Dave Haddleton

02:00 pm — L04: INVITED LECTURE
Multicomponent reactions in polymer science: from versatile tuning of structure and properties to sequence defined macromolecules
Prof. Dr. Michael Meier
Karlsruhe Institute of Technology, Karlsruhe (DE)

02:45 pm — L05: CONTRIBUTED LECTURE
Preclinical test strategies using the shell less hen's egg test
Prof. Dr. Dagmar Fischer
Friedrich Schiller University Jena, Jena (DE)

03:15 pm — L06: CONTRIBUTED LECTURE
Insight into the structure and architecture of polymer nanoparticles obtained by transmission electron microscopy techniques
PD Dr. Stephanie Höppener
Friedrich Schiller University Jena, Jena (DE)

03:45 pm — L07: CONTRIBUTED LECTURE
Reactive polysaccharide nanoparticles for biomedical applications
Dr. Martin Gericke
Friedrich Schiller University Jena, Jena (DE)

04:15 pm — COFFEE BREAK

SCIENTIFIC PROGRAM

SESSION 3
Session Chair: Prof. Dr. Michael Meier

04:45 pm — L08: INVITED LECTURE
Polymer microgels: permeability of soft colloidal particles leads to sophisticated properties
Prof. Dr. Igor Potemkin
Lomonosov Moscow State University, Moscow (RU)

05:30 pm — L09: CONTRIBUTED LECTURE
Nanoscale structure sensitive investigation of bio-polymers - chances and challenges
Prof. Dr. Volker Deckert
Friedrich Schiller University Jena, Jena (DE)

06:00 pm — L10: CONTRIBUTED LECTURE
Different strategies to overcome the endosomal barrier for efficient gene delivery
Dr. Anja Träger
Friedrich Schiller University Jena, Jena (DE)

06:30 pm — L11: INVITED LECTURE
Synthesis and characterization of redoxresponsive hydrogels based on stable nitroxide radicals
Prof. Dr. Jean-François Gohy
Catholic University of Louvain, Louvain-la-Neuve (BE)

SCIENTIFIC PROGRAM

Tuesday, 16 July 2019

09:00 am — LAB TOURS
Meeting point:
Foyer of the Center for Applied Research (ZAF)

SESSION 1
Session Chair: Prof. Dr. Sébastien Lecommandoux

10:30 am — L12: INVITED LECTURE
Fine-tuning composite polymer colloids
Prof. Dr. Jose M. Asua
University of the Basque Country UPV/EHU, San Sebastian (ES)

11:15 am — L13: CONTRIBUTED LECTURE
Preparation and application of functional polymeric nanoparticles as drug delivery devices
Dr. Stephanie Schubert
Friedrich Schiller University Jena, Jena (DE)

11:45 am — L14: CONTRIBUTED LECTURE
Bridging light and electron microscopy
Prof. Dr. Rainer Heintzmann
Friedrich Schiller University Jena, Jena (DE)

12:15 pm — L15: CONTRIBUTED LECTURE
Raman spectroscopic imaging reveals changes in the micellar conformation dictating pharmacokinetic properties
Dr. Anuradha Ramoji
Leibniz-Institute for Photonic Technology / Jena University Hospital, Jena (DE)
Dr. Adrian Press
Jena University Hospital, Jena (DE)

SCIENTIFIC PROGRAM

12:45 pm LUNCH BREAK

SESSION 2
Session Chair: Prof. Dr. Kazunori Kataoka

01:45 pm L16: INVITED LECTURE
Clickable copoly(2-oxazoline)s for drug inclusion/API attachment and selective cell adhesion
PD Dr. Frank Wiesbrock
Graz University of Technology, Graz (AT)

02:30 pm L17: CONTRIBUTED LECTURE
Multimodal characterization of polymer nanoparticles: Chemical specificity, structural information and mechanical properties on the nanometer scale
Dr. Christiane Höppener
Friedrich Schiller University Jena, Jena (DE)

03:00 pm L18: INVITED LECTURE
Nanostructured macromolecular assemblies as controlled drug release carriers: From intelligent drug release to high efficiency drug solubilization with nanomicelles of self-assembling block copolymers possessing hyperbranched segments
Prof. Dr. Béla Iván
Eötvös Loránd University, Budapest (HU)

03:45 pm COFFEE BREAK

SCIENTIFIC PROGRAM

SESSION 3
Session Chair: Prof. Dr. Jose M. Asua

04:15 pm — L19: CONTRIBUTED LECTURE
In silico design of polymer nanocarriers for biomedical applications
Prof. Dr. Marek Sierka
Friedrich Schiller University Jena, Jena (DE)

04:45 pm — L20: INVITED LECTURE
Some biomedical applications of temperature responding polymers
Prof. Dr. Andrzej Dworak
Centre of Polymer and Carbon Materials, Polish Academy of Sciences, Zabrze (PL)

05:30 pm — POSTER SESSION AND DRINKS

SCIENTIFIC PROGRAM

Wednesday, 17 July 2019

09:00 am — LAB TOURS
Meeting point:
Foyer of the Center for Applied Research (ZAF)

SESSION 1
Session Chair: Prof. Dr. Jean-François Gohy

10:30 am — L21: INVITED LECTURE
Copper mediated living radical polymerisation in the presence of oxygen
Prof. Dr. Dave Haddleton
University of Warwick, Warwick (UK)

11:15 am — L22: CONTRIBUTED LECTURE
In situ analysis of polymers and nanoparticle systems for the nanomedicine
PD Dr. Ivo Nischang
Friedrich Schiller University Jena, Jena (DE)

11:45 am — L23: CONTRIBUTED LECTURE
PeptoMicelles in tuberculosis therapy
Dr. Matthias Barz
Johannes Gutenberg University, Mainz (DE)

12.15 pm — L24: INVITED LECTURE
Biomimetic polymersomes as innovative nanomedicines
Prof. Dr. Sébastien Lecommandoux
University of Bordeaux, Bordeaux (FR)

01.00 pm — FAREWELL
Prof. Dr. Ulrich S. Schubert
Chairman, Friedrich Schiller University Jena, Jena (DE)

01.15 pm — LUNCH BREAK

SCIENTIFIC PROGRAM

02.15 pm PARALLEL WORKSHOPS

Workshop 1:
EO-Polymerization
Spacebox first floor
Dr. Jürgen Vitz
Friedrich Schiller University Jena, Jena (DE)

Workshop 2:
Formulation of polymeric nanoparticles
Lecture hall
Dr. Stephanie Schubert
Friedrich Schiller University Jena, Jena (DE)

Workshop 3:
Electron microscopic characterization
Spacebox ground floor
PD Dr. Stephanie Höppener
Friedrich Schiller University Jena, Jena (DE)

Workshop 4:
Solution characterization
CEEC Jena, room 108
PD Dr. Ivo Nischang
Friedrich Schiller University Jena, Jena (DE)

Workshop 5:
Microwave assisted synthesis
CEEC Jena, seminar room (E 009)
Dr. Christine Weber
Friedrich Schiller University Jena, Jena (DE)

SOCIAL PROGRAM

Monday, 15 July 2019

08:00 pm **CONFERENCE DINNER**

Botanical Garden Jena
Fürstengraben 26
07743 Jena
Enjoy a memorable evening in the relaxed atmosphere of the "green lung of Jena"!

Tuesday, 16 July 2019

07:00 pm **THURINGIAN BARBECUE**

Center for Applied Research (ZAF)
Thuringia is world famous for its "Bratwurst"! Enjoy a typical Thuringian barbecue evening with us - including stimulating conversations with colleagues and friends.

Abstracts of Oral Contributions

ABSTRACTS OF ORAL CONTRIBUTIONS

L01: Self-assembled supramolecular nanosystems for smart diagnosis and targeted therapy of intractable diseases

Kazunori Kataoka[a]
[a]Innovation Center of NanoMedicine, Kawasaki Institute of Industrial Promotion, Kawasaki, Japan
Institute for Future Initiatives, The University of Tokyo, Tokyo, Japan
kataoka@bmw.t.u-tokyo.ac.jp

Nanotechnology-based medicine (Nanomedicine) has received progressive interest for the treatment of intractable diseases, such as cancer, as well as for the non-invasive diagnosis through various imaging modalities. Engineered polymeric nanosystems with smart functions play a key role in nanomedicine as drug carriers, gene vectors, and imaging probes. This presentation focuses present status and future trends of supramolecular nanosystems self-assembled from designed block copolymers for therapy and non-invasive diagnosis of intractable diseases. Nanosystems with 10 to 100 nm in size can be prepared by programmed self-assembly of block copolymers in aqueous entity. Most typical example is polymeric micelle (PM) with distinctive core-shell architecture. PMs have several properties relevant for nanosystems, including controlled drug release, tissue penetrating ability, and reduced toxicity.[1] Furthermore, smart functionalities, such as pH- and/or redox potential responding properties, can be integrated into the PM structure. These smart PMs loaded with various chemotherapy reagents were evidenced to have a significant utility in the treatment of intractable and metastatic cancers, including pancreatic cancer, glioblastoma, and tumors harboring recalcitrant cancer stem cells (CSCs). Eventually, five different formulations of the PMs developed in our group have already been in clinical trials world-wide, including Japan, Asia, USA and European countries.

Versatility in drug incorporation is another relevant feature of PMs for drug delivery. Nucleic acid-based medicine can be assembled into PM through the electrostatic interaction with oppositely-charged polycationic block copolymers. In this way, siRNA- or antisense oligo (ASO)-loaded PMs were prepared, and their utility in molecular therapy of cancer has been revealed. Recently, PM-based imaging reagents were developed, opening a new avenue for the novel type of theranostic nanomedicines. PM-based nanosysems hold promise for the treatment of intractable diseases other than cancer. Very recently, we developed PMs decorated with glucose to crossing blood-brain barrier by recognizing glucose-transporter overexpressing on brain endothelial cells, indicating a novel route to deliver versatile drugs into brain for the treatment of neurodegenerative diseases, including Alzheimer's disease.

References

[1] H. Cabral, K. Miyata, K. Osada, K. Kataoka, *Chem. Rev*. **2018**, *118*, 6844-6892.

ABSTRACTS OF ORAL CONTRIBUTIONS

L02: Glycopolymer code: Towards selective lectin recognition tuned by sequence and folding in macromolecules

C. Remzi Becer[a,b]
[a]Department of Chemistry, University of Warwick, Coventry, United Kingdom
[b]School of Engineering and Materials Science, Queen Mary University of London, London, United Kingdom
remzi.becer@warwick.ac.uk

Sequence controlled polymers have been attracting more and more attention to deliver the desired properties to the advanced materials by the help of their precisely controlled compositions and architectures.[1] Understanding the specific multivalent carbohydrate-protein interactions is crucial to determine the structure-property relationships and to design accordingly the next generation of functional glycomaterials. Therefore, we investigate the structure -property relationships between the mammalian lectins and multivalent carbohydrate polymers, which may have applications for anti-adhesion therapy. Moreover, we have investigated the affinity of poly(mannose-methacrylate), helical glycocopolypeptides, gp120, start shaped glycopolymers, and cyclodextrin centered glycopolymers with a selected mannose binding lectin (DC-SIGN) that exists on dendritic cells, using SPR technique.[2-4] Selected members of a glycopolymer library were used to demonstrate the interactions between DC-SIGN and mannose rich polymers. We extend this study to a broader set of polymers to examine the effect of chain length, end group, architecture, thermoresponsive block, and number of arms in the star shaped polymers on the lectin binding.[5]

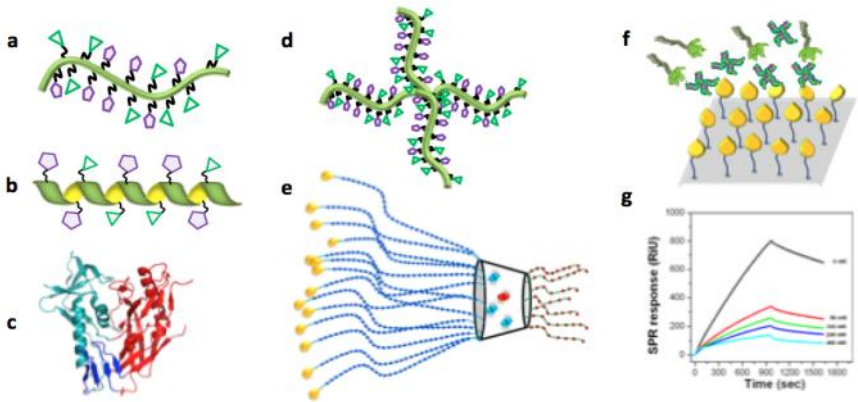


Fig. 1: Schematic representation of (**a**) linear GP, (**b**) helical glycocopolypeptide, (**c**) glycoprotein 120 (gp120), (**d**) star shaped GP, (**e**) cyclodextrin centred GP, (**f**) SPR measurement on glycopolymer-DCSIGN competition in solution, (**g**) SPR response-time for the interaction of DC-SIGN & gp120.

ABSTRACTS OF ORAL CONTRIBUTIONS

References

[1] C.Lavilla, G. Yilmaz, V. Uzunova, R. Napier, C. R. Becer, A. Heise, *Biomacromolecules* **2017**, *18*, 1928-1936.

[2] C. R. Becer, *Macromol. Rapid Commun*. **2012**, *33*, 742-752.

[3] Q. Zhang, L. Su, G. Chen, R. Wallis, D. A. Mitchell, D. M. Haddleton, C. R. Becer, *J. Am. Chem. Soc*. **2014**, *136*, 4325-4332.

[4] A. Blakney, G. Yilmaz, P.F. MacKay, C. R. Becer, R.J. Shattock, *Biomacromolecules* **2018**, *19*, 2870-2879.

[5] G. Yilmaz, V. Uzunova, R. Napier, C. R. Becer, *Biomacromolecules* **2018**, *19*, 3040-3047.

ABSTRACTS OF ORAL CONTRIBUTIONS

L03: Poly(2-oxazoline)s as drug delivery vehicles

Richard Hoogenboom[a]

[a]Supramolecular Chemistry Group, Centre of Macromolecular Chemistry (CMaC) Department of Organic and Macromolecular Chemistry, Ghent University, Krijgslaan 281-S4, 9000 Ghent Belgium
richard.hoogenboom@ugent.be

The living cationic ring-opening polymerization of 2-oxazolines has been studied in great detail since its discovery in 1966. The versatility of this polymerization method allows copolymerization of a variety of 2-oxazoline monomers to give a range of tunable polymer properties that enable, for example, hydrophilic, hydrophobic and fluorophilic materials. Moreover, the chemical versatility allows orthogonal end-group and side-chain modification of the polymers. However, this class of polymers was almost forgotten in the 1980s and 1990s because of the long reaction times and limited application possibilities. In the new millennium, a revival of poly(2-oxazoline)s has arisen because of their potential use as biomaterials and thermoresponsive materials, as well as the easy access to defined amphiphilic structures for (hierarchical) self-assembly.

Within this lecture, the challenges that are posed for biomaterials will be addressed based on improved synthetic methodologies and screening of in vitro and in vivo toxicity of the materials.[1] Altogether, we aim to develop poly(2-oxazoline)s as biomaterials by providing in depth studies on the basic questions, such as biocompatibility and renal clearance as well as by providing proof of concept for use of poly(2-oxazoline)s for various specific applications, such as excipients for oral formulations, tissue adhesives[2] and polymer therapeutics.[3] Finally, we are working towards the commercialization of poly(2-oxazoline)s under the name Ultroxa®, see www.ultroxa.com.

References

[1] L. Wyffels, T. Verbrugghen, B. Monnery, M. Glassner, S. Stroobants, R. Hoogenboom, S. Staelens, *J. Controlled Release* **2016**, *235*, 63.
[2] M. A. Boerman, E. Roozen, M. J. Sánchez-Fernández, A. R. Keereweer, R. P. Félix Lanao, J. C. M. E. Bender, R. Hoogenboom, S. C. Leeuwenburgh, J. A. Jansen, H. Van Goor, J. C. M. Van Hest, *Biomacromolecules* **2017**, *18*, 2529-2538.
[3] O. Sedlacek, B. D. Monnery, J. Mattova, J. Kucka, J. Panek, O. Janouskova, A. Hocherl, B. Verbraeken, M. Vergaelen, M. Zadinova, R. Hoogenboom, M. Hruby, *Biomaterials* **2017**, *146*, 1-12.

ABSTRACTS OF ORAL CONTRIBUTIONS

L04: Multicomponent reactions in polymer science: From versatile tuning of structure and properties to sequence defined macromolecules

Michael A. R. Meier[a]
[a]Institute of Organic Chemistry (IOC), Karlsruhe Institute of Technology (KIT), Straße am Forum 7, 76131 Karlsruhe, Germany
m.a.r.meier@kit.edu

Multicomponent reactions are an established tool in organic chemistry. They offer high atom-economy, straightforward practical procedures and most importantly structural diversity can easily be achieved by variation of the used components. Only recently, the benefit of these one-pot reactions was realized for macromolecular engineering. Especially the Passerini three-component (P-3CR) and Ugi four-component (U-4CR) reactions demonstrate attractive tools for polymer synthesis.[1] Several approaches will be discussed, focusing on the preparation of highly defined polymeric architectures. For instance, star-shaped block copolymers were prepared via multicomponent step-growth polymerization[2] and subsequently modified with PEG to obtain water soluble unimolecular micelles that show an interesting encapsulation property (Figure 1).[3] Moreover, multicomponent reactions are an excellent tool for the design of monodisperse macromolecules, including sequence defined polymers,[4,5] also in combination with other methods of sequence definition.[6] Their synthesis and first applications for data storage and transportation will be highlighted.[7,8]

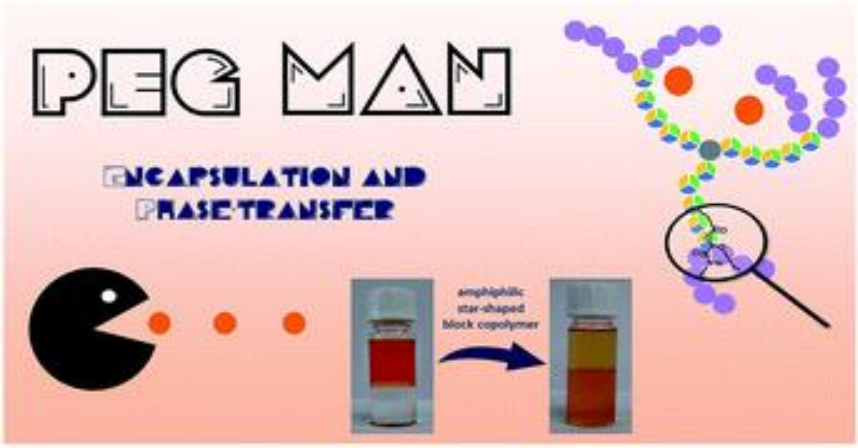


Fig. 1: Encapsulation of guest molecule by a star-shaped block copolymer prepared via the P-3CR.[3]

References

[1] A. Sehlinger, M. A. R. Meier, *Prog. Polym. Sci.* **2015**, 269, 61-86.
[2] S. Oelmann, S. C. Solleder, M. A. R. Meier, *Polym. Chem.* **2016**, *7*, 1857-1860.
[3] S. Oelmann, M. A. R. Meier, *RSC Adv.* **2017**, *7*, 45195-45199.
[4] S. C. Solleder, M. A. R. Meier, *Angew. Chem. Int. Ed.* **2014**, *53*, 711-714.
[5] S. C. Solleder, D. Zengel, K. S. Wetzel, M. A. R. Meier, *Angew. Chem. Int. Ed.* **2016**, *55*, 1204-1207.
[6] S. C. Solleder, S. Martens, P. Espel, F. Du Prez, M. A. R. Meier, *Chem. Eur. J.* **2017**, *23*, 13906-13909.
[7] A. C. Boukis, K. Reiter, M. Frölich, D. Hofheinz, M. A. R. Meier, *Nat. Commun.* **2018**, *9*, 1439.
[8] A. C. Boukis, M. A. R. Meier, *Eur. Polym. J.* **2018**, 104, 32-38.

