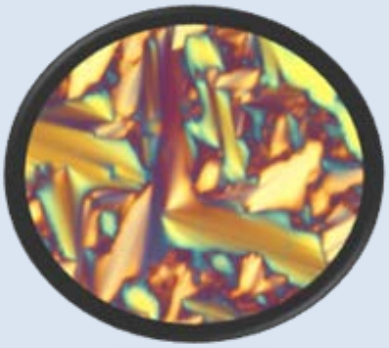
ERC Grantees Conference 2016

August 31 - September 2 | Zandvoort | The Netherlands



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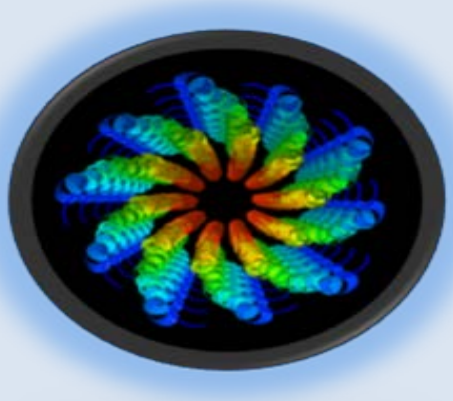

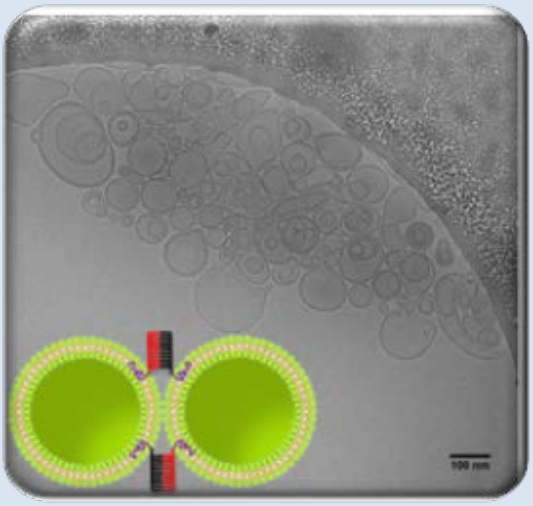

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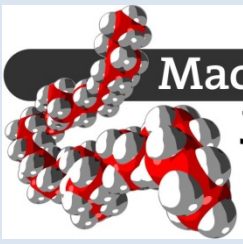

Macromolecular Journals

university of groningen / faculty of mathematics and natural sciences / zernike institute for advanced materials

August 31, 2016

Dear Participants,

Welcome to the 3rd ERC Grantees Conference 2016 in Zandvoort!

We hope that you will enjoy the meeting and the location at one of the most famous beaches in the Netherlands. Two very successful ERC laureate conferences were already organized in 2012 in Strasbourg and in 2014 in Berlin. With this meeting, we would like to continue this series by inviting Europe's leading experts in the arena of chemistry with an emphasis on soft materials ranging from small molecule systems over polymers to bioinspired macromolecular assemblies.

The field of organic- and biological materials is moving very fast with established applications in electronics, diagnostics and the biomedical sector. For this conference we have chosen current topics including biohybrid- and biointeractive systems, dynamic self-organization, out-of-equilibrium structure formation, molecular systems designed by evolutionary techniques, adaptive and switchable (macro)molecular structures, minimal artificial live, and bionanochemical systems, which are presented in 23 talks and 35 posters. We will hear about latest results in these areas and will see how they possibly impact future chemical research and development. There will be enough breaks to enter face-to-face discussions with your colleagues either at coffee or lunch times, during a poster session or at the joint barbecue.

Moreover, this conference will offer young scientists the possibility to get in touch with leading researchers who are supported by the European Research Council (ERC) and to learn more about the opportunities offered from the European Commission through the ERC. There will be two poster prizes for young researchers sponsored by Wiley-VCH, one for molecular systems and one for polymer architectures.

