Projekthaus NanoBioMater

SummerSchool 2015

June 22-24

Bad Herrenalb, Germany

Contents

Welcome from the Organizing Committee

Dear friends of NanoBioMater,

mix a cup of hydrogel with three tablespoons of biomineral, add half a teaspoon of tobacco mosaic viruses and pour the blend into a lovely Black Forest conference center – and you shall get a wonderful summer school? Or may you rather rely on inviting knowledgeable experts, motivated students, enthusiastic young and experienced researchers and give them suitable room for exchange of thoughts and fruitful discussions in a friendly atmosphere?

Such were the questions arising prior to this summer school, and we hope to have sorted it out well. We are looking curiously forward to find out, if the three team leaders of our Projekthaus NanoBioMater and the two of us have mixed all "ingredients" correctly to experience three days worthy of pleasant remembrance here in Bad Herrenalb in mid June 2015.

Yours sincerely

Christina Wege & Günter Tovar

Coordinators of the

Projekthaus NanoBioMater

Universität Stuttgart

General Information

Congress Site

The summer school will take place in Bad Herrenalb, in the Black Forest, located 30 km south of Karlsruhe and 80 km east of Stuttgart. The congress venue is the "Haus der Kirche - Evangelische Akademie Baden" (Dobler Str. 51, 76332 Bad Herrenalb).

Internet Access

Free WiFi access will be available at the congress venue, the required user name and password will be handed to each participant upon their arrival.

Instructions for Speakers

In the lecture room, a computer for PowerPoint or PDF presentations will be available. Please make sure to transfer your presentation slides to this computer before the start of your session. There will be technical staff assisting you with this. Please inform the technical staff if you want to use your own computer for your presentation.

Instructions for Poster Presentation

All participants who are present with a poster are kindly asked to mount their posters onto the poster boards according to their poster numbers upon their arrival. The poster boards are numbered consecutively. Please take your poster with you when you leave.

During the official poster sessions, the presenting authors are requested to remain near their posters. The three best poster presentations will be awarded with one of three poster prizes.

Each participant in the summer school will get two free drinks which can be claimed at the poster session using the vouchers you will find at the end of this booklet.

Invited Speakers

Dr. Leonie Barner

Forschungsschwerpunkte:
Polymersynthese und –charakterisierung, kontrollierte/'lebende' radikalische Polymerisation (RAFT, ATRP), Ringöffnende Polymerisation, Partikelsynthese und –charakterisierung, Hydrogele, Oberflächenmodifikation und –charakterisierung, *click* Chemie Keywords: controlled polymerisation, surfaces modification, hydrogels'.

Akademische Ausbildung mit Abschluss:
Diplom Chemie (1989 – 1994)
Gesamthochschule Kassel – Universität des Landes Hessen (Vordiplom)
Georg-August-Universität Göttingen, Diplom, Betreuer: Prof. M. Buback

Wissenschaftliche Abschlüsse:
Promotion: Chemie, Georg-August-Universität, 01/1998, Betreuer: Prof. M. Buback

Beruflicher Werdegang ab Studienabschluss:
Seit 06/2013, Adjunct Accociate Professor, Queensland University of Technology, Brisbane, Australien
Seit 10/2011, Leitung, Soft Matter Synthesis Lab' am Institut für Biologische Grenzflächen, und stellvertretende Abteilungsleitung am Institut für Funktionelle Grenzflächen, Karlsruhe Institute of Technology
10/2008 – 09/2011, Wissenschaftliche Mitarbeiterin, Fraunhofer Institut für Chemische Technologie (ICT), Pfinztal
07/2007 - 06/2008, Research Manager und Senior Research Fellow, Centre for Advanced Macromolecular Design, University of New South Wales, Sydney, Australien
12/2003 - 06/2007, Research Manager und Senior Research Associate, Centre for Advanced Macromolecular Design, University of New South Wales, Sydney, Australien
10/2002 - 11/2003, Senior Research Associate, Centre for Advanced Macromolecular Design, University of New South Wales, Sydney, Australien
02/2001 – 09/2002, Research Associate, Centre for Advanced Macromolecular Design, University of New South Wales, Sydney, Australien
10/1998 - 01/2001, Wissenschaftliche Mitarbeiterin, Sartorius AG, Göttingen, Deutschland
02/1998 – 09/1998, Wissenschaftliche Mitarbeiterin, Institut für Physikalische Chemie, Georg-August-Universität, Göttingen, Deutschland

Sonstiges:
07/12-08/12, Gastwissenschaftlerin an der University of Canterbury, Christchurch, Neuseeland
08/07-09/07, Gastwissenschaftlerin an der Universität Bayreuth, Makromolekulare Chemie II (Prof. Axel Müller), Bayreuth, Deutschland
03/95-05/95 Gastwissenschaftlerin an der University of Sydney (Prof. Bob Gilbert), Sydney, Australien
07/93-09/93 Erasmus-Stipendiatin, University of Bangor, Wales, UK

Dr. Nadia Benkirane is Research director and head of the "Osteoarticular and Dental regenerative Nanomedicine" laboratory, at INSERM (French National Institute for Health and Medical Research), UMR 1109, Strasbourg, France. She was leader of "Active Biomaterials and Tissue Engineering" team INSERM 977. She received her Ph.D. from University Louis Pasteur, ULP, Strasbourg, France for the work on Development of pseudopeptides as synthetic vaccines. Dr. Jessel (Benkirane) then held a postdoctoral position in collaboration with the Institut Pasteur, Paris, France, working on Immunotherapy HIV, and another postdoctoral position on the application of modified peptides as vaccines against FMDV (Plum Island Animal Disease Center, ARS, USDA, Greenport, NY 11944-0848, USA). She joined the INSERM U595 in 2002 as a post-doc, and received the diploma to direct the research (HDR) in 2004. Dr. Jessel got the permanent position (CR1) in the INSERM 595 laboratory in 2004 and Research Director (DR2) position in the INSERM 977 and head of "active Biomaterials and Tissue Engineering team from 2009 until 2012). Currently Research Director (DR1) in the INSERM UMR 1109 (Osteoarticular and Dental Regenerative Nanomedicine" and heads the team. Dr. Jessel possesses expertise in diverse fields of molecular and cellular biology, immunochemistry, tissue engineering and biomedical engineering. In the last 10 years, she focused her research on the bio-functionalization of multilayered polyelectrolyte architectures with emphasis on the use of these architectures to induce specific cellular responses and gain control over cell proliferation and differentiation. Dr. Benkirane-Jessel is a co-author of 60 peer-reviewed publications in high impact factor journals (Proc. Nat. Acad. Sci. USA; Adv. Mater.; Adv. Funct. Mater.; Small; Nanoletters, Biomaterials, ACS Nano), 5 chapters reviews and 5 international patents, she is a regular referee for a number of scientific journals (Nature nanotechnology, Nature Materials, ACS nano, Biomaterials, Nanoletters…). She is under the contract (Interface INSERM/Clinic 2008-2013) and she got also (Prime d'Excellence Scientifique from the INSERM, 2010-2014).

Scientific topics:

- Material Science
- Nanomedicine
- Regenerative Medicine
- Tissue Engineering

Helmut Cölfen is full professor for physical chemistry at the university of Konstanz. He studied chemistry at the Gerhard-Mercator University Duisburg and did his PhD work on "Analytical Ultracentrifugation of gels". His current research interests are in the area of nucleation, classical and non-classical crystallization, Biomineralization, synthesis of functional polymers, directed self assembly of nanoparticles and fractionating methods of polymer and nanoparticle analysis – especially Analytical Ultracentrifugation. His group has made contributions in high-resolution particle size analysis with Angström resolution in solution, Mesocrystals, Nonclassical Crystallization, Prenucleationb clusters, $CaCO_3$ crystallization and additive controlled crystallization.

He serves on the editorial /advisory boards for *Crystal Engineering Communications, Inorganics; Journal of Biomaterials and Nanobiotechnology; Journal of Crystallography; Macromolecular Bioscience; Particle & Particle Systems Characterization; The Scientific World Journal and Journal of Materials Chemistry B*, is editor in chief of *Crystals*, co-editor of *Current Nanoscience* and is member of the German Chemical Society and Fellow of the Royal Society of Chemistry. He received several awards including the Hermann Schnell price of the German Chemical Society, the Academy Award of the Berlin-Brandenburg Academy of Science and Humanities, the ECIS-Solvay price and recently the LUKS award for excellent teaching at the University of Konstanz. He has also been listed in the Thomson Reuters and Times Higher Education Index lists of top 100 chemists worldwide for the years 2000 – 2010 – a list including several nobel laureates.

Dr. Yuri Gleba has over 30 years of research and management experience in plant genetics and biotechnology. (M. Sc., Kiev University, 1971; Ph.D., Institute of Botany, Academy of Sciences of Ukraine, 1974; D.Sc., Leningrad University, 1980).

Dr. Gleba's pioneering research in plant genetics, physiology and biotechnology was published in more than 200 research papers, books and over 30 patent families, and has earned the respect of the international scientific community as is evidenced by his election to the World Academy of Arts and Science (Rome), the European Academy (*Academia Europaea*, London), the National German Academy *Leopoldina* (Halle), the National Ukrainian Academy of Sciences (Kiev), the Lithuanian Academy of Science (Vilnius) and the Bavarian Academy of Sciences (Munich). He received a *Doctor Honoris Causa* title from his *alma mater*, Kiev State University. In recognition of his outstanding scientific contributions, he also received numerous international and national awards and prizes, including Koerber Prize (Hamburg), A. von Humboldt Prize (Bonn), USSR State Prize (Moscow), State Prize of Ukraine (Kiev), etc.

He founded the Institute of Cell Biology and Genetic Engineering, Ukrainian Academy of Sciences, Kiev, Ukraine, in 1989, and was serving as its Director until 2010; currently, he is Honorary Director of the Institute.

Dr. Gleba left former USSR in 1991 and joined American Cyanamid Company, Princeton, NJ, where he developed research efforts in plant biotechnology and genomics and crop engineering, first as a group leader/manager, and, since 1997, as a Director of Crop Engineering Department. Dr. Gleba left American Cyanamid/American Home Products in 1999 and founded Icon Genetics, Princeton/Munich/Halle, a plant biotechnology company group; he has been serving since its inception as its CEO. Under his leadership, Icon has developed multiple plant expression technologies, including the magnICON® transient technology that has been brought to a commercial level and cGMP compliance and has been used to support clinical trials of the product candidates developed by Icon/Bayer. Icon has created one of the best IP portfolios in plant biotechnology that currently includes over 450 issued patents representing 42 patent families of patents/applications. He also co-founded/founded three other companies, Phytomedics Inc., USA, Nomad Bioscience GmbH, Germany, and Nomads UAB, Lithuania. In January 2012, Dr. Gleba engineered the acquisition of Icon Genetics from Bayer by Nomad Bioscience.

During his entire carrier, Dr. Gleba was involved in university education. He was a supervisor of 35 Ph D students and was lecturing or holding adjunct positions for many years at the universities of USSR, USA, Belgium, Germany and Ukraine.

Dr. Gleba actively managed or supervised many international foundations: UNESCO Plant Biotechnology Program (Paris), International Soros Foundation (New York-Moscow), International Soros Science Education Program (Washington-Moscow), Renaissance Foundation (Kyiv), INTAS (Brussels), EPSO (Brussels), etc.

Prof. Jürgen Groll holds the chair for Functional Materials in Medicine and Dentistry at the University of Würzburg. The research in his department features applied polymer chemistry for life sciences, hierarchical and biomimetic scaffolds, immunomodulatory materials and scaffolds, nanobiotechnology, and biofabrication. Within biofabrication, he currently coordinates a large European integrated project that focuses on the printing of layered constructs for cartilage regeneration (HydroZONES; www.hydrozones.eu). Since 2014, he also holds an ERC consolidator grant that concerns the evaluation of design criteria for immunomodulatory scaffolds through precise control over geometry and surface chemistry.

Prof. Groll studied chemistry at the University of Ulm and received his Ph.D. from the RWTH Aachen University with summa com laude in 2005. From 2005 to 2009, he worked in industry in the field of functional coatings and biocomposite materials, where he was part of a team that brought a polymer for surface treatment to industrial scale production and a Hydroxyapatite-gelatine nanocomposite to a commercial product. In parallel, he built up a research group on polymeric biomaterials at the DWI Interactive Materials Research Institute in Aachen.

He is co-author of over 90 peer-reviewed publications and inventor of 10 patents. He is board member of the international society for biofabrication and editorial board member of the journal Biofabrication, and his work has been recognized by several awards such as the PhD thesis award of the German Society for Biomaterials in 2005, the Henkel Innovation Award in 2007, the Bayer Early Excellence in Science Award 2009, the Reimund-Stadler award of the Division of Macromolecular Chemistry of the German Chemical Society in 2010 and the Unilever Prize of the Polymer Networks Group in 2014.

Since 2012 **Cornelia Lee-Thedieck** is head of the junior research group “Stem Cell-Material-Interactions” at the Karlsruhe Institute of Technology (KIT), Institute of Functional Interfaces. From 2007 to 2009 she was a Postdoctoral Fellow and from 2009 to 2012 she was a group leader at the Max Planck Institute for Intelligent Systems in the department of Prof. Spatz, where she started to investigate the impact of physical parameters on stem cells. She received her Diploma in Biochemistry (2004) and her Ph.D. in Biology (2007) from the University of Tübingen.

Name: **Robert LISKA**
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Main research areas
Photopolymerization, Dental materials, Biocompatible and biodegradable polymers

Education

June 2006	Habilitation in the field of macromolecular chemistry (Ao. Univ. Prof) at the Institute of Applied Synthetic Chemistry
May 1998	Graduation, Dr. tech. (Ph.D.)
1995-1998	Dissertation at the Vienna University of Technology, Institute of Chemical Technology of Organic Materials: "Synthesis and Testing of New Photoinitiators for High-Performance Applications"
June 1995	Graduation, Dipl.-Ing. in Technical Chemistry
1994-1995	Diploma Thesis performed at the Institute of Chemical Technology of Organic Materials: "Synthesis and Testing of new Photoinitiators based on Imines"
1988-1995	Vienna University of Technology; Course of Studies: Organic Chemistry
1983-1988	Engineering College (TGM), Dept. for Plastics Engineering in Vienna
1979-1983	High School in Vienna

Professional Experience

Since 2012	Head of the Christian Doppler Laboratory for Photopolymers in digital and restorative dentistry
Since 2013	Member of the Austrian Tissue Regeneration Cluster
Since 1998	University Assistant at the Vienna University of Technology, Institute of Chemical Technology of Organic Materials and the Institute of Applied Synthetic Chemistry, respectively
1995-1997	Contract Assistant at the Vienna University of Technology, Institute of Chemical Technology of Organic Materials

Scientific publications

Publications in peer-reviewed international journals	>110
Patents and patent applications	>30
Contribution to Proceedings	>200
Books and Book sections	9
Talks and Poster Presentations	>200
Invited scientific lectures	>40
Citations according to Google Scholar:	> 1500
h-index (Google Scholar):	23

George Lomonossoff graduated from the University of Cambridge in 1976 and studied for his His Ph.D. at MRC Laboratory of Molecular Biology (LMB), Cambridge. He moved to the John Innes Centre, Norwich in 1980 and has continued to work there ever since apart from two periods of sabbatical leave in the USA. George's research has focused on the molecular biology of RNA plant viruses and their use in bio- and nanotechnology. He is an honorary professor at the University of East Anglia and has co-ordinated several EU Framework consortia. In 2012 he was named “BBSRC Innovator of the year” for his work on plant-made pharmaceuticals and was named the Colworth Prize Lecturer in 2015 for his work on translational research.

Frédéric Marin has a 26-years experience in biomineralization research. He defended his PhD in 1992 (University Paris XI) on calcium carbonate skeletons in molluscs, corals and sponges. After his military service (1992-1993) and a first post-doctoral position (1993-1994), he developed his own post-doc project at the University of Leiden (The Netherlands, 1994-2000), in the geobiochemistry group of Pr. P. Westbroek, under different supports including one Marie Curie Fellowship. In 1998, he received the Vening-Meinesz Price (25 000 guldens) for his research on the origin of animal skeleton. In 2001, the Dutch biotech company IsoTis hired for two years. In 2003, F. Marin was recruited by CNRS in Dijon, where he set up the biomineralization lab, owing to different regional, national and international supports. He defended his accreditation for leading research ('habilitation') in 2009 and became research director at CNRS in 2012. He was involved as partner in different French or European consortia: GDR ADEQUA on Polynesian pearls (2008-2012); ANR ACCRO-Earth (2007-2011); BioMinTec network (ITN Marie Curie, see www.biomintec.de, 2008 - 2012). He has contributed to establish a European network on biomineralization (COST action TD0903, 2009-2014), from which he was the Chair (2012-2014). This network comprised 17 countries and 34 research groups. Frédéric Marin has signed or co-signed about 100 scientific papers.

Michael J. Schöning received his diploma degree in electrical engineering (1989) and his Dr.-Ing. (1993), both from the Karlsruhe University of Technology. In 1989, he joined the Institute of Radiochemistry at the Research Centre Karlsruhe. Since 1993, he has been with the Institute of Thin Films and Interfaces (now, Peter Grünberg Institute) at the Research Centre Jülich, and since 1999 he was appointed as full professor at Aachen University of Applied Sciences, Campus Jülich. Since 2006, he serves as a director of the Institute of Nano- and Biotechnologies (INB) at the Aachen University of Applied Sciences. He has been authored more than 400 technical papers, review articles and chapters in books. He serves as editorial board member for *sensors* (editor in chief: 2004-2005), IEEE Sensors Journal, The Open Electrochemistry Journal, International Journal of Electrochemical Science, and Armenian Journal of Physics. His main research subjects concern silicon-based chemical and biological sensors, thin-film technologies, solid-state physics, microsystem and nano(bio-)technology.