ABSTRACTS OF ORAL CONTRIBUTIONS

L05: Preclinical test strategies using the shell less hen's egg test

Paul Warncke[a], Lenka Applová[b], Christian Grune[a], Martin Rabel[a], Blerina Shkodra-Pula[c], Anna Czapka[d], Robert Müller[e], Ondrej Stranik[e], Wolfgang Fritzsche[e], Ulrich S. Schubert[c], Oliver Werz[d], Přemysl Mladěnka[b], Dagmar Fischer[a]
[a]Pharmaceutical Technology and Biopharmacy, Friedrich Schiller University Jena, 07743 Jena, Germany
[b]Department of Pharmacology and Toxicology, Charles University, Faculty of Pharmacy in Hradec Králové, Czech Republic
[c]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, 07743 Jena, Germany
[d]Department of Pharmaceutical/Medicinal Chemistry, Friedrich Schiller University Jena, 07743 Jena, Germany
[e]Department of Nanobiophotonics, Leibniz Institute of Photonic Technology, 07745 Jena, Germany
dagmar.fischer@uni-jena.de

In the early stages of the preclinical development, the irritation potential or toxicity of materials has to be assessed. For this purpose, the hen's egg test on the chick area vasculosa (HET-CAV) offers a flexible test platform to address different questions in the preclinical toxicity testing of materials under dynamic conditions in a biological surrounding. Furthermore, aspects in the field of inflammation and infection can be addressed.

Fertilized eggs were transferred into petri dishes to obtain the planar CAV. Local or systemic administration of nanomaterials were performed to obtain a toxicity profile. Therefore, hemorrhage, vascular lysis, thrombosis and embryonic lethality were assessed. Video fluorescence microscopy of particles after systemic injections was used to analyze the flow profile pattern of particles within the blood stream. Moreover, impact of the protein corona on the toxicological profile of the nanoparticles was investigated. Data ex ovo correlated with data from static 2D in vitro experiments.

Besides toxicology testing, a hen's egg based infection model was developed by cultivating different microorganisms on the CAV. Parallel antimicrobial treatment was used to confirm the antimicrobial efficacy and biocompatibility of antimicrobial drugs or formulations. Moreover, systemic injections of potential antithrombotic flavonoid metabolites followed by induction of thrombosis by local arachidonic acid application showed the suitability of the HET-CAV as a model for thrombosis. Analysis of the blood samples can be used to identify genotoxic substances by micronucleus induction.

In conclusion, the HET-CAV offers a flexible alternative test system to investigate a variety of different drugs or nanomaterials in a biological surrounding according to the 3R concept of animal testing.

We acknowledge the DFG CRC PolyTarget (SFB 1278, C02, Z01) and the BMBF (project 03XP0003, NanoBEL).

ABSTRACTS OF ORAL CONTRIBUTIONS

L06: Insight into the structure and architecture of polymer nanoparticles obtained by transmission electron microscopy techniques

Daniel Friedrich[a], Pelin Sungur[a], Aisha A. Womiloju[a], Maren T. Kuchenbrod[a], Steffi Stumpf[a], Stephanie Hoeppener[a]
[a]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, 07743 Jena, Germany
s.hoeppener@uni-jena.de

The architecture and chemical properties of polymer nanoparticles is of tremendous influence on their biophysical interactions with cells and tissue.[1,2] A precise knowledge about the size, shape, and interaction of nanoparticles with cellular compartments can provide a deeper insight into the mode of action and impact of potential drug delivery vehicles. Modern Transmission Electron Microscopy methods facilitate directly studying essential properties of the nanoparticle system and can provide valuable information on the level of the individual nanoparticle as well as in the environment of a cellular system.

For polymer nanoparticles cryo-TEM investigations are essential and provide a suitable method to study the nanoparticles in their solution-like state by avoiding destructive drying effects. In particular stimuli-responsive polymer systems demand for alternative investigation tools. Here, new developments in the utilization of ionic liquids will be presented to study polymer systems in a dynamic fashion.[3]

With TEM and TEM tomography investigations the fate of nanoparticles can be studied additionally in the cellular systems. This includes their localization within cellular organelles as well as questions on their cellular internalization or their degradation. We will introduce promising polymer, metal, and polymer-metal hybrid nanoparticle systems and report on TEM studies which can help to understand their interaction with cells.

References

[1] M. Reifarth, S. Hoeppener, U.S. Schubert, *Adv. Mater.* **2018**, *30*, 1703704.
[2] M. Reifarth, U.S. Schubert, S. Hoeppener, *Adv. Biosyst.* **2018**, *2*, 1700254.
[3] U. Mansfeld, S. Hoeppener, U.S. Schubert, *Adv. Mater.* **2012**, *25*, 761-765.

ABSTRACTS OF ORAL CONTRIBUTIONS

L07: Reactive polysaccharide nanoparticles for biomedical applications

Martin Gericke[a], Thomas Heinze[a]
[a]Institute of Organic Chemistry and Macromolecular Chemistry, Friedrich-Schiller-University of Jena
martin.gericke@uni-jena.de; *thomas.heinze@uni-jena.de*

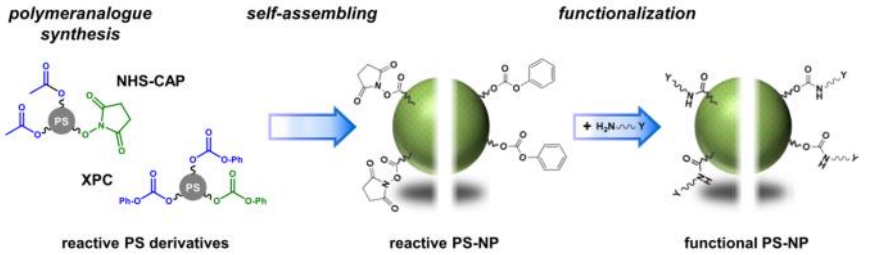
Polysaccharide nanoparticles (PS-NP) can easily be obtained by self-assembling of hydrophobically modified PS derivatives. Due to their inherent biocompatibility and facile preparation, they are highly attractive for biomedical applications, e.g., immobilization of dyes, drugs, and bioactive molecules. For the designated task, a key challenge is their functionalization. Thus, "ready-to-use" PS-NP with reactive groups were developed that enabled direct immobilization and high coupling efficiencies under mild conditions. Two synthesis approaches were pursued to obtain PS derivatives that combine hydrophobic groups (particle formation) and reactive groups (functionalization) within the polymer backbone:

(I) PS-NP with activated NHS-ester groups: Cellulose acetate phthalate (CAP), a NP-forming PS derivative, was chemically modified by polymeranalogue derivatization to introduce activated N-hydroxysuccinimide- (NHS) ester moieties for a subsequent immobilization of amines by amide bond formation.[1] The NHS-CAP products formed spherical NP in the range of 200-400 nm.

(II) PS-NP with reactive carbonate groups: Xylan phenyl carbonates (XPC) with different degrees of substitution were prepared by using ionic liquids as homogeneous reaction media.[2] The derivatives showed a high reactivity towards various types of functional amines leading to the formation of carbamates.[3] The carbonate groups likewise acted as reactive and hydrophobic groups, thus, enabling self-assembling of XPC into PS-NP with diameters of 100-200 nm.

PS-NP with both types of reactive moieties (NHS-esters and aryl carbonates) on the particle surfaces were stable under aqueous conditions and enabled direct immobilization of amine functionalized dyes and enzymes under aqueous conditions with high coupling efficiencies of up to 90%. Moreover, the novel PS-NP were demonstrated to be non-cytotoxic.

ABSTRACTS OF ORAL CONTRIBUTIONS



References

[1] P. Schulze, M. Gericke, T. Heinze, *Cellulose* **2019**, *26*, 475-490.

[2] M. Gericke, L. Gabriel, K. Geitel, S. Benndorf, P. Trivedi, P. Fardim, T. Heinze, *Carbohydr. Polym*. **2018**, *193*, 45-53.

[3] L. Gabriel, M. Gericke, T. Heinze, *Carbohydr. Polym.* **2019**, *207*, 782-790.

ABSTRACTS OF ORAL CONTRIBUTIONS

L08: Polymer Microgels: Permeability of Soft Colloidal Particles Leads to Sophisticated Properties

Rustam A. Gumerov[a,b], Ivan V. Portnov[a,b], Sergey A. Filippov[a], Andrey A. Rudov[a,b], Igor I. Potemkin[a,b]
[a]Physics Department, Lomonosov Moscow State University, Leninskie Gory 1-2, Moscow 119991, Russian Federation
[b]DWI-Leibniz Institute for Interactive Materials, Forckenbeckstr. 50, Aachen 52056, Germany
igor@polly.phys.msu.ru

Internal structure of nano- and microgels resembles elements of macroscopic polymer network: linear chains (subchains) are covalently linked with each other into three-dimensional frame of the size in the range between tens of nanometers and few microns. As a result, the microgels reveal the properties of soft colloidal particles which are permeable for solvent and dissolved (macro)molecules. The most remarkable property of the microgels is their ability to swell and collapse under variation of environmental conditions (temperature, pH, etc.). This property can efficiently be exploited in many applications, in particular, for uptake and release of guest molecules.[1,2] It has been shown recently that the spherical microgels can serve as "soft", penetrable and stimuli sensitive alternative of solid particles which can stabilize emulsions. Such emulsions have peculiar properties and can easily be destroyed under external stimuli leading to desorption of the microgel particles.[3]

In the present paper, we report about few effects which are characteristic for the microgels. In particular, we demonstrate ability of polyampholyte core-shell microgels to serve as Coulomb trap, when charged shell of the microgel can serve as a potential barrier enforcing similarly charged nanoparticles (proteins) to "levitate" inside the core prohibiting their escape.[4] Amphiphilic microgels adsorbed at water-oil interface reveal peculiar behavior comprising ability to homogeneously mix two immiscible liquids (oil and water) inside the microgel.[5-7] They demonstrate very efficient catalytic activity in reactions for which two immiscible reactants can be mixed in the presence of a catalyst inside the microgel and react. Interaction of the amphiphilic microgels with lipid bilayers is considered.

References

[1] A. J. Schmid, J. Dubbert, A. A. Rudov, J. S. Pedersen, P. Lindner, M. Karg, I. I. Potemkin, W. Richtering, *Sci. Rep.* **2016**, *6*, 22736.
[2] W. Richtering, I. I. Potemkin, A. A. Rudov, G. Sellge, Ch. Trautwein, *Nanomedicine* **2016**, *11*, 2879-2883.
[3] S. Wiese, A. C. Spiess, W. Richtering, *Angew. Chem. Int. Ed.* **2013**, *52*, 576-579.
[4] R. Schroeder, A. A. Rudov, W. Xu, I. V. Portnov, W. Richtering, I. I. Potemkin, A. Pich, *Biomacromolecules*, submitted.

[5] R. A. Gumerov, A. M. Rumyantsev, A. A. Rudov, A. Pich, W. Richtering, M. Moeller, I. I. Potemkin, *ACS Macro Lett.* **2016**, *5*, 612-616.

[6] A. M. Rumyantsev, R. A. Gumerov, I. I. Potemkin, *Soft Matter* **2016**, *12*, 6799-6811.

[7] R. A. Gumerov, S. A. Filippov, W. Richtering, A. Pich, I. I. Potemkin, in preparation.

ABSTRACTS OF ORAL CONTRIBUTIONS

L09: Nanoscale structure sensitive investigation of bio-polymers - chances and challenges

Volker Deckert[a,b], Tanja Deckert-Gaudig[a,b]
[a]Institute of Physical Chemistry, Helmholtzweg 4, 07742 Jena
[b]Leibnitz Institute of Photonic Technology, Albert-Einstein-Str. 9, 07745 Jena
volker.deckert@leibniz-ipht.de

Recent developments in optical microscopy allow the investigation of objects far below the diffraction limit. Here the possibilities of label-free vibrational spectroscopy approaches will be presented. Raman spectroscopy under specific conditions, namely plasmonic enhancement, is capable to address even sub-nanometer domains. Hence, a direct sequencing of the single units of polymers based on the vibrational finger print is potentially possible. The application of the method towards the investigation of biopolymers like DNA/ RNA and/or protein structures will be discussed specifically emphasising the challenges when working under conditions far from statistical averaging.[1-3]

References

[1]Z. He, Z. Han, M. Kizer, R. J. Linhardt, X. Wang, A. M. Sinyukov, J. Wang, V. Deckert, A. V. Sokolov, J. Hu, M. Scully, *J. Am. Chem. Soc.* **2019**, *141*, 753-757.
[2]C. Helbing, T. Deckert-Gaudig, I. Firkowska-Boden, G. Wei, V. Deckert, K. D. Jandt, *ACS Nano* **2018**, *12*, 1211-1219.
[3]T. Deckert-Gaudig, A. Taguchi, S. Kawata, V. Deckert, *Chem. Soc. Rev.* **2017**, *46*, 4077-4110.

ABSTRACTS OF ORAL CONTRIBUTIONS

L10: Different strategies to overcome the endosomal barrier for efficient gene delivery

Anja Traeger[a,b], Friederike Richter[a,b], Jana Solomun[a,b], Meike N. Leiske[a,b], Liam Martin[a,b], Ulrich S. Schubert[a,b], Johannes Brendel[a,b]
[a]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstraße 10, 07743 Jena, Germany
[b]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
anja.traeger@uni-jena.de

The controlled delivery of genetic material into eukaryotic cells is needed for the development of novel therapeutic agents. Beside evolutionary qualified and efficient viral transfection, non-viral delivery using polymeric systems is of high interest. Cationic polymers are able to complex the negatively charged genetic material to promote cellular uptake. Taken up by endosomal processes the complexes of polymer and genetic material has to reach their place of action, the cytoplasm or cell nuclei. Therefore, the endosomal membrane has to be crossed. This mechanism is identified by the bottle neck for efficient gene delivery. Herein we present polymers using different strategies for successful gene delivery by efficient endosomal release mechanisms, what was studied in more detail using calcein release studies, lipid-interaction, live cell confocal laser scanning microscopy and flow cytometry. On the one hand, polymeric micelles of block copolymers were investigated.[1,2] On the other hand polymers bearing pH-dependent primary amine or tertiary amines as well as pH-independent guanidinium functionalities were studied. Both systems showed superior transfection efficiency. In the case of micelles the pH-dependent protonation of the cationic polymers can cause a change of shape and size leading to enhanced release of the particles from endosomal compartments. We will further show, that even polymers showing low level of transfection can be tuned to efficient carriers if used as a micelle. Besides, the library of polymers with different amino groups showed efficient transfection of polymers containing guanidinium moieties showing no pH-dependence behavior. Herein, specific interaction with endosomal elements will be discussed. The results will highlight different polymeric strategies for the design of gene delivery polymers with efficient endosomal release.

References

[1] A. C. Rinkenauer, A. Schallon, U. Günther, M. Wagner, E. Betthausen, U. S. Schubert, F. H. Schacher, *ACS Nano* **2013**, *7*, 9621-9631.
[2] M. N. Leiske, F. H. Sobotta, F. Richter, S. Hoeppener, J. C. Brendel, A. Traeger, U. S. Schubert, *Biomacromolecules* **2018**, *19*, 748-760.

ABSTRACTS OF ORAL CONTRIBUTIONS

L11: Synthesis and characterisation of redox-responsive hydrogels based on stable nitroxide radicals

Miriam Khodeir[a], Jean-François Gohy[a]
Institute of Condensed Matter and Nanosciences (IMCN), Université catholique de Louvain, Place L. Pasteur 1, 1348 Louvain-la-Neuve, Belgium
jean-francois.gohy@uclouvain.be

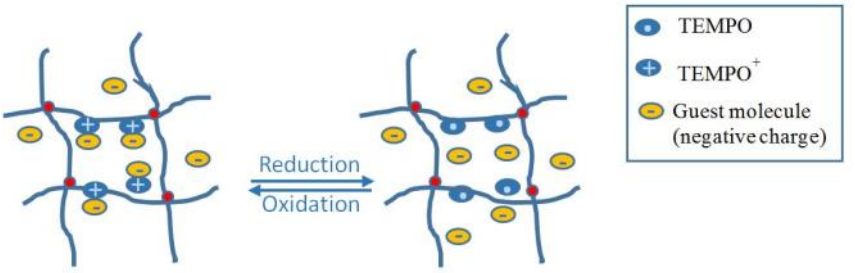
Hydrogels have received considerable attention over the past 50 years due to their exceptional promise in a wide range of applications. Hydrogels can be defined as polymer networks consisting of inter- and intra-molecularly connected polymer chains that possess the ability to absorb large amounts of water while maintaining their three-dimensional structure. The stimuli-responsive hydrogels (SRHs), also called 'smart' hydrogels, represent a broad class of hydrogels being actively investigated, and some of them have been considered for practical use. SRHs can be defined as hydrogels that are able to modify their equilibrium swelling in response to external stimuli such as pH, temperature, redox, light, and electrical field.

As far as redox responsive SRHs are concerned much less work has been performed. Hydrogels based on disulphide cross-linkers can be cited, where the gels dissolve and release their guest molecules when the disulphide bonds are broken. Other systems involve ferrocene functions that can change the hydrophilic-hydrophobic balance of the gel depending on the redox state of the ferrocene moieties. Other examples of redox responsive polymers involve conducting polymers, such as polyaniline (PANI) or polypyrrole (PPy), where clusters of conductive polymer are entrapped into the hydrogels. When submitted to an electrical current the conducting polymer becomes hydrophilic and allows the encapsulated drug to diffuse out of the hydrogel.

Our strategy is to design a redox responsive hydrogel that can encapsulate negatively charged hydrophilic molecules upon oxidation and release them upon reduction. To obtain this redox responsive hydrogel, we decided to focus our attention on the 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) group as redox-active component. TEMPO is a stable nitroxide radical that can be easily oxidised into its oxoammonium counterpart or reduced into an aminoxyl functions. Nitroxide radicals, and especially TEMPO derivatives, are largely used in chemistry for the synthesis of organic molecules or polymers, and in the biomedical field as imaging enhancer in electron spin resonance (ESR) techniques or as radical scavenger of reactive oxygen species (and thus anticipated as valuable candidates for anti-oxidant therapies). In the present work, we have introduced this polymer into a hydrogel in order to produce redox responsive SHRs.

A precursor of the hydrogel will be firstly synthetized by conventional radical polymerisation. This polymeric network will be obtained from a mixture of 2,2,6,6-tetramethylpiperidin-4-yl methacrylate (TMPM), oligo(ethylene glycol)

methyl ether methacrylate with an average molar mass of 300 g/mol (OEGMA300) and di(ethylene glycol) dimethacrylate (OEGMA2) as cross-linker. In the second step, the secondary amine of TMPM units will be oxidised into TEMPO-methacrylate (TEMPO) to obtain the desired redox responsive hydrogel. The final step will be the oxidation of the nitroxide radical units of TEMPO into oxoammonium ones (TEMPO+). In this case the encapsulation of the molecules would be driven by electrostatic interactions between the anionic molecules and the positively charged TEMPO+ units of the hydrogels. The reduction of the TEMPO+ into TEMPO will finally allow the disappearance of those electrostatic interactions and thus the diffusion of the guest molecules out of the hydrogel (Figure).



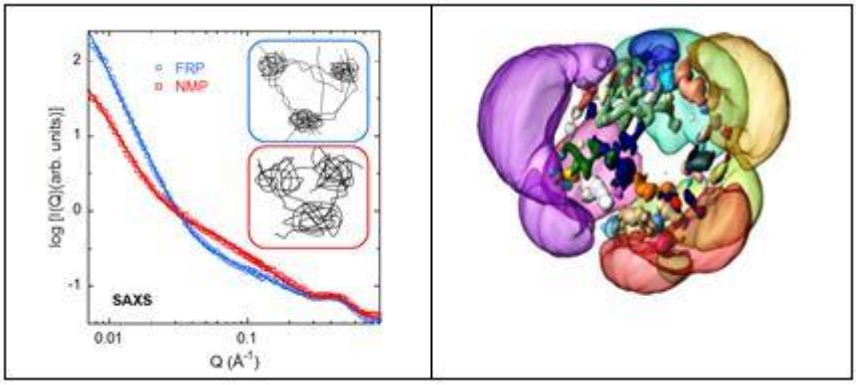
ABSTRACTS OF ORAL CONTRIBUTIONS

L12: Fine-tuning composite polymer colloids

José M. Asua[a]
[a]POLYMAT, University of the Basque Country UPV/EHU, Joxe Mari Korta Zentroa, Tolosa Hiribidea 72, 20018, Donostia-San Sebastián, Spain
jm.asua@ehu.es

Polymer colloids are used in a broad range of applications including adhesives, coatings, paper, carpet backing, additives for textiles and leather, impact modifiers for plastics, water treatment, lithography and biomedical applications. Composite particles offer the possibility to enlarge the portfolio of properties by including within each particle different materials. The promise of new and improved properties has catalyzed research in this area aimed at controlling the multiple characteristics of the composite polymer colloids (polymer composition, chemical composition distribution, MWD, polymer chain architecture, particle morphology, particle size distribution, surface composition ...). This has led to impressive advances in the control of many of these characteristics, but the architecture of crosslinked polymers and the particle morphology still present unsolved challenges, in part due to the difficulties encountered in their detailed characterization.