We wish you a successful conference with many new interactions, ideas and collaborations and hope that you have a good time at the beach in Zandvoort.

Sijbren Otto
Stratingh Institute for Chemistry
University of Groningen
(Conference organizer)

Andreas Herrmann
Zernike Institute for Advanced Materials
University of Groningen
(Conference organizer)

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Programme

Wednesday 31-08-2016

12.30 – 14.00	**Arrival and Registration**	
14.00 – 14.15	**Welcome**	
	Chair: Andreas Herrmann	
14.15 – 14.45	**Ben Feringa** (University of Groningen, Netherlands)	From Molecules to Dynamic Molecular Systems
14.45 – 15.15	**Andreas Walther** (University of Aachen, Germany)	Trapped and Driven Non-Equilibrium Self-Assemblies and Dynamic Materials
15.15 – 15.45	**Gonen Ashkenasy** (Ben Gurion University, Israel)	Emergence of Complex Functions in Synthetic Replication Networks
15.45 – 16.15	**Coffee break**	
	Chair: Hans Börner	
16.15 – 16.45	**Oren Scherman** (University of Cambridge, United Kingdom)	Smart Supramolecular Sensing with Cucurbit[n]urils
16.45 – 17.15	**Gerard Roelfes** (University of Groningen, Netherlands)	Artificial Metalloenzymes: Design and Application
17.15 – 17.45	**Nicolas Giuseppone** (University of Strasbourg, France)	Supramolecular Self-Assemblies of Triarylamines: Structures, Dynamics, Functions
17.45 – 18.15	**Stefan Hecht** (Humboldt University, Germany)	Controlling Dynamic Covalent Chemistry by Light

Thursday morning 01-09-2016

	Chair: Stefan Hecht	
09.00 – 09.30	**Klaus Müllen** (Max Planck Institute for Polymer Research, Germany)	A POLYMER CHEMISTRY OF GRAPHENES: Synthesis, Processing, Applications
10.00 – 10.30	**Tanja Weil** (Max Planck Institute for Polymer Research, Germany)	Fluorescent Nanodiamonds for Precision Sensing & Drug Delivery Applications
10.30 – 11.00	**Coffee break**	
11.00 – 11.30	**Bert Meijer** (Eindhoven University of Technology, Netherlands)	Supramolecular materials
11.30 – 12.00	**Hans Börner** (Humboldt University, Germany)	Specifically Interacting Polymers
12.00 – 13.30	**Lunch**	

Thursday afternoon 01-09-2016

	Chair: Gerard Roelfes	
13.30 – 14.00	**Tim Liedl** (Ludwig-Maximilians University, Germany)	Molecular sensing with DNA origami
14.00 – 14.30	**Jean-Francois Lutz** (Institut Charles Sandron, France)	Design and Applications of Digital Polymers
14.30 – 15.00	**Olli Ikkala** (Aalto University, Finland)	Biomimetics for functional materials
15.00 – 15.30	**Coffee break**	
15.30 – 16.00	**Alexander Kros** (University of Leiden, Netherlands)	Drug Delivery via Cell Membrane Fusion using Lipopeptide Modified Liposomes
16.00 – 16.30	**Scott Cockroft** (University of Edinburgh, United Kingdom)	Transmembrane Nanopores: from Sensors to Logic Devices and Molecular Machines
16.30 – 17.00	**Jeroen Cornelissen** (University of Twente, Netherlands)	Assembly of Proteins into Cages and Tubes
17.00 – 19.00	Posters	
19.00	**BBQ & bar is open**	