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Heinrich-Mußmann-Str. 1, 52425 Jülich

Keywords:
- Silicon-based (bio-)chemical sensing
- Thin-film technologies
- Nanotechnology

PhD studies
- Chemical microsensors with silver halide layers

Renko de Vries was trained as a theoretical physicist and has done a PhD thesis on the theory of forces in stacks of fluctuating bilayer membranes (such as lipid or surfactant bilayers). After his PhD he switched to experiments, initially still in the field of surfactants. Later, at Wageningen University, he started working on protein materials.

Keywords: Recombinant proteins, Polymers, Hydrogels, Nanoparticles, Bioinspiration

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A. EDUCATION

Institution	Year	Degree	Major and (Minor)
Technische Universität München Faculty of Chemistry, Biology and Geosciences Institute of Organic Chemistry	1996	Diploma	Chemistry
Technische Universität München Faculty of Forestry, Institute for Wood Research	2000	Dr. rer. silv.	Forest and Wood Sciences
University of Erlangen-Nuremberg Department of Materials Science and Engineering Glass and Ceramics	2009	Habilitation	Materials Science – Bioinspired Materials

B. APPOINTMENTS

2000-2002	• Post-Doc Position: Department of Materials Science and Engineering - III- Glass and Ceramics, University of Erlangen-Nuremberg
2003-9/2011	• Senior Researcher: Department of Materials Science and Engineering - III- Glass and Ceramics:, University of Erlangen-Nuremberg Head of Group Bioengineered Ceramics
since 10/2011	• Associate Professor, Technische Universität München (TUM) Straubing Science Centre for Renewable Resources
2010	• Visiting Professor at the University of Rennes, France
2015	• Visiting Professor at the University of Natural Resources and Life Sciences, Vienna, Austria

C. RESAERCH INTERESTS

- Biogenic Polymers and Bioplastics
- Bioinspired Materials Engineering
- Bioinspired Functional Materials
- Ultrastructure Analysis of Biological and Hybrid Material Composites
- Materials Processing involving Pyrolysis and High-Temperature Reactions

Chairs

Eva Hoch studied Biological Chemistry at the University of Applied Sciences in Mannheim. Her diploma thesis at the Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB in Stuttgart focused on the preparation and characterization of cell culture substrates for selective cultivation of skin keratinocytes. In 2013 she finished her PhD at the University of Stuttgart, which dealt with the development of functional biomaterials for fabrication of biomimetic articular cartilage applying 3D printing technology. Since then she continues her bioprinting activities at Stuttgart University as holder of a postdoc scholarship from the Peter and Traudl Engelhorn Stiftung.

Anna Schenk studied chemistry and earned her master's degree in Leipzig, Germany, and Uppsala, Sweden in 2007. She performed graduate research on polymer-mineral hybrid materials at the Max Planck Institute of Colloids and Interfaces in Potsdam and received her PhD degree in physical chemistry in 2011. From 2011–2013 she worked as a postdoctoral research fellow in the group of Prof. Fiona Meldrum at the University of Leeds, UK, studying the crystallization of calcium carbonate and other minerals under biomimetic conditions. Anna Schenk joined the Institute of Polymer Chemistry at the University of Stuttgart as a postdoctoral researcher in 2013. Her current research in the group of Prof. Sabine Ludwigs focuses on the translation of bio-inspired concepts into synthesis strategies for functional oxide ceramics and polymer-based hybrid materials.

Since 2009, **Sabine Eiben** has been working on the application of tobacco mosaic virus (TMV) for nanotechnology and materials science. Initially as a postdoc in the DFG project PAK410 (Tobacco mosaic viruses as biotemplate for oxide ceramics) and since 2011 as project leader in the DFG SPP1569 (Genetically optimized tobacco mosaic viruses as scaffold for the in vitro generation of semiconductor bio/metal-oxide nanostructured architectures), her special interest is in the rational design of TMV variants, their structure and surface properties. They are applied in different systems, for instance as templates for the deposition of semi-conductive layers enabling the preparation of field-effect transistors at ambient conditions, but also for coupling of enzymes and other proteins used e.g. for 'lab-on-a chip' applications. She obtained her PhD in 2007 at the Institute of Technical Biochemistry (ITB), University of Stuttgart, working on bioctalysis with P450 monooxygenases. Afterwards she switched to archaebacterial enzymes and lipases and was the head of the Molecular Biotechnology group at the ITB from August 2008 till March 2009.

Dirk Rothenstein graduated in Biology at the University of Stuttgart. His diploma thesis was awarded in 2000 by the Fraunhofer-Gesellschaft with the Hugo-Geiger-Prize in the field of life science. He received his Ph.D. in molecular biology from the University of Stuttgart, Germany in 2004. After a short research period at the Max Planck Institute for Plant Breeding Research, Cologne, Germany, he joined the plant breeding company Selecta, Germany for a targeted research project. From 2007 to 2009 he was research associate at the Max Planck Institute for Intelligent Systems, formerly Material Research and Institute for Material Science at the University of Stuttgart, Germany. Since 2009 he completely joined the Institute for Material Science. Dr. Rothenstein's research focuses on the interaction of bioorganic and inorganic materials as well as the design of functional peptides and biotemplates for the synthesis of nanostructured hybrid materials.

Alexander Southan studied chemistry with macromolecular chemistry at the Philipps University Marburg (Germany). In his diploma thesis in the group of Prof. Dr. Markus Motzkus, he worked on the development of Multiplex CARS microscopy for the investigation of reactions in polymer matrices. In 2014, he received his Ph.D. from the Institute of Interfacial Process Engineering and Plasma Technology IGVP (head: Prof. Dr. Thomas Hirth) of the University of Stuttgart (Germany) under the supervision of Prof. Dr. Günter Tovar. Dr. Southan´s research is focused on functional polymers and hydrogels.

Scientific Program

List of Invited Lectures and Time Schedule

Chair: Sabine Eiben [SE], Eva Hoch [EH], Dirk Rothenstein [DR], Anna Schenk [AnSch], Alexander Southan [AS]

Monday, 22. June 2015		
11:00 – 13:30	Registration and reception	
12:30 – 13:30	Lunch	
13:30 – 14:30	Christina Wege, Günter Tovar, Sabine Eiben, Dirk Rothenstein, Alexander Southan	Welcome to the NanoBioMater Summer School and Presentation of the Projekthaus NanoBioMater
14:30 – 15:30	**Jürgen Groll** [Chair: AS]	Stimuli-sensitive Hydrogels for Biomedicine: From Drug Delivery to 3D Printing
15:30 – 16:00	Coffee break	
16:00 – 17:00	**Robert Liska** [Chair: AS]	Advanced Photopolymers for Tissue Engineering
17:00 – 18:00	**George Lomonossoff** [Chair: SE]	Plant Viruses and Virus-like Particles as Building Blocks for Bionanotechnology
18:00	Dinner	
19:30 – 22:00	**Poster session** and Get together	

Tuesday, 23. June 2015		
9:00 – 10:00	**Renko de Vries** [Chair: SE]	De-novo Designed Self-assembling Protein Polymers
10:00 – 11:00	**Nadia Benkirane-Jessel** [Chair: EH]	Advanced Therapeutics Medicinal Implants Equipped with Active Nanoreservoirs of Growth Factors and Stem cells for Regenerative Medicine
11:00 – 11:30	Coffee break	
11:30 – 12:30	**Michael Schöning** [Chair: DR]	Silicon-based Sensor Approaches @INB with Organic Molecules
12:30 – 13:30	Lunch	
13:30 – 14:30	**Leonie Barner** [Chair: AS]	Precision Macromolecular Design in Solution and Surfaces: From Thermal to Photochemical Control
14:30 – 15:30	**Yuri Gleba** [Chair: SE]	New Pharmaceuticals, Biomaterials and Nanoscaffolds from Plant Viral Vectors
15:30 – 16:00	Coffee break	
16:00 – 17:00	**Cordt Zollfrank** [Chair: DR]	Inorganic Structural and Functional Materials from Biotemplates
17:00 – 18:30	**Poster session**	
18:30	Barbeque	

Wednesday, 24. June 2015		
9:00 – 10:00	**Helmut Cölfen** [Chair: AnSch]	Additive Controlled Mineralization and Analytical Ultracentrifugation
10:00 – 11:00	**Cornelia Lee-Thedieck** [Chair: EH]	Poly(ethylene glycol) Hydrogel-Based Biomaterials for Hematopoietic Stem Cells
10:30 – 11:00	Coffe break	
11:00 – 12:00	**Frédéric Marin** [Chair: AnSch]	Animal Calcium Carbonate Skeletons and their Organic Matrix
12:00 – 12:30	Sabine Laschat	Closing remarks
12:30 – 13:30	Lunch	

List of Poster Presentations

PO-1	**Karishma K. Adatia, Alexander Southan, Günter E. M. Tovar** Surface functionalization of Hydrogel Foams for Additive Manufacturing
PO-2	**Vanessa L. Albernaz, Alexander Southan, Achim Weber, Monika Bach** Surface active monomers: building blocks for particle functionalization
PO-3	**Klara Altintoprak, Axel Seidenstücker, Alexander Welle, Hartmut Gliemann, Alfred Plettl, Othmar Marti, Christina Wege** Fabrication of genetically engineered viral nucleoprotein pore adaptors for oriented insertion into nano-porous solid-state membranes
PO-4	**Bernhard Baumann, Rainer Wittig, Mika Lindén** Mesoporous silica nanoparticle containing injectable hybrid hydrogel for drug delivery and tissue engineering
PO-5	**Michaela Beck, Tamoghna Mandal, Christian Buske, Mika Lindén** Targeting of leukaemia stem cells by monoclonal antibody functionalized mesoporous silica nanoparticles
PO-6	**Felix Boldt, Weina Liu, Yu Tokura, Seah Ling Kuan, Yuzhou Wu, Tanja Weil** Bioprogrammable Artificial Fusion Proteins
PO-7	**Katharina Braun, Alexander Pochert, Mika Lindén** Adsorption and desorption kinetics of antimicrobial peptides on mesoporous silica nanoparticles
PO-8	**Christiane Claaßen, Alexander Southan, Günter E. M. Tovar, Boris V. Stanzel, Kirsten Borchers** Light-responsive hydrogels for sustained growth factor delivery
PO-9	**Christian Debus, Maria Siglreitmeier, Baohu Wu, Tina Kollmann , Dietmar Schwahn, Vitaliy Pipich, Damien Faivre, Dirk Zahn, Helmut Cölfen** Multifunctional Layered Magnetic Composites
PO-10	**Sabine Eiben, David Brodbeck, Alexander Southan, Patricia Hegger, Maike Martini** Application of tobacco mosaic virus in hydrogels
PO-11	**Rahel Eisele, Dirk Rothenstein, Sandra J. Facey, Bernhard Hauer, Joachim Bill** Deposition of zirconium-based materials on biotemplates
PO-12	**Alexandra M. Greiner, Benjamin Richter, Clemens M. Franz, Martin Bastmeyer** Micro- / Nano-Engineered Polymeric 3D Environments for Cell Culture Studies
PO-13	**Eva Hoch, Achim Weber, Thomas Hirth[2], Günter E. M. Tovar, Kirsten Borchers** Fabrication of zonal cartilage by bioprinting technology
PO-14	**Maximilian Hörner, Natascha Hotz, Raphael Gübeli, Erik Christen, Josef Madl, Winfried Römer, Jan Pruszak, Matias Zurbriggen, Wilfried Weber** Engineering of a light-tunable extracellular matrix
PO-15	**Martin Humenik, Kristin Schacht, Thomas Scheibel** Spider Silk Fibrils as New Building Blocks for Assembly of Hierarchical Structures
PO-16	**J. Maxi Kanold, Françoise Immel, Frédéric Marin, Franz Brümmer** Biomineralization studies in sea urchins
PO-17	**Philipp Keckeis, Helmut Cölfen** Bio-inspired, multifunctionalized polymers to dissolve high-risk, endogenous deposits
PO-18	**Stefan Kilper, Dirk Rothenstein, Pouya Moghimian, Vesna Srot, Nina Stitz, Peter A. van Aken , Joachim Bill** Phage-templated inorganic multilayer assemblies
PO-19	**Jennifer A.S. Knaus, Elena Rosseeva, Hemut Cölfen** Apatite-Protein Nanocomposites - From Biological to Biomimetic Materials
PO-20	**Claudia Koch, Katrin Wabbel, Fania Geiger, Peter Krolla-Sidenstein, Hartmut Gliemann, Sabine Eiben, Christina Wege** Nano-scaffolds: modified *tobacco mosaic virus* (TMV) particles as carriers for active enzymes
PO-21	**Hannah Köhring, Iris Bellinghausen, Joachim Saloga, Holger Frey** Allergen-loaded pH-Sensitive Poly(ethylene glycol) Nanogels for Specific Immunotherapy
PO-22	**KaJohn Boonrod, Mario Braun, Verona Rink, Christine Müller-Renno, Christiane Ziegler, Gabi Krczal** Genetically improved Tomato Bushy Stunt Virus particles as functional macromolecular building blocks

PO-23	**Julia Kupka, Marcus Mateescu, Sabine Laschat** Studies on the Synthesis of Pyridine Acrylate and Acrylamide Cross-linking Molecules
PO-24	**Weina Liu, Yu Tokura, Felix Boldt, Yuzhou Wu, Tanja Weil** Single strand DNA modified nanodiamond for origami and cell targeting
PO-25	**Benjamin Madeja, Helmut Cölfen** Calcium Silicate Hydrate Mesocrystals
PO-26	**Dirk Rothenstein, Julia Maxi Kanold, Franz Brümmer, Joachim Bill** Insight into calcium carbonate biomineralization
PO-27	**Nicole Schädel, Maike Martini, Julia Kupka, Esra Oruc, Sabine Laschat** Synthesis of novel cross-linkers for bio-inspired hydrogels
PO-28	**Anna S. Schenk, Lukas Reith, Sabine Eiben, Alexander N. Kulak, Fiona Meldrum, Christina Wege, Holger Jeske, Sabine Ludwigs** Superstructures of Cobalt(II,III) Oxide Formed by Co^{2+}-Mediated Association of Tobacco Mosaic Viruses
PO-29	**Angela Schneider, Fabian Eber, Christina Wege, Sabine Eiben** Toehold-mediated assembly of tobacco mosaic virus nanotubes with defined subdomain structure
PO-30	**Romina Schröder, Hannah Köhring, Timo Schüler, Martin Panthöfer, Ronald E. Unger, Holger Frey, Wolfgang Tremel** Transformation of vaterite nanoparticles to hydroxycarbonate apatite in poly(ethylene glycol)-based hydrogel scaffolds
PO-31	**Alexander Southan, Eva Hoch, Veronika Schönhaar, Kirsten Borchers, Christian Schuh, Michaela Müller, Monika Bach, Günter E.M. Tovar** Side chain thiol-functionalized poly(ethylene glycol) by postpolymerization modification of hydroxyl groups: synthesis, crosslinking and inkjet printing
PO-32	**Hanna J. Wagner Raphael J. Gübeli, Balder Rebmann, Desirée Hövermann, Wilfried Weber** Stimulus-Responsive Hydrogel Vaccine Depots
PO-33	**Nana L. Wenz, Sylwia Piasecka, Clemens Richert, Christina Wege** Towards porous bio-functional materials based on virus-derived nucleoprotein domains and branched DNA hybrid linkers
PO-34	**Eduard Wiedenbeck, Helmut Cölfen** Liquid Precursors of Pharmaceutical Compounds

Abstracts of Invited Lectures

Stimuli-sensitive Hydrogels for biomedicine: From Drug delivery to 3D printing

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Keywords: hydrogels, nanogels, stimuli-sensitive, biofabrication

Hydrogels are three-dimensionally cross-linked hydrophilic polymer networks that can swell up to more than 90% weight content with water. They can be tuned regarding their chemical composition and three-dimensional physical structure enabling control over water content, mechanical properties and biocompatibility. Due to their similarity to the ECM, cells can be embedded into hydrogels, and cell encapsulation by hydrogels has been an active field of research for decades.
Only recently, the combination with 3D printing has led to development of printable hydrogels for direct generation of hierarchical structures. Moreover, the polymer network in hydrogels protects embedded bioactives such as proteins and peptides from degradation, and the degradability of the network can be adjusted through the chemical design of the polymers and the choice of cross-linking mechanism. Nanogels, hydrophilic cross-linked hydrogel-particles, may thus be exploited for delivery of peptides and proteins. This lecture will introduce into the field and present the activities of my group with the focus on redox-sensitive nanogels for drug delivery and approaches to 3D-printable hydrogels for biofabrication.

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Advanced Photopolymers for Tissue Engineering

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Keywords: Photopolymerization, Additive Manufacturing Technology, Biomaterials, Hydrogels.

UV curing of photopolymerizable formulations has been used for more than a half century for protective and decorative coatings of paper, wood, metals or plastics. Advantages can for sure been found in the high curing speed that allows the conversion of typically (meth)acrylate-based monomers within the fraction of a second. Furthermore, a large variety of monomers is commercially available so that the mechanical properties and other polymer characteristics can be easily tuned.
In the last decade there has been a strong demand for the curing of thicker layers or even to print arbitrarily shaped 3D cellular structures out of these materials. Especially in the field of dental filling materials curing of the filled cavity with a single initial light flash is desired to save precious time. Therefore, frontal polymerization is a hot topic that is still not satisfactorily solved. Herein we present a new concept for functional peroxides that show good storage stability but also give surprisingly good frontal polymerization.