This lecture presents our work in these areas. Combination of asymmetric-flow field-flow fractionation and small angle X-ray scattering (SAXS) led to a much better description of the network structure. Scanning transmission electron microscopy with high angular dark field (STEM HAADF) combined with image reconstruction was used to obtain a 3D quantitative characterization of the morphology of composite particles. This allowed unveiling unexpected mechanisms and developing mathematical models that pave the way to both process optimization and online control of these characteristics.



ABSTRACTS OF ORAL CONTRIBUTIONS

L13: Preparation and application of functional polymeric nanoparticles as drug delivery devices

Stephanie Schubert[a], Paul Klemm[a], Turgay Yildirim[a]
[a]Pharmaceutical Technology and Biopharmacy, Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena
stephanie.schubert@uni-jena.de

The development of functional polymeric nanoparticles is essential for breakthroughs in nanomedicine. By tuning the polymer characteristics and subsequently applying optimized formulations for the procedure of nanoparticles, tailored nanoparticles with varying release properties, degradation behavior, targeting groups and size distributions can be developed. For the preparation of polymeric nanoparticles, nanoprecipitation is one good choice since it is a facile, mild, and low energy input process. In combination with high-throughput devices such as microfluidics, pipetting robots, inkjet printers, and automated analytical instrumentation, the abilities of nanoprecipitation can broaden tremendously with significant effects on new applications. But also emulsion techniques have the potential as versatile tool for the efficient production of particles of interest. The particle characteristics are strongly driven by formulation conditions but also by the polymer features. Selected examples in the field of gene- and drug delivery vehicles will be presented, e.g. dual pH-value and redox responsive nanoparticles and polymersomes based on a methacrylate copolymer library[1,2] and pH-sensitive dextran based nanomaterials. Targeting ligands for the directed guidance of the nanoparticles to the side of action can be introduced directly within the original polymer structure or attached to the nanoparticle surface. The functionalization of the polymers with Raman active targeting structures further enables the label-free visualization of cell uptake processes.[3]

References

[1] T. Yildirim, I. Yildirim, R. Yanez-Machias, S. Stumpf, C. Fritzsche, S. Hoeppener, C. Guerrero-Sanchez, S. Schubert, U. S. Schubert, *Polym. Chem.* **2017**, *8*, 1328-1340.
[2] T. Yildirim, A. Traeger, P. Sungur, S. Hoeppener, C. Kellner, I. Yildirim, D. Pretzel, S. Schubert, U. S. Schubert, *Biomacromolecules* **2017**, *18*, 3280-3290.
[3] T. Yildirim, C. Matthäus, A. T. Press, S. Schubert, M. Bauer, J. Popp, U. S. Schubert, *Macromol. Biosci.* **2017**, *17*, 1700064.

ABSTRACTS OF ORAL CONTRIBUTIONS

L14: Bridging Light and Electron Microscopy

Fengjiao Ma,[a,b] Daniel Friedrich,[c,d] Stephanie Hoeppener,[c,d] Rainer Heintzmann[a,b]
[a]Institute of Physical Chemistry and Abbe Center of Photonics, Friedrich-Schiller-Universität Jena, Helmholtzweg 4, 07743 Jena, Germany
[b]Leibniz Institute of Photonic Technology, Albert-Einstein Str. 9, 07745 Jena, Germany
[c]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstr. 10, 07743 Jena, Germany
[d]Jena Center for Soft Matter, Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
rainer.heintzmann@uni-jena.de

Fluorescence microscopy is a common tool for studying the internal structure of cells. By specific labeling of the proteins of interest, one can easily study their role in the cell. However, due to the Abbe limit, even if using the existing superresolution microscope technology, ultra-structures in the cell are still difficult to discern. The use the electron microscopy enables to further observe the cell's microstructure down to the nanoscale level. However, Transmission electron microscopy's low and relatively unspecific contrast makes it difficult to conclude on the role of individual molecules.

This project is aimed at investigating optimized approaches to combine the mutual benefits of both imaging modalities: (fluorescence) light microscopy (LM) and electron microscopy (EM). The aim is to obtain molecule specific information by the LM measurement and to join it with the ultra-structure seen in the EM. This shall be implemented by a custumized algorithm to enable an EM-guided deconvolution. The basic idea is to use the high-resolution information of the EM image to guide the deconvolution process of the LM images via a tailored regularisation. This will, for example, help the study of changes in the ultrastructural environment in response to nanoparticle uptake. We demonstrate that our EM-guided deconvolution of light microscopy images, achieves better results than state of the art regularized deconvolution of LM data only.[1]

References

[1] P. J. Verveer, M. J. Gemkow, T. M. Jovin, *J. Microsc.* **1999**, *193.1*, 50-61.

ABSTRACTS OF ORAL CONTRIBUTIONS

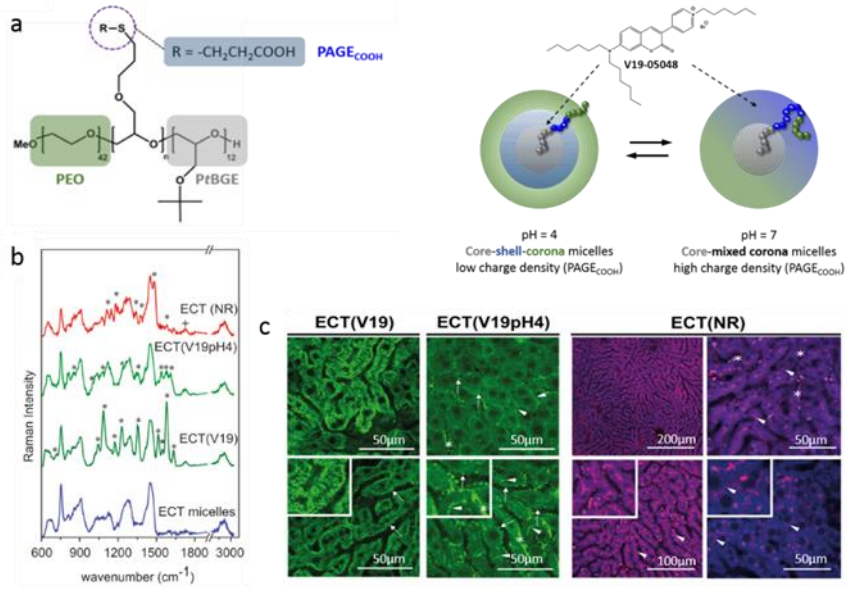
L15: Raman spectroscopic imaging reveals changes in the micellar conformation dictating pharmacokinetic properties

Anuradha Ramoji[a,b], Adrian T. Press[a,b], Carsten Roessel[d], Ute Neugebauer[a,b,e,f,g], Felix H. Schacher[d], Juergen Popp[a,b,e,f,g], Michael Bauer[b,c,g]
[a]Leibniz-Institute for Photonic Technology, Albert-Einstein-Straße 9, D-07745 Jena, Germany
[b]Center for Sepsis Control and Care, Jena University Hospital, Am Klinikum 1, 07747 Jena, Germany
[c]Department of Anesthesiology and Intensive Care, Jena University Hospital, Am Klinikum 1, 07747 Jena, Germany
[d]Institute or Organic Chemistry and Macromolecular Chemistry, Friedrich-Schiller-University Jena, Lessingstraße 8, D-07743 Jena, Germany
[e]Institute of Physical Chemistry and Abbe Center of Photonics, Friedrich Schiller University, Lessingstr. 10, 07743 Jena, Germany
[f]InfectoGnostics Research Campus Jena, Philosophenweg 7, 07743 Jena, Germany
[g]Jena Biophotonics and Imaging Laboratory, Albert-Einstein-str. 9, 07745 Jena, Germany
anuradha.ramoji@med.uni-jena.de

Strategies to deliver drugs using nanocarriers, which are passively or actively targeted to their alleged site of action might affect benefit-risk-profiles of novel therapeutics favorably. We recently demonstrated interactions within or in-between carrier and cargo are influencing the pharmacokinetic properties such as biodistribution, hence must be considered while designing translational nanocarrier platforms.

To understand the surface changes affecting the biomedical applications in sub-50 nm micelles suitable methods are missing. Here we present Raman imaging, an automatable vibrational spectroscopy platform, which probes molecular bond vibrations revealing structure conformation, so far only detectable by synchrotron SAXS.

On the basis of in vitro and in vivo evidence we propose that intramolecular changes introduced e.g. by cargo-carrier interactions alters the micellar corona influencing the pharmacokinetic profile. Thus, these interactions have to be considered when a carrier system is selected to achieve optimal delivery to a given tissue. Raman imaging presents an innovative platform to tackle the current bottle necks in the clinical translation of nanocarriers.



a) An ABC-triblock terpolymer is assembled to sub-50 nm (diameter) micelles (ECT) carrying different hydrophobic cargos (V19-07059, V19 or NileRed, NR) with hypothesized impact on the micellar conformation, b) Raman imaging reveals significant changes in the PEO corona due to cargo-carrier interactions with c) consequences on the *in-vivo* distribution. (V19=green, NT=magenta, liver tissue=blue).

References

[1] A. T. Press, A. Ramoji, M. vd Lühe, A. C. Rinkenauer, J. Hoff, M. Butans, C. Rössel, C. Pietsch, U. Neugebauer, F. H. Schacher, M. Bauer, *NPG Asia Mater.* **2017**, *9*, e444.

ABSTRACTS OF ORAL CONTRIBUTIONS

L16: Clickable copoly(2-oxazoline)s for drug inclusion/API attachment and selective cell adhesion

Frank Wiesbrock[a]
[a]Polymer Competence Center Leoben GmbH, Roseggerstrasse 12, 8700 Leoben, Austria
f.wiesbrock@tugraz.at

Poly(2-oxazoline)s and corresponding copolymers are under intense investigation as potential replacement for poly(ethylene glycol)s as stealth polymers for in-vivo applications including drug delivery and provision of antimicrobial surfaces. As pseudo-polyamides, their properties can be varied over a broad range by careful choice and polymeranalogous manipulation of the side-chains of the corresponding repetition units.

UV-mediated thiol-ene and thiol-yne click chemistry have evolved as prominent techniques for the crosslinking of poly(2-oxazoline)s bearing unsaturated functionalities by oligothiols. The degree of hydrophilicity/hydrophobicity of such gels can be fine-tuned by variation of the repetition units[1], enabling for the diffusion-mediated inclusion of drugs into solvent-stored gels and subsequent release of the drugs only upon network degradation in aqueous environments. Esterases can degrade the poly(2-oxazoline)-based networks if ester-functionalized thiols were used for crosslinking (Figure 1)[2]; acid-mediated hydrolysis, on the other hand, would yield protonated ethylene imine repetition units, which act as contact biocides: Such permanent biocides have excellent antimicrobial activity against various bacteria and fungi if hydrophobic side-chains like in poly(2-nonyl-2-oxazoline) repetition units are present in addition to the cationic charges of the protonated poly(ethylene imine) repetition units[3].

In addition, the thiol-ene click reaction can be used for the surface functionalization of (water-insoluble) poly(2-oxazoline)-based particles by cysteine-bearing cyclic RGD-pentapeptides: The surface-functionalized particles show preferred adhesion towards BON pancreatic cancer cells over healthy endothelial cells[4]. Following orthogonal synthetic approaches, amphiphilic block copoly(2-oxazoline)s can be functionalized with azide-containing APIs such as antiretrovirally active Zidovudine according to the Huisgen cycloadditions and subsequently be crosslinked in micellar shape by thiol-ene click reactions with glycol dimercaptoacetate: The radii of the non-crosslinked micelles of the diblock copolymers of 2-ethyl-2-oxazoline and 2-dec-9'-enyl-2-oxazoline increase with increasing hydrophobicity of the copolymer, whereas the crosslinked micelles of these polymers behave opposite. The micelles of the Zidovudine-containing copolymer are larger than those of the similar API-free diblock copolymer, which could be a result of the introduction of a polar molecule into the hydrophobic core.

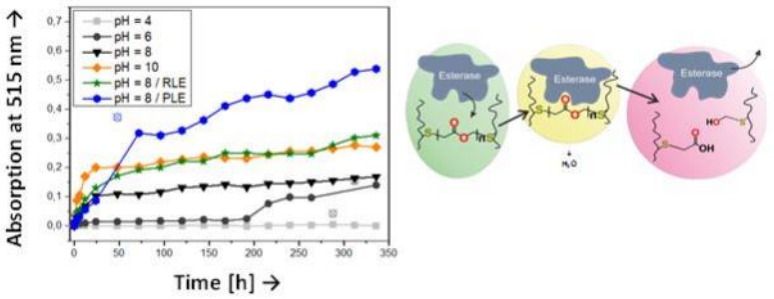


Figure 1: Esterase-mediated and pH-mediated degradation of poly(2-oxazoline)-based networks and compound release from the degraded networks. RLE: rabbit liver esterase; PLE: porcine liver esterase.

References

[1] A.M. Kelly, A. Hecke, A., B. Wirnsberger, F. Wiesbrock, *Macromol. Rapid Commun.* **2011**, *32*, 1815-1819.
[2] K.P. Luef, C. Petit, B. Ottersböck, G. Oreski, F. Ehrenfeld, B. Grassl, S. Reynaud, F. Wiesbrock, *Eur. Polym. J.* **2017**, **88**, 701-712.
[3] A.M. Kelly, V. Kaltenhauser, I. Mühlbacher, K. Rametsteiner, H. Kren, C. Slugovc, F. Stelzer, F. Wiesbrock, *Macromol. Biosci.* **2013**, *13*, 116-125.
[4] V. Schenk, E. Rossegger, C. Ebner, F. Bangerl, K. Reichmann, B. Hoffmann, M. Höpfner, F. Wiesbrock, *Polymers* **2014**, *6*, 264-279.

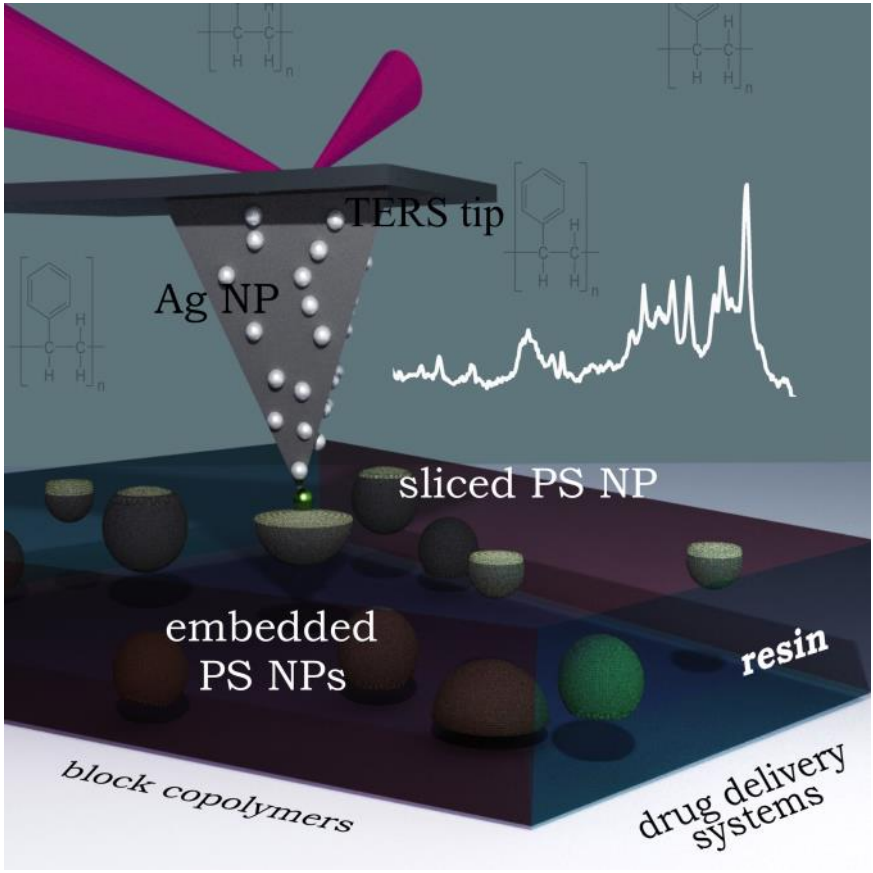
ABSTRACTS OF ORAL CONTRIBUTIONS

L17: Multimodal characterization of polymer nanoparticles: Chemical specificity, structural information and mechanical properties on the nanometer scale

Christiane Höppener[a,b], Moritz Köhler[c], Felix H. Schacher[c], Volker Deckert[a,b]

[a] Leibniz Institute of Photonic Technologies (IPHT), Albert-Einsteinstraße 3, 07745 Jena, Germany
[b] Institute for Physical Chemistry, Friedrich Schiller University Jena, Helmholzweg 4, 07743 Jena, Germany
[c] Institute of Organic Chemistry and Macromolecular Chemistry (IOMC), Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Lessingstraße 8, 07743 Jena, Germany
christiane.hoeppener@leibniz-ipht.de

Polymers have attracted high interest in medical science due to their prospect to be used as materials for drug delivery systems. Formulation of polymers into nanostructures with designed site-specific functions has been successfully demonstrated. However, understanding the underlying uptake and release mechanisms, and the impact of environmental influences on these functions requires complementary information on these systems. Due to their size high resolution techniques have to be utilized, which provides high chemical specificity, nanoscale structural information and provide insight into the mechanical properties. Hence, a multimodal approach is required for their investigation. Tip-enhanced Raman Spectroscopy (TERS) is applied to obtain chemical and structural information of the polymer nanoparticles with nanometer resolution.[1,2] These investigations are supplemented by means of mapping the adhesion and elasticity by means of Atomic Force Microscopy (AFM). Information on the interior of the nanoparticles are accessed by investigations of sliced polymer nanoparticles. This approach is also used to study the formation of a protein corona on the surface of polystyrene nanoparticles. Furthermore, block copolymer nanoparticles and micelles are investigated by means of this multimodal approach.



References

[1] M. Richard-Lacroix, Y. Zhang, Z. Dong, V. Deckert, *Chem. Soc. Rev.* **2017**, *46*, 3922-3944.

[2] S. Trautmann, J. Aizpurua, I. Götz, A. Undisz, J. Dellith, H. Schneidewind, M. Rettenmayrc, V. Deckert , *Nanoscale* **2016**, *9*, 391-401.

ABSTRACTS OF ORAL CONTRIBUTIONS

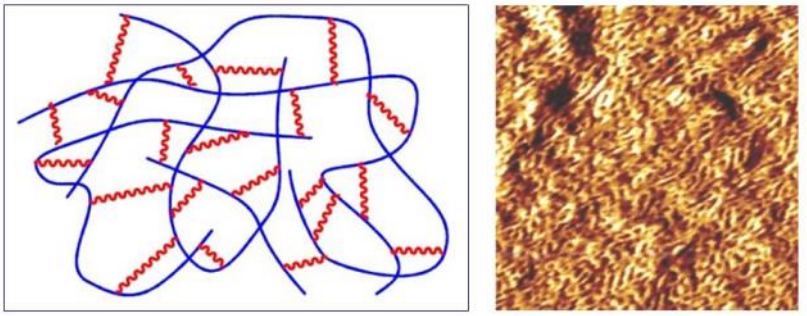
L18: Nanostructured macromolecular assemblies as controlled drug release carriers: from intelligent drug release to high efficiency drug solubilization with nanomicelles of self-assembling block copolymers possessing hyperbranched segments

Béla Iván[a], Márton Haraszti[a], György Kasza[a], Dóra Fecske[a], Gergő Gyulai[b], Kata Horváti[c], Márk Szabó4, Györgyi Szarka[a], Éva Kiss[b], Attila Domján[d], Szilvia Bősze[c]
[a] Polymer Chemistry Research Group, Institute of Materials and Environmental Chemistry, Research Centre for Natural Sciences Hungarian Academy of Sciences, H-1117 Budapest, Magyar tudosok krt. 2, Hungary
[b] Laboratory of Interfaces and Nanostructures, Institute of Chemistry, Eötvös Loránd University, H-1117 Budapest, Pázmány Péter sétány 1/A, Hungary
[c] MTA-ELTE Research Group of Peptide Chemistr, Eötvös Loránd University, H-1117 Budapest, Pázmány Péter sétány 1/A, Hungary
[d] NMR Laboratory, Research Centre for Natural Sciences, Hungarian Academy of Sciences, H-1117 Budapest, Magyar tudósok körútja 2, Hungary
ivan.bela@ttk.mta.hu

Due their various exceptional properties, amphiphilic conetworks (APCNs),[1,2] composed of covalently bonded, otherwise immiscible hydrophilic and hydrophobic polymer chains, have recently received significant interest. These cross-linked polymer assemblies belong to a new class of rapidly emerging nanostructured materials. Unique bicontinuous (cocontinuous) nanophase separated morphology exists in APCNs in a broad composition window.[1,2] Poly (methacrylic acid) (PMAA) containing APCNs [2] exhibit unprecedented pH-responsive (smart, intelligent) behavior. Encapsulation of drugs, sensitive to the low pH and enzymes in the stomach, has been utilized by us in the PMAA nanophases of APCNs for obtaining conetwork hydrogels with pH-dependent controlled drug release in terms of both the extent of loading and release rates.