Friday 02-09-2016

	Chair: Jeroen Cornelissen	
09.00 – 09.30	**Wesley Browne** (University of Groningen, Netherlands)	Photo- and Electrochemical switching at interfaces; challenges and opportunities
09.30 – 10.00	**Rafal Klajn** (Weizmann Institute of Science, Israel)	Light-controlled self-assembly of non-photoresponsive nanoparticles
10.00 – 10.30	**Ivan Huc** (Institut Européen de Chimie et Biologie, France)	Molecular recognition using aromatic foldamers
10.30 – 11.00	**Coffee break**	
	Chair: Sijbren Otto	
11.00 – 11.30	**Patricia Dankers** (Eindhoven University of Technology, Netherlands)	Functional, bio-inspired supramolecular polymeric materials – the interplay between covalent and non-covalent bonds
11.30 – 12.00	**David Margulies** (Weizmann Institute of Science, Israel)	Molecules that Generate 'Fingerprints': A New Class of Fluorescent Probes for Chemical Biology and Cryptography
12.00 – 14.00	**Poster prizes, lunch, and farewell**	

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Lecture Abstracts

From Molecules to Dynamic Molecular Systems

Ben L. Feringa

Stratingh Institute for Chemistry, University of Groningen

Nijenborgh 4, 9747 AG Groningen, The Netherlands

b.l.feringa@rug.nl

Keywords: Switches, Motors, Photopharmacology

Summary. Among the major challenges ahead in the design of complex artificial molecular systems is the control over dynamic functions and responsive far-from-equilibrium behaviour. Chemical systems ultimately require control over structure, organization and function of multi-component dynamic molecular assemblies at different hierarchical levels. A major goal is the control over translational and rotary motion.
In this presentation the focus is on the dynamics of functional molecular systems as well as triggering and assembly processes. We design switches and motors in which molecular motion is coupled to specific functions. Responsive behaviour will be illustrated in photopharmacology. The design, synthesis and functioning of rotary molecular motors will also be presented with a prospect toward future dynamic molecular systems

Information on http://www.benferinga.com

- Molecular Machines: *Nature, September 2015*
- Molecular Switches: *Chemistry World, June 2016*

Trapped and Driven Non-Equilibrium Self-Assemblies and Dynamic Materials

Andreas Walther

DWI-Leibniz Institute for Interactive Materials, Forckenbeckstr. 50, 52056 Aachen, Germany

walther@dwi.rwth-aachen.de

The modulation of energy landscapes of self-assembling systems using kinetic control mechanism, energy dissipation schemes and feedback mechanisms provides means to generate new non-equilibrium structures and fundamentally new functionalities inaccessible with classical self-assembly schemes.[1] Some of the most attractive functionalities include adaptation, evolution, self-replication and self-regulation. If designed properly, such systems can be energy-autonomous (for a certain period of time) and show autonomous dynamics that may be pre-orchestrated by setting appropriate starting conditions.
In this talk, I will present a kinetic pathway orchestration to make well-defined hierarchically, structured and compartmentalized particles by a single step heating procedure starting from sequence controlled multiblock copolymers.
Secondly, the talk will cover our approaches towards autonomously dynamic self-assembling systems and hydrogel materials, that can be preprogrammed with lifetimes by imposing simple feedback mechanisms.[2]

References:

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[2] a) T. Heuser, A.-K. Steppert, C. Molano Lopez, B. Zhu, A. Walther, *Nano Lett.* **2015**, *15*, 2213-2219; b) T. Heuser, E. Weyandt, A. Walther, *Angew. Chem. Int. Ed.* **2015**, *54*, 13258-13262.