If one wants to have arbitrarily shaped 3D cellular structures, additive manufacturing technology (AMT), also called Rapid Prototyping, is the method of choice. Different setups are commercially available that allow the printing of photopolymerizable formulations from a simple CAD model. Laser or DLP (Digital light processing) based systems fabricate polymer parts with a feature resolution of about 10 µm. In recent days not only prototypes are of interest, also small number of individual parts that can be used in the automotive industry or for medical applications are important. Especially in the latter case monomers and polymers with low toxicity should be used. Vinylcarbonates represent a new and interesting class of photopolymers with exceptionally low cytotoxicity and suitable photoreactivity. Degradation can be easily tuned giving non-toxic low molecular polyvinyl alcohol as degradation product and various non-toxic alcohols such as glycerol or polyethylene glycol. In vivo experiments demonstrated excellent biocompatibility. Furthermore, a thiol-ene system was used to tune the polymer architecture to achieve elastomer-like properties with low brittleness that can be printed by AMT and are suitable as vascular grafts.

Two photon photopolymerization (TPP) is another rapid prototyping technique that allows a real 3D writing process with feature resolutions of about 200 nm. Using suitable monomers and photoinitiators we were able to write with a femtosecond pulsed laser in the presence of tissue (Caenorhabditis elegans) without harming them. With newly designed two photon initiators we were also able to show the 3D printing of vinylester-modified gelatine with free thiol-groups of bovine serum albumin, for potential tissue engineering application. Other suitable polymer substrates that were modified with low toxic reactive groups belong to natural polymers like hyaluronic acid or synthetic polymers like polyvinyl alcohol. By multi-photon grafting one is able to make site-selective modifications of hydrogels in the µm scale.

For real-time study of the photocuring behaviour a special setup based on a combination of photorheometry coupled with an FTIR spectrometer will be presented.

Plant viruses and virus-like particles as building blocks for bionanotechnology

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The capsids of most plant viruses are simple and robust structures consisting of multiple copies of one or a few types of protein subunit arranged with either icosahedral or helical symmetry. The capsids can be produced in large quantities either by the infection of plants. In view of their relative simplicity and ease of production, plant virus particles have attracted much interest over the past 20 years for applications in both bio- and nanotechnology. During these studies, plant virus particles have been subjected to both genetic and chemical modification, and have been incorporated into supramolecular structures.

Despite the fact that much interesting data has been obtained using virus particles produced via infection, the use of such particles suffers from several disadvantages: the particles are themselves infectious, albeit only to plants; the need to propagate via infections means the particles must be functional in a virological sense, limiting the range of modifications that can be made; the particles contain the genomic nucleic acid, thereby limiting the degree to which additional, foreign material can be incorporated. To overcome these limitations, attention has turned to the use of virus-like particles (VLPs). These consist of just the protein shell of the virus and can be produced by the expression of the virus coat protein subunit(s) in a variety of heterologous systems, including plants, and relying on the ability of the subunits to self-assemble into VLPs. Such VLPs are not infectious, do not have be functional in a virological sense and can be used to encapsulate foreign material.

This presentation will review the various ways that both virus and virus-like particles have been exploited for use in bionanotechnology over the past two decades.

De-novo designed self-assembling protein polymers

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Many structural proteins such as collagen, elastin and silk feature characteristic patterns of amino acid sequences that are repeated many times within a protein sequence. Such rather simple and repetitive natural sequences, that could be called “protein polymers” are a perfect starting place to start engineering new self-assembling protein materials for specific biomaterial applications. In my lecture I will emphasize how my specific background, in theoretical physics, polymer science and soft matter science has benefited my work in the highly interdisciplinary field of protein polymers. I will first give a brief overview of structural proteins that are currently being used as a template for engineering new protein materials. Next I will present an overview of the protein polymer work in my group. Finally, I will zoom in on a recent project that showcases how natural structural protein sequence motifs can be “recycled” to design self-assembling multiblock protein polymers with specific properties, namely a project on designing a minimalistic artificial viral coat protein.

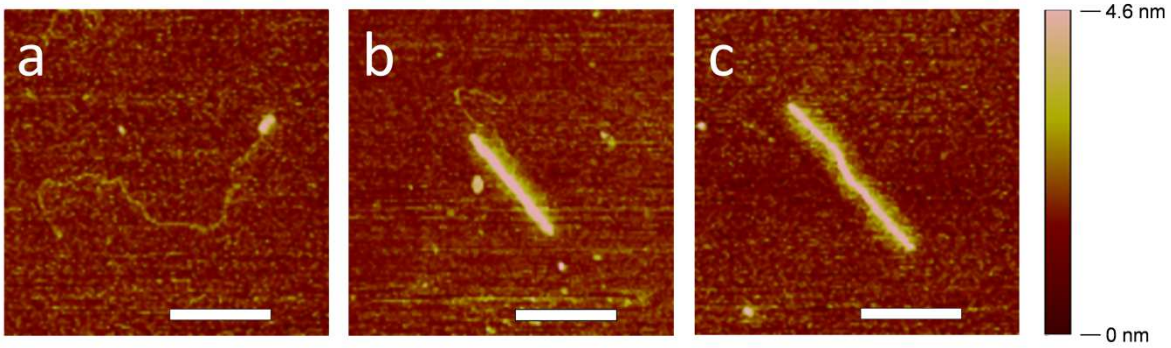

Figure 1. - Encapsulation of single linear dsDNA molecule (2.5kb) by de-novo designed recombinant protein polymer, into rod-shaped, virus-like particle. Taken from Ref. 1

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Advanced Therapeutics Medicinal Implants Equipped with Active Nanoreservoirs of Growth factors and Stem cells for Regenerative Medicine

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Keywords: Active living Biomaterials, Osteo-Articular Systems, Bone-tooth unit regeneration

Recently, we have reported a "Smart Hybrid Materials Equipped by Nanoreservoirs of Therapeutics and stem cells ". This unique nanotechnology strategy is used to entrap, protect, and stabilize therapeutic agents into polymer coatings acting as nanoreservoirs enrobing nanofibers of implantable membranes. Upon contact with cells, therapeutic agents become available through enzymatic degradation of the nanoreservoirs. As cells grow, divide, and infiltrate deeper into the porous membrane, they trigger slow and progressive release of therapeutic agents that, in turn, stimulate further cell proliferation. This constitutes the first instance of a smart living nanostructured hybrid membrane for regenerative medicine. The cell contact-dependent bioerodable nanoreservoirs described here will permit sustained release of drugs, genes, growth factors, etc., opening a general route to the design of sophisticated cell-therapy implants capable of robust and durable regeneration of a broad variety of tissues.

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Silicon-based sensor approaches @INB with organic molecules

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Keywords: Silicon-based biosensor, field-effect, microelectrode, biomolecule, electrochemical sensor

The rapid progress in semiconductor-based micro- and nano-technologies has stimulated the design of new sensor concepts that combine (bio-)chemical recognition processes together with silicon chip fabrication technologies. Typical examples are sensor arrays such as “lab on a chip” devices, µTAS (micro total analysis systems) or electronic tongues. In spite of these high-sophisticated multi-parameter sensor systems, the chemical sensors or biosensors as part of those set-ups play a key role with regard to their analytical behaviour.

Among the multitude of concepts and different types of chemical sensors and biosensors discussed in literature, the strategy to integrate chemical or biological recognition elements together with semiconductor-type field-effect devices is one of the most attractive approaches. In this context, typical examples are the capacitive EIS (electrolyte-insulator-semiconductor) sensor, the LAPS (light-addressable potentiometric sensor) or the ISFET (ion-sensitive field-effect transistor). Alternatively, microelectrodes can also serve as an electrochemical transducer for microsensing.

These different kinds of devices are currently being the basic structural element in a new generation of chemical and biological microsensors, fabricated by means of silicon planar technology. Moreover, they provide a lot of potential advantages over conventional approaches such as the small size and weight, the fast response time, the possibility of an on-chip integration of sensor arrays, the high robustness, the possibility of low-cost fabrication, etc. At the same time, their possible field of application reaches from medicine, biotechnology, process control and environmental monitoring through food and drug industries up to defense and security requirements.

This paper gives an overview on recent examples of silicon-based (bio-)chemical sensors @INB, dealing with different receptor molecules such as enzymes, polyelectrolytes or DNA molecules, respectively, as well as their device concepts (amperometric and potentiometric sensor (arrays) up to biomolecular logic gates). Additionally, different immobilization strategies will be presented and discussed.

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Precision Macromolecular Design in Solution and Surfaces: From Thermal to Photochemical Control

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Keywords: Macromolecular Chemistry, Polymer Surface Design, Grafting-To, Grafting-From, Thermal and Photochemical Modular Ligation

The lecture will discuss our latest advances in the field of constructing high precision polymers via light induced ligation protocols with a particular emphasis of patterning polymers onto solid substrates for cell guiding applications via light induced grafting-to technologies.[1,2] In addition, efficient methodologies for the non-spatially resolved design of dense polymer brush regimes via controlled/living grafting-from techniques will be discussed.[3,4] Importantly, the latest advances in the photo-chemically driven design of sequence controlled polymers[5] as well as photo-reactive polymers will be presented.[6,7] Particular emphasis will be placed on the characterization methodologies employed for the surface characterization including X-ray photoelectron spectroscopy (XPS), time-of-flight secondary ion mass spectrometry (ToF-SIMS) as well as ellipsometry.

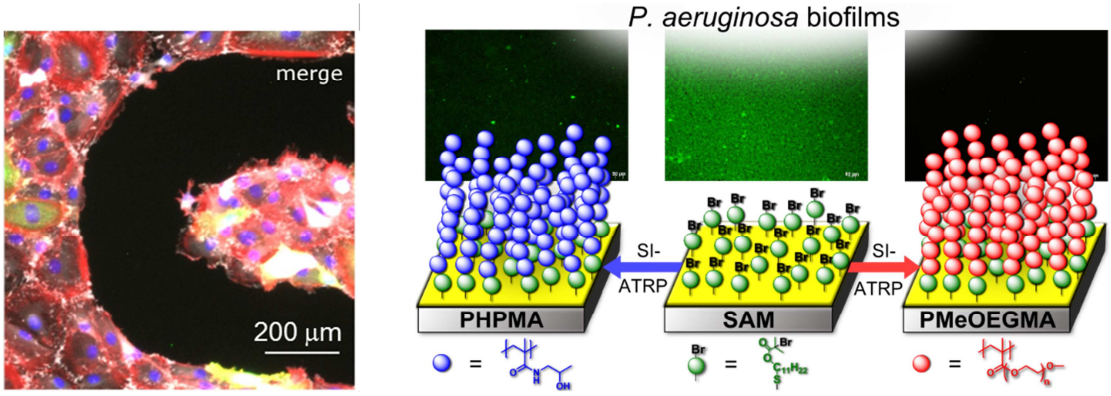

Figure1. (Left) Protection of a silicon surface from biological impact (rat fibroblast cells, stained) via the photochemical patterning of ultra-low antifouling polymer strands.[1] (Right) Global protection of surfaces against biofilm adhesion via the controlled grafting of dense anti-fouling polymer brush regimes.[4]

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New Pharmaceuticals, Biomaterials and Nanoscaffolds from Plant Viral Vectors

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Transient expression technologies such as magnICON® developed by Icon Genetics are new generation processes for biopharmaceutical and biomaterial production that are simple and indefinitely scalable protocols for heterologous protein expression in plants, which are devoid of stable genetic transformation of a plant, but instead rely on transient amplification of viral vectors delivered to multiple areas of a plant body (systemic delivery) by Agrobacterium. These eclectic technologies effectively address most of the major shortcomings of earlier plant-based technologies such as low speed of manufacturing, low expression levels, lack of versatility and high manufacturing cost. The technologies have been brought to the GMP-compliant level and are currently being used to manufacture materials for clinical trials by Icon Genetics, Nomad Bioscience, KBP, Fraunhofer USA, IBio, Mapp Biopharmaceuticals and others. Current Ebola virus outbreak and apparently successful use of ZMapp antibody cocktail manufactured using magnICON® technology and tested on several patients demonstrate the power of transient technologies.
Transient technologies are also applicable for generating biomaterials, novel biotemplates including virus–based nanoscaffolds and novel agronomic traits. The core process in development today at Nomad Bioscience is a technology that allows to rapidly temporarily re-program metabolism of green plants using agrobacteria sprays, thus generating valuable traits and bio-based materials. Because of its speed and versatility, the agrospray technology has a potential to become a disruptive new process that will redefine agriculture business as we know it.

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Inorganic structural and functional materials from biotemplates

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Keywords. Biotemplating, hierarchical materials, inorganic actuator.

Bioinspired materials research is a continuously growing field in interdisciplinary materials science and –engineering with large potential for novel functional materials [1-3]. Biotemplating is a technique, which employs naturally occurring structured resources (plant tissue, wood, lignocellulosics, beetle and butterfly scales, microorganisms, algae, bacteria, viruses etc.) and processed materials (paper, cardboard, fiberboard, composites) as starting materials for the manufacturing of inorganic compounds. Natural structures and composites used as biotemplates are therefore promising for the formation of patterned and hierarchically structured inorganic functional and structural materials. Owing to their structural diversity, natural materials can be used at various levels from the molecular scale up to complex three-dimensional parts. The replication of structural details of complex biological tissues over several levels of hierarchy down to the nanometer level is still a major challenge, figure 1 [4].

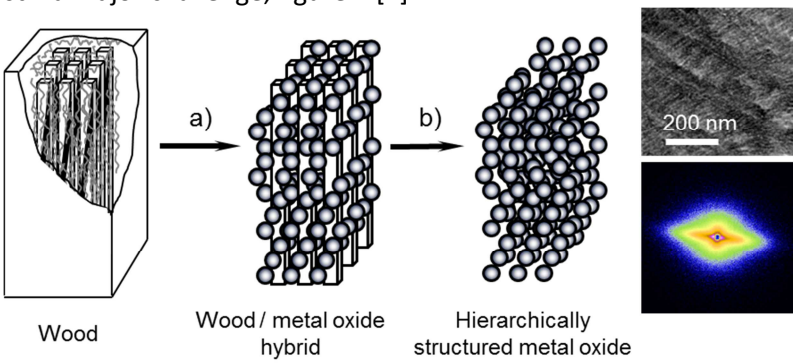

Figure 1: Scheme for hierarchical biotemplating of wood: a) Chemical modification and infiltration metalorganic precursor, b) calcination at elevated temperature yields the hierarchically structure material; insets: transmission electron micrograph and small angle X-ray pattern of the hierarchical inorganic products.

The biological templates need to be (made) accessible for the precursor materials down to nanometers, and the desired inorganic replica often require a final (high-) temperature treatment with the danger of collapse of the nanostructure. The presentation introduces the current knowledge about the replication of hierarchical biological materials into structural and functional inorganic with the special emphasis on wood as a template. It will be shown that hierarchical replication down to the nanoscale requires a careful pre-preparation of the biological template, followed by elaborate template infiltration via gas or liquid phases and their transformation into a solid material, and finally, the gentle removal of the template. Not very surprisingly, retaining the replicated material in an amorphous or nanocrystalline state is a key-requirement for a successful nanoscale replication of biological materials [4].

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Additive controlled Mineralization and Analytical Ultracentrifugation

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Biomineralisation, bio-inspired mineralisation, organic - inorganic interaction, crystallization control, Analytical Ultracentrifugation

Nature is teaching excellent lessons about sophisticated crystallization control of inorganic minerals by organic molecules in the process of Biomineralization. While insoluble molecules (structural matrix) serve as scaffold to produce a confined space for the mineralization process, soluble (macro)molecules (functional matrix) serve as crystallization modifier in various ways starting from the process of nucleation and ending with morphogenesis of an organic-inorganic hybrid material. Sophisticated examples for the modification of mineralization processes are also known for synthetic molecules as additives. Various of these examples will be discussed with a focus on the organic-inorganic interactions and how the mineralization process is guided by the organic molecules along different pathways. Several of these additive controlled crystallization pathways will be highlighted.

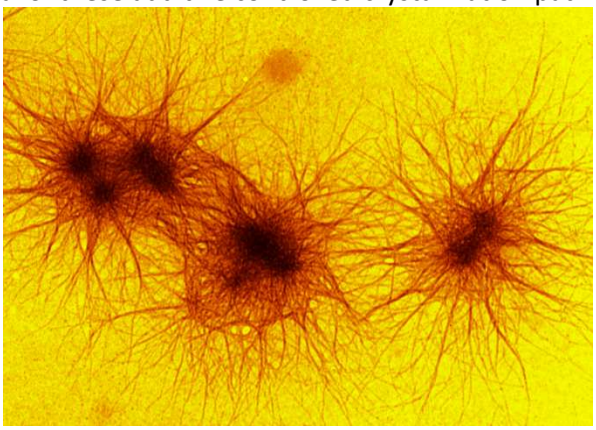

Figure 1: Hydroxyapatite mineralized in presence of a PEO-b-PMAA block copolymer modified by alkane chains

Analytical Ultracentrifugation is a very powerful tool to study macromolecules and nanoparticles as well as their interactions in solution over the entire colloidal range. The technique will be introduced and examples given how high resolution particle size distributions can be obtained as well as (macro)molecule characterization. It will be shown that not only size but also shape distributions can be obtained and that the technique is able to quantitatively deliver stoichiometry and interaction constants in case of interacting species.