In another approach, amphiphilic ABA branched-linear-branched triblock copolymers of hyperbranched polyglycerol (HbPG) and telechelic poly (tetrahydrofuran) (PTHF) were obtained by quasiliving multibranching ring-opening polymerization of glycidol by using PTHF as macroinitiator. Such block copolymers offer broad range of biomedical application possibilities unexplored until now. The HbPG-PTHF-HbPG block copolymers form nanomicelles in aqueous media with diameters of ~10-20 nm. Solubility increase by more than 700 times was obtained with these nanomicelles for drugs with low solubility, such as the naturally existing hardly soluble curcumin. High stability and sustained release with long effective release times were observed with these novel nanocarriers.[3]

Acknowledgements. Support by the National Research, Development and Innovation Office, Hungary (OTKA NN129366, 112094) and the BIONANO_GINOP-2.3.2-15-2016-00017 project (Hungary) is acknowledged.



Schematic structure of an amphiphilic conetwork (APCN) composed of a polymer cross-linked with telechelic macromonomer, and an AFM phase image of the bicontinuous nanophasic morphology of an APCN sample (image size: 250x250 nm).

References

[1] C. Fodor, G. Kali, R. Thomann, Y. Thomann, B. Iván, R. Mülhaupt, *RSC Adv.* **2017**, *7*, 6827-6837.

[2] B. Iván, M. Haraszti, G. Erdődi, J. Scherble, R. Thomann, R. Mülhaupt, *Macromol. Symp.* **2005**, *227*, 265-274.

[3] G. Kasza, D. Fecske, G. Gyulai, K. Horváti, M. Szabó, Gy. Szarka, É. Kiss, A. Domján, Sz. Bősze, B. Iván, submitted.

ABSTRACTS OF ORAL CONTRIBUTIONS

L19: In silico design of polymer nanocarriers for biomedical applications

Marek Sierka[a], Andreas Erlebach[a]
[a]Otto-Schott-Institut für Materialforschung, Friedrich-Schillller-Universität Jena
marek.sierka@uni-jena.de

Efficient encapsulation of biologically active substances in polymeric nanocarriers is of fundamental importance, among others, for the targeted drug delivery in nanomedicine. However, experimental trial-and-error optimization of the encapsulation efficiency is often cumbersome and time-consuming. In contrast, computer simulations can potentially not only efficiently predict the polymer-active compatibility, but also provide a detailed understanding of the underlying interactions. Atomistic simulations combined with the Flory-Huggins (FH) theory have been successfully used for prediction of the polymer-active miscibility (e.g., Ref.[1]). However, such predictions fail for mixtures involving strong specific interactions (e.g., hydrogen bonding), making an improved thermodynamic modelling indispensable for reliable solubility predictions[2]. Here, we derive corrections to the FH theory based on atomistic simulations including not only specific interactions but also steric effects of the intermolecular structure on the polymer-active miscibility. Comprehensive test calculations show that the corrected FH model allows rapid, qualitative solubility predictions. Quantitative predictions, however, require more accurate models such as the perturbed hard sphere chain (PHSC) equation of state[3]. The in silico parametrized PHSC predicts physicochemical properties of polymer mixtures in good agreement with experimental observations facilitating an efficient design of polymeric nanocarriers.

References

[1] A. Erlebach, T. Ott, C. Otzen, S. Schubert, J. Czaplewska, U. S. Schubert, M. Sierka, *J. Comput. Chem.* **2016**, *37*, 2220-2227.
[2] B. D. Anderson, *J. Pharm. Sci.* **2018**, *107*, 24-33.
[3] Y. Song, S. M. Lambert, J. M. Prausnitz, *Chem. Eng. Sci.* **1994**, *49*, 2765-2775.

ABSTRACTS OF ORAL CONTRIBUTIONS

L20: Some biomedical applications of temperature responding polymers

Andrzej Dworak[a]
[a]Centre of Polymer and Carbon Materials, Polish Academy of Sciences, PL-41-819 Zabrze
adworak@cmpw-pan.edu.pl

Under the term "temperature responding polymers" a group of macromolecular materials is generally understood which undergo rapid and reversible changes of properties under the influence of changes of temperature of the surrounding medium. This class of macromolecular compounds has been studied in many details, its behavior is in general well understood.

Some of the temperature responding polymers exhibit behavior related to the occurrence of the lower critical solution temperature: they are soluble below a certain temperature in medium. In most cases water has been studied. Is this temperature exceeded, the polymer precipitates, to become soluble again when the temperature is lowered. Are the macromolecules crosslinked, the gels formed, also micro- or nanogels, shrink or expand when the temperature is changed. If the temperature responding polymers are immobilized on surface, the affinity of such surface to medium (the contact angle), water most frequently, changes.

Some of the temperature responding polymers are biocompatible. This makes tem suitable for construction of biomedical devices. Some examples will be discussed in this talk.

Under proper conditions the precipitation of some temperature responding polymers from water solution may be controlled. Small nanoparticles, the mesoglobulas, of polymers are formed. Is a medically active species attached to such polymers or is it encapsulated inside of the mesoglobula a way to carriers of therapeutics is open.

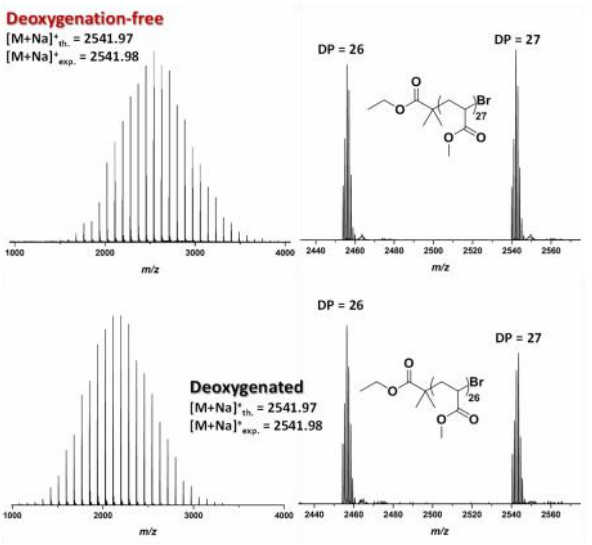
Two examples of such potential carriers are discussed. The basic carrier polymer consists of the polymers of (oligoethylene glycol) methacrylates, a biotolerable thermoresponsive polymer, or of ppoly(N-isopropyl acrylamide), a well-known and well-studied thermoresponding material. Doxorubicin or met-enkephalin are attached to the chains forming mesoglobules. The mesoglobules their selves, being thermodynamically unstable at physiological temperature range, are stabilized either by click-reaction induced crosslinking or by surrounding the by a cross-linked polymer layer. Controlled release of the biologically active species is thus achieved.

The last example of the use of temperature induced changes deals with the temperature induced changes of properties of surfaces intended as substrates for the growth of skin sheets. This application, studied before by several researchers and induced in this case by burn treatment surgeons, bases upon some thermoresponsive polymers, polyoxazolines being most promising. It was developed up to the level of clinical experiments.

L21: Copper mediated living radical polymerisation in the presence of oxygen

David M. Haddleton
University of Warwick, Department of Chemistry, Coventry, UK
d.m.haddleton@warwick.ac.uk

We report a fully oxygen photoinduced RDRP system, independent of any externally added oxygen quenchers, reducing agents or deoxygenation methods. The efficient elimination of headspace gives access to a range of monomer families, such as methyl acrylate (MA) even in molecular weights as high as ~ 53,000, ethylene glycol methyl ether acrylate (EGA) and the hydrophilic poly(ethylene glycol methyl ether acrylate) (PEGA480). Moreover, the hydrophobic monomers such as n-butyl acrylate (n-BA) and hexyl acrylate (HA), as well as the protected and expansively functionalized tert-butyl acrylate (t-BA) are polymerized in different solvents. Additionally, utilizing 2,2,2-trifluoroethanol (TFE) as solvent, the semi-fluorinated poly(2,2,2-trifluoroethyl acrylate) (PTFEA) and poly(2,2,2-trifluoroethyl methacrylate) (PTFEMA) are obtained. Surprisingly, this approach is efficiently scalable from extremely low volumes such as 5 µL, to high scale reactions of 0.5 L. The experimental data generating from the oxygen probe demonstrate preliminary insights into the oxygen consumption mechanism and the role of the different components that comprise a deoxygenation-free polymerization.



References

E. Liarou, R. Whitfield, A. Anastasaki, N. G. Engelis, G. R. Jones, K. Velonia, D. M. Haddleton, *Angew. Chem.* **2018**, *57*, 8998-9002.

ABSTRACTS OF ORAL CONTRIBUTIONS

L22: In situ analysis of polymers and nanoparticle systems for the nanomedicine

Ivo Nischang[a,b], Mandy Grube[a,b], Ulrich S. Schubert[a]
[a] Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstraße 10, 07743 Jena, Germany
[b] Solution Characterization Group (SCG), Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
ivo.nischang@uni-jena.de

Soft matter nanoscale objects in solution can physically be described by their density, sedimentation / flotation, and diffusion. Together with their (tailored) chemistry, such properties determine the technological applications. Particularly, this concerns the entire colloidal size range of only a few nanometers to several hundreds of nanometers, last but not least in the diverse area of the life sciences.

In our research, we measure these very first principle properties of soft matter materials in solution by a technique called analytical ultracentrifugation (AUC). AUC allows in situ observation of the solution behavior of colloids and individual colloid system components for the broadest size spectrum currently available. There are virtually no limits for the choice of the solvent systems including simulated physiological conditions (e.g. buffers, salts, complex biological media, etc.). Due to the experimental setup, mass balances are conserved in the defined solution volume during analysis, i.e. also the absence of global dilution. Careful choice of forces allows selective observation of individual system components, entirely reference-free.

Based on these assets of AUC, examples of the quantitative study of neutral1,2 and charged pharmapolymers, polymer drug conjugates, and polymer aggregates3 will be shown. Furthermore, we present results of quantitative AUC experiments with multiple speed and time profiles enabling the compositional analysis of nanoscale colloid systems containg nanoparticles, drug components, and targeting dye as well as surfactants. In addition to compositional analysis, the sizing of system components and assessment of their heterogeneity is simultaneously possible.

References

[1] I. Nischang, I. Perevzayko, T. C. Majdanski, J. Vitz, G. Festag, U. S. Schubert, *Anal. Chem.* **2017**, *89*, 1185-1193.
[2] M. Grube, M.N. Leiske, U. S. Schubert, I. Nischang, *Macromolecules* **2018**, *51*, 1905-1916.
[3] I. Muljajew, C. Weber, I. Nischang, U. S. Schubert, *Materials* **2018**, *11*, 528.

ABSTRACTS OF ORAL CONTRIBUTIONS

L23: PeptoMicelles in tuberculosis therapy

Matthias Barz[a]
[a]Institute of Organic Chemistry, Johannes Gutenberg University, Duesbergweg 10-14, Mainz
barz@uni-mainz.de

The enormous potential of polymeric nanomedicines arises from the possibility to combine desirable material properties with compartmentalized functionalities in one distinct nanoparticle,[1] to encapsulate and deliver drugs more specifically to the desired site of action and/or maintain sustained release over elongated time frames. The current treatment of tuberculosis requires administration of four drugs over six months and the patients are likely to suffer from side effects such as liver toxicity. This leads to poor patient compliance and thus promotes the development of multi-drug-resistant and extensively drug-resistant strains of Mtb. Nanosized drug delivery systems may address these current limitations. Griffiths and co-workers have recently demonstrated that even i.v. injected PeptoMicelles can accumulate passively at granulomas in zebrafish embryo and mouse models, which provides a novel approach for tuberculosis therapy.[2] The accumulation process, however, requires stealth-like nanoparticles with enhanced serum stability.[3] With respect to these needs we established polypept(o)ide-based micelles and cylindrical polymer brushes, which are all stabilized nanoparticles. In the core of micelles various anti-TB drugs can encapsulated by either hydrophobic interactions, π-π stacking or covalent attachment, while the corona can be modified with ligands for active targeting. Therefore, we have access to nanoparticles of controlled size, shape and functionality enabling us to tailor them for drug delivery in tuberculosis therapy. We demonstrate that drug loaded PeptoMicelles can reduce bacterial burden and enhance long time survival substantially in zebra fish embryo and mice models.

References

[1] Q. Sun, M. Barz, B. G. De Geest, M. Diken, W. E. Hennink, F. Kiessling, T. Lammers, Y. Shi, *Chem. Soc. Rev.* **2019**, *48*, 351-381.
[2] F. Fenaroli, U. Repnik, Y. Xu, K. Johann, S. Van Herck, P. Dey, F. M. Skjeldal, D. M. Frei, S. Bagherifam, A. Kocere, R. Haag, B. G. De Geest, M. Barz, D. G. Russell, G. Griffiths, *ACS Nano* **2018**, *12*, 8646-8661.
[3] I. Negwer, A. Best, M. Schinnerer, O. Schäfer, L. Capeloa, M. Wagner, M. Schmidt, V. Mailänder, M. Helm, M. Barz, H.-J. Butt, K. Koynov, *Nat. Commun.* **2018**, *9*, 5306.

ABSTRACTS OF ORAL CONTRIBUTIONS

L24: Biomimetic polymersomes as innovative nanomedicines

Sébastien Lecommandoux[a]
[a] Laboratoire de Chimie des Polymères Organiques, Univ. Bordeaux, CNRS UMR 5629, Bordeaux-INP ENSCBP, Pessac, France
Lecommandoux@enscbp.fr

We report on the self-assembly of amphiphilic block copolymers into different nanomedicines, mainly focusing on polymer vesicles, also referred as polymersomes, and their applications in loading and controlled release of both hydrophilic and hydrophobic molecules and biomolecules.

We pay special attention to polysaccharide and polypeptide-based block copolymer vesicles and their development in nanomedicine.[1-5] Indeed, the field of synthetic polypeptides has seen many significant advances in recent years, including studies on block and hybrid copolypeptides that form vesicles, fibrils, and other structures with potential applications in medicine and materials chemistry. However, the development of glycosylated polypeptides has not kept pace, primarily due to the inability to readily synthesize glycopolypeptides in a controlled manner. In this context, we developed over the last years synthetic strategies for the design of glycosylated polypeptides and polysaccharide-polypeptide biohybrids with controlled placement of sugar functionality. We were especially interested in designing amphiphilic copolymers able to self-assemble into well-defined micelles and vesicles that can advantageously be loaded with drugs and present a surface with multivalent presentation of bioactive saccharides or oligosaccharides. The ability of these nanoparticles for different biomedical applications, from drug-delivery to inhibitor, will be presented. We especially evidenced the particular benefit of nanoparticles and their multivalency toward the interaction with biological receptors.[6-7]

Finally, our recent advances in using “biomimicry approaches” to design complex, compartmentalized and functional protocells will be proposed. Such a system constitutes a first step towards the challenge of structural cell mimicry and functionality, and may act in the future as an autonomous artificial cell that can sense and cure in situ any biological deregulation.[8-11]

References

[1] C. Bonduelle, S. Lecommandoux, *Biomacromolecules* **2013**, *14*, 2976-2983.
[2] C. Bonduelle, J. Huang, E. Ibarboure, A. Heise, S. Lecommandoux, *Chem. Commun.* **2012**, *48*, 8353-8355.
[3] J. Huang, C. Bonduelle, J. Thévenot, S. Lecommandoux, A. Heise, *J. Am. Chem. Soc.* **2012**, *134*, 119-122.
[4] V. Jeannot, S. Smazzaferro, J. Lavaud, M. Arboléas, V. Josserand, J.-L. Coll, S. Lecommandoux, C. Schatz, A. Hurbin, *Nanomedicine: NBM* **2016**, *4*, 921-932.

[5] V. Jeannot, C. Gauche, S. Mazzaferro, M. Couvet, L. Vanwonterghem, M. Henry, C. Didier, J. Vollaire, V. Josserand, J.-L. Coll, C. Schatz, S. Lecommandoux, A. Hurbin, *J. Control. Release* **2018**, *275*, 117-128.
[6] C. Bonduelle, J. Huang, T. Mena-Barragán, C. Ortiz-Mellet, C. Decroocq, E. Etamé, A. Heise, P. Compain, S. Lecommandoux, *Chem. Commun.* **2014**, *50*, 3350-3352.
[7] C. Bonduelle, H. Oliveira, C. Gauche, A. Heise, S. Lecommandoux, *Chem. Commun.* **2016**, *52*, 11251-11254.
[8] M. Marguet, L. Edembe, S. Lecommandoux, *Angew. Chem. Int. Ed.* **2012**, *51*, 1173-1176.
[9] R. J. R. W. Peters, M. Marguet, S. Marais, M. W. Fraaije, J. C. M. Van Hest, S. Lecommandoux, *Angew. Chem. Int. Ed.* **2014**, *53*, 146-150.
[10] A. Peyret, E. Ibarboure, A. Tron, L. Beauté, R. Rust, O. Sandre, N. McClenaghan, S. Lecommandoux, *Angew. Chem. Int. Ed.* **2017**, *56*, 1566-1570.
[11] A Peyret, E Ibarboure, J.-F. Le Meins, S. Lecommandoux, *Adv. Sci.* **2018**, *5*, 1700453.

List of Poster Presentations

LIST OF POSTER PRESENTATIONS

P01	Synthesis of spermine-based polyamines for nucleic-acid delivery *Dr. Friederike Adams* *Ludwig-Maximilians-Universität München, München (DE)*
P02	Biocompatible polyglycerols as versatile platform for biomedical applications *Vahid Ahmadi* *Freie Universität Berlin, Berlin (DE)*
P03	Controlling the degradation behavior of polymeric nanoparticles by structurally tailored thermal properties *Damiano Bandelli, Karl Scheuer* *Friedrich Schiller University Jena, Jena (DE)*
P04	MOFs templated polymer networks for bio-applications *Dr. Salma Begum* *Karlsruhe Institute of Technology, Karlsruhe (DE)*
P05	Guanidinium bearing methacrylamide based terpolymers mimicking secondary amphipathic peptides for gene delivery *Ceren Cokca* *Friedrich Schiller University Jena, Jena (DE)*
P06	Quantifying the distribution of nanoparticle- and micelle-based cargo delivery using image-based systems biology techniques *Dr. Zoltan Cseresnyes* *Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute, Jena (DE)*

LIST OF POSTER PRESENTATIONS

P07	In vitro cytotoxicity and cytolocalization of RAFT nano-polymeric carriers *Dr. Marco Antonio De Jesus-Tellez* *Friedrich Schiller University Jena, Jena (DE) / Centro de Investigacion y Estudios Avanzados (Cinvestav), Mérida (MX)*
P08	Cellular uptake of polymeric nanoparticles invesigated by correlative light and electron microscopy *Daniel Friedrich* *Friedrich Schiller University Jena, Jena (DE)*
P09	Influence of micelle structure on immune response, uptake properties and hemocompatibility *Elena Gardey* *Jena University Hospital, Jena (DE)*
P10	Protein-polymer conjugates: synthesis strategies and applications as natural membrane mimics and therapeutic agents *Dr. Ulrich Glebe* *Fraunhofer Institute for Applied Polymer Research, Potsdam-Golm (DE)*
P11	Prodrug nanoparticles to target conidia of the human-pathogenic fungus Aspergillus fumigatus in macrophages *Katherine González Rojas* *Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute, Jena (DE)*
P12	Highly disperse carboxymethyl celluloses - a characterization challenge *Mandy Grube* *Friedrich Schiller University Jena, Jena (DE)*

LIST OF POSTER PRESENTATIONS

P13	A green organic solvent-free formulation method for nanoparticulate drug delivery systems *Christian Grune* *Friedrich Schiller University Jena, Jena (DE)*
P14	Hydroxyethyl starch - poly(ethylene imine) conjugates as potential targeted gene carriers in inflammatory diseases *Franz Hack* *Friedrich Schiller University Jena, Jena (DE)*
P15	Amphiphilic Nylon-3 polymers for enhanced siRNA delivery into glioblastoma cells *Natascha Hartl* *Ludwig-Maximilians-University Munich, Munich (DE)*
P16	Self-immolative drug-delivery-systems based on polycarbonate compounds *Dimitri Jung* *Paderborn University, Paderborn (DE)*
P17	Trivalent sialosides as inhibitors of influenza virus *Pallavi Kiran* *Freie Universität Berlin, Berlin (DE)*
P18	Raman spectroscopic characterization of the linkage- and interaction mechanism of nanocarriers and drugs with hepatic stellate cells *Paul Klemm* *Friedrich Schiller University Jena, Jena (DE)*