Emergence of Complex Functions in Synthetic Replication Networks

Gonen Ashkenasy

Ben-Gurion University of the Negev, Beer Sheva, Israel

gonenash@bgu.ac.il

Like many other open systems in nature, living organisms are replete with rhythmic and oscillatory behavior at all levels, to the extent that oscillations have been termed as a defining attribute of life. Additionally, living organisms contain internal circadian clocks that produce rhythms of a 24 hour cycle. Recently, we have started to investigate an important challenge in contemporary Systems Chemistry, that is, to synthetically construct "bottom-up" molecular networks that display such complex behavior. Towards this aim, we utilize catalytic replication networks, which have already served to study emergent phenomena in complex mixtures.[1,2] In the first part of this talk, I will describe the kinetic behavior of small networks of coupled oscillators, producing various functions such as logic gates, integrators, counters, triggers and detectors. These networks are also utilized to simulate the connectivity and network topology observed for the Kai-proteins circadian clocks from the S. elongatus cyanobacteria, thus producing rhythms whose constant frequency is independent of the input intake rate and robust towards concentration fluctuations.[3,4] Then, in the second part, I will disclose our experimental results, showing for the first time that the replication process can also lead to bistability in product equilibrium distribution.[5] We believe that these recent studies may help further reveal the underlying principles of complex enzymatic processes in cells and may provide clues into the emergence of biological clocks.

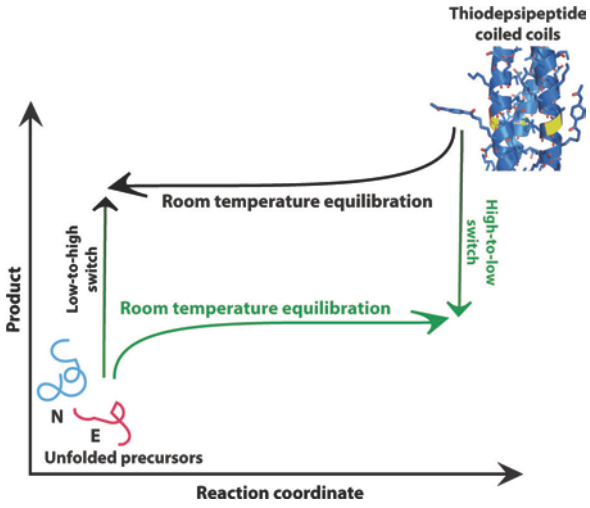

Figure 1. Bistable behavior observed along thiodepsipeptide equilibration experiments.[5]

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[1] Z. Dadon, N. Wagner, G. Ashkenasy, *Angew. Chem. Int. Ed.* **2008**, *47*, 6128.

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[5] R. Mukherjee, R. Cohen-Luria, N. Wagner, G. Ashkenasy *Angew. Chem. Int. Ed.* **2015**, 54, 12452.

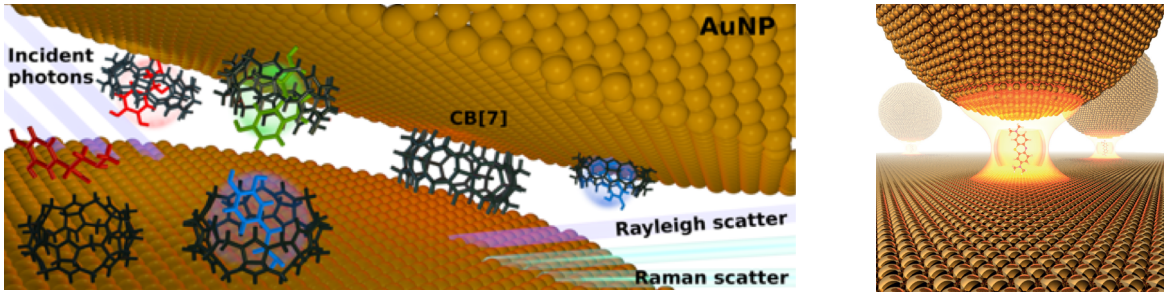
Smart Supramolecular Sensing with Cucurbit[n]urils