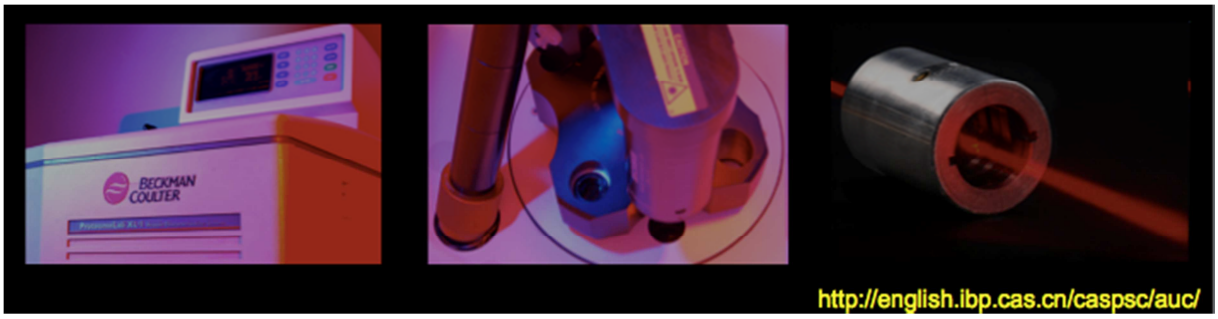

Fig. 2: Analytical Ultracentrifugation

Poly(ethylene glycol) hydrogel-based biomaterials for hematopoietic stem cells

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Keywords: Hydrogels, stem cell niche, hematopoietic stem cells, 3D biomaterials

Hematopoietic stem cells (HSC) replenish the blood system with all types of blood cells, including red blood cells and immune cells, throughout an entire lifespan. Since more than 50 years these cells are applied to treat patients who suffer from hematological disorders such as leukemia. Nevertheless, the clinical usage of HSCs is restricted because of the limited availability – per patient one matching donor has to be found – and the non-satisfying results when trying to proliferate them outside of the body. The only place where HSCs can proliferate and maintain at the same time their full stem cell potential is their natural microenvironment – their niche in the bone marrow. Therefore, understanding the stem cell-niche interactions and mimicking them with the help of biomimetic materials seems to be an attractive approach to improve HSC proliferation.
The HSC niche is a complex, three-dimensional (3D) environment, in which HSCs are in contact with other cells and the extracellular matrix. They are influenced by biological signals such as cell-cell-contacts as well as biophysical cues including substrate nanostructure and elasticity, which are not reflected by standard cell culture in two-dimensional (2D) tissue culture plates. Therefore, we design biomaterials to study the influence of nanostructure, mechanical properties and architecture (2D versus 3D) of the environment on HSCs. The results of these studies show that not only the biochemical composition but also the physical properties of the microenvironment influence HSC behaviour and, therefore, should be considered for approaches of HSC proliferation in biomaterial-based approaches.

Animal calcium carbonate skeletons and their organic matrix

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Keywords: biomineralization, calcium carbonate, molluscs, calcifying matrix, proteomics.

In metazoans, the secretion of skeletal tissues made of calcium carbonate is regulated by a complex array of extracellular macromolecules, namely proteins and polysaccharides - and sometimes lipids - that collectively constitute the skeletal matrix. Because of its ability to 'sculpt' the biominerals and to organize spatially crystallites in well-defined microstructures, this matrix, in particular, its protein moieties, has been the focus of several studies covering five decades of research in biomineralization. However, it is only in the last few years that the use of high-throughput techniques (proteomics alone or transcriptomics and proteomics together) has allowed identifying several sequences (partial or complete) of proteins that are putatively associated to the skeletal matrix, in different model and non-model organisms: corals, molluscs, brachiopods or sea urchins. This growing dataset allows now establishing large comparisons between the 'molecular kits' of different species, from phylum to phylum, and within one given phylum.
The obtained data show a remarkable diversity of the proteins involved in mineral deposition, in term of primary structures and of putative functions deduced from in silico sequence analysis. This diversity invites to refine the existing molecular models of mineral deposition and to integrate the role of the calcifying epithelium/calcifying cells facing the front of mineral growth. As illustrated by the mollusc nacre on the one hand, and by examples taken from other phyla on the other hand, it appears that 'similar' microstructures may emerge from very different protein 'toolkits'; this finding puts into question past attempts to use the matrix for taxonomic purposes. It reveals the astonishing plasticity of the 'calcifying matrix'; furthermore, it emphasizes that the matrix of extant species is built by the co-option of ancient and recent functions. In a counterintuitive manner, proteomic data suggest that the skeletal matrix is less evolutionary constrained than suspected and exhibits a true 'evolvability', while maintaining stable and perennial the associated microstructures.

Abstracts of Poster Presentations

PO1: Surface functionalization of Hydrogel Foams for Additive Manufacturing

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Keywords: surface functionalization, hydrogel, hydrogel foam, 3D-printing.

The research will focus on the development of defined, microstructured hydrogel foams for additive manufacturing by specific polymer engineering. One key aspect hereby is the surface functionalization of the hydrogel foams with molecular anchor points at the interface. These anchors can for example be used for covalent coupling of biological active compounds to form bioactive, three dimensional hydrogels. Furthermore, a hardening- and foaming process for the hydrogel foams will be investigated, which should be compatible with 3D-inkjet printing. Therefore a suitable composition of hydrogel- and foaming agents for 3D-inkjet printing will be explored in order to fabricate surface functionalized, 3D-printable hydrogel foams. Such materials could have an application as polymer scaffolds for personalized implants in the field of tissue engineering.

PO2: Surface active monomers: building blocks for particle functionalization

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Keywords: surfmer, polymerizable surfactants, polymeric nanoparticles, particle functionalization.

There is a rising interest in the development of efficient ways to synthesize novel polymeric materials possessing functional surfaces due to the wide range of possible applications that they have, especially in the field of biotechnology. Surface active monomers (often referred to as “surfmers”) are polymerizable surfactants that may carry a functional group, representing an improved path to the functionalization of polymeric particles. Due to the surface-active properties, these molecules are largely on the particle surface and, during surfactant-based emulsion polymerization processes, the surfmers are directly incorporated into the particle's polymeric backbone. Thus, increasing the particle's stability and allowing for controlled display of the functional groups on the surface of the particles (Fig. 1). Therefore, this particle configuration is highly suitable for conjugation with biomolecules. This work aims to synthesize two surfmer molecules and develop polymer particles using these surfmers as comonomers in a UV-initiated miniemulsion polymerization system, in order to obtain particles with a reactive surface functionality, with the objective to ensure that it reacts with biomolecules (Fig. 2). A wide range of biomolecules can be immobilized and, among them, viruses have turned out to be molecules of great interest. The configured particles with customized functional surfaces are promising candidates for multifunctional platforms suitable for biomedical applications.

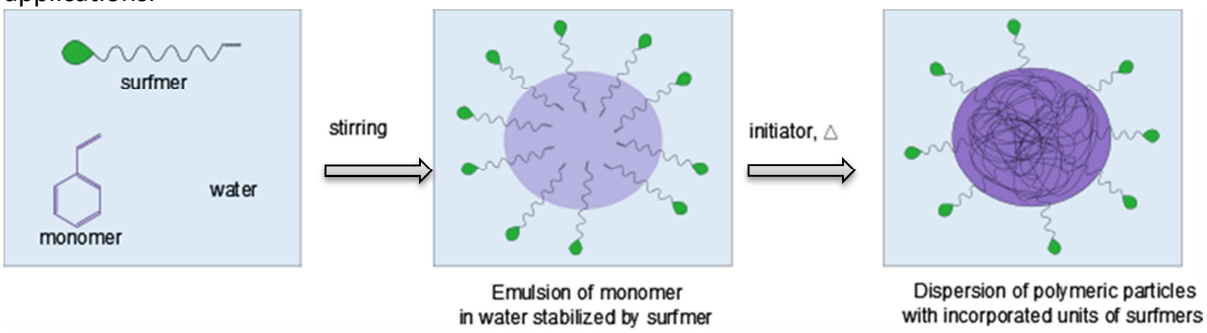

Figure 1. Preparation of polymeric dispersions with functionalized surface.

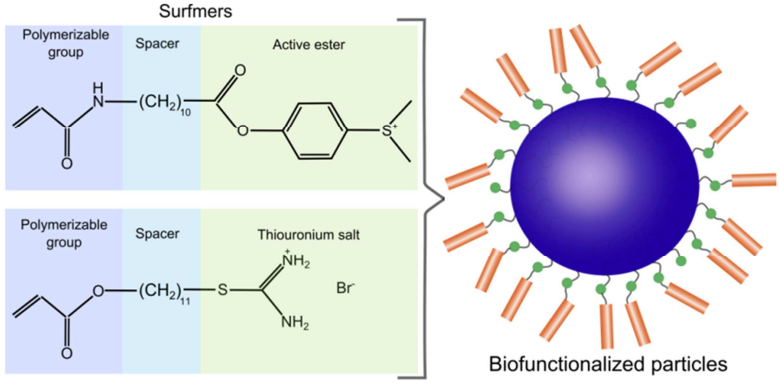

Figure 2: Graphical abstract of the project.

PO3: Fabrication of genetically engineered viral nucleoprotein pore adaptors for oriented insertion into nano-porous solid-state membranes

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Keywords: biohybrid membrane; bio-inorganic interface; bio-mineralization; nano-pores; tobacco mosaic virus

Nanoporous materials with well-defined pore size and chemistry have a high potential for sorting and separating small molecules. As it is difficult to produce for example solid-state membranes (SSMs) with large numbers of homogeneous pores of nanometric diameter and adjustable charge, uniform protein adapters fitting into inorganic membrane backbones might offer a versatile novel route towards the fabrication of stable nanopore arrays for different applications.
Precisely shaped pore-adapters were generated of tobacco mosaic virus intermediates, which are helical assemblies of 68 coat proteins stabilized by short single-stranded RNA constructs of a disk-like structure. Their central pores have a size of 4 nm, and their outer rim can be functionalized by covalently bound molecules such as linkers, fluorescent dyes or peptides. Proper orientation of the viral protein pore adopters inside the SSM pores will be achieved by electrophoretically driven insertion of appropriate designed novel nucleoprotein constructs with attached negatively charged double-stranded RNA, resulting in a disk-on-a-leash construct.
Mineral deposition-inducing peptides are applied to fine-tune silica formation at the viral pore-adapters outer surface, allowing gap sealing inside conical silica-containing holes of SSMs by means of biomineral precipitation between protein and inorganic template. Individual functionalization inside or close to the protein pore will extend the applicability of such bio-hybrid nanoporous membranes, customized for special approaches.

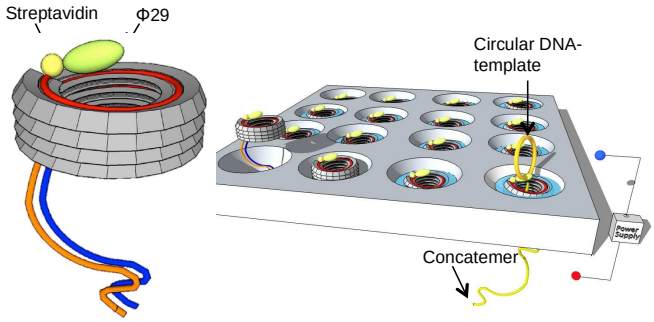

Figure 1: Functional extension of the protein pore: outline of enzyme-streptavidin complex immobilization to biotinylated RNA accessible at the pore rim. In this example, Phi29 polymerase is used to generate concatemeric DNA-sequences from a circular DNA-template by rolling circle amplification (RCA). Newly synthesized DNA may translocate through the protein pore in an electric field, and collected from there at high concentration for further analyses.

PO4: Mesoporous silica nanoparticle containing injectable hybrid hydrogel for drug delivery and tissue engineering

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Keywords: Tissue engineering, hydrogel, mesoporous silica nanoparticles

Stem cell-based tissue engineering carries high promises in the field of regenerative medicine. Here, scaffolds mimicking the target organ matrix both in terms of structure and mechanical properties are often applied. For *in vivo* approaches injectable systems are very beneficial because of their ease of administration. However, problems may arise due to low stem cell survival, limited proliferation and uncontrolled differentiation. Both stem cell proliferation and differentiation can be influenced by adding specific drugs. We therefore aim at developing an injectable hybrid hydrogel scaffold based on the combination of functionalized mesoporous silica nanoparticles (MSN) as drug delivery vehicles with the self-assembling peptide RADA16-I. RADA16-I forms a hydrogel as soon as it is in contact with the surrounding biological medium. The resulting network has a fibrillar diameter of about 10 nm and generates pores of 5-200 nm[1]. The structure of the formed hybrid hydrogel was analyzed by scanning electron microscopy (SEM) and focus ion beam-SEM ((FIB)-SEM), transmission electron microscopy (TEM) and confocal raman microscopy. The *in vitro* uptake by cells of MSNs incorporated in the hybrid hydrogels was followed by confocal laser microscopy as well as flow cytometry (FACS). A homogeneous distribution of particles and an efficient uptake of particles by cells within the hydrogel were observed. This proof-of-concept study indicates that hydrogel-MSN combinations are promising for cell-directed drug delivery in tissue engineering applications.

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PO5: Targeting of leukaemia stem cells by monoclonal antibody functionalized mesoporous silica nanoparticles

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Keywords: Mesoporous silica nanoparticles – targeting – drug delivery

Selective targeting of a special cell type is one of the new strategies in the treatment of cancers in order to reduce side effects dramatically. Mesoporous silica nanoparticles (MSN) are suitable candidates for such an approach due to high pore volumes for the delivery of hydrophobic drugs and the possibility of various surface functionalization such as antibodies or peptides for selective targeting. Especially the therapy of leukaemia would benefit from such systems as in comparison to solid tumors the treatment of blood cancer has to face the challenge to eradicate free circulating cancer stem cells. In order of high similarity of healthy and malignant stem cells standard chemotherapeutic approaches reveal in high side effects.
In this work we present a MSN based system for the selective B220 receptor targeting. B220 is a receptor expressed on leukaemic stem cells which initiate and propagate acute myeloid leukaemia (AML). MSN modified with differently charged organic groups were further functionalized with the antibody anti-human/mouse CD45R (B220) and selective uptake was analysed in vitro via flow cytometry (FACS). Based on this uptake studies the most promising particles were further loaded with the lipophilic tracer DiR or the anthracycline cancer drug daunorubicin. Co-localization of the model drug DiR and the fluorescent labelling of the particles as well as the successful delivery of daunorubicin into B220 positive cells could be shown. Due to this in vitro results the antibody functionalized and daunorubicin loaded particles seem to be very promising candidates for the selective eradication of a subpopulation of AML propagating cells.

PO6: Bioprogrammable Artificial Fusion Proteins

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Keywords: Synthetic Biology, Protein Modifications, Oligonucleotides, Medicinal Chemistry

Controlling biostructures at the nanoscale level is one of the major challenge in biomedicine.[1] Today nature has achieved with various building blocks a precision which is unsurpassed by any in vitro method. On the other hand, artificially engineered structures with such a high precision can only be achieved by DNA hybridization,[2] most notably DNA origami. Nevertheless beside aptamers and ribozymes, DNA has no biofunctionality. In comparison, proteins contain a wide variety of biological functions ranging from structural proteins and motor proteins to enzymes. Therefore the coupling of proteins to DNA is highly attractive. An alternative system, which is used more extensively to couple to biomacromolecules together nowadays is the avidin/biotin coupling. The binding of avidin and biotin is the strongest noncovalent binding known. Avidin can bind simultaneously to four biotin molecules therefore limiting the versatility of this system to form dimers due to steric hindrance. We established a solid phase system[3] which enables the monofunctionalization of avidin without the need of tedious fusion protein preparation. Using these elegant semi-synthetic approaches we prepared different protein heterodimers. Our goal is to assemble different bioactive proteins to create a new molecule which combines both functionalities. In addition to that the method can be extended to decorate DNA origami structures with proteins.

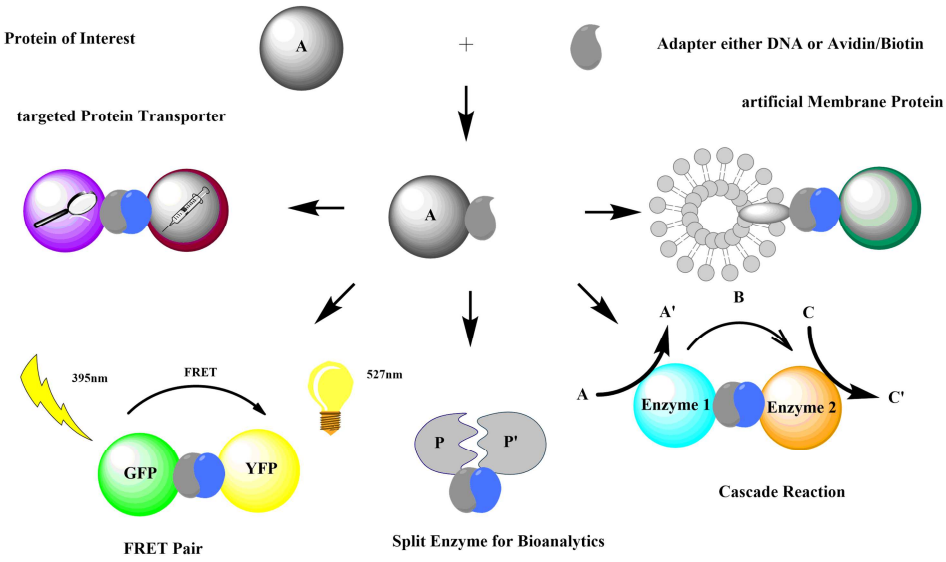

Figure 1: Schematic representation of the proposed protein assemblies

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P07: Adsorption and desorption kinetics of antimicrobial peptides on mesoporous silica nanoparticles

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Keywords: peptide, mesoporous silica, nanoparticle, adsorption, desorption

Mesoporous silica nanoparticles exhibit several characteristics that could be beneficial for administration of peptides, including a narrow pore size distribution that can lead to efficient protection inside the mesopore system of the cargo until the point of release. Particle size and shape can be adjusted as well as it's possible to modify the surface with different functional groups. These characteristics can be utilized to optimize mesoporous silica nanoparticles as carriers with respect towards peptide adsorption, release characteristics and formulation properties. High pore volumes and their large surface area are also advantageous for a high drug loading capacity.[1] Beside diffusion-mediated release it is possible to control release via pH, redox potential, ion concentration, enzymatic activity, light or thermal stimulation.[2] Here we present adsorption kinetics and salt mediated desorption kinetics of the peptide LL37 on mesoporous silica nanoparticles of different sizes and surface functionalities, as well as on non-porous Stöber particles. LL-37 is a 37-mer cationic peptide with an isoelectric point at a pH of 11.4 and a net charge of 6 at pH 7, which shows antimicrobial activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus*, in a time- and concentration-dependent manner.[3]

Mesoporous particles were synthesized via sol-gel process via a modified synthesis of Rosenholm *et al.*[4] under basic conditions and were modified post-synthetically. Morphology, size and porosity were determined with nitrogen sorption, dynamic light scattering and transmission electron microscopy. Adsorption and desorption kinetics were determined via peptide quantification in the supernatant using fluorescamine assay.[5] The peptide could be adsorbed on differently charged mesoporous silica nanoparticles as well as on non-porous Stöber particles. Non-porous Stöber particles followed Langmuir adsorption behaviour, whereas for mesoporous particles strong adsorption at low concentration could be observed. Non-functionalized mesoporous silica particles showed the maximum adsorption capacity for LL-37. Release kinetics of these peptide-loaded particles were studied. Almost complete release in TRIS could be observed after 48 h of all mesoporous silica nanoparticles whereas non-porous particles only released a small amount of the adsorbed peptide. Addition of sodium chloride leads to a much faster release of the same amount already after 24 h.