LIST OF POSTER PRESENTATIONS

P19	Stability of PEO-b-PAGE-b-PCL triblock terpolymers upon presence of nucleophilic substituents in the PAGE segment *Moritz Köhler* *Friedrich Schiller University Jena, Jena (DE)*
P20	Anaylsis of polymeric micelles and soft molecular assemblies by cryo-transmission electron microscopy *Maren T. Kuchenbrod* *Friedrich Schiller University Jena, Jena (DE)*
P21	Enhancing the comparability and reproducibility of quantitative analyses of the nanoparticle protein corona by integrating QconCATs into a new standardized LC-MS workflow *Christian Leps* *Johannes Gutenberg University Mainz, Mainz (DE)*
P22	Tailored nanoparticles with two step release pattern: new tool for drug delivery *Henry Lindemann* *Friedrich Schiller University Jena, Jena (DE)*
P23	Tailor-made multifunctional polymers and nanoparticles with optimized compatibility between biodegradable core and encapsulated drug *Irina Muljajew* *Friedrich Schiller University Jena, Jena (DE)*
P24	Microfluidic manufacture of PLGA nano- and microparticle drug delivery vehicles using the NanoAssemblr® Benchtop *Martin Rabel* *Precision NanoSystems Inc., Vancouver (CA)*

LIST OF POSTER PRESENTATIONS

P25	Light-triggered backbone-cleavable polycarbonates from (2-nitro-1,4-phenylene)dimethanol *Tarik Rust* *Paderborn University, Paderborn (DE)*
P26	Biomedical system based on precision biomacromolecular polymers with repetitive peptide entities *Dr. Stefan M. Schiller* *University of Freiburg, Freiburg (DE)*
P27	Improving the bioavailability of BRP-187: Encapsulation of a potent inhibitor of leukotriene biosynthesis into biodegradable polymers for drug delivery *Blerina Shkodra-Pula* *Friedrich Schiller University Jena, Jena (DE)*
P28	Photo-responsive polymeric nanostructures based on 1-naphthol *Maria Sittig* *Friedrich Schiller University Jena/Leibniz Institute of Photonic Technology Jena, Jena (DE)*
P29	Stimuli-responsive layer-by-layer nanoparticles for specific delivery of nucleic acids *Jana Solomun* *Friedrich Schiller University Jena, Jena (DE)*
P30	Micellar doxorubicin with dendritic polyglycerol sulfate shell for targeted tumor therapy *Yinan Zhong* *Freie Universität Berlin, Berlin (DE)*

Abstracts of Poster Presentations

ABSTRACTS OF POSTER PRESENTATIONS

P01: Synthesis of spermine-based polyamines for nucleic acid delivery

Friederike Adams[a], Olivia M. Merkel[a]
[a]Lehrstuhl für Pharmazeutische Technologie und Biopharmazie, Ludwig-Maximilians-Universität München, Butenandtstr. 5-13, 81377 München
friederike.adams@cup.uni-muenchen.de

RNA interference by small interfering RNA (siRNA) is an efficient strategy to silence genes and thus to prevent translation. However, the application of siRNA faces challenges, since siRNA is a negatively charged macromolecule. It cannot cross cell membranes, the cellular uptake is limited and siRNA is unstable in blood due to rapid enzymatic degradation. Consequently, several carriers for siRNA have been developed in which polymeric vectors showed advantages over viral vectors regarding safety, immunogenicity, production costs and risk of mutagenicity. In these systems, siRNA is condensed with polycationic polymers through electrostatic interactions to so-called polyplexes. Among these polymers, poly(ethyleneimine) (PEI) offers the highest positive charge density and a proton-sponge effect over a broad pH range, however, high molecular weight PEI is cytotoxic due to its high positive charge.[1] Our group develops new polymeric vectors for siRNA encapsulation and delivery which are based on oligo- and polyspermines. The naturally occurring spermine is a potential nucleic-acid delivery vehicle, as it is a small tetraamine consisting of two primary and two secondary amines. However, spermine shows low ability to condense siRNA due to its low molecular weight. Therefore, spermine was modified via oligomerization, polymerization or coupling with other copolymers to obtain higher molecular weights and different functionalities (e.g. amphiphilic properties). Different modification strategies, including living-radical polymerization, polycondensation and protection-group chemistry, were used to obtain various polyamine architectures consisting of spermine-moieties. In further characterization studies, oligospermines displayed lower cytotoxicity and more efficient siRNA condensation than PEI. In addition, the morphology of the polyplexes was effected by the different architectures.[2]

References

[1] O. M. Merkel, M. Zheng, H. Debus, T. Kissel, *Bioconjugate Chem.* **2012**, *23*, 3-20.
[2] M. Elsayed, V. Corrand, V. Kolhatkar, Y. Xie, N. H. Kim, R. Kolhatkar, O. M. Merkel, *Biomacromolecules* **2014**, *15*, 1299-1310.

ABSTRACTS OF POSTER PRESENTATIONS

P02: Biocompatible polyglycerols as versatile platform for biomedical applications

Vahid Ahmadi[a], Magda Ferraro[a], Michael Tully[a], Paria Pouyan[a], Ehsan Mohammadifar[a], Rainer Haag[a]
[a]Institut für Chemie und Biochemie Organische Chemie, Freie Universität Berlin, Takustr. 3, 14195 Berlin, Germany
haag@chemie.fu-berlin.de

Linear and hyperbranched polyglycerols (lPG and hPG) have attracted tremendous attention in a broad range of biomedical fields, from drug delivery to pathogen interaction and anti-inflammatory applications.[1,2] Hyperbranched polyglycerols can be also employed as a building block for the preparation of two and three dimensional nanogels.[3] Here we present the employment of diverse structures based on PG.

Two-dimensional hPG for multivalent interactions

Herein, we report a new and efficient method for the synthesis of 2D polyglycerol using a pH-sensitive functionalized graphene template. Thermally reduced graphene oxide (TRGO) functionalized with triazine and a pH-sensitive linker, was conjugated to hPG with 10% azide functional groups. Afterwards it was crosslinked 2-dimensionally by a click-reaction and cleaved from the surface of TRGO by mild acidification. After sulfation, a low IC50 against herpes virus was observed, making the two-dimensional polyglycerol network (2DPN) sheets promising virus inhibitors.

Linear polyglycerols (lPG)

Due to the potential toxicity of PEG, alternatives are under investigation. lPG presents promising characteristics to substitute PEG. As PEG, it is based on a polyether backbone, but due to its numerous hydroxyl groups it is more hydrophilic and can be further modified. In this study a model peptide was conjugated to lPG with different molecular weights (5, 10, 20 and 40 kDa) as well as PEG with comparable molecular weights, to study the effect of the conjugation on the structure of the peptide.

Biodegradable polyglycerol sulfates

Dendritic polyglycerol sulfate (dPGS) has been shown to possess anti-inflammatory characteristics, but lacks biodegrability. Hence, we have developed a new copolymer which can bind L-selectin and therefore inhibit leukocyte recruitment. Moreover, it is biologically degradable thanks to the presence of ester bonds.

References
[1] M. Ferraro, K. Silberreis, E. Mohammadifar, F. Neumann, J. Dernedde, R. Haag, *Biomacromolecules* **2018**, *19*, 4524–4533.
[2] M. Weinhart, I. Grunwald, M. Wyszogrodzka, L. Gaetjen, A. Hartwig, R. Haag, *Chem. Asian J.* **2010**, 5, 1992-2000.
[3] Y. Zheng, S. Li, Z. Weng, C. Gao, *Chem. Soc. Rev.* **2015**, 44, 4091-4130.

P03: Controlling the degradation behavior of polymeric nanoparticles by structurally tailored thermal properties

Karl Scheuer[a], Damiano Bandelli[b,c], Christine Weber[b,c], Klaus D. Jandt[a], Ulrich S. Schubert[b,c]

[a]Chair of Materials Science (CMS), Department of Materials Science and Technology, Otto Schott Institute of Materials Research (OSIM), Faculty of Physics and Astronomy, Friedrich Schiller University Jena, Löbdergraben 32, 07743 Jena, Germany

[b]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstr. 10, 07743 Jena, Germany

[c]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany

karl.scheuer@uni-jena.de; damiano.bandelli@uni-jena.de

Polyesters represent biodegradable and biocompatible polymers making them useful for medical applications.[1] In particular, applications aiming at the release of actives from polyester-based nanoparticles are in focus of our research. The degradation and release behavior is affected by the crystallinity of the polyesters, however, the exact role of this feature is difficult to quantify as additional factors such as the hydrophilicity play a major role as well. Our approach is therefore directed to obtain tailor-made polyesters that vary in their crystallinity but maintain the same hydrophilic / hydrophobic balance (HHB). In this contribution, we show the synthesis and the characterization of homo- and co-polyesters mimicking the HHB of PCL and PLA.[2] Tailor made polyesters were obtained via the ring opening polymerization (ROP) of lactones or substituted glycolides, yielding well defined homo- and co-polymers. The resulting materials were characterized by means of size exclusion chromatography, nuclear magnetic resonance, matrix assisted laser desorption ionization mass spectrometry, differential scanning calorimetry, thermogravimetric analysis and atomic force microscopy to assess the structural, thermal and mechanical properties of the bulk materials. Stable aqueous nanoparticle suspensions of varying size were prepared by changing the polymer concentration during the process. Nanoparticles from all the polymers were investigated in detail by atomic force microscopy, dynamic light scattering and scanning electron microscopy. As proof of concept, fluorescence spectroscopy of pyrene loaded nanoparticles for the PLA series confirmed constant hydrophobicity, validating our approach. All techniques consistently hint towards an altered internal structure of the nanoparticles with constant HHB.

References

[1] N. Kamaly, B. Yameen, J. Wu, O. C. Farokhzad, *Chem. Rev.* **2016**, *116*, 2602-2663.

[3] D. Bandelli, C. Helbing, C. Weber, M. Seifert, I. Muljajew, K. D. Jandt, U. S. Schubert, *Macromolecules* **2018**, *51*, 5567-5576.

ABSTRACTS OF POSTER PRESENTATIONS

P04: MOFs templated polymer networks for bio-applications

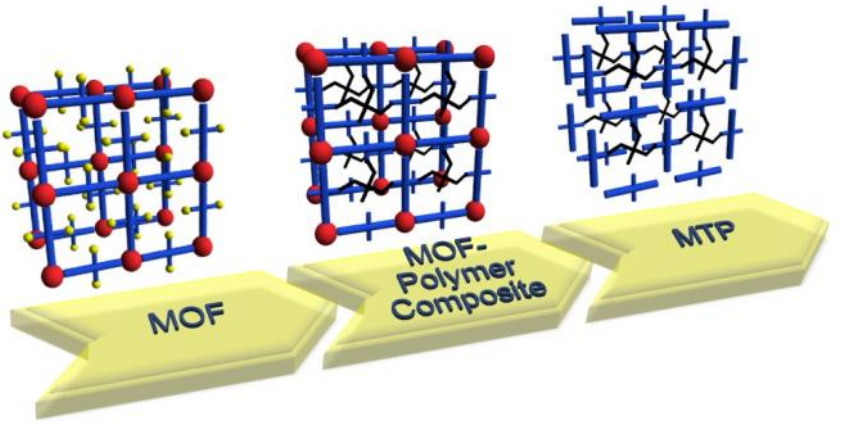
Begum Salma[a], Sophia Schmidt[a], Krolla Peter[a], Julia Hümmer[a], Cornelia Lee-Thedieck[a], Sylvain Grosjean[b], Zhou Wencai[a], Bräse Stefan[b], Wöll Christof[a], Manuel Tsotsalas[a,b]

[a]Institute of Functional Interfaces (IFG), Karlsruhe Institute of Technology (KIT), Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany

[b]Institute for Organic Chemistry (IOC), Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany

salma.begum@kit.edu

Metal-organic frameworks (MOF)-templated polymers (MTP) have emerged as persistent modular materials that can be tailored for desired bio-functions. This class of polymer materials combine the advantages of the structurally well-defined MOFs with that of covalently connected soft polymer networks.[1] We designed biocompatible metal-free polymer network via crystal-controlled polymerization process that facilitate the simultaneous synthesis and morphology control of polymer materials on a molecular level. In this approach bis-azido functionalized organic linker units are chemically arranged at nanoscale within a MOF structure, afterwards the organic linker units are covalently connected via a secondary linker applying azide-alkyne click chemistry. Removal of the metal ions of the MOF-polymer composite result in water-stable bio-compatible MTPs that demonstrate their suitability for bio-applications, such as bioactive particles or coatings for cells adhesion and stimuli responsive drug-release platform in in vitro cell culture studies.[2] Similarly, incorporation of porphyrin moieties within the polymer network demonstrate high antibacterial activity against pathogens via visible light promoted singlet oxygen generation.[3]



References

[1] M. Tsotsalas, J. Liu, B. Tettmann, S. Grosjean, A. Shahnas, Z. Wang, C. Azucena, M. Addicoat, T. Heine, J. Lahann, J. Overhage, S. Bräse, H. Gliemann, C. Wöll, *J. Am. Chem. Soc.* **2014**, *136*, 8-11.

[2] S. Schmitt, M. Silvester, M. Tsotsalas, A.L. Winkler, A. Shahnas, S. Grosjean, F. Laye, H. Gliemann, J. Lahann, S. Bräse, M.Franzreb, C. Wöll, *ACS Nano* **2015**, *9*, 4219-4226.

[3] W. Zhou, S. Begum, Z. Wang, P. Krolla, D. Wagner, S. Bräse, C. Wöll, M. Tsotsalas, *ACS Appl. Mater. Interfaces* **2018**, *10*, 1528-1533.

P05: Guanidinium bearing methacrylamide based terpolymers mimicking secondary amphipathic peptides for gene delivery

Ceren Cokca[a], Leon Zartner[b], Andrew Njau[b], Franz Hack[b], Dagmar Fischer[b], Kalina Peneva[a]
[a]Institute of Organic and Macromolecular Chemistry, Friedrich Schiller University Jena, Lessingstrasse 8, 7743 Jena, Germany.
[b]Institute of Pharmacy, Friedrich Schiller University Jena, Lessingstrasse 8, 07743 Jena, Germany.
ceren.cokca@uni-jena.de

The naked gene delivery is not possible due to the degradation of gene material by nucleases and rapid clearance from blood circulation, interfering with the cellular uptake process. Therefore, the utilization of polymers as a carrier system is an advantage to create a safe transport of genetic material to its target site. For this purpose, cationic polymers have been explored and demonstrated significant transfection efficiency.[1] The monomer selection and the distribution in the polymer chain are important factors for the efficient polyplex formation.[2] However, the higher cationic charge content ends up with either failure of release of the genetic material during transfection or higher cytotoxicity. Hence, it is crucial to adjust this charge balance to get the optimum transfection efficiency with less cytotoxicity. In this study, we designed an amphipathic terpolymer structure embodying the combination of cationic and hydrophobic methacrylamide monomers. Well-defined polymer samples were synthesized through aqueous reversible addition-fragmentation chain-transfer polymerization with low dispersity index (Đ~1.2). The plasmid DNA (pDNA) and NF-κB oligonucleotides binding capacity and their complex formation with copolymers and terpolymers were tested by gel electrophoresis and Accu Blue assay. At low polymer nitrogen to nucleic acid phosphate ratios, NF-κB oligonucleotides represented good biocompatibility beside no in vitro hemotoxicity. The polyplexes evaluated using the hen´s egg test (HET-CAV). A luciferase reporter was used to assess polyplex transfection capability. Overall, incorporation of hydrophobic monomer units into cationic copolymer structure dramatically improved transfection efficiency of pDNA. These findings enable further fine tuning of polymer structures to improve transfection efficiency while maintaining low cytotoxicity.

References

[1] I. Tabujew, K. Peneva, Cationic Polymers in Regenerative Medicine. **2014**, 1-29.
[2] Paper submitted.

P06: Quantifying the distribution of nanoparticle-and micelle-based cargo delivery using image-based systems biology techniques

Zoltan Cseresnyes[a], Marc T. Figge[a,b]
[a]Applied Systems Biology, Hans Knöll Institute, Jena, Germany
[b]Faculty of Biological Sciences, Friedrich Schiller University, Jena, Germany
zoltan.cseresnyes@hki-jena.de; thilo.figge@leibniz-hki.de

The targeted delivery of anti-pathogenic compounds is of special interest when it comes to fighting diseases caused by treatment-resistant fungi or bacteria. Properly designed polymer-based nanoparticles (NP) and micelles (MC) can provide a very efficient way to deliver the cargo directly to the target organ(s), whilst minimizing the off-target release and activation of the active compound. It is necessary to be able to follow the anatomical pathway of the particles' movements and their endpoint spatial distribution in the body, so as to be able to precisely design the targeting and releasing mechanisms, as well as the minimum effective dosage. In order to support such effort, we have developed an array of systems biology tools that allow us to visualize and quantify the distribution of such compound-carrying NPs and MCs. By combining fluorescence confocal or two-photon microscopy with dark-field imaging, we were able to individually identify NPs down to the 100 nm size range. For the much smaller size MCs, we used the fluorescence signal of the released cargo, as well as the a priori knowledge of the anatomical structure of the targeted organs to identify the endpoint location of the delivery, as well as the relative amount of active compounds delivered to various anatomical regions. Examples include the characterization of MC-mediated liver-targeted compounds to protect the organ from undergoing cirrhosis. By using 3D and 4D (3D plus time) confocal microscopy, we also characterized the NP and MC uptake probability as a function of the NP and MC morphometry. In summary, a combination of microscopy techniques with proprietary and open source software, we developed a workflow that allows the quantitative characterization of the spatio-temporal distribution of NPs and MCs.

References

[1] Z. Cseresnyes, K. Kraibooj, M.T. Figge, *Cytometry Part A* **2018**, *93*, 346-356.

P07: In vitro cytotoxicity and cytolocalization of RAFT nano-polymeric carriers

Marco A. D. Jesus-Tellez[a,b], Patricia Quintana-Owen[b], Guadalupe Ayora-Talavera[c], Emily Sauri-Medina[c], Raul Mena-Rosado[c], Carolina Ventura-Hunter[d], Enrique Saldivar-Guerra[d], Carlos Guerrero-Sanchez[a], Ulrich S. Schubert[a]
[a]Jena Center Soft Matter (JCSM), Friedrich Schiller University of Jena (FSU).
[b]Centro de Investigacion y Estudios Avanzados (Cinvestav) unidad Mérida.
[c]Universidad Autónoma de Yucatan (UADY).
[d]Centro de Investigación en Química Aplicada (CIQA).
marco.dejesus.tellez@uni-jena.de

Research in nanomaterials has increased exponentially due to their exceptional optical, electrical, magnetic, biological and mechanical properties; with applications in electronics, biotechnology, healthcare, pharmaceutics, etc.[1] RAFT permits to synthesize compounds with architectures and molar mass controlled. In addition, this methodology can be applied in diversity of monomers. Therefore, this polymerization favors obtaining accurate structures that are ideal for materials development or creation of new products.[2] RAFT strategies can be applied in pharmaceutical and biomedical field, where there is an increasing interest in the development of tools that allow efficient and safe drug delivery. However, several challenges have restricted protein-based drug delivery methods to extracellular targets making nanostructured polymers a very attractive solution to use as intracellular carriers to treat or prevent diseases.[2,3] In this work, toxicity of RAFT polymers was firstly evaluated and secondly the location of them into contact with the cell was determined. The in vitro cytotoxicity and cytolocalization of a series of five RAFT polymers was assessed using Madin-Darby Canine Kidney as an adherent cell line via MTT Cell Proliferation Assay to evaluate cell metabolic activity and proliferation along with Crystal Violet Cell Viability Assay as a complementary test to determine cell viability and microscopic morphology. Cytolocalization was evaluated by means of fluorescent microscopy in the fluorescein conjugated polymers. Results obtained from evaluation via MTT assay indicate low cytotoxicity of polymers except PDMAEMA. Crystal Violet assay showed similar results of cell viability and analysis of morphological changes and cell integrity confirmed these findings. In addition, studies by confocal microscopy have detected the exact position of the fluorescent polymer respect to the cells.

References

[1] I. Capek, Nanotechnology and nanomaterials; Studies in Interface Science; Elsevier Science. **2006**, *23*, 1-69.
[2] B. Fairbanks, P. Gunatillake, L. Meagher, *Adv. Drug Deliv. Rev.* **2015**, *91*, 142-152.
[3] D. Pissuwan, C. Boyer, K. Gunasekaran, T. Davis, V. Bulmus, *Biomacromolecules* **2010**, *11*, 412-420.