Oren A. Scherman

Oren A. Scherman, Melville Laboratory for Polymer Synthesis, Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, UK

oas23@cam.ac.uk

We have utilised the chemistry of cucurbit[n]uril, CB[n], macrocycles for a variety of different applications at interfaces. CB[n]s have attracted increased attention on account of their excellent recognition properties and high binding affinities. The immobilisation of CB[n], especially CB[8], onto surfaces has been a major focus of the Scherman group in the last few years. Recently, we reported the immobilisation of the larger CB[8] macrocycle onto a gold substrate through the formation of a catenane-like structure.[1] This chemically robust motif is able to encapsulate small molecule second guests such as dopamine and detect concentrations as low as 5 x 10^{-8} M. The CB[8] homoternary complex exhibits chemical, redox and photo-responsive behaviour and thus allows for a variety of applications including the formation of polymer brushes[2] on surfaces and nano patterning via colloidal tempting.[3] Moreover, the immobilisation of CB[8] via the formation of a surface-bound catenane structure was recently shown on silica nanoparticles and used as a recyclable nanoplatform for peptide separation.[4] The interactions of CB[n] with gold colloids has also been an area of interest within the group. The use of CB[n] as a molecular ruler to control the aggregation of Au NPs and subsequently bind and detect analyte molecules at room temperature within their cavity is a major area of research in the group.[5] Simple, robust CB[7]-AuNP constructs have shown the ability to detect neurotransmitters through the formation of 1:1 complexes. Using SERS, the detection of these biomolecules within the CB[7] cavity in the CB[7]-AuNP construct was possible. Moreover, this system is capable of performing quantitative multiplexing in biological media such as urine.[6]



(Left) Multiplexing of neurotransmitters in CB[7]-Au NP aggregates. (Right) Single molecule detection at room temperature.

References:

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Artificial Metalloenzymes: Design and Application

Gerard Roelfes

Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands. Email: j.g.roelfes@rug.nl. Web: https://roelfesgroup.nl

The catalytic efficiency and high selectivities achieved by natural metalloenzymes are a source of inspiration for the design of novel bio inspired catalysts. A powerful approach for creating artificial metalloenzymes involves incorporating a synthetic transition metal catalysts into a biomolecular scaffold such as a protein or DNA. We have developed a new concept for the design of artificial metalloenzymes that involves creation of a novel active site at the dimer interface of the transcription factor LmrR (Lactococcal multidrug resistance Regulator) [1]. LmrR was selected as the protein scaffold because it contains an unusual large hydrophobic pocket on the dimer interface. Here, two novel classes of LmrR-based artificial metalloenzymes will be presented, involving either supramolecular anchoring of the metal complex[2] or biosynthetic incorporation of an unnatural metal binding amino acid using expanded genetic code methodology [3]. These artificial metalloenzymes have been applied successfully in catalytic asymmetric C-C bond forming and hydration reactions. Finally, our recent insights into how to design the second coordination sphere will be discussed.

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Supramolecular Self-Assemblies of Triarylamines: Structures, Dynamics, Functions

Nicolas Giuseppone*

University of Strasbourg, Institut Universitaire de France (IUF), Institut Charles Sadron - CNRS, 23 rue du Loess, BP 84047, 67034 Strasbourg Cedex 2, France

giuseppone@unistra.fr

Supramolecular organic electronics rests on the use of bottom-up chemical self-assembly processes in order to design conducting components at the 5–100 nm scale. Challenges in this field are both the construction of 1D-nanostructures displaying optimized transport properties and their precise connections to electrodes. By externally controlling light-responsive supramolecular polymerization processes of tailored triarylamine molecules, and by using appropriate methods of orientation, we have now demonstrated that it becomes possible to pre-determine the accurate positioning of organic interconnects within patterned nano-circuitry.[1–3] Along this main line, we will describe the detailed mechanism of this very original self-assembly process.[4] We will show that supramolecular polymerization can be extended to a number of advanced triarylamine derivatives for the production of various nanostructures.[5–7] We will also discuss the optical and electronic properties of these supramolecular polymers which reveal optical, magnetic, and electronic metallic signatures; the nature of their through-space conduction will be described. Furthermore, the supramolecular dynamics of these assemblies allows for the creation of novel soft materials not accessible with conducting conjugated polymers. In particular, we will show that some triarylamine-based nanofibers demonstrate a mechanism of defect repair driven by polaron diffusion through their supramolecular stacks.[8] We will finally highlight how the presence of such metallic electrons in these organic materials can be used for the first time in the formation of supramolecular plasmonic waveguides and interconnects.[9,10]