In conclusion we could show that LL-37 could be adsorbed on mesoporous silica nanoparticles with different surface functionalities as well as on non-porous silica nanoparticles. Release kinetics could be stimulated by adding salts to the release medium. Therefore mesoporous silica nanoparticles could serve as vehicles for the distribution of peptides via different administration pathways, e.g. topical or pulmonary application.

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P08: Light-responsive hydrogels for sustained growth factor delivery

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Keywords: retinal tissue engineering, therapeutic angiogenesis, controlled release, responsive hydrogel.

The retinal pigment epithelium (RPE) is a cellular monolayer involved in metabolism between the choroid and photoreceptors, as well as in the visual process [1]. Functional impairment of the RPE plays an important role in the pathophysiology of age-related macular degeneration (AMD) [2], which is the leading cause of blindness in industrialized countries [3]. There are currently no disease-altering therapies available for the vast majority of AMD patients.
Replacement of dysfunctional submacular RPE with tissue engineering grafts represents a potentially curative treatment strategy [2]. Long-term function of transplanted RPE may be achieved by using functionalized cell carriers promoting angiogenesis and thereby biointegration of the transplant in the subretinal space. Growth factor concentration and duration of delivery are critical factors to sustain angiogenesis [4]. Stimuli-responsive hydrogels allow for the controlled release of therapeutic agents into the surrounding matrix [5]. There are first approaches for the light-responsive release of proteins from synthetic hydrogels via photodegradable macromers [6] as well as for the two-photon induced delivery of drugs into the eye [7].
If covalent immobilization of growth factors into hydrogels through photocleavable linkers and their functional light-responsive release in the subretinal space is possible, biointegration and long-term function of the transplant could be achieved.

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PO9: Multifunctional Layered Magnetic Composites

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Keywords: Biomimetic mineralisation, nacre, chiton tooth, layered composite, gelatin, magnetite.

Biominerals are an interesting example for natural organic-inorganic hybrid materials. One such material is nacre which consists of layered aragonite tablets, adding hardness to the material, surrounded by a chitin/protein matrix, adding elasticity. This hybrid structure makes nacre 3000 times more fracture resistant than aragonite itself, which makes up approx. 95 % of this structure [1]. Another astonishing biomaterial is the chiton tooth. The tooth's shell is formed by magnetite nanoparticles embedded into a protein/polysaccharide gel matrix, showing very high abrasion resistance and the highest hardness and stiffness among the known biominerals, being for example three times harder than human tooth enamel [2].
To combine the advantageous properties of these biominerals we established a synthesis method to infiltrate a demineralized nacre chitin scaffold with gelatin and consecutively mineralize the gelatin hydrogel with magnetite nanoparticles of adjustable size [3]. Degrees of mineralization of up to 70 wt.-% could be achieved as well as a hardness and elastic modulus comparable to human bone and dentin. This hybrid material possesses the layered "brick-mortar" structure seen in nacre, showing anisotropic mechanical and magnetic properties.
One step to further improve the mechanical properties will be the increase of overall mineral content by an additional, "filler" mineral, embedding the magnetite nanoparticles. Suitable minerals that will be examined are silica, calcium carbonate and calcium phosphate/apatite. We also want to stiffen the gelatin matrix by incorporation of calcium ions into the triple helix. To allow upscaling of our approach, we try to create a substitute for the natural chitin scaffold by freeze-casting of chitosan.

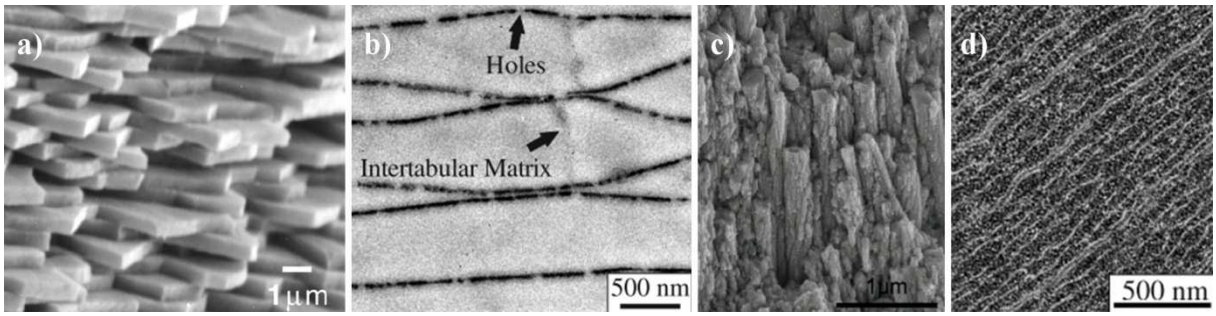

Figure 1. a) SEM image of nacre aragonite platelets; b) TEM cross section of the nacre chitin matrix; c) SEM image of the magnetite rods forming chiton teeth; d) TEM cross-section of hybrid chitin/gelatin/magnetite material.

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PO10: Application of tobacco mosaic virus in hydrogels

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Tobacco mosaic virus, hydrogels

Tobacco mosaic virus (TMV) can easily be produced in planta or in vitro. With its unique structure, 300 nm long hollow rods with inner and outer diameters of 4 and 18 nm, it is an ideal scaffold for nanoscaled materials.Hydrogels are versatile materials for a variety of applications including nano-diagnostics, biocatalysis or as a matrix for tissue engineering. Here we combine both, TMV-based structures with their high multivalency, 2130 CP per particle, and hydrogels, allowing simultaneous cross-linking of the virus with the hydrogel matrix and coupling of functional groups such as mineralizing peptides, enzymes or antibodies.

So far we have investigated two hydrogel systems in combination with TMV in both cases, a TMV mutant with an accessible cystein on its surface was used (TMVCys). The thiol group can be used for Michael type addition and thus can be covalently linked to the different gel matrices. The first system is based on a hydrogel matrix of poly(ethyleneglycol)700(PEG-DA) (120-250 mg/ml) and very low amounts of TMVCys (300-1000 µg/ml). While PEG-DA monomers can bind to the thiol group on TMV at room temperature on their own, cross-linking is initiated by activation of photo-inducible Irgacure. In addition to the use of unmodified TMVCys, virus with bound alkaline phosphatase (AP) was also investigated. The resulting gels showed, upon incubation in a Ca-glycerophosphate solution, enhanced mineralization properties in comparison to pure PEG-Da-, TMVCys containing- but also only alkaline phosphatase containing hydrogels. Rheology measurements on PEG-DA and PEG-DA/TMV hydrogels revealed that at these low concentrations, the TMVCys had no impact on mechanical properties of the gel.

In the second gel system a newly synthesized bifunctional cross-linker and thiolated hyaluronic acid (HA) as gel matrix were combined with much higher TMV concentrations. Here the ratio of TMVCys to HA had a clear impact on gel elasticity. These gels were further investigated by transmission electron microscopy and the fine structure of TMV in the hydrogels could be visualized.

PO11: Deposition of zirconium-based materials on biotemplates

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rahel.eisele@imw.uni-stuttgart.de Keywords: Bio-inspired mineralization, ZrO_2, biotemplate, M13 bacteriophage, phage display, organic-inorganic hybrid material

Due to its chemical, mechanical and thermal resistance and its semiconducting properties zirconia (ZrO_2) is often used in fuel cell technology[1], as mechanical or heat resistant protective layer[2] and in optical applications[3]. Conventional synthesis methods of ZrO_2 often require harsh reaction conditions. Inspired by biomineralization processes in living nature an energy extensive synthesis strategy for ZrO_2 under moderate reaction conditions was established where M13 bacteriophages are used as bio-organic templates for the deposition of a zirconium-based material. Moreover, inspired by the architecture of nacre, an alternating organic-inorganic multilayer system based on M13 bacteriophages and zirconium will be generated.

To get a stronger interaction between the biotemplate and the inorganic layer and influence the deposition rate of the zirconium-based material on M13 phages specific ZrO_2-binding peptides were displayed on the phage body. Their influence on the mineralization of the inorganic phase and the mechanical properties of the multilayer system will be characterized.

For mineralization a $ZrOCl_2$ solution in an ethanol-water solvent was used[4]. To obtain small particles at relatively high pH, the temperature, salt concentration, and ethanol-water ratio were systematically varied. At 25°C a 20 mM $ZrOCl_2$ solution in an ethanol-water ratio of 5:1 exhibits particle sizes from 12 to 22 nm at a pH of 2.12. With increasing temperature, salt-concentration, and ethanol-water ratio the particle size increased.

ZrO_2-binding peptides were isolated by phage display (Ph.D.-7; New England Biolabs). According to the low pH of the mineralization solution the binding step to a monocrystalline cubic and a polycrystalline tetragonal ZrO_2 substrate was carried out at pH 2. The peptides were eluted at pH 10. Among the isolated peptides after the 4th and 5th biopanning round, the six most abundant peptide sequences were selected to functionalize the phage templates (table 1). Additionally, there exists a putative binding motive with the amino acid sequence “SXS”. In further work the isolated ZrO_2-binding peptides will be expressed on the biotemplate to use them for mineralization.

Table 1: Sequences and frequency of the six most abundant peptides. *4th Amino acid G is partially substituted by R.

peptide	amino acid sequence	peptide-frequency [%]			
		c-ZrO_2		*t*-ZrO_2	
		4th round	5th round	4th round	5th round
a51	SLLGQTP	16.1	14.8	2.7	3.8*
b51	GSLSRFI	3.2	11.1	0	0
c52	GQSEKHL	0	1.9	10.8	21.4
a58	HGGVRLY	0	9.3	8.1	7.1
a53	QLAVAPS	0	14.8	0	5.4
e53	TVNFKLY	0	0	2.7	17.9

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PO12: Micro- / Nano-Engineered Polymeric 3D Environments for Cell Culture Studies

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Keywords: Direct Laser Writing, Photopolymerization, 3D Cell Culture Substrates, Biocompatibility, Cell and Nuclear Volume, Cell-Matrix Adhesion

Cells in physiological three-dimensional (3D) environments often vary considerably in morphology and differentiation status from those growing in 2D tissue culture. Naturally derived 3D polymer systems are frequently used to study cells in 3D. These 3D matrices are often challenging to use with respect to their (bio)chemical composition, mechanical properties, and geometry. Therefore, there exists a demand for well-defined 3D cell culture in order to methodically investigate cell behavior in 3D environments. Bio-functionalized three-dimensional (3D) structures which can be easily fabricated by Direct Laser Writing (DLW) (a photopolymerization technique) are structurally and mechanically well-defined and thus ideal for systematically investigating the influence of three-dimensionality and substrate stiffness on cell responses.
We show that different fibroblast-like and epithelial cell lines maintain normal proliferation rates and form functional cell-matrix contacts in both soft and stiff DLW scaffolds. Furthermore, the molecular composition of cell-matrix contacts forming in 3D micro-environments and under conventional 2D culture conditions is identical, based on the analysis of several marker proteins (paxillin, phospho-paxillin, phospho-focal adhesion kinase, vinculin, β1-integrin). However, fibroblast-like and epithelial cells differ markedly in the way they adapt their total cell and nuclear volumes in 3D environments. While fibroblast-like cell lines display significantly increased cell and nuclear volumes in 3D substrates compared to 2D substrates, epithelial cells retain similar cell and nuclear volumes in 2D and 3D environments. Despite differential cell volume regulation between fibroblasts and epithelial cells in 3D environments, the nucleus-to-cell (N/C) volume ratios remain constant for all cell types and culture conditions. Thus, changes in cell and nuclear volume during the transition from 2D to 3D environments are strongly cell type-dependent, but independent of matrix stiffness, while cells maintain the N/C ratio regardless of culture conditions.

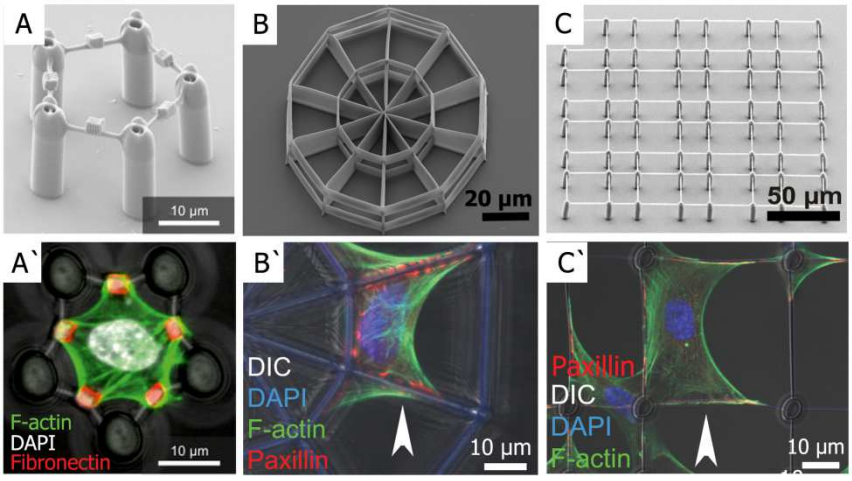

Figure 1. A two-photon polymerization technique (Direct Laser Writing) is used to fabricate physically and chemically well-defined synthetic 3D cell culture scaffolds. **(A-C)** Scanning electron microscopy images of different 3D architectures. **(A'-C')** The specific responses of single cells adherent to the biofunctionalized tailored 3D environments can be systematically studied with respect to e.g., geometrical, biochemical, and mechanical aspects of the 3D culture environment.

PO13: Fabrication of zonal cartilage by bioprinting technology

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Keywords: Cartilage tissue engineering, zonal cartilage models, bioprinting, biopolymers

Because of the limited capacity for spontaneous repair, articular cartilage damage is a serious problem. Cartilage tissue engineering approaches have been investigated for over two decades, but have not yet advanced to guarantee clinical success. One of the potential reasons for this is that current engineered cartilage constructs do not hold the cartilage-specific zonal structure that, however, is crucial for tissue function.

In order to develop artificial biomimetic structures, which perform as well as natural ones, we need fabrication processes that do not set any limits to the generation of shapes. Thus, current research activities focus on the application of freeform fabrication methods, e.g. dispensing printing, for the deposition of cells and biomaterials into spatial orientations and geometries to reproduce the complexity of native tissues in a controllable and automated manner. This so called bioprinting requires biomaterials that are printable and, at the same time, hold appropriate physical, chemical, and biological properties. Thereby, biomolecules from the extracellular matrix (ECM) of native tissues constitute very promising materials as they hold natural signaling motifs for the stimulations of cell adhesion, migration and function.

In this study, photo-crosslinkable derivatives of the ECM biopolymers gelatin, chondroitin, and hyaluronan are prepared by derivatization with methacrylic anhydride. [1,2] To furthermore achieve printable and dispensable bioinks, the viscous behavior of gelatin precursor solutions is adapted to the requirements of the printing technologies by additional acetylation. [3] The developed bioinks are used for bioprinting with articular chondrocytes to proof cytocompatibility. [2] For fabrication of zonal cartilage models bioinks with appropriate biopolymer composition for replication of the three cartilage zones (superficial, middle, deep) are determined. Criteria for evaluation are the visco-elastic properties of the resulting hydrogels, such as mechanical strength, swellability, and degradability, as well as their potential to preserve cell viability and functionality. Finally, three-dimensional, zonal cartilage models were fabricated and evaluated for their quality.

We present biopolymer-based biomaterials which are processable by inkjet printing and dispensing technology and which can be crosslinked into hydrogels with cartilage-like properties. Furthermore, three-dimensional cartilage equivalents with biomimetic hierarchical structure as potential cartilage substitutes are presented.