P08: Cellular uptake of polymeric nanoparticles invesigated by correlative light and electron microscopy

Daniel Friedrich[a,b], Fengjiao Ma[c,d], Martin Reifarth[a], Rainer Heintzmann[c,d], Stephanie Hoeppener[a,b]
[a]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldstr. 10, 07743 Jena, Germany
[b]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
[c]Leibniz Institut of Photonic Technology (IPHT), Albert-Einstein-Str. 9, 07745 Jena, Germany
[d]Institute of Physical Chemistry (IPC) and Abbe Center of Photonics (ACP), Friedrich Schiller University Jena, Helmholtzweg 4, 07743 Jena, Germany
daniel.friedrich@uni-jena.de

The elucidation of cellular uptake mechanisms and the subsequent fate of polymeric drug delivery systems within cells and tissue is of high importance to assess their desired as well as their side effects.[1,2] In this project we implement correlative light and electron microscopy (CLEM) as an outstanding analysis tool, since each of the methods provide their own specific advantages. In this context, the informative values of superresolution fluorescence microscopy, i.e., structures illumination microscopy (SIM) and transmission electron microscopy (TEM) are discussed and special focus is placed on the complementary information that can be obtained by the correlation of both methods. In particular, the distribution as well as the changes in the cellular ultrastructure induced by the polymer nanoparticles will be investigated. CLEM benefits here from a large field of view and a resolution down to the cellular membrane level. Furthermore, a user-friendly software package will be implemented that can colocalize the fluorescence labeled structures (i.e., nanoparticles and actin filaments) in the obtained correlative images.

Specific challenges encountered during the implementation of suitable preparation techniques are highlighted as well as the question of the development of suitable correlative dyes. Based on an number of illustrative examples the specific benefit of correlative light and electron microscopy will be demonstrated. These examples utilize CLEM for the localization of polymer nanoparticles or introduce tailor-made correlative dyes consisting of metal-complex polymers conjugated with coordinative metal compounds.[3,4]

References

[1] M. Reifarth, S. Hoeppener, U.S. Schubert, *Adv. Mater.* **2018**, *30*, 1703704.
[2] M. Reifarth, U.S. Schubert, S. Hoeppener, *Adv. Biosyst.* **2018**, *2*, 1700254.
[3] T. Bus, C. Englert, M. Reifarth, P. Borchers, M. Hartlieb, A. Vollrath, S. Hoeppener, A. Traeger, U.S. Schubert, *J. Mater. Chem. B.* **2017**, *5*, 1258-1274.
[4] M. Reifarth, E. Preussger, U.S. Schubert, R. Heintzmann, S. Hoeppener, *Part. Part. Syst. Charact.* **2017**, *34*, 1700180.

P09: Influence of micelle structure on immune response, uptake properties and hemocompatibility

Elena Gardey[a,d], Fabian H. Sobotta[c,d], Tony Bruns[a,b], Johannes C. Brendel[c,d], Andreas Stallmach[a,d]
[a]Department of Internal Medicine IV (Gastroenterology, Hepatology, and Infectious Diseases), Jena University Hospital, Jena, Germany.
[b]The Integrated Research and Treatment Centre for Sepsis Control and Care (CSCC), Jena University Hospital, Jena, Germany.
[c]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Jena, Germany.
[d]Jena Centre for Soft Matter (JCSM), Friedrich Schiller University Jena, Jena, Germany
elena.gardey@med.uni-jena.de

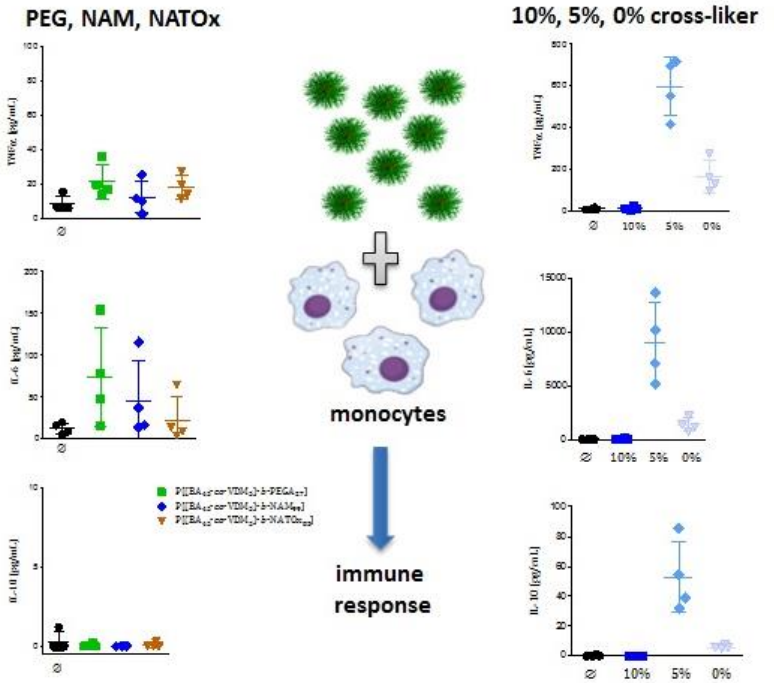
Block copolymer micelles have received increasing attention in the last decades, in particular for their appealing properties in nanomedicine.[1] An important, but barely investigated aspect is the biological response to these materials and their stability in a biological environment. It has been shown that the shell-crosslinking micelles induce less immune response and less cytotoxic than the non-crosslinked micelles.[2] But the biocompatibility and hemocompatibility of nanoparticles also depend on their core, shell, charge and surface chemistry.[3]

Here we demonstrate novel block copolymer micelles with the same hydrophobic core and various hydrophilic shells ranging from common poly (ethylene glycol) derivatives to materials based on *N*-acrylomorpholine (NAM) or *N*-acryloylthiomorholine oxide (NATOx). The influence of these shells on immune response and the lysis of erythrocytes were studied in detail. In addition, we investigated the impact of the cross-link density in the core using PNAM-micelles with 10%, 5% and 0% of cross-linker.

While the different shells had only a minor impact on the immune response, micelles with reduced crosslinking density (5% or 0%) enhanced the release of inflammatory cytokines such as tumour necrosis factor alpha, interleukin-6, interleukin-10 in monocytes isolated from the peripheral blood of healthy donors.

The uptake into monocytes was significantly higher for non-crosslinking micelles compared to both crosslinking materials (5% and 10%).

ABSTRACTS OF POSTER PRESENTATIONS



References

[1] J. C. Brendel, F. H. Schacher, *Chem. Asian. J.* **2018**, *13*, 230-239.

[2] M. Elsabahy, S. Zhang, F. Zhang, Z. J. Deng, Y. H. Lim, H. Wang, P. Parsamian, P. T. Hammond, K. L. Wooley, *Sci. Rep.* **2013**, *3*, 3313.

[3] F. Schlenk, S. Werner, M. Rabel, F. Jacobs, C. Bergemann, J. H. Clement, D. Fischer, *Arch. Toxicol.* **2017**, *91*, 3271-3286.

ABSTRACTS OF POSTER PRESENTATIONS

P10: Protein-polymer conjugates: synthesis strategies and applications as natural membrane mimics and therapeutic agents

Ulrich Glebe[a], Maria Mathieu[a], Magnus Schwieters[a], Johannes Martin[a], Himanshu Charan[a], Xiaolin Dai[a], Zhiyong Sun[a], Changzhu Wu[a], Alexander Böker[a]
[a]Fraunhofer Institute for Applied Polymer Research IAP, Geiselbergstr. 69, 14476 Potsdam-Golm, Germany
ulrich.glebe@iap.fraunhofer.de

The synthesis of protein-polymer conjugates via the grafting-from strategy and a controlled radical polymerization technique became increasingly popular from 2005 on and conjugates find applications in drug delivery among others. The poster gives an overview about the synthesis and characterization of various protein-polymer conjugates performed in our lab. In the case of transmembrane proteins, the conjugates can be crosslinked at interfaces to form ultrathin membranes with the protein nanochannels acting as uniform pores. Furthermore, stable capsules were formed exploiting the formation of Pickering emulsions.[1,2] In the case of enzymes, the efficiency of interfacial biocatalysis was improved due to the higher stability and interfacial activity of the conjugates.[3]

In addition to grafting-to and grafting-from approaches, we are also focusing on enzymatic strategies for the synthesis of protein-polymer conjugates. Site-specific polymer attachment, 1:1 stoichiometry and bio-friendly reaction conditions are especially advantageous for the synthesis of defined conjugates and could be applied for therapeutic proteins in future. Moreover, the enzymatic ligation allows for protein immobilization with uniform orientation.

References

[1] H. Charan, J. Kinzel, U. Glebe, D. Anand, T. M. Garakani, L. Zhu, M. Bocola, U. Schwaneberg, A. Böker, *Biomaterials* **2016**, *107*, 115-123.
[2] H. Charan, U. Glebe, D. Anand, J. Kinzel, L. Zhu, M. Bocola, T. Mirzaei Garakani, U. Schwaneberg, A. Böker, *Soft Matter* **2017**, *13*, 2866-2875.
[3] Z. Sun, U. Glebe, H. Charan, A. Böker, C. Wu, *Angew. Chem. Int. Ed.* **2018**, *57*, 13810-13814.

ABSTRACTS OF POSTER PRESENTATIONS

P11: Prodrug nanoparticles to target conidia of the human-pathogenic fungus Aspergillus fumigatus in macrophages

Katherine González Rojas[a,b], Gauri Gangapurwala[c,d], Julien Alex[c,d], Antje Vollrath[c,d], Thorsten Heinekamp[a], Christine Weber[c,d], Zoltán Cseresnyés[a], Marc Thilo Figge[a], Carlos Guerrero Sánchez[c,d], Ulrich S. Schubert[c,d], Axel A. Brakhage[a]
[a]Leibniz Institute for Natural Product Research and Infection Biology – Hans-Knöll-Institute Beutenbergstraße 11a, 07745 Jena, Germany
[b]Institute of Microbiology, Friedrich Schiller University Jena, 07745 Jena, Germany
[c]Jena Center for Soft Matter, Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
[d]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, 07745 Jena, Germany
katherine.gonzalez@leibniz-hki.de; christine.weber@uni-jena.de; thorsten.heinekamp@hki-jena.de

Aspergillus fumigatus is one of the most important airborne fungal pathogens of the immunocompromised patient. The fungus causes life-threatening pulmonary aspergillosis, which has a mortality rate of 60 to 90%.[1] Several virulence factors have been identified, which, allow the fungal spores (conidia) to survive inside macrophages.[2,3] To fight invasive aspergillosis, clinically used drugs and their combination with humidimycin are planned to be employed. Humidimycin was recently discovered to prevent the caspofungin paradoxical effect by countering the salvage pathway that A. fumigatus employs under a high dose of caspofungin.[4]

To develop strategies for targeting intracellular pathogens, we generated polymer-based nanoparticles with a size range from 100 to 600 nm and different drug ratios of caspofungin-based methacrylate polymers. This way, we aim at targeting conidia residing in macrophages. Therefore, we decorated the nanoparticles with mannose and glucans moieties. These carbohydrates are recognized by specific cell receptors and this recognition appears to accelerate the endocytosis of nanoparticles. An important question also concerns the ability of these nanoparticles to enter a mature phagolysosome and thus to reach a phagocytosed pathogen.

To follow the fate of endocytosed nanoparticles, the macrophage cell line RAW 264.7 was treated with a variety of nanoparticle formulations and was analyzed by confocal laser scanning microscopy. To determine the intracellular localization of the particles the macrophage cells were transfected with genes encoding GFP fusion proteins that are located in endosomal and lysosomal compartments. Additionally, the cytotoxicity of the nanoparticles was tested by resazurin assay. We observed uptake of nanoparticles of the different sizes and co-localization of the 555 nm particles at the conidium-phagolysosome.

References

[1] A. A. Brakhage, *Curr. Drug. Targets* **2005**, *6*, 875-86.

[2] S. Amin, A. Thywissen, T. Heinekamp, H. P. Saluz, A. A. Brakhage, *Int. J. Med. Microbiol*. **2014**, *304*, 626-36.

[3] T. Akoumianaki, I. Kyrmizi, Isabel Valsecchi, M. S. Gresnigt, G. Samonis, E. Drakos, D. Boumpas, L. Muszkieta, A. Zachariou, D. P. Kontoyiannis, T. Chavakis, M. G. Netea, F. L.van de Veerdonk, A. A. Brakhage, Jamel El-Benna, A. Beauvais, J.-P. Latge and G. Chamilos, *Cell, Host & Microbe* **2016**, *19*, 79-90.

[3] V. Valiante, M. C. Monteiro, J. Martín, R. Altwasser, N. El Aouad, I. González, O. Kniemeyer, E. Mellado, S. Palomo, N. de Pedro, I. Pérez-Victoria, J. R. Tormo, F. Vicente, F. Reyes, O. Genilloud, A. A. Brakhage, *Antimicrob. Agents Chemother*. **2015**, *59*, 5145-53.

P12: Highly disperse carboxymethyl celluloses - a characterization challenge

Mandy Grube[a,b], Igor Perevyazko[c], Thomas Heinze[a,b], Ulrich S. Schubert[a,b], Ivo Nischang[a,b]
[a]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstraße 10, 07743 Jena, Germany
[b]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
[c]Department of Molecular Biophysics and Physics of Polymers, St. Petersburg State University St. Petersburg, 7/9 Universitetskaya nab., St. Petersburg, 199034, Russian Federation
mandy.grube@uni-jena.de

Cellulose is one of the most abundant natural macromolecule and commercially available in a variety of forms and chemical derivatives. One of the most significant markets concerns carboxymethyl cellulose (CMC), an important ionic cellulose ether because of its widespread implementation as a biomaterial and in industrial processes. As a consequence, the properties of CMCs are elucidated for a rather long time by a selection of techniques. A known challenge for characterization and quality control purposes is their inherent molecular dispersity, resolved by analyst depending on the methods utilized for their characterization.

In our study, we employ a global analytical approach for their characterization by a combination of molecular hydrodynamic methods, i.e. intrinsic viscosities as a measure for rotational friction as well as sedimentation and diffusion analysis as a measure for translational friction. Such combination of methods aims at identifying the range of concentrations suitable for molecular hydrodynamic analysis by sedimentation velocity experiments and diffusion coefficient estimations. Orthogonally, absolute molar masses are also determined by size exclusion chromatography coupled to multi-angle laser light scattering. Using these different absolute approaches in determining the molecular properties of the CMCs, we subsequently utilize the classical exponential scaling relationships, the molecular hydrodynamic chain parameter estimations, and conformation zone plots to pin down the conformation type these CMCs adopt in aqueous sodium chloride. Our multi-dimensional experimental approach on the same samples provides an opportunity for a comprehensive characterization of dissolved / dispersed biomaterials even at very high degrees of dispersity. This is enabled by statistical averaging and verification of molecular hydrodynamic parameters of all techniques utilized.

References

[1] M. Grube, I. Perevyazko, T. Heinze, U. S. Schubert, I. Nischang, submitted.

ABSTRACTS OF POSTER PRESENTATIONS

P13: A green organic solvent-free formulation method for nanoparticulate drug delivery systems

Christian Grune[a], Anna Czapka[b], Jana Thamm[a], Stephanie Höppener[c], Oliver Werz[b], Dagmar Fischer[a,c]
[a]Pharmaceutical Technology and Biopharmacy, Institute for Pharmacy, Friedrich Schiller University Jena, Lessingstraße 8, 07743 Jena, Germany
[b]Pharmaceutical and Medicinal Chemistry, Institute for Pharmacy, Friedrich Schiller University Jena, Philosophenweg 14, 07743 Jena, Germany
[c]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
christian.grune@uni-jena.de

The emulsion-diffusion-evaporation technique (EM) is a classical and worldwide accepted method to prepare poly(D,L-lactide-co-glycolide acid) (PLGA) nanoparticles (NP) as drug delivery systems. One major drawback of this technique is the usage of organic solvents to dissolve the water-insoluble polymer. Organic solvents can be environmental damaging, toxic and harmful to the human health. Therefore, great efforts must be made to recover, reuse and recycle the organic solvents and to clean the final product from residuals. This is associated with immense costs, especially when it comes to large industrial manufacturing. This study aims at finding an alternative technique for the preparation of PLGA-NP by a fast, non-toxic, cost-efficient and green organic solvent-free method. The prepared NP showed a comparable particle size, size distribution and zeta potential like obtained by the conventional EM. It was shown that the green method changed the crystallinity of the particles which allows a modified drug release. A reduction of the process time by more than half with less preparation steps was achieved, which is a huge benefit in terms of manufacturing costs and process automatization. The NP showed no *in vitro* hemotoxicity and a good biocompatibility after systemic injection into the dynamic blood flow of a shell-less hen's egg test (HET-CAV). As a proof of concept, several hydrophilic and lipophilic drugs such as rosuvastatin, atorvastatin and the indirubin-derived 6BIGOE were encapsulated to demonstrate the general eligibility of the green method. A quality by design approach was used to evaluate the process and make a risk assessment. In conclusion, the green method is a fast, simple, non-toxic and cost-efficiency technique to prepare PLGA-NP avoiding all the drawbacks associated with organic solvents.

P14: Hydroxyethyl starch - poly(ethylene imine) conjugates as potential targeted gene carriers in inflammatory diseases

Franz Hack[a], Ekram Ahmed Chowdhury[c,d], Behnam Noorani[c,d], Dagmar Fischer[a,b], Ulrich Bickel[c,d]
[a]Friedrich Schiller University Jena, Pharmaceutical Technology and Biopharmacy, Lessingstrasse 8, 07743 Jena, Germany
[b]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
[c]Texas Tech University Health Sciences Center, School of Pharmacy, Center for Blood-Brain-Barrier Research, 1400 S Coulter Street, Amarillo, USA
[d]Texas Tech University Health Sciences Center, School of Pharmacy, Department of Pharmaceutical Sciences, 1400 S Coulter Street, Amarillo, USA
dagmar.fischer@uni-jena.de

The endothelial cells of the blood brain barrier (BBB) represents a significant hurdle in getting therapeutic compounds into the brain. Compared to lipophilic small molecules the situation is even more challenging for macromolecules such as plasmid DNA (pDNA), oligonucleotides (ODN) or small interfering RNA (siRNA) necessitating targeted delivery to the brain. Among others, poly(ethylene imine) (PEI) has been the most popular non-viral vector utilized for nucleic acid delivery. PEI disadvantages are like being cytotoxic to cells, tending to agglomerate and getting easily taken up by the reticuloendothelial system without appropriate shielding.[1] To avoid unspecific reactions in the body, shielding agents such as hydroxyethyl starch (HES) have been introduced for PEI to deliver genes in vitro.[2] HES, a biodegradable polymer, has long been used as a plasma volume expander in humans and shows promise to be used with PEI for targeted delivery to the brain.

In this work we HESylated® PEI followed by linkage to streptavidin via biotin. Polyplexes were formed with nuclear factor (NF)-kappaB decoys and physicochemically (DLS, LDA) and biologically (MTT assay) characterized. Polyplexes at N/P ratios of 6 were prepared in a size range from 200 to 400 nm showing zeta potentials from -10 to +10 mV. HES conjugates showed lower cytotoxicity compared to PEI polyplexes.

However, since HES and PEI are available in various molecular weights and chemical structures, optimization studies are necessary to elucidate the best combination of HES and PEI in terms of molecular weight and condensation properties. Moreover, the anti- inflammatory effects of pDNA, ODN and siRNA need to be compared.

References

[1]D. Fischer, R. Bhattacharya, B. Osburg, U. Bickel, *J. Gene Med.* **2005,** *7*, 1063-1076.
[2]M. Noga, D. Edinger, E. Wagner, G. Winter, A. Besheer, *Biomater. Sci.* **2014,** *25*, 855-871.

P15: Amphiphilic Nylon-3 polymers for enhanced siRNA delivery into glioblastoma cells

Natascha Hartl, Friederike Adams, Gabriella Costabile, Runhui Liu, Olivia Merkel
Ludwig-Maximilians-University Munich, Munich (DE), Pharmaceutical Technology and Biopharmaceutics, Department of Pharmacy, Butenandtstrasse 5, 81377 München, Germany
natascha.hartl@lmu.de

Glioblastoma multiforme is the most common devastating type of primary malignant tumor of the central nervous system. Thus, any new therapeutic strategy to target this tumor is of significant benefit. Small interference RNA (siRNA) is intensively investigated for the treatment of a broad range of diseases e.g. for brain diseases such as glioblastoma. Limitations in application of naked siRNA caused by rapid degradation, immune response and low passive cell uptake are bypassed by using polymers to encapsulate the nucleic acids by electrostatic interactions in order to shield them from the environment and to assist cellular internalization. As a new class of cationic amphiphilic polymers, our group established Nylon-3 polymers for siRNA delivery.[1] Various random Nylon-3 copolymers with different ratios of hydrophobic and cationic subunits in the polymer chain were synthesized. Due to their amphiphilicity these polymers form micelle-like nanoparticles by efficiently encapsulating siRNA even at low concentrations. In comparison to well-investigated highly cationic systems, Nylon-3 polymers showed advantages in their biocompatiblity, lower cytotoxicity and improved transfection efficiencies. Characterization of the formed siRNA-polymer complexes (polyplexes) was performed regarding physicochemical properties, stability and in vitro behavior. In our experiments, Nylon-3 polymers with the highest hydrophobic amounts showed the best performance in matters of polyplex characteristics, cell internalization and gene knockdown ability in glioblastoma cells. We suggest that hydrophobic subunits in the polymer enable the fusion of polyplexes and the membrane of cells. In conclusion, Nylon-3 polymers were demonstrated to be a promising class of siRNA delivery system for future treatment of glioblastoma.