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Controlling Dynamic Covalent Chemistry by Light

Stefan Hecht

Humboldt-Universität zu Berlin, Department of Chemistry & IRIS Adlershof,

Brook-Taylor-Str. 2, 12489 Berlin, Germany

sh@chemie.hu-berlin.de

Photoswitchable systems are at the heart of our research program in order to obtain spatio-temporal control over chemical processes, materials' properties as well as the function of optoelectronic devices. For this purpose we are exploring light as a highly selective, non-invasive external stimulus that provides superior resolution in space and time in combination with photochromic molecules, which allow for reversible switching. Our work is therefore devoted to developing and improving photoswitches on the one hand and exploring them in a various settings to gate and thereby control the physicochemical properties of its environment on the other hand.

This presentation will focus on our group's recent work to control thermal chemical reactions by light [1]. For this purpose we have been developing photoswitchable systems, which engage in dynamic covalent chemistry and allow us to influence and even shift chemical equilibria by light [2]. Based on these photocontrolled dynamic covalent systems, we could influence the degree and dynamics of covalent crosslinking in polymeric materials and thereby control the intrinsic self-healing [3] as well as thermal healing properties [4]. The advantages of the new light-programmable soft materials will be discussed and their underlaying design principle will be analyzed from a general mechanistic perspective.

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A POLYMER CHEMISTRY OF GRAPHENES: Synthesis, Processing, Applications

Klaus Müllen

Max Planck Institute for Polymer Research, Mainz, Germany

Graphene is a two-dimensional polymer and thus not only a playground for physics, but also a true challenge for materials synthesis. Herein we present, both, “bottom-up” synthesis and “top-down” fabrication protocols toward graphene, but above all highlight the importance of structural precision in controlling function. The resulting materials properties cover an enormous breadth ranging from batteries, supercapacitors, oxygen reduction catalysts, photodetectors and spin-valves to semiconductors. Graphene nanoribbons (GNRs) hold promise as a new generation of semiconductors with special value for miniaturization of devices. GNRs can be synthesized with ultrahigh molecular weights by both classical solution synthesis and by on-surface synthesis under in-situ STM control. Particularly exciting from, both, a chemical and physical viewpoint are GNRs with zigzag edges.

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Tunneling Junctions Comprising Self-Assembled Monolayers