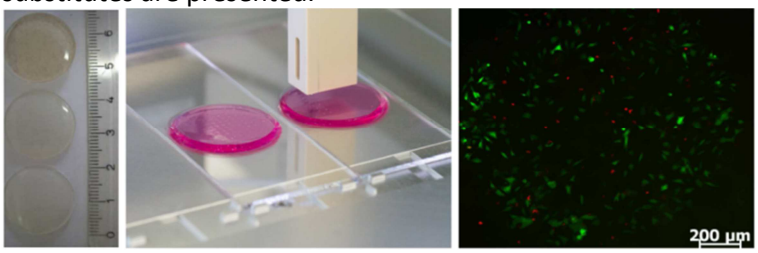

Fig. 1: Left: EZM-based hydrogels of different mechanical properties. Middle: Inkjet-printing of cell-laden biopolymer-based bioink onto hydrogel substrates. Right: Porcine chondrocytes after inkjet printing (green: viable cells, red: dead cells).

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PO14: Engineering of a light-tunable extracellular matrix

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Keywords:Biohybrid hydrogel, Optogenetics, Extracellular matrix, Substrate elasticity

The stiffness of the microenvironment of cells has significant influence on cellular signaling pathways and can even direct cell differentiation. However, only few studies have investigated the impact of dynamic changes in substrate elasticity on cells. Therefore our aim was to engineer a synthetic cell matrix which stiffness can be reversibly adjusted by light illumination. This was realized by combining light-gated molecular switches from the field of optogenetics with cell-compatible polymers from material sciences. To this end, we covalently coupled the cyanobacterial phytochrome Cph1 to an eight-arm polyethylene glycol thus forming a biohybrid hydrogel. Illumination with red light triggers dimerization of Cph1, thereby increasing the number of crosslinks within the hydrogel and thus enhancing its stiffness. Vice versa, far-red light illumination induces Cph1 monomerization and decreases hydrogel stiffness. Due to the fast switching properties of Cph1, the stiffness can be modulated reversibly within seconds. By incorporation of RGD cell adhesion motifs our hydrogel serves as suitable matrix for primary cells as well as cell lines.

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PO15: Spider Silk Fibrils as New Building Blocks for Assembly of Hierarchical Structures

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Keywords: spider silk, self-assembly, fibrils, hierarchical association, ribbons, rafts, hydrogels

Self-organization properties of the recombinant spider silk protein eADF4(C16) [1], an engineered variant of *Araneus diadematus* dragline silk ADF4, enables assembly of different structures such as nano-fibrils, microspheres or capsules [2]. Cross-β fibrils are mechanically, environmentally and chemically stable and therefore represent versatile building blocks for preparation of higher-ordered materials such as ribbons, rafts or hydrogels [3; 6].
Recombinant spider silk eADF4(C16) and short oligonucleotides were chemically modified and conjugated using a copper catalyzed "click" reaction [5]. It has been demonstrated that short nucleic acid moieties do not change the self-assembly mechanism of the silk moiety; as such it results in morphologies and protein secondary structures of the nano-fibrils which are identical to those of the unmodified silk protein. The conjugated fibrils also had accessible nucleic acid strands, which enabled sequence specific binding of DNA-modified gold nanoparticles, which were arranged along the fibrils [5]. Specific complementarity of DNA moieties on the conjugate fibrils also enabled their hierarchical association into nano-scopic ribbons using steep gradient temperature conditions. Conversely, their prolonged incubation at constant temperatures close to DNA melting led to an association of the conjugate fibrils into microscopic rafts with fibrous patterns [3]. We therefore expect that hierarchical DNA-silk scaffolds will enable patterning of gold nano-particles resulting in compound materials with photonic or plasmonic properties.
Moreover, nano-fibrils assembled from eADF4(C16) could be processed into hydrogels based on fibril hydrophobic interactions [6]. Such physical crosslinking allows injectable properties of the hydrogels which were used to prepare 3D printed cell-loaded constructs. Cells were able to adhere and proliferate over at least one week within these scaffolds. Fusion of RGD cell binding motif with the spider silk protein further enabled fine-tuned control over cell–material interactions [4]. Thus, considering also the biocompatibility and biodegradability of the spider silk [7] the hydrogels represent a highly attractive novel bioink for biofabrication [4].

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PO16: Biomineralization studies in sea urchins

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Keywords: biomineralization, sea urchin, organic matrix, saccharides, mechanical properties, *in vivo* and *in vitro*

Sea urchins are commonly used model organisms for developmental biology, but further they are highly suitable for biomineralization research since they offer great opportunities to study this process on different levels, from single cells to the adult animal. Additionally they possess several different structures, such as the test, spine and teeth, which display a variety of shapes and mechanical characteristics, which makes them also attractive for architectural constructions [1, 2].
The Mediterranean sea urchin species *Arbacia lixula* is rarely used for biomineralization studies, so far. However it is highly interesting to investigate this species since it belongs to the order Arbacioida, which diverged more than one hundred million years ago from the order Camarodonta that includes commonly investigated species in respect to biomineralization. One focus of our studies is the characterization of the organic matrix from adult structures of *A. lixula*. By using different biochemical and analytical methods, we were able to identify several peptide sequences and saccharide motifs that are part of the organic matrix [3-5]. Further, we performed *in vivo* studies on developing larvae of this species, in order to identify whether an increased presence of magnesium ions in the surrounding seawater would influence the composition of the formed biomineral and its mechanical properties [6]. At last, we established a protocol for isolating and cultivating the primary mesenchyme cells (PMCs), i.e. the cells that are responsible for mineral formation during embryonic development, in order to investigate the process of biomineralization on this single cell type.
A great advantage of this species is that the adult animals can be cultured at our department in Stuttgart and larvae are available to us during the whole year. Therefore, by combining methods from biology and material science, this model organism is suitable for biomineralization studies and the results contribute to a better and broader understanding of the biomineralization process in sea urchins.

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PO17: Bio-inspired, multifunctionalized polymers to dissolve high-risk, endogenous deposits

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Keywords: Arteriosclerosis, cholesterol, nano medicine, poly peptides, polymer micelles.

Coronary arteriosclerosis and the related cardiovascular diseases constitute one of the most serious health problems in the Western Hemisphere, which causes around 40 % of all deaths. [1] Based on the high lethal number of coronary diseases, a new fundamental approach shall be established (Figure 1, A). Plaque-sensitive macro surfactants are assumed to partially extract arteriosclerotic compounds, encapsulate them into stable aggregates, followed by renal excretion.

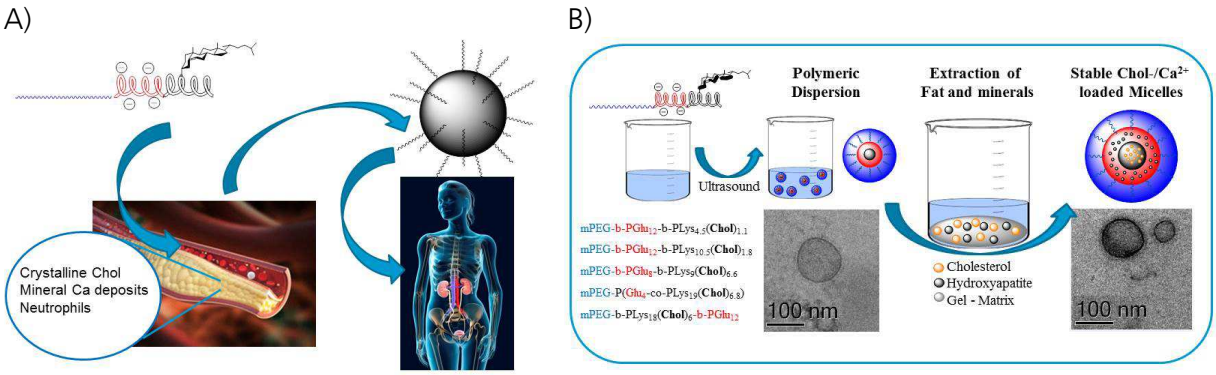

Figure 1. Fundamental approach of the project (A). Synthesized polymers; structural characterization in blood-mimicking media; extraction of gel-covered hydrophobic and mineral compounds (B).

A new generation of bio-inspired multifunctional surfactants was synthesized, targeted to dissolve arterial arteriosclerotic plaque. The plaque is complexly composed of solid blood components, hydrophobic components like cholesterol, but also of inorganic deposits of calcium minerals. A multifunctional copolymer with covalently attached cholesteryl and anionic moieties is assumed to achieve interactions with hydrophobic and mineral parts of the arterial deposit. Moreover pendant polyethylene glycol increases the water solubility. Complementary analytical techniques (DLS, AUC, NMR, cryo-TEM, tensiometry, zeta-potential measurements) suggested an oriented arrangement of the polymer into particles with a distinct shape, a negatively charged surface and a size within 50 and 150 nm (Figure 1, B) in a blood-mimicking media. The polymeric dispersions were able to extract solid cholesterol and calcium ions bound in mineral structures, which where embedded in a κ-carrageenan gel matrix. Moreover the extracted compounds were entrapped in stable micelles. Furthermore, cytotoxicological assays against human kidney epithelial cells negated toxic impacts of the polymers.

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PO18: Phage-templated inorganic multilayer assemblies

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Keywords: Bioinspired mineralization, organic/inorganic hybrid material, bio-template, M13 bacteriophages, zinc oxide, artificial nacre, mechanical properties.

The formation of inorganic materials by living organisms is referred as biomineralization [1]. The materials formed by this mechanism are nearly unlimited in size, shape, and properties. Different organic molecules, e.g. proteins, function as templates in such materials [2]. Researchers aim to use this natural toolbox for the synthesis of nanostructured organic/inorganic hybrid materials for technical applications. In this context, viruses like the filamentous M13 bacteriophage are a particularly interesting group of bio-templates. Due to their length of ~ 1 µm and a diameter of ~ 6-7 nm they can be used as templates for nanowires and other multiple nanostructured materials [3, 4]. The high aspect ratio causes a concentration dependent liquid crystal behavior of the bacteriophages in solution and therefore highly ordered and self-structuring templates can be formed with e.g. convective assembly [4]. The aim of this work was the formation of multilayered assemblies with alternating organic and inorganic layers, which is inspired by the natural model nacre. The wild type M13 bacteriophage was used as bio-template for the deposition of the inorganic ZnO. In order to generate a homogenous template structure, the bacteriophages were aligned by convective assembly. Based on the model of fiber reinforced materials the subsequent M13 bacteriophage layers were aligned in different orientations relatively to each other, in order to influence the mechanical performance of the multilayer assemblies [5].The ZnO layers, composed of nanocrystallites, were mineralized by chemical bath deposition at ambient conditions. It was shown that multilayer assemblies with up to 10 bacteriophage/ZnO layers can be synthesized. Furthermore, structural and mechanical properties of the new hybrid material were investigated. No distinct differences in hardness, Young's modulus and fracture toughness between the multilayer systems with differently aligned M13 bacteriophage layers were found. Therefore it can be concluded that the mechanical performance of the hybrid material is mainly dominated by the ZnO-M13 bacteriophage and the bacteriophage-bacteriophage interactions and not by the orientation of aligned M13 bacteriophages. Further investigations aim on hybrid materials with genetically modified M13 bacteriophages.

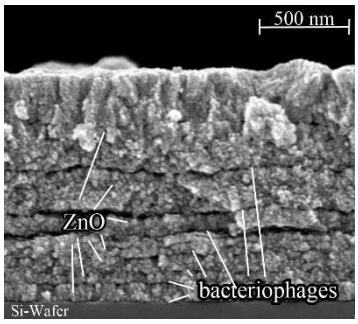

Figure 2: SEM- cross section of a ZnO/wt M13 bacteriophage multilayer hybrid material. The ZnO layers are separated by the M13 bacteriophage layers.

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PO19: Apatite-Protein Nanocomposites - From Biological to Biomimetic Materials

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Keywords: Hard tissues, biomimetic, nanocomposites, apatite-gelatine nanocomposites

Hard tissues in living organisms are comprised of biominerals, which display complex hierarchical structures and unique physical properties from the microscale down to the nanoscale. Such structures and composition render for example enamel one of the hardest mineralized tissues of vertebrates. The *in vivo* formation of hierarchical nanocomposite structures as main components of bone and teeth in biological hard tissues are highly sophisticated and evolutionary optimized. Exploring the underlying biomineralization processes involved in the formation of apatite-based hard-tissues in vertebrates and determining the structure-property relations enable the development of efficient biomimetic syntheses for different types of apatite protein nanocomposites (figure 1). These provide valuable guidelines for the fine-tuning of the biomimetic materials parameters, which can build the basis for the development of advanced functional materials for biomedical applications, such as dental repair materials and bone implants.[1, 2]

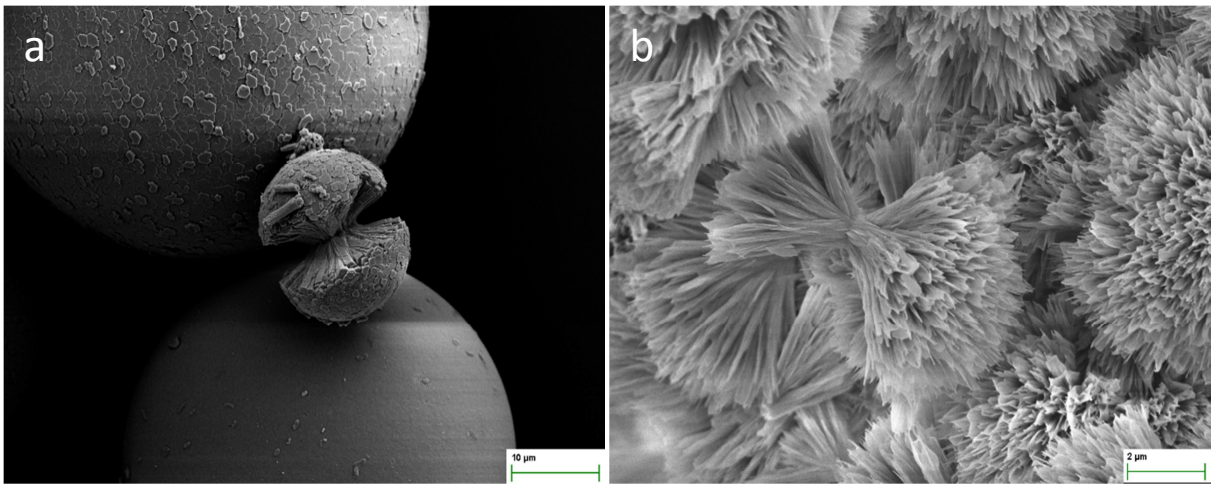

Figure 3: Scanning electron microscope images of fluorapatite-gelatine nanocomposites (a) and magnesium substituted fluorapatite-gelatine nanocomposites (b).

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PO20: Nano-scaffolds: modified *tobacco mosaic virus* (TMV) particles as carriers for active enzymes

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Keywords: tobacco mosaic virus, biotemplate, enzyme cascade system, biosensing, diagnostics, nano-scaffolds

Tobacco mosaic virus (TMV) is a rigid nanotubular plant virus with a length of 300 nm and a diameter of 18 nm. The native TMV capsid consists of 2130 identical coat proteins (CP) which self-assemble into a helical structure around the positive-sense single-stranded viral RNA (6395 bases long). Numerous studies have demonstrated a huge potential of the robust TMV particles to serve as versatile building blocks of hierarchically structured functional materials. So far, TMV has proven to be an effective carrier not only for inorganic compounds, but also for the display of foreign peptides, fluorescent dyes and antibodies. We now present a proof-of-principle for TMV-based nanoscaffolds enabling an ultradense immobilization of active enzymes. The use of a TMV mutant (TMV_{Cys}) carrying a reactive cysteine residue on the surface of every CP subunit allowed the coupling of bifunctional maleimide-PEG-biotin linkers resulting in biotinylated TMV-nanorods (TMV_{Cys}/Bio). The highly specific biotin-streptavidin bond enabled the immobilization of streptavidin [SA]-conjugated enzymes (glucose oxidase ([SA]-GOx) and horseradish peroxidase ([SA]-HRP)) on TMV_{Cys}/Bio sticks for the detection of glucose.
We found that at least 50 % of the CPs were equipped with a maleimide-PEG-biotin linker and virtually all thereof carrying an active enzyme. This was also reflected by transmission electron microscopy (TEM) analyses showing a high density and homogeneous distribution of the coupled enzymes over the complete nanotube surface as well as the structural integrity of the underlying TMV scaffold. Further, the TMV_{Cys}/Bio sticks served as a surface-increasing adapter system by forming multiple layers ("haystacks") in immobilization experiments. Moreover, the TMV-exposed enzymes showed considerably increased reusability indicating a stabilizing effect by the TMV stick environment. The findings of this study and the potential of TMV as modular nanobiotemplate suggest TMV to be a suitable scaffold for the ordered presentation of highly active enzymes in biosensors and diagnostic systems.

PO21: Allergen-loaded pH-Sensitive Poly(ethylene glycol) Nanogels for Specific Immunotherapy

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Keywords: Poly(ethylene glycol), degradable nanogel, allergy, targeted transport

During the last decades, the number of allergic patients has increased dramatically (about 300 Mio patients worldwide). The only available causal oriented therapy is the specific immunotherapy (SIT). SIT reduces the allergic symptoms, but also exhibits some disadvantages, i.e., it is a long-lasting procedure, and in a few cases severe side effects like an anaphylactic shock can occur. In this work, we have developed a method to encapsulate the allergen used during specific immunotherapy into nanoparticles to avoid severe side effects during treatment.

Nanoparticles derived from biocompatible and degradable macromonomers gain increasing attention for a variety of biomedical applications. These polymer nanoparticles protect therapeutic proteins, e.g., allergens, or drugs from degradation, permitting higher local concentrations and enable targeted transport.[1,2] Degradable nanocarriers combine the advantage of providing a physical barrier between the encapsulated cargo and the biological environment as well as responding to certain local stimuli (like pH) to release their payload.[3]

We have synthesized a novel type of difunctional, water soluble poly(ethylene glycol) dimethacrylate macromonomer with acetal-sites which degrade at acidic pH. The allergen and the macromonomer were entrapped inside liposomes as templates produced by dual centrifugation. Radical polymerization of the methacrylate groups inside the liposomes generated PEG-nanogels.