References

[1] V. Nadithe, R. Liu, B. A. Killinger, S. Movassaghian, N. H. Kim, A. B. Moszczynska, K. S. Masters, S. H. Gellman, O. M. Merkel, *Mol. Pharm.* **2015**, *12*, 362-374.

P16: Self-immolative drug-delivery-systems based on polycarbonate compounds

Dimitri Jung, Timo Schoppa, Klaus Langer, Dirk Kuckling
Paderborn University, Warburger Str. 100, 33098 Paderborn
dimitri.jung@uni-paderborn.de

The application of a drug-delivery-system is a facile approach to fight adverse drug effects and enhance the cellular uptake and distribution of certain drugs in a medical therapy. Polycarbonates are known for their biocompatibility and can be modified to respond to certain stimuli, e.g. redox-reactions, light irradiation and acidic environments. The implementation of stimuli-responsive side-groups empower the fabrication of suitable drug-delivery-systems. By applying a certain trigger, the responsive side-group cleaves off and liberates a nucleophile which can intramolecularly backbite into the polymer backbone and subsequently lead to the degradation of the polymer chain into smaller molecules. The side-groups of polycarbonates act as a chemical handle to further modify the monomer to respond to a variety of stimuli.

References

[1] J. Sun, D. Jung, T. Schoppa, J. Anderski, M.-T. Picker, Y. Ren, D. Mulac, N. Stein, K. Langer, D. Kuckling, **2019**, submitted.
[2] J. Sun, W. Birnbaum, J. Anderski, M.-T. Picker, D. Mulac, K. Langer, D. Kuckling, *Biomacromolecules* **2018**, *19*, 4677-4690.
[3] J. Sun, J. Anderski, M.-T. Picker, K. Langer, D. Kuckling, *Macromol. Chem. Phys.* **2019**, *220*, 1800539.

ABSTRACTS OF POSTER PRESENTATIONS

P17: Trivalent sialosides as inhibitors of influenza virus

Pallavi Kiran[a]*, Sumati Bhatia[a]*, Daniel Lauster[b], Stevan Aleksic´[c], Carsten Fleck[d], Natalija Peric[d], Wolfgang Maison[d], Susanne Liese[e,f], Bettina G. Keller[c]
[a]Institut fer Chemie und Biochemie Organische Chemie, Freie Universität Berlin, Takustr. 3, 14195 Berlin (Germany)
[b]Institut fer Biologie, Molekulare Biophysik, IRI Life Sciences, Humboldt-Universit-t zu Berlin, Invalidenstr. 42, 10115 Berlin (Germany)
[c]Institut fer Chemie und Biochemie, Physikalische und Theoretische Chemie, Freie Universität Berlin, Takustr. 3, 14195 Berlin (Germany)
[d]Fachbereich Chemie, Institut für Pharmazie, Universität Hamburg, Bundesstr. 45, 20146 Hamburg (Germany)
[e]Department of Mathematics, University of Oslo, P.O Box 1053 Blinder, 0316 Oslo (Norway)
[f]Department of Physics, Freie Universit-t Berlin, Arnimallee 14, 14195 Berlin, (Germany)
*These authors contributed equally to this work.
jhapallavi@zedate.fu-berlin.de

Yearly Influenza Virus vaccination yields dissatisfactory protection and the efficacy of existing drugs is limited due to the development of resistant virus strains. Hence, novel drugs are needed urgently.

Inhibition of influenza A virus (IAV) infection by multivalent sialic acid (SA) inhibitors preventing viral hemagglutinin binding to host cells of the respiratory tract is a promising strategy.

Here, in this work we tried to emphasize on the importance of the scaffold rigidity and the challenges associated with the spacer length optimization.

References

[1] S. Bhatia, D. Lauster, M. Bardua, K. Ludwig, S. Angioletti-Uberti, N. Popp, U. Hoffmann, F. Paulus, M. Budt, M. Stadtmeller, T. Wolff, A. Hamann, C. Böttcher, A. Herrmann, R. Haag, *Biomaterials* **2017**, *138*, 22 -34.
[2] M. Mammen, S.-K. Choi, G. M. Whitesides, *Angew. Chem. Int. Ed*. **1998**, *37*, 2754 -2794.

ABSTRACTS OF POSTER PRESENTATIONS

P18: Raman spectroscopic characterization of the linkage- and interaction mechanism of nanocarriers and drugs with hepatic stellate cells

Paul Klemm[a,b], Sophie Huschke[c], Nadia Ehteshamzad[a,b], Marko Rodewald[d], Tobias Meyer[d], Michael Schmitt[d,e], Adrian Press[c], Jürgen Popp[a,d,e], Michael Bauer[a,c], Stephanie Schubert[a]

[a]Jena Center for Soft Matter (JCSM), Friedrich-Schiller University Jena, Philosophenweg 7, 07743 Jena

[b]Laboratory of Organic and Macromolecular Chemistry, Friedrich-Schiller University Jena, Humboldtstrasse 10, 07743 Jena

[c]Jena University Hospital, Department of Anesthesiology and Intensive Care Medicine, Am Klinikum 1, 07747 Jena

[d]Institute of Physical Chemistry and Abbe Center of Photonics, Albert-Einstein-Straße 6, 07745 Jena

[e]Leibniz Institute of Photonic Technology, Albert-Einstein-Straße 9, 07745 Jena

paul.klemm@uni-jena.de

The chemical sensitivity of linear and non-linear Raman-based imaging approaches is utilized for the characterization of the interaction mechanism of nanoparticles and drugs with (i) hepatic stellate cells (HepSC) and (ii) their uptake kinetics, aggregation behavior, and vitamin A (vit. A) release within the cells. The specific role of HepSC in vit. A uptake and storage offers the ability to purposefully use this function as a targeting moiety at least in early stages of their transformation. A library of poly(methacrylate) based functional polymers will be presented that can be formulated into well defined vit. A decorated nanoparticles carrying siRNA for HepSC treatment. Basic investigations of the induced liver fibrosis in a mouse model are essential to monitor benchmark parameters that are later needed to identify a successful HepSC treatment. In addition to immunohistology and gene expression, CARS (Coherent Anti-Stokes Raman Scattering), TPEF (Two-Photon Excited Fluorescence) and SHG (Second Harmonic Generation) imaging provide useful information for the differentiation between healthy and fibrotic tissue.[1]

References

[1] T. Yildirim, C. Matthäus, A. T. Press, S. Schubert, M. Bauer, J. Popp, U. S. Schubert, *Macromol. Biosci.* **2017**, *17*, 1700064.

P19: Stability of PEO-*b*-PAGE-*b*-PCL triblock terpolymers upon presence of nucleophilic substituents in the PAGE segment

Moritz Köhler[a,b], Carsten Rössel[a,b], Felix H. Schacher[a,b]
[a]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstrasse 10, 07743 Jena
[b]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena
moritz.koehler@uni-jena.de

Amphiphilic block copolymers (BCP) provide access to nanostructured materials in aqueous media.[1] Micelles from amphiphilic BCP are of high interest because they can overcome polarity limits of pharmaceutically relevant drugs and thus improve their biomedical applicability. Besides enhanced drug solubility and chemical stability, the delivery of drugs with BCP in so-called drug delivery systems (DDS) is a huge research field, in terms of maximizing the therapeutic efficiency and minimizing negative side effects.[2] Loading of hydrophobic drugs inside the micellar core of amphiphilic BCP micelles protects the drug against hydrolysis, enzymatic degradation and, in case of a poly(ethylene oxide) (PEO) corona, due to their "stealth" properties, also preliminary elimination from the bloodstream.[3] Ideally such BCP micelle DDSs show biodegradable properties so the targeted body can excrete them after the delivery of the drug.

We synthesized a polyether/-ester based triblock terpolymer and functionalized it with different amine groups in the middle block. We were mainly interested in whether the presence of different nucleophilic amines has an influence on hydrolytic stability of the polyester segment.

The triblock terpolymer poly(ethylene oxide)-block-poly(allylglycidyl ether)-block-poly(caprolactone) (PEO-*b*-PAGE-*b*-PCL) was synthesized by ring opening polymerization (ROP) of AGE using a PEO macroinitiator and a subsequent block extension by catalyzed ROP of ε-caprolactone (CL). Post-polymerization modifications with different amine-thiol compounds via thiol-ene click reaction gave access to the desired functionalized materials, which were characterized using size exclusion chromatography (SEC), 1H nuclear magnetic resonance (^{1}H-NMR) and elementary analysis.

References

[1] P. Alexandridis, B. Lindman, *Amphiphilic Block Copolymers: Self-Assembly and Applications*, Elsevier Science, **2000**.
[2] Y. Zhang, H. F. Chan, K. W. Leong, *Adv. Drug Delivery Rev.* **2013**, *65*, 104-120.
[3] A. Rösler, G. W. M. Vandermeulen, H.-A. Klok, *Adv. Drug Delivery Rev.* **2001**, *53*, 95-108.

P20: Anaylsis of polymeric micelles and soft molecular assemblies by cryo-transmission electron microscopy

Maren T. Kuchenbrod[a,b], Aisha A. Womiloju[a,b], Stephanie Hoeppener[a,b]
[a]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstr. 10, 07743 Jena, Germany
[b]Jena Center for Soft Matter (JCSM), Philosophenweg 7, 07743 Jena, Germany
maren.kuchenbrod@uni-jena.de

Polymeric structures are easily manipulated to form self-organized aggregates such as micelles, vesicles or higher ordered structures.

In order to drive the the polymeric system to aggregate into a desired configuration, specific key parameters have to be carefully chosen during synthesis. Such key parameters include the composition of the polymer as well as its properties, the block-structure, the polymer length and fraction, preparation procedure and the connected surrounding parameters (e.g. preparation temperature).[1]

Such systems consisting of soft matter materials are best characterized by cryo-Transmission Electron Microscopy (TEM). The advances in structural analysis that could be achieved by this technique were recently awarded with the noble price of chemistry (2017). Key for the success of the analysis technique is the ability to measure samples dissolved in water (aqueous medium) in a native state, therefore skipping long and error-prone embedding steps or drying. The technique is able to cover a wide range of molecular masses and requires only a small amount of sample compared to other techiques such as X-ray crystallography.[2,3]

We present different aspects of soft matter characterization by TEM. Special focus is placed also on alternative techniques to characterize stimuli-responsive systemes to follow morphological progression with respect to pH and temperature changes. As well as multifunctional staining approaches to add stimuli-responsiveness towards external triggers (e.g. reactive oxygen species in cellular environments).

References

[1] M. Reifarth, S. Hoeppener, U. S. Schubert, *Adv. Mater*. **2018**, *30*, 1703704.
[2] E. Callaway, *Nature* **2017**, *550*, 7675.
[3] K. Murata, M. Wolf, *BBA-General Subjects* 1862 **2018**, 324-334.

ABSTRACTS OF POSTER PRESENTATIONS

P21: Enhancing the comparability and reproducibility of quantitative analyses of the nanoparticle protein corona by integrating QconCATs into a new standardized LC-MS workflow

Christian Leps[a], Malte Sielaff[a], Stefan Tenzer[a]
[a]Institute for Immunology, University Medical Center of the Johannes Gutenberg University Mainz, Langenbeckstr. 1, 55131 Mainz, Germany
chrileps@uni-mainz.de

When a Nanoparticle (NP) enters a biological fluid (e.g. blood), a layer of proteins, termed the protein corona (PC), immediately forms around its surface, defining the NP's biological identity.[1]To enable the use of NPs as medical agents, detailed investigations about the composition of the PC are therefore required. The use of Liquid Chromatography - Mass Spectrometry (LC-MS) is one of the most commonly used techniques for these investigations, since it provides reliable information and deep insights into the corona proteome. The inter-lab comparability of different studies aiming to characterize the protein corona is currently suboptimal, due to variations in sample preparation and LC-MS workflows.

In the present study, we established a new LC-MS workflow that implements the use of quantification concatemers (QconCATs) for the absolute quantification of NP-PC components.[2] These recombinantly expressed proteins contain standard peptides, representing the 100 most abundant proteins in the protein corona, which enable the absolute quantification of PC proteins and furthermore allow reliable comparison of PCs derived from different NPs and laboratories.[3]

References

[1] M. P. Monopoli, C. Åberg, A. Salvati, K. A. Dawson, *Nat. Nanotechnol.* **2012**, *7,* 779–786.
[2] J. M. Pratt, D. M. Simpson, M. K. Doherty, J. Rivers, S. J. Gaskell, R. J. Beynon, *Nat. Protoc.* **2006**, *1, 2,* 1029-1043.
[3] Leps, C., Tenzer S. unpublished data.

ABSTRACTS OF POSTER PRESENTATIONS

P22: Tailored nanoparticles with two step release pattern: new tool for drug delivery

Thomas Heinze[a], Henry Lindemann[a], Thorsten Heinzel[a], Susanne Hofmann[a], Marie Kühne[a]
[a] Friedrich Schiller Universität Jena, Institut of Organic Chemistry and Macromolecular Chemistry, Institut of Biochemestry and Biophysics
henry.lindemann@uni-jena.de

Polysaccharides (PS) are valuable polymers for medical application as they are non-toxic, biocompatible and biodegradable. Their structure and, hence, properties can be widely modified. Valproic acid (VPA) is a histone deacetylase inhibitor (HDACi) and can be bound to PS via an ester linkage. PS valproates can be shaped to nanoparticles (NP).[1,2] These NPs may be used as carriers for additional HDACi, e.g. Ex-527.[3] HDACi acts on the acetylation of histones and non -histone proteins thereby influencing various cellular processes through altered signaling and gene expression. Interestingly, HDACi shows anti-inflammatory properties and benefits in the treatment of inflammation and sepsis. Since the free drugs have a short serum half-life time and side effects, binding to NPs could overcome these drawbacks and lead to a controlled two step release.[2,3] PS valproate were prepared as HDACi carrier with different degree of substitution (DS). The esterification was carried out in DMA/LiCl or ionic liquid in presents of p-toluenesulfonic acid, N,N-carbonyldiimidazol or iminium chloride as activating agent. The resulting hydrophobic polymer will be shaped to NP by nanoprecipitation or emulsification. The NPs prepared by emulsification are spherical and have diameters from 135 to 150 nm, which was determined by DLS, SEM/TEM, AF4 and AUC.

Cellular uptake of rhodamine B-labeled cellulose, dextran and pullulan valproate NPs was demonstrated by live cell imaging in tumor cells in vitro. Z-stacks made with confocal microscopy prove localization of the NPs within the cells. Co-localization studies with Mitotracker and TEM revealed the subcellular localization of the NPs in mitochondria. In addition, the liver organoid was used as a model to investigate NP distribution in tissue and potential treatment of sepsis.

References

[1] S. Hornig, H. Bunjes, T. Heinze, *J. Colloid Interface Sci.* **2009**, *338*, 56-62.
[2] M. Göttlicher, S. Minucci, P. Zhu, O. H. Krämer, A. Schimpf, S. Giavara, J. P. Sleeman, F. Lo Coco, C. Nervi, P. G. Pelicci, T. Heinzel, *EMBO J.* **2001**, *20*, 6969-6978.
[3] M. Wieczorek, T. Ginter, P. Brand, T. Heinzel, O. H. Krämer, *Cytokine Growth Factor Rev.* **2012**, *23*, 293-305.

P23: Tailor-made multifunctional polymers and nanoparticles with optimized compatibility between biodegradable core and encapsulated drug

Irina Muljajew[a,b], Marek Sierka[c], Ulrich S. Schubert[a,b]
[a]Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstr. 10, 07743 Jena, Germany
[b]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
[c]Otto Schott Institute of Materials Research (OSIM), Friedrich Schiller University Jena, Löbdergraben 32, 07743 Jena, Germany
marek.sierka@uni-jena.de, ulrich.schubert@uni-jena.de

Tailored polymeric nanocarriers that efficiently encapsulate and release biologically active substances are designed by combining experiments and atomistic simulations. For this purpose, hydrophobic poly(esteramide)s (PEA) were systematically altered by variation of monomers and by introduction of hydrophilic blocks based on poly(2-oxazoline)s. The PEAs were obtained through two complimentary reaction pathways. Firstly, the step growth approach including the polyaddition of carboxylic diacids and 2,2'-bis(2-oxazoline) benefited from experimental simplicity as well as from the range of commercially available aliphatic diacids.[1] Secondly, the chain growth approach by ring opening polymerization (ROP) of different morpholine-2,5-diones yielded copolymers of animo acids (glycine, alanine, valine, leucine, or isoleucine) and glycolic acid. Kinetic studies of the ROP utilizing TBD as catalyst revealed that the molar masses and dispersities (Đ < 1.2) could be well controlled.[2] In addition, block copolymers were synthesized utilizing poly(2-ethyl-2-oxazoline) as macroinitiator for the ROP. Atomistic simulations by calculation of solubility parameters revealed that the intermolecular interactions of the synthesized polymers could indeed be systematically varied by changing the chemical structure. In addition, the calculated solubility parameters of the polymers and different drugs allowed qualitative predictions of the thermodynamic compatibility for determination of promising polymers that effectively solubilize particular drugs.[3] However, such predictions failed in case of mixtures involving strong specific interactions such as hydrogen bonding. Therefore, computationally more demanding simulations were used for refined modeling of the thermodynamic compatibility facilitating efficient, in silico guided design of polymeric drug nanocarriers.

References

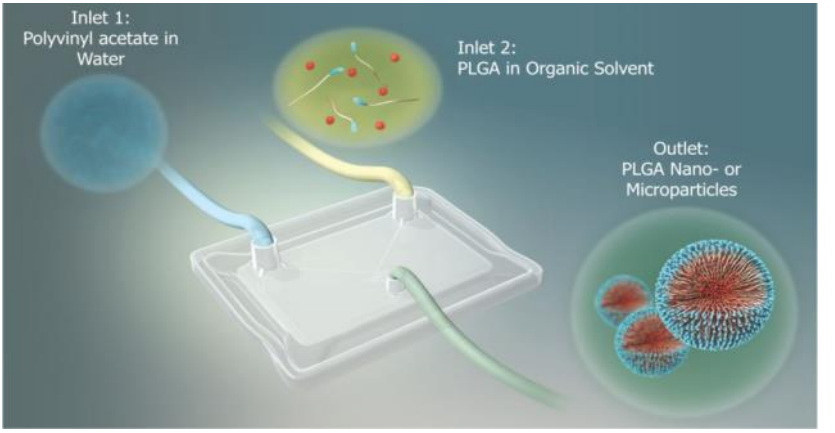
[1] I. Muljajew, A. Erlebach, C. Weber, M. Sierka, U. S. Schubert, *Manuscript in preparation*.
[2] M. Dirauf, D. Bandelli, C. Weber, H. Görls, M. Gottschaldt, U. S. Schubert, *Macromol. Rapid Commun.* **2018**, 1800433.
[3] A. Erlebach, T. Ott, C. Otzen, S. Schubert, J. Czaplewska, U. S. Schubert, M. Sierka, *J. Comput. Chem.* **2016**, *37*, 2220-2227.

P24: Microfluidic manufacture of PLGA nano- and microparticle drug delivery vehicles using the NanoAssemblr® Benchtop

S. M. Garg[a], A. Thomas[a], T. J. Leaver[a], A. W. Wild[a], M. Rabel[a], S. Clarke[a], E. C. Ramsay[a]
[a]Precision NanoSystems Inc., 50 - 655 West Kent Ave. N., V6P 6T7 Vancouver, BC, Canada
mrabel@precision-nano.com

Several methods exist for the production of both nanoparticles and microparticles composed of hydrophobic biodegradable polymers as drug delivery vehicles for numerous therapeutic applications. However, maintaining consistent particle quality, tuning particle size, and scalability remain challenging. Here we demonstrate using the NanoAssemblr Benchtop to produce both microparticles and nanoparticles composed of polylactic-co-glycolic acid (PLGA). NanoAssemblr technology uses microfluidics to control self-assembly to eliminate user variability and enable reproducible and scalable manufacture. We further describe optimization strategies to control particle size from 75 nm to 5 µm.