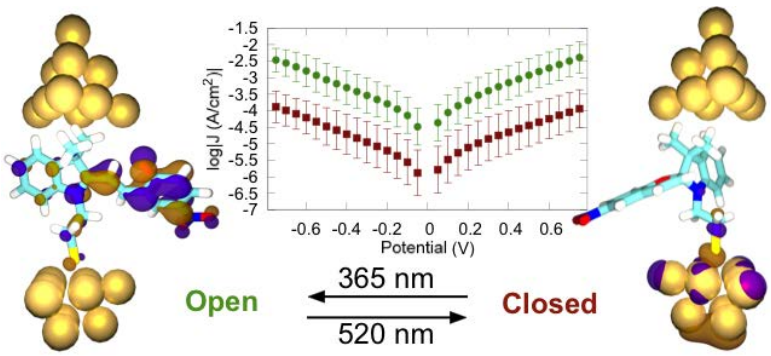
Ryan C. Chiechi

Stratingh Institute for Chemistry and Zernike Institute for Advanced Materials

University of Groningen, Groningen, 9747 AG, The Netherlands

r.c.chiechi@rug.nl

Self-assembled monolayers (SAMs) that define the smallest dimension of a molecular junction serve as a template for both the physical dimensions and electrical details of the tunneling barrier.[1] They are relatively straightforward to address experimentally because the SAM and bottom electrode can be interrogated *ex situ*, but are quite complex on a single-molecule level; defects, domains, boundaries, etc. all affect tunneling charge transport. This talk will focus on efforts to understand the electrostatics of SAMs in junctions formed using eutectic Ga-In and nano-gap electrodes by systematically altering the compounds used to form the monolayers, the conditions under which the junctions are formed, and the local environment of the molecules. In particular, we find that, by including embedded dipole moments and through-space elements in the tunneling pathway, the current that flows through these junctions is dominated by one conformer and the average structure of the monolayer (i.e., determined spectroscopically) and is sensitive to collective effects arising from the crystalline nature of self-assemble monolayers.[2,3] While the details of transport are complicated by the ensemble nature of monolayers, gross features in simulated transmission spectra on single molecules as well as collective effects unique to their two-dimensional structure are clearly reproduced in J/V data. Light-induced switching and gating effects are similarly captured by these relatively straightforward zero-bias calculations.[4] Furthermore, light-induced switching can give insights into the supramolecular structure of SAMs by comparing photoelectron spectra and conductance-switching ratios to the conditions under which the SAMs are formed (shown in the figure below).



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Fluorescent Nanodiamonds for Precision Sensing & Drug Delivery Applications

Tanja Weil[1,2], Martin Plenio[1], Fedor Jelezko[1]

[1] Ulm University, Albert-Einstein-Allee 11, 89081 Ulm, Germany
[2] Max-Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

Fluorescent nanodiamonds (FNDs) are emerging as highly promising nanomaterials for biomedical applications and precision sensing due to their unique optical and magnetic properties.[1] FNDs are obtained by implementing elemental defects into the carbon lattice, such as the nitrogen vacancy (N-V), giving unconditionally stable fluorescence without bleaching or blinking even after several months of continuous excitation. The emission wavelength of FNDs is not size-dependent and is tuneable from the visible to the near infrared region according to the elemental defects. In addition, the N-V center in FNDs serves as single-spin sensor[2] that locally detects various physical properties offering great potential for atomic resolution imaging under physiological conditions. The advent of diamond quantum sensing promises solving the longstanding goal of single molecule detection with atomic resolution under ambient conditions[1] There is currently no other nanomaterial that would offer such features.

The preparation of high quality N-V diamonds and the chemistry of surface modification with i.e. biopolymers[3-4] and proteins[2] provides the basis for quantum sensing and drug delivery in living biological environments. In addition, functionalization of N-V diamonds with proteins or DNA provides access to precisely assembled diamonds on DNA origami to access sophisticated quantum devices[4].

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Supramolecular materials

E.W. Meijer

Institute for Complex Molecular Systems, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, the Netherlands. E-mail: e.w.meijer@tue.nl

The intriguing prospects of molecular electronics, nanotechnology, biomaterials, and the aim to close the gap between synthetic and biological molecular systems are important ingredients to study the cooperative action of molecules in the self-assembly towards functional supramolecular materials and systems. The design and synthesis of well-defined supramolecular architectures require a balanced choice between covalent synthesis and the self-assembly of the fragments prepared. For synthetic chemists, the non-covalent synthesis of these supramolecular architectures is regarded as one of the most challenging objectives in science: How far can we push chemical self-assembly and can we get control over the kinetic instabilities of the non-covalent architectures made? How can we go from self-assembly to self-organization? Where the number of different components is increasing, the complexity of the system is increasing as well. Mastering this complexity is a prerequisite to achieve the challenges in creating functional systems and materials. In the lecture we illustrate our approach towards novel supramolecular materials. In the lecture, the choice between organic liquid crystals, monodisperse polymers or discrete oligomers will be illustrated with examples showing intriguing options for ferroelectricity, nanolithography and polymers with unusual optical and electrical properties.