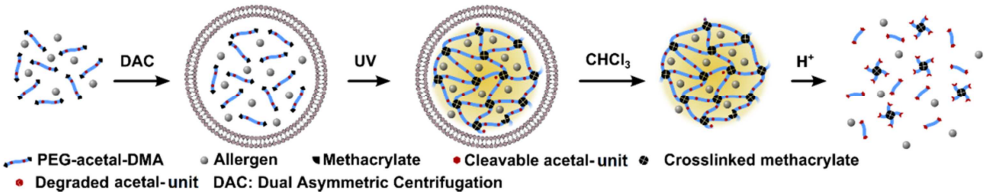

Figure 1. Schematic overview of the encapsulation concept: entrapment of both macromonomers and allergen in liposomes, followed by photo initiated radical polymerization. Acid-triggered degradation leads to release of encapsulated protein cargo.

The allergen-loaded nanogels were approximately 150-200 nm in size and showed low molecular weight distribution. *In-vitro* studies demonstrated that dendritic cells (DCs) internalize the protein-loaded, non-toxic PEG-nanogels. Furthermore, we demonstrated that the nanogels effectively shield the allergen cargo from detection by immunoglobulins on the surface of basophilic leucocytes, which is supported by cellular antigen stimulation tests. Uptake of nanogels into DCs does not lead to cell maturation; however, the released allergen was capable of inducing immune responses.[4]

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PO22: Genetically improved Tomato Bushy Stunt Virus particles as functional macromolecular building blocks

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Keywords: Functionalized TBSV particles, self-assembly, optimized monolayers, 3-dimensional structures

Plant viruses are promising biomolecules for nanotechnology, since they have simple structures and large potential for self-assembly. Spherical plant viruses like the tomato bushy stunt virus (TBSV) allow for multiple applications in nanotechnology due to their shape and size. We created different types of virus particles by extending coat protein (CP) subunits at their carboxylic termini with two differently charged amino acids. The CPs subunits carried either 6 cysteine (negative charge) or 4 histidine (positive charge) residues. The surface structures formed by these viral particles by self-assembly on mica were investigated by scanning force (SFM) and scanning electron microscopy (SEM) [1]. Depending on the particle type, the self-organizing behavior showed pronounced differences in the surface arrangement under the same convective assembly conditions: Electrostatic interactions between virus particles and virus particles and the substrate surface significantly influenced the building of mono-layers by viral self-assembly. Finding a compromise between the best possible electrostatic attraction between the (mica) carrier and the different types of virus particles and a minimal repulsion between these particles resulted in an optimal coating and a monolayer over macroscopic-length scales. These electrostatic interactions could be optimally adjusted by varying the pH value of the virus solution used for coating with the different particles types.
Moreover we will use genetically modified TBSV particles to establish more complex structures. In particular the link between Ni ions and histidine will be exploited in several ways. This comprises the binding of the virus to the substrate as well as the modification of the virus surface, e.g. through metallization mediated by histidine and other side chains like material binding peptides. Currently we dispose of modified TBSV particles carrying peptides to bind gold and hematite. To build 3-dimensional structures, we will link viral layers via a peptide (12mers) exposed on the CP units exhibiting a specific binding affinity for the viral capsid itself
We will also establish systems for the loading of the capsid with different compounds e.g. gold particles. We currently try to actively assemble modified CP subunits around a gold core as well as to dis- and re-assemble viral particles to trap gold particles in the assembly suspension.

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PO23: Studies on the Synthesis of Pyridine Acrylate and Acrylamide Cross-linking Molecules

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Keywords: Bio-inspired cross-linking molecules, aza/thio-Michael addition, hydrogels

Recent biomaterial designs have shown the importance of elasticity and tensile strength to the field of tissue engineering, focusing on artificial, biodegradable hydrogels.[1] Inspired by desmosine we developed new structural elements composed of a charged or an uncharged pyridine core with flexible side chains. These chains are comprised of alkyl or PEG spacers bearing acrylate or acrylamide end groups, and are connected to the core via ester or amide bonds. [2]

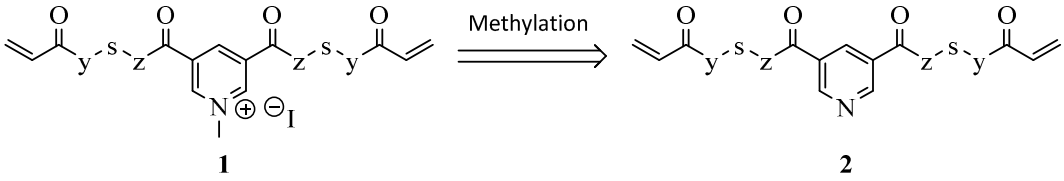

Figure 1: Retrosynthesis of pyridine core cross-linkers. [2]

We were able to achieve compound **2** on either the linear synthetic route or the convergent synthetic route. Irrespective of the synthesis route the key step is the esterification, respectively the amidation, which is followed by a methylation reaction. We designed these pyridine cross-linkers in order to polymerise them via a thio- or aza-Michael addition.[2]

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PO24: Single strand DNA modified nanodiamond for origami and cell targeting

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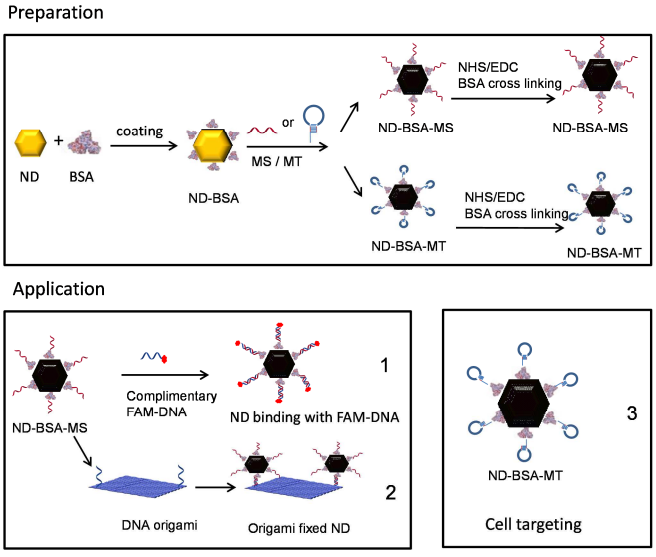
Keywords: Nanodiamond, bio-coating stabilization, staple DNA, origami, sgc8 aptamer DNA

Nanodiamond (ND) with excellent biocompatibility, chemical stability as well as special optical property has been studied a lot in biomedical or physical applications. Stable monodispersed nanodiamond was prepared by Native bovine serum albumin (BSA) coating to prevent ND from aggregation and for further modification [1]. Single strand DNA (ssDNA) with maleimide group was synthesized by solid phase method and applied to modify the BSA coated ND via covalent coupling with cysteine group of coating material BSA. By this coupling post coating process, the functional staple DNA as well as aptamer DNA was on the surface of the modified ND, which is superior for further application. Fluorescent ND dimer with close distance of energy center (less than 10 nm) was calculated to have increased coupling or magnetic effect. DNA origami was a great platform to place ND at specific position with accurate distance between the functional nanoparticles. To position the ND on origami, Staple DNA (MS) was synthesized to modify ND-BSA and bind with the sticky end in specific location on origami to form ND dimer. Sgc8 DNA aptamer (MT) would specifically target CCRF-CEM (T-cell acute lymphoblastic leukemia, T-cell ALL) cells with the over expressed receptor protein tyrosine kinase 7 (PTK7), and the targeting system can be delivered specifically to the CCRF-CEM cells to get improved delivery efficiency. MT DNA was synthesized and modified with ND, and the cell targeting efficiency were studied with confocal and flow cytometry.



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PO25: Calcium Silicate Hydrate Mesocrystals

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Keywords: calcium silicate hydrate, mesocrystal, bionics, material engineering

This project was inspired by an unexpectedly discovered feature of the sea-urchin spin. Although it consists of 92% calcite, a very brittle material, roughly of 8 % amorphous calcium carbonate and less than of 0.01% protein - this structure is very hard but still flexible [1]. The special arrangement of the calcite building blocks which are embedded into a shock-absorbing matrix is responsible for the mechanical strength (Fig. 1). This highly ordered, mesoscale assembly of primary nanocrystals is called a *mesocrystal.*

Regarding this interesting concept (Fig. 1) a new cement-based (mostly calcium silicate hydrate, CSH) material was synthesized: Starting from a solution in which the reactants were mixed and nanocrystals were formed, the stable dispersion was later destabilized by simply adding sodium hydroxide. The polymer (PVP*co*PAA, 5 wt.%) which adheres on the surface of the CSH nanocrystals dissolves from it while the pH is being increased. This results is a well-structured agglomeration of the nanocrystals - at first in a gel-like form. Later, after drying under nitrogen atmosphere, a macroscopic structure with both – flexible and hard properties was formed.

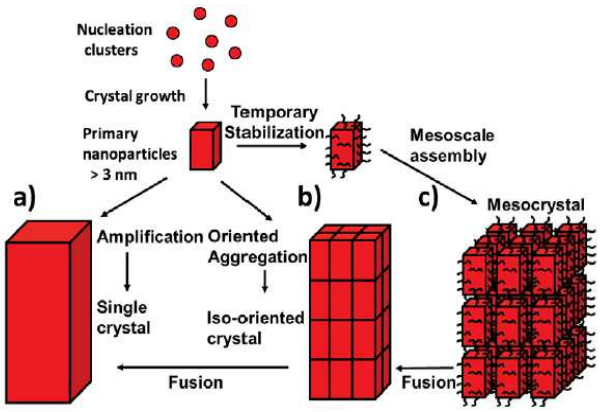

Figure 4. Scheme of different pathways of crystallization.

A mesocrystal is a highly-ordered assembly of crystals over several length-scales. To prove its formation (see Fig. 1 pathway c)) different analytical methods were used. TEM suggested the formation from a single crystal to the whole CSH-Mesocrystal. XRD and POM as macroscopic techniques prove the crystallinity and the high orientation of the crystal.

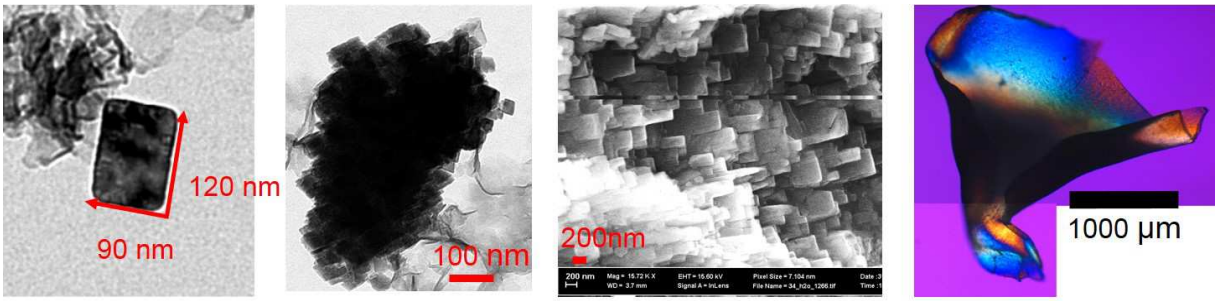

Figure 2. Different microscopy techniques for characterization. f.l.t.r: TEM image of a primary nanoparticle; TEM image of a CSH cluster with approx. 1000 nanocrystals; SEM image of the fracture surface; POM image of a macroscopic CSH-Mesocrystal

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PO26: Insight into calcium carbonate biomineralization

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Keywords: Phage display, inorganic-binding peptides, biomineralization

Biomineralization is the formation of inorganic materials by living nature. Thereby, organic molecules like proteins control the formation of an inorganic phase *in vivo*, resulting in an organic-inorganic hybrid material. The inorganic material synthesis is accomplished at ambient reaction conditions, e.g. moderate pH and temperature in an aqueous environment. Moreover, the material properties can exceed those compared to the pure inorganic material[1] and delicate structures in the nanometer regime can be locally mineralized[2]. Both, the material properties and morphologies of such hybrid materials are controlled, among other effectors, by the organic phase.
To use biomineralization processes as a tool for the *in vitro* formation of hybrid materials, specific biomineralizing peptides have to be identified. However, since natural mineralizing organisms are complex systems, the identification of proteins controlling biomineralization is difficult. In addition, for the synthesis of non-natural inorganic materials specific inorganic-binding peptides, mediating the biomineralization processes, have to be identified from e.g. random peptide libraries[3].
In order to investigate the biological controlled calcium carbonate ($CaCO_3$) mineralization, peptides which specifically bind to the $CaCO_3$ target substrate were selected by phage display from a random peptide library. As target substrates single crystalline aragonite and calcite substrates were selected. The aragonite- and calcite-binding peptide pools, respectively, vary from each other regarding isoelectric points of peptides and amino acid composition. Common binding motives and frequent peptides were identified.
The effect of these peptides on the mineralization of $CaCO_3$ *in vitro* will be investigated and compared to natural protein isolate from adult sea urchin structures[4,5].

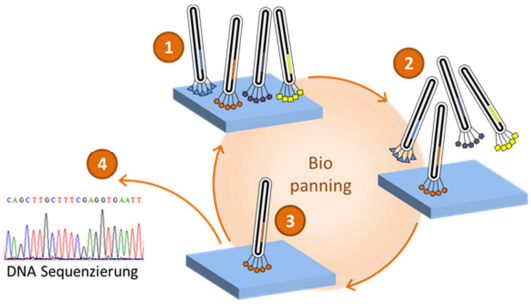

Figure 1: Schematic drawing of phage display method. 1) Phages expressing a random peptide library (colored symbols at the phage tip) are incubated with the target substrate. 2) Non-binding phage species are excluded by washing with appropriate buffer systems. 3) Specifically binding phage/peptide entities are eluted from the target substrate. These steps (1-3) are repeated several times (process called Biopanning). 4) Peptides were analyzed by sequencing corresponding DNA sequence.

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PO27: Synthesis of novel cross-linkers for bio-inspired hydrogels

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Keywords: desmosine analogues, cross-linking molecules, hydrogels

Elastin is a natural polymer found in the extracellular matrix of connective tissue. It consists of protein chains that are cross-linked via desmosine **1** and isodesmosine and is responsible for the high elasticity and tensile strength of human tissue.[1] We recently reported the synthesis of the desmosine analogues **2a,b** (Figure 1). These molecules were used to cross-link natural and synthetic polymers to form hydrogels.[2, 3]

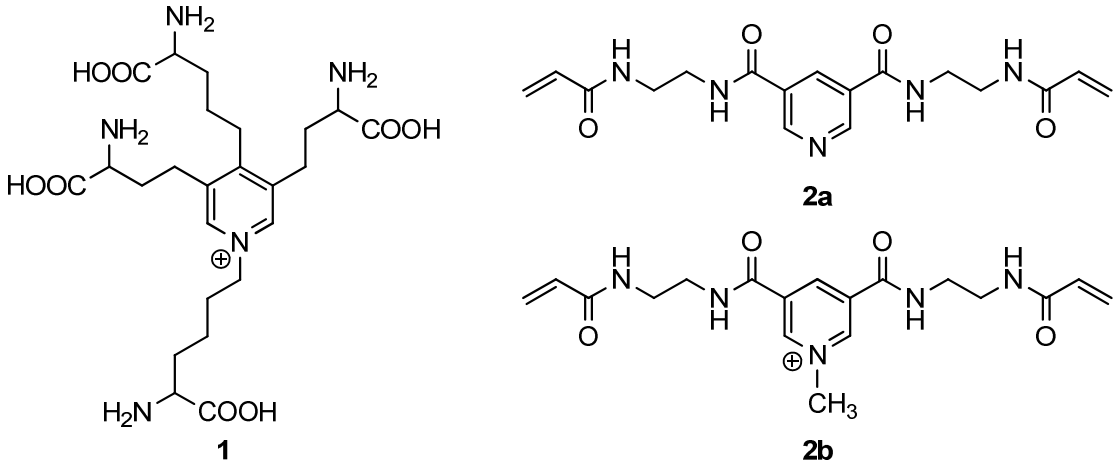

Figure 1. Desmosine **1** and cross-linkers **2a** and **2b**.

In this project, we wish to synthesize novel desmosine analogues which consist of a pyridine or pyridinium core unit and two amino acid side chains. The target molecules shall then be used for the cross-linking of natural or synthetic polymers and the influence of the cationic charge on the material properties shall be investigated.

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PO28: Superstructures of Cobalt(II,III) Oxide Formed by Co^{2+}-Mediated Association of Tobacco Mosaic Viruses

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Keywords: bio-inspired mineralization, cobalt oxide, tobacco mosaic virus, self-assembly, catalyst

Spinel cobalt(II,III) oxide (Co_3O_4) represents a highly promising material for a wide range of technological applications, particularly in the field of heterogeneous catalysis,[1] where the catalytic activity of the functional oxide largely depends on its morphology (exposed lattice planes), nanostructure and specific surface area (porosity).[2] Therefore, eco-efficient routes towards nanostructured cobalt oxide need to be established.