Using a water-miscible organic solvent, PLGA nanoparticles could be tuned from 75 - 300 nm by systematically exploring the parameter space. Changing the organic solvent to a partially miscible solvent enabled the development of particles tunable between 1 to 5 microns with PDI ~0.2. In general, increasing PLGA concentrations in the solvent phase led to an increase in the size of both PLGA nanoparticles and microparticles. Increasing the TFR led to a decrease in the size of both nanoparticles and microparticles. Scanning electron micrographs indicated a spherical morphology. Thus, we have successfully demonstrated the utility of NanoAssemblr technology as a tool in the scalable development of both nanoparticles and microparticles.



Microfluidic mixing: homogeneous solvent/antisolvent precipitation.

ABSTRACTS OF POSTER PRESENTATIONS

P25: Light-triggered backbone-cleavable polycarbonates from (2-nitro-1,4-phenylene)dimethanol

Tarik Rust[a], Timo Schoppa[a], Klaus Langer[a], Dirk Kuckling[a]
[a]Paderborn University, Department of Chemistry, Warburger Str. 100, 33098 Paderborn, Germany
Trust@mail.upb.de

During past years, smart polymer based biomaterials have attracted significant attention for numerous biomedical applications, e.g. drug delivery, tissue engineering or tissue adhesives. As a response to a certain stimulus such smart polymers can undergo a change of structure, polarity or solubility and therefore enable a fast controlled release of payloads, for example. Among different stimuli like pH, redox or temperature, light can be applied remotely with high temporal and spatial precision by simply adjusting the wavelength, irradiation intensity or irradiation time.[1,2] Herein a novel light-triggered backbone-cleavable polycarbonate based on the ortho-nitrobenzyl unit shall be reported. Polycondensation in the melt with diphenylcarbonate as the carbonylation reagent and Liacac as the catalyst was used to synthesize a polycarbonate with a high molar mass (M_n) and a reasonable polydispersity (PDI). Furthermore the light-triggered degradation of the polycarbonate was investigated with SEC and UV-VIS spectroscopy. By using the solvent evaporation technique, nanoparticles were formed and the stability as well as the degradation behavior were analyzed via DLS and SEM.

References

[1] J. Sun, J. Anderski, M.-T. Picker, K. Langer, D. Kuckling, *Macromol. Chem. Phys.* **2019**, *220*, 1800539.
[2] J. Sun, W. Birnbaum, J. Anderski, M.-T. Picker, D. Mulac, K. Langer, D. Kuckling, *Biomacromolecules* **2018**, *19*, 4677-4690.

ABSTRACTS OF POSTER PRESENTATIONS

P26: Biomedical system based on precision biomacromolecular polymers with repetitive peptide entities

Stefan M. Schiller[a]
[a]Albert-Ludwigs-Universität Freiburg, Zentrum für Biosystemanalyse (ZBSA), Habsburger Str. 49, 79104 Freiburg
stefan.schiller@frias.uni-freiburg.de

Macromolecular precision assemblies & networks (MPNs) with adjustable multi-stimulus responsive behavior are interesting for applications in microsystems technology and medicine. Varying composition and sequence order of the repetitive units combined with advanced prototype 3D structuring enables access to a new generation of materials. They are yielded in via a novel combination of biosynthetic methods including the site-selective cotranslational introduction of noncanonic amino acids with functional site chains and bioorthogonal functionalization e.g. via click chemistry. The yielded selectively functionalized macromolecules are further site-specifically crosslinked via photoredox reactions rendering them designable multistimulus responsive material system. The photocrosslink can be facilitated at various length scales also including two-photon structuring via direct laser writing (DLW) with micro-features. The environmental control of structure/ conformation of the specific fold/sequence of the macromolecular network segments allows to „program" responsive and adaptive molecular systems (responsive to temp. pH, Cion) constituting defined materials with new properties. The ability to design molecularly defined amphiphilic block-copolymers with a variety of supramolecular architectures ranging from micells over tubular structures and networks to vesicles creates a tool-box of molecular systems with a wide range of applications. Some compositions achieve extraordinary stability against environmental conditions such as temperature up to 100 °C, high ionic strength solutions above 1 M and pH from 2-13. Hence, MPNs provide a system with multiple applications in biomedicine. Recently we realized controlled delivery and encapsulation application and new surgical materials.[1-3]

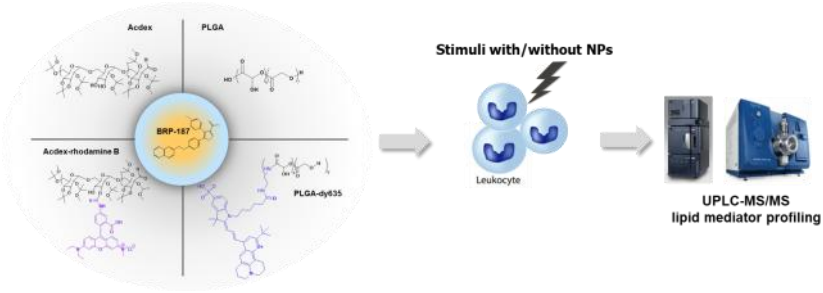
References

[1] M. Huber, A. Schreiber, K. Benz, S. M. Schiller, *Biomaterials* **2014**, *35*, 8767-8779
[2] M. Huber, A. Schreiber, P. von Olshausen, B. R. Varga, O. Kretz, B. Joch, S. Barnert, R. Schubert, S. Eimer, P. Kele, S. M. Schiller, *Nat. Mater.* **2015**, *14,* 125-132
[3] S. Klein, T. Auung, R. M. Haas, F. Nedved, S. Schiller, O. Felthaus, J. H. Dolderer, *Handchir. Mikrochir. plast. Chir.* **2018**, *50,* 83-92

P27: Improving the bioavailability of BRP-187: Encapsulation of a potent inhibitor of leukotriene biosynthesis into biodegradable polymers for drug delivery

Blerina Shkodra-Pula[a], Christian Kretzer[b], Paul Klemm[a], Antje Vollrath[a], Stephanie Schubert[c,d], Oliver Werz[b,c], Ulrich S. Schubert[a,c]
[a] Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstrasse 10, 07743 Jena, Germany
[b] Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, Friedrich Schiller University Jena, Philosophenweg 14, 07743 Jena, Germany
[c] Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany
[d] Department of Pharmaceutical Technology and Biopharmacy, Institute of Pharmacy, Friedrich Schiller University Jena, Lessingstrasse 8, 07743 Jena, Germany
blerina.shkodra-pula@uni-jena.de

Dual inhibitors of 5-lipoxygenase activating protein (FLAP) and microsomal prostaglandin E2 synthase-1 (mPGES-1) display better anti-inflammatory efficacy and lower risks of side effects versus non-steroidal anti-inflammatory drugs (NSAIDs).[1-3] Despite the high potential for better efficacy, these dual inhibitors are acidic lipophilic molecules with strong tendency for plasma protein binding. In this study, we present the encapsulation of BRP-187 into biocompatible polymers - acetaleted dextran (Acdex) and poly(lactic-co-glycolic acid) (PLGA) - via nanoprecipitation. Nanoparticles (NPs) containing BRP-187 were characterized by dynamic light scattering and SEM for the hydrodynamic diameter (D_h) and particle morphology, and UV-VIS spectroscopy for the determination of encapsulation efficiency of the drug. NPs were tested in isolated leukocytes or macrophages and in whole blood experiments to determine the drug uptake, the cytotoxicity and the efficiency of BRP-187 loaded NPs to inhibit the 5-lipoxygenase (5-LO) product formation. Fluorescent BRP-187 NPs were also designed, which showed high cellular uptake by immune cells when analyzed by confocal microscopy. Our results reveal that encapsulation into Acdex and/or PLGA improve the bioavailability since BRP-187 is less active than encapsulated compound after 5 h preincubation. In the human whole blood assay the Acdex NPs showed the ability to inhibit the leukotrien formation by themselves. While PLGA-particles showed an increasing potency over time. With prolonged incubation times we could see that NPs with encapsulated BRP-187 have a better bioavailability and higher efficacy than free drug.



References

[1] U. Garscha, S. Voelker, S. Pace, J. Gerstmeier, B. Emini, S. Liening, A. Rossi, C. Weinigel, S. Rummler, U. S. Schubert, et al., *Biochem. Pharmacol.* **2016**, *119*, 17-26.

[2] T. Hanke, F. Dehm, S. Liening, S. Popella, J. Maczewsky, M. Pillong, J. Kunze, C. Weinigel, D. Barz, A. Kaiser, et al., *J. Med. Chem.* **2013**, *56*, 9031−9044.

[3] A. Koeberle, A. Rossi, J. Bauer, F. Dehm, L. Verotta, H. Northoff, L. Sautebin, O. Werz, *Front. Pharmacol.* **2011**, 1-10.

ABSTRACTS OF POSTER PRESENTATIONS

P28: Photo-responsive polymeric nanostructures based on 1-naphthol

Maria Sittig[a,b,c], Jessica Tom[a,d], Felix Wendler[a,d], Benjamin Dietzek[a,b,c], Felix H. Schacher[a,d]

[a]Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany

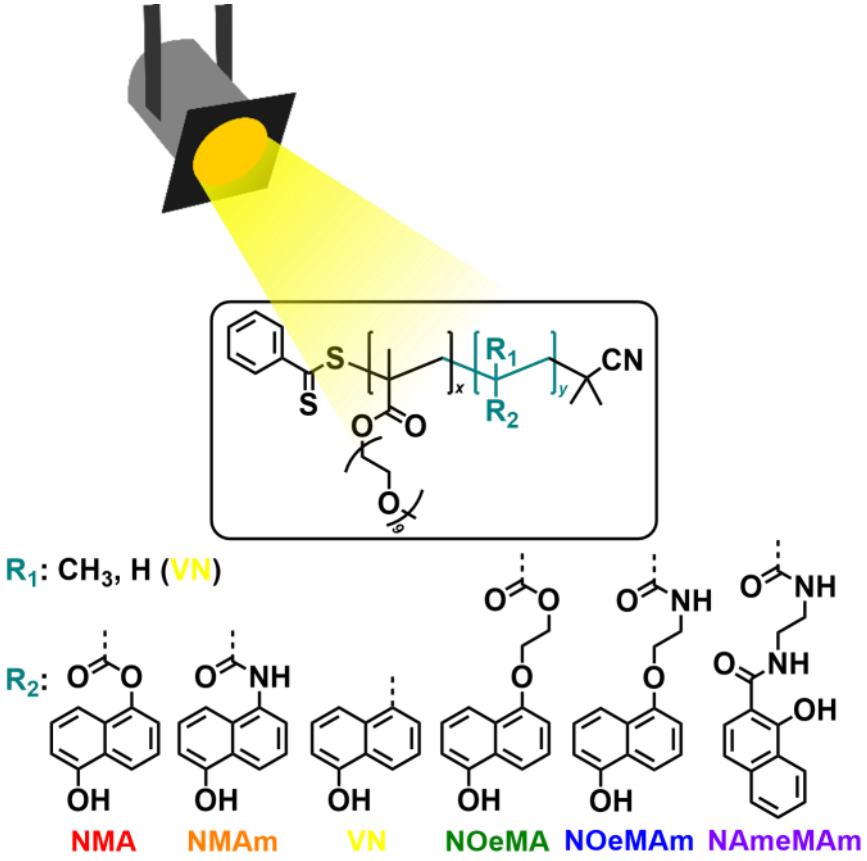
[b]Institute of Physical Chemistry and Abbe Center of Photonics, Friedrich-Schiller-University Jena, Helmholtzweg 4, 07743 Jena, Germany

[c]Leibniz Institute of Photonic Technology Jena, Department Functional Interfaces, Albert-Einstein-Straße 9, 07745 Jena, Germany

[d]Institute of Organic Chemistry and Macromolecular Chemistry (IOMC), Friedrich Schiller University, Jena, Humboldtstraße 10, 07743 Jena, Germany

maria.sittig@uni-jena.de

Photoacids are a class of molecules that display a marked increase in acidity in their electronic excited state compared to their ground state.[1] By incorporating photoacid moieties into block copolymer micelles we aim to trigger the targeted release of an encapsulated cargo upon light exposure and improve drug delivery and efficacy, which offers both temporal and spatial control. We have previously shown that hydrophobic terpolymers featuring a 1-naphthol pendant moiety can encapsulate and release Nile Red, a hydrophobic dye, upon illumination with UV light.[2] These preliminary results confirm that 1-naphthol-containing polymers are promising candidates for drug delivery applications. We have since designed a number of photoacid precursors based on 1-naphthol (see Figure), which vary in the nature of attachment to the polymer backbone in order to study how this influences their photoactivity, i.e., their photostability and photoacidity. Functional copolymers containing varying amounts of 1-naphthol can be easily synthesized by reversible addition - fragmentation chain-transfer (RAFT) polymerisation with high chain-end fidelity, which permits the formation of block copolymers capable of self-assembly to encapsulate bioactive species. To study the proton transfer in the excited state in aqueous media, a set of water-soluble copolymers were first prepared with a hydrophilic comonomer, oligo(ethylene glycol) methyl ether methacrylate (OEGMA). The photoacidity and reversibility of the deprotonation were examined via absorption and emission spectroscopy. A series of well-defined amphiphilic block copolymers featuring 1-naphthol moieties within the hydrophobic block were then prepared, and their self-assembly examined to determine their suitability for use in controlled drug delivery.



References

[1] E. Pines, D. Pines, T. Elsaesser, H. J. Bakker, Eds. Springer Netherlands: Dordrecht, **2002**; p 155.

[2] F. Wendler, K. R. A. Schneider, B. Dietzek, F. H. Schacher, *Polym. Chem*. **2017**, *8*, 2959.

P29: Stimuli-responsive layer-by-layer nanoparticles for specific delivery of nucleic acids

Jana Solomun[a,b], Liam Martin[a,b], Franziska Stanzel[a,b], Elisabeth Moek[a,b], Anja Träger[a,b]

[a] Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena, Philosophenweg 7, 07743 Jena, Germany

[b] Laboratory of Organic and Macromolecular Chemistry (IOMC), Friedrich Schiller University Jena, Humboldtstrasse 10, 07743 Jena, Germany

jana.solomun@uni-jena.de

For efficient systemic in vivo delivery of nucleic acids, several physiological barriers must be overcome, such as stability in biological fluids, immunogenic recognition and the endothelial barrier to reach the targeted cells.[1] Once taken up by the targeted cells the genetic material subsequently has to be released from the endosome to reach the site of action in its active form. Therefore, an efficient delivery system needs the ability to bind, protect and deliver the genetic material and beyond that should be biocompatible and non-immunogenic when used for in vivo applications.

In this study we use a layer-by-layer approach to develop stimuli-responsive nanoparticles for the systemic delivery of genetic material, which are designed to overcome the various physiological barriers and furthermore enable targeted delivery to the desired site of action.

Cationic and pH-responsive terpolymers with substantial hydrophobic character P(DMAEMA-co-MMA-co-BMA) are used to encapsulate negatively charged genetic material into stable nano-sized particles below 200 nm in diameter via electrostatic as well as hydrophobic interactions. To prevent unspecific uptake by immune cells and unspecific interactions in vivo, the remaining positive charge needs to be masked.[2] In our approach block copolymers P(NAM-b-CEAm) composed of a block containing pH-responsive anionic block (PCEAm) and a „stealthy" block (PNAM) were used. We investigated the pH-dependent layering, stability against serum proteins, cellular uptake and the cyto- as well as hemocompatibility of the resulting coated particles. In further studies targeting moieties were introduced to the particle surface and cellular uptake was investigated.

References

[1] H. Yin, R. L. Kanasty, A. A. Eltoukhy, A. J. Vegas, J. R. Dorkin, D. G. Anderson, *Nat. Rev. Genet.* **2014**, *15*, 541.

[2] A. C. Rinkenauer, A. T. Press, M. Raasch, C. Pietsch, S. Schweizer, S. Schwörer, K. L. Rudolph, A. Mosig, M. Bauer, A. Traeger, U. S. Schubert, *J. Control. Release* **2015**, *216*, 158-168.

P30: Micellar doxorubicin with dendritic polyglycerol sulfate shell for targeted tumor therapy

Yinan Zhong[a], Mathias Dimde[a], Zhiyuan Zhong[b,*], Rainer Haag[a,*]
[a]Institut für Chemie und Biochemie, Freie Universität Berlin, Berlin, 14195, Germany.
[b]Biomedical Polymers Laboratory, and Jiangsu Key Laboratory of Advanced Functional Polymer Design and Application, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou, 215123, P. R. China.
zhongyinan@126.com, haag@chemie.fu-berlin.de, zyz-hong@suda.edu.cn

Most current polymeric nanocarriers are based on poly(ethylene glycol) (PEG) shells, however, the significant immunogenic potential, modest tumor targeting and poor tumor cell uptake of PEG always leads to unsatisfactory results, hampering the development of PEG-based nanomedicine. Dendritic polyglycerol (dPG) and its derivatives, which are biocompatible, water-soluble, and functional, provide multivalently arranged ligands on the surface, presenting one of the appealing platforms in targeted cancer therapy. Particular interesting is dPG-sulfate (dPGS), which was identified to have an intrinsic targetability to inflammation. Here, taking advantages of the osculating relationship between tumor and inflammation, we designed redox-sensitive biodegradable micelles based on dPGS-SS-poly(ε-caprolactone) amphiphilic block copolymer for targeted cancer therapy.[1] Intriguingly, doxorubicin-loaded micelles exhibited extraordinary tumor accumulation and markedly accelerated drug release at the tumor site (Fig. 1A&B), resulting in complete tumor suppression with relative tumor volume of 1.1 (vs 9.1 of PBS group) on day 29 (Fig. 1C), diminishing adverse effects with little body weight change, and significantly improved survival rate (100% within 76 d) as compared to free drug (all died within 13 d) in MCF-7 human breast tumor-bearing nude mice (Fig. 1D). Dendritic polyglycerol sulfate with well-defined structures, excellent biocompatibility and superior tumor homing ability to PEG has provided a new platform to advanced cancer nanomedicines.

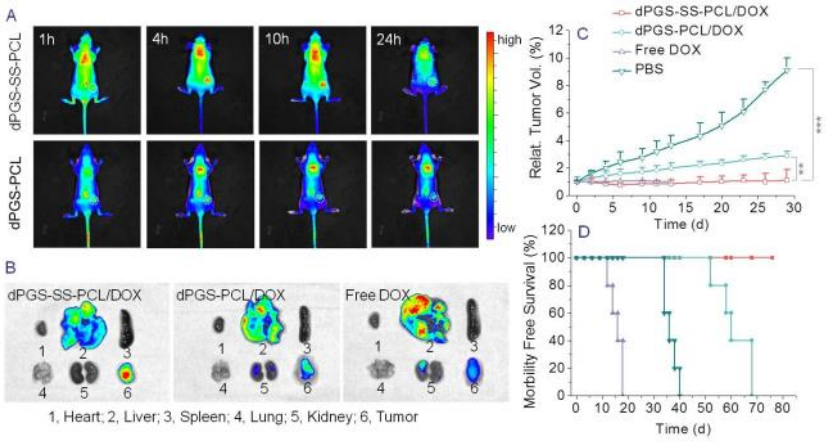


Fig. 1 In vivo F.L. images at different time points (A) and ex vivo F.L. images at 10 h (B) of MCF-7 human breast tumor-bearing mice following injection of DIR-loaded micelles; tumor volume change (C) and Kaplan-Meier survival curves (D) of MCF-7 tumor-bearing mice treated by different groups.

References

[1] Y. Zhong, M. Dimde, D. Stöbener, F. Meng, C. Deng, Z. Zhong, R. Haag, *ACS Apply. Mater. Inter*. **2016**, *8*, 27530-27538.

NOTES

CONTACT

Friedrich Schiller University Jena
Jena Center for Soft Matter (JCSM)
Prof. Dr. Ulrich S. Schubert
apl. Prof. Dr. Michael Gottschaldt
Ms. Ulrike Kaiser
Philosophenweg 7
07743 Jena
Germany

Phone: +49 3641 9-48987
Fax: +49 3641 9-48202
E-Mail: polytarget@uni-jena.de

ISBN 978-3-00-063235-8

Publisher: Jena Center for Soft Matter (JCSM)
Photos: FSU Jena (Jan-Peter Kasper, Anne Günther, Dr. David Pretzel), pixabay (Stefan Schweihofer), DominoPlus Jena
Layout: Communications Office FSU Jena
ISBN 978-3-00-063235-8

www.polytarget.uni-jena.de