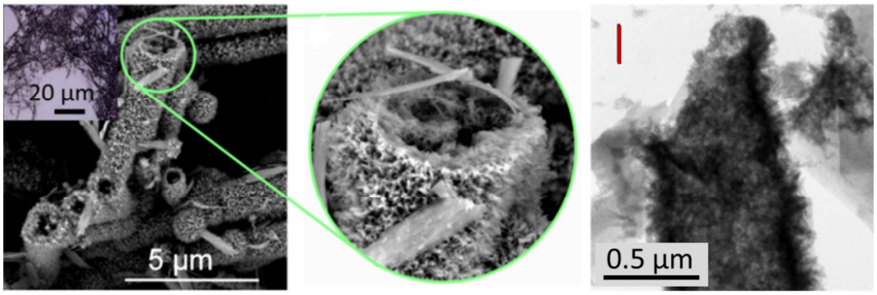

Figure 1. left, center: Scanning electron micrographs of tubular mineral-virus hybrid particles. The inset (upper left corner) shows metal-bridged aggregates of TMV before mineralization. right: Transmission electron micrograph showing a mineralized shell of the precursor-virus composite and a core of lower density. Measuring up to 30 µm in length the tubular aggregates are ca. 2 orders of magnitude larger than an individual tobacco mosaic virus (schematic illustration true to scale in the upper left corner).

The here presented work explores a bio-inspired approach, in which a thermally unstable cobalt hydroxide carbonate precursor[3] is precipitated in the presence of tobacco mosaic viruses (TMV) as structure-directing additives.[4] We demonstrate that µm-sized tubular superstructures of cobalt hydroxide carbonate, can be prepared in aqueous solution by mineralizing ordered aggregates of pre-assembled wild-type TMV cross-linked by Co(II)-ions (Figure 1). Calcination of the obtained mineral rods leads to thermal conversion of the precursor into an array of interconnected Co_3O_4 nanoparticles, while the gross morphology of the initial metal-virus complexes is retained. The virus-templated mineral phases are analyzed before and after calcination using a range of imaging, spectroscopic and x-ray scattering techniques. Particular emphasis is put on the nanostructural characterization of the specimens by means of electron microscopy (SEM and TEM) and small-angle x-ray scattering (SAXS) as well as the evaluation of their catalytic activity with respect to the anodic oxygen evolution reaction[3] (cyclic voltammetry). In view of the potential generality of this procedure, we additionally explore the effects of replacing Co^{2+} with other divalent transition metal ions such as Ni^{2+} or Cu^{2+} as well as mixed metal species. Furthermore, different genetically modified virus variants exposing a higher proportion of either cysteine or lysine on the surface of the coat protein are used as templates.

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PO29: Toehold-mediated assembly of tobacco mosaic virus nanotubes with defined subdomain structure

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*[1] University of Stuttgart, Institute of Biomaterials and Biomolecular Systems, Department of Molecular Biology and Plant Virology, Stuttgart, Germany, * **Correspondence**: Sabine Eiben, Institute of Biomaterials and Biomolecular Systems, Department of Molecular Biology and Plant Virology, University of Stuttgart, Pfaffenwaldring 57, 70569 Stuttgart, Germany email: sabine.eiben@bio.uni-stuttgart.de*

Keywords: tobacco mosaic virus, strand-displacement, RNA-directed self-assembly, bio/inorganic hybrid semiconductive layer, bio-inspired mineralization

Tobacco mosaic virus (TMV) is a ss(+)RNA plant virus with a tube-like structure of 18 nm diameter x 300 nm length. TMV is comprised of its genomic RNA of 6395 nt and 2130 identical subunits of the coat protein (CP). Due to its well-characterized properties TMV is often employed for nanobiotechnological applications [1], ranging from medical in vivo diagnostics [2] up to its use as template for bio-inspired mineralization to generate bio/inorganic hybrid semiconductive layers for electronic devices in our team [3]. Preparing TMV with precisely defined and clearly distinguishable longitudinal subdomains provides the possibility to investigate even minor changes in the TMV surface charge distribution which can affect e. g. its mineralization and may thus enable the fabrication of novel nanosized electronic components.

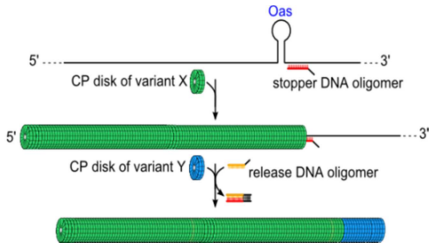

Figure 1: Schematic illustration of the "stop-and-go" principle.

Additionally, such domains allow the spatially defined presentation of specific peptides or polymers in exact regions thus enlarging the TMV toolbox.
Therefore a "stop-and-go" principle was used to obtain defined domains of distinct CP types (Fig. 1). First a stopper (partially complementary to TMV-RNA, second portion serving as "toehold") is hybridized to the RNA and blocks its assembly with CP, resulting in partially assembled TMV particles with a defined nucleoprotein tube length. Using strand-displacement hybridization, the stopper is detached from the RNA by addition of a release oligomer (fully complementary to the respective stopper), and assembly can proceed with another CP variant, provided that the first CP was removed by suitable purification steps. This will create particles with two distinct domains.
Four different stoppers were designed, two to bind on the 5' (A1B, A2B), and two on the 3' site (BA5, BA6) of the origin of assembly (OAs), respectively. We could show that the 3' stopper BA5 blocks the RNA efficiently and leads to partially assembled nanotubes of around 250 nm length. Furthermore, its toehold-release by addition of oligomer R5 is working well, resulting in fully assembled nanotubes filled-up by the CPs still present in the solution. In contrast, stopping the assembly in 5’ direction was not successful under the conditions applied. This probably reflects the high assembly velocity of TMV in this direction, which is known to result from an integration of higher-order CP aggregates towards the 5' end of the viral RNA. Consequently, the stoppers on the 5' site were displaced by the CP added here, resulting in fully assembled TMV particles.

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PO30: Transformation of vaterite nanoparticles to hydroxycarbonate apatite in poly(ethylene glycol)-based hydrogel scaffolds

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Keywords: vaterite nanoparticles, hydroxycarbonate apatite, hydrogel, biomaterial, bone grafting materials, biodegradable, simulated body fluid, endotoxin, biocompatible.

Bone grafting biomaterials have been gaining increasing importance for the use in bone regeneration applications due to their unlimited availability, low risk of infection and reduced morbidity compared to autologous tissues. Native bone is composed of organic (mainly collagen) and inorganic (non-stoichiometric hydroxyapatite (HA) with ion substitutions)[1] compounds, which are responsible for the special mechanical properties of elasticity and extremely hardness at the same time. Most of the bone grafting materials used in clinical applications are based on synthetic calcium phosphates (e.g. HA and β-tricalcium phosphate), however, their brittleness, low elasticity and very slow resorption are disadvantageous.[1,2]

In our work we demonstrate a promising alternative for the use of biomaterials for bone regeneration based on a biodegradable poly(ethylene glycol)-acetal-dimethacrylate (PEG-acetal-DMA) hydrogel loaded with vaterite nanoparticles as mineral storage. Vaterite, the least stable crystalline polymorph of calcium carbonate, was chosen as inorganic precursor for the bone mineral to ensure the presence of a potential ion buffer for bone regeneration. Due to the instability and relative solubility of vaterite, a sufficient reactivity is achieved that allows the transformation from vaterite to hydroxycarbonate apatite (HCA) upon incubation in simulated body fluid (SBF) at human body temperature within several hours to days. Much attention has been paid to bonelike HCA as a novel biomaterial, since HCA is very similar to apatite in terms of living bone in its chemical composition and structure.[2] Furthermore HCA shows effective compatibility in cell attachment, proliferation and differentiation, as well as good bioresorbability.[2] We were able to show the transformation from free vaterite nanoparticles as well as vaterite nanoparticles incorporated in a PEG-acetal-DMA hydrogel to HCA. In various *in vitro* experiments vaterite nanoparticles and vaterite-containing hydrogels were evaluated for endotoxin, toxicity and biocompatibility, and initial results indicate that vaterite may have prospects for future applications in the treatment of bone tissue engineering.

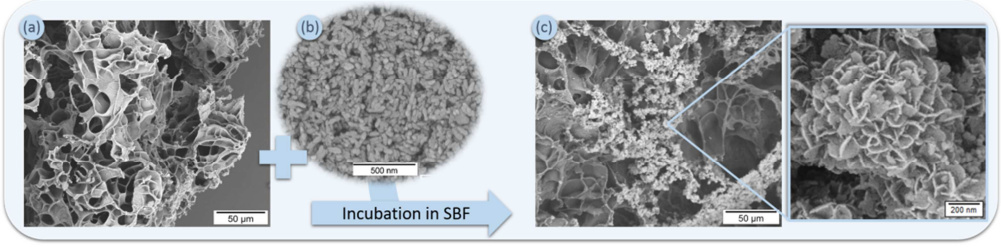

Figure 1. SEM images of (a) PEG-acetal-DMA hydrogel, (b) vaterite nanoparticles, (c) vaterite-loaded hydrogel after 24 h incubation in SBF.

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PO31: Side chain thiol-functionalized poly(ethylene glycol) by postpolymerization modification of hydroxyl groups: synthesis, crosslinking and inkjet printing

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Keywords: Functional poly(ethylene glycol), hydrogels, inkjet printing

Poly(ethylene glycol) (PEG) is a non-toxic, hydrolytically stable and water-soluble polymer.[1] It has been used for various applications, *e.g.* in drug delivery, tissue engineering or surface coatings.[2] In order to broaden the scope of PEGs, a general aim involves the introduction of functional groups which allow cross-linking of the polymers to hydrogels or the covalent attachment of *e.g.* drugs. In this study, polymers with a poly(ethylene glycol) backbone and mercaptomethyl side chains were developed, characterized, cross-linked to polymer networks using acrylate crosslinkers, and processed by inkjet printing.

The synthetic strategy to the polymers contained post-polymerization modification of hydroxymethyl side chains. As the starting point of the synthetic route, linear copolymers of ethylene oxide and glycidol with molar contents of glycidol repeating units of approximately 20, 40, 60, 80 and 100% were used. The polymer-bound hydroxyl groups were converted to thiol groups in three steps, comprising tosylation, introduction of a triphenylmethyl protected thiol and thiol deprotection by acid treatment. The degree of thiol-functionalization was controlled by the degree of functionalization of the starting material. The degree of conversion of hydroxyl groups to thiol groups determined by ^{1}H NMR spectroscopy was quantitative for copolymers with approximately 20 and 40% glycidol repeating units and 92, 81 and 87% for copolymers with approximately 60, 80 and 100% glycidol repeating units, respectively. Exemplarily, poly(glycidylthiol) obtained by conversion of poly(glycidol) was crosslinked with poly(ethylene glycol) diacrylate (PEG-DA) to yield hydrogels which supported adhesion and proliferation of human fibroblasts 48 h after cell seeding. Spatially defined and surface attached gel structures were fabricated by subsequent inkjet printing of poly(glycidylthiol) and PEG-DA solutions onto acrylated glass slides.

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PO32: Stimulus-Responsive Hydrogel Vaccine Depots

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Keywords: biohybrid materials, stimulus-responsive, vaccination, hydrogels

Vaccination is one of the most powerful and effective preventive health measure to protect people from infectious diseases. However, most vaccines require boost injections leading to poor patient compliance and thus to a significant percentage of the population which is not well protected. Reducing the number of required medical consultations and hence simplification of the vaccination regime might be a promising approach to increase the global health. We present a novel strategy to reduce repetitive vaccine injections using a biohybrid hydrogel depot that enables the timely controlled release of the boost vaccine in response to an orally available stimulus. To maximize safety and biocompatibility the hydrogel design was exclusively based on components routinely used in the clinics. The drug depot can be administered together with the primary vaccine dose thereby replacing subsequent injections with oral application of a trigger tablet. Vaccination of mice against the oncogenic human papilloma virus type 16 demonstrated the functionality and safety of our hydrogel depots mediating an immunoprotection equivalent to the classical multi-injection vaccination regime.[1] We propose that our hydrogel depot represents a rather generally applicable design for custom-tailored stimulus-responsiveness and patient compliant delivery of vaccines or even other cargo pharmaceuticals.

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PO33: Towards porous bio-functional materials based on virus-derived nucleoprotein domains and branched DNA hybrid linkers

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Keywords: Tobacco mosaic virus, nucleic acid scaffold, 3D nucleoprotein lattice, bio-functional material

Tobacco mosaic virus (TMV) derivatives offer promising perspectives as biotemplate building blocks for nanotechnological applications. We aim to generate a novel type of porous bio-functional material by assembling functionalized TMV-like particles into nucleic acid lattices with control over their spatial arrangement by use of branched DNA hybrid linker molecules.
TMV is a tube-shaped plant virus with a length of 300 nm, an outer diameter of 18 nm and a hollow channel of 4 nm width. The exceptionally stable TMV nanotube consists of a single-stranded 6395 nt RNA that is helically encapsulated by a well-defined number of identical coat protein (CP) subunits in a predetermined geometry. Modifying the CPs genetically and chemically allows for selective coupling of functional molecules. By combining CPs with RNA constructs that include a TMV origin of assembly sequence, novel nanostructures can be designed and assembled *in vitro*.
To arrange numerous TMV particles into higher-order super-structured materials in a spatially controlled manner, we used DNA hybrid molecules as branched linkers. They each consist of an organic core and four dinucleotide DNA arms [1]. The tetrahedron shape of each DNA hybrid enables the formation of a three-dimensional nucleic acid lattice that may be interspersed with non-DNA domains, such as TMV.
For the covalent conjugation of TMV-RNA termini to the dinucleotide arms of the DNA hybrids, three different ligases were evaluated: T4 RNA ligase 1 [2], T4 RNA ligase 2 and T4 DNA ligase. The latter two were tested in the presence of deoxyoligonucleotide splints as they recognize double-stranded RNA/DNA as substrates, while T4 RNA ligase 1 is able to ligate single-stranded RNA or DNA. We could show that T4 RNA ligase 1 is the only enzyme catalyzing the ligation of DNA-termini of DNA hybrids as well as of test substrates (DNA oligomers of comparable molecular weight) to the RNA termini. A ratio of about 1:1 of DNA to RNA termini was crucial for the efficiency of the reaction and promoted the formation of DNA hybrids with RNA linked to all four DNA arms, which was confirmed by a gel shift assay. It showed that hybridization of complementary DNA oligos to the ligated RNA arms reduced the products' mobility in the gel, while incubation with non-complementary DNA oligos did not.
The RNA-guided self-assembly of stiff TMV-like particles together with the rigid tetrahedral DNA hybrids as linker molecules is expected to provide the possibility of creating 3D nucleoprotein lattices with adjustable pore size and selectively addressable protein domains. These may give rise to novel functional materials for various applications.

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PO34: Liquid Precursors of Pharmaceutical Compounds

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Keywords: PILP, precursor, dissolution, analgesic, ibuprofen, diclofenac.

With the advent of high-throughput screening in the pharmaceutical industry, nowadays highly potent candidates can be discovered more frequently. However, these new chemical entities exhibit poor solubility in water which restrains the resorption of the drug and consequently, reaching the site of action. Due to this issue, up to 75 % of these newly discovered drugs are poorly soluble in water [1]. The formulation of these compounds for oral delivery presents one of the greatest challenges to formulation scientists in the pharmaceutical industry today.
A completely new approach for enhanced dissolution is given by the generation of the polymer-induced liquid precursor (PILP) phase of a pharmaceutical compound. This procedure represents a versatile method to create different products with enhanced dissolution rate. By employing different pH values, the size and composition of the PILP droplets can be tuned and furthermore the properties of the final products. The droplets can be crystallized to obtain objects on the micrometer scale (Fig. 1 a). Also, the PILP mixture can be lyophilized in order to yield a three-dimensional network with increased surface area, assessed by nitrogen sorption (Fig. 1 b). *In vitro* dissolution studies in simulated intestinal fluid proved the superior dissolution rate of this formulation in comparison with the milled powder. Further research could provide a better understanding of the crystallization of organic molecules and pave the way for accessing efficient formulations of a variety of pharmaceutical compounds.

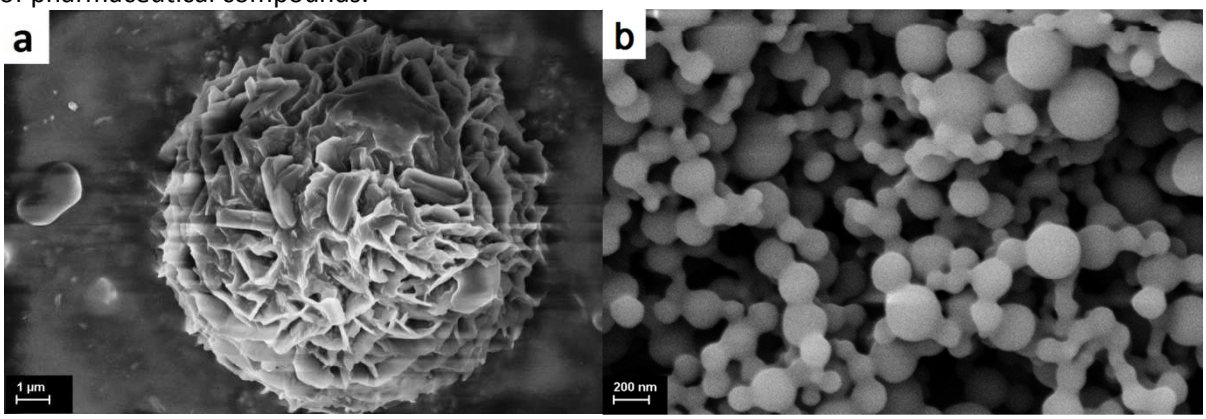

Figure 1. Crystallized microparticle of an ethanol/water/diclofenac/PEI PILP mixture (a). Amorphous diclofenac nanoparticles obtained from the PILP mixture after lyophilization (b). The particles build up a three-dimensional network with increased surface area for enhanced dissolution.

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Notes:

Voucher for one drink (beer/wine) at the poster session

Voucher for one drink (beer/wine) at the poster session