Specifically Interacting Polymers

Hans G. Börner

Humboldt-Universität zu Berlin, Department of Chemistry, Laboratory for Organic Synthesis of Functional Systems, Brook-Taylor-Str. 2, 12489 Berlin, Germany

H.Boerner@HU-Berlin.de

Recently enormous efforts have been spend to advance polymer synthesis methods, enabling monomer sequence control.[1, 2] Methods of controlled radical polymerization played one major role to precisely position functionalities in synthetic polymers.[3] After principles of advanced precision polymer synthesis routes have been established, one of the upcoming challenges will be finding applicable sequences to demonstrate the potentials of fully synthetic polymers, which exhibit a defined monomer sequence. Here we summarize recent advances and present our approach to extract interesting primary structures by combinatorial means and finding minimal sequences by sequence analysis to design precision polymers. Those polymers offer the possibility to mimic aspects of functional biomacromolecules with non-biological monomer building blocks and might enlarge the functional space available for polymers useful for drug delivery,[4-6] adhesives[7] or nanoengineering of surfaces.[8-10]

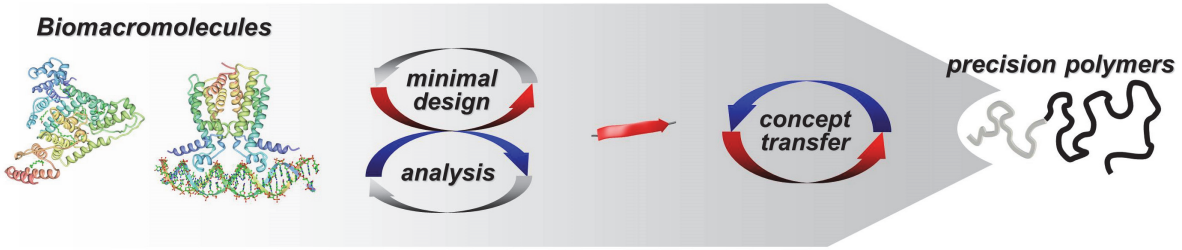

Figure 1. Abstracting principles from peptides to design precision polymers

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Molecular sensing with DNA origami

Tim Liedl

Ludwig-Maximilians-Universität München, Department of Physics, Geschwister-Scholl-Platz 1, 80539 München, Germany, tim.liedl@physik.lmu.de

We use the DNA origami method [1] for the fabrication of functional self-assembled nanoscopic objects and materials [2]. By offering attachment sites for active nano-components on these DNA objects, we have realized complex and nanometer-precise assemblies of fluorophores and plasmonic nanoparticles [3].

Currently we are exploring plasmonic nanoantennas made by DNA origami that can be used as reliable and efficient probes for surface enhanced Raman spectroscopy (SERS). The nanoantennae are built up by pairs of gold nanoparticles on DNA origami templates at separation distances between 9 nm and 4 nm in order to achieve plasmonic coupling and the formation of strong plasmonic 'hot spots' [4].

In recent, unpublished experiments we studied force interactions between biomolecules. Well-established techniques such as atomic force microscopy and magnetic or optical tweezers are usually applied to investigate protein folding or biopolymer – particularly DNA – elasticity. Here we present a nanoscopic DNA origami based single-molecule force spectroscopy device without any physical connection to a micrometer-sized bead or cantilever. We exploit the entropic elasticity of single-stranded DNA to apply tension on a system mounted on the device [5] and single-molecule Förster Resonance Energy Transfer (smFRET) is used as a readout to study two dynamic systems under different tensions: the transition behavior of a Holliday junction and the bending of a DNA promotor sequence induced by the TATA-binding protein (TBP). We are able to generate reliable single-molecule force spectroscopy data in the piconewton range in a high throughput fashion. Our DNA origami force spectrometer can in principle be employed with a wide variety of DNA interacting biomolecules.

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Design and Applications of Digital Polymers

Jean-François Lutz

Precision Macromolecular Chemistry, Institut Charles Sadron

23 rue du Loess, 67034 Strasbourg, France.

jflutz@unistra.fr

Information-containing macromolecules are polymers that contain a message encrypted in their comonomer sequences.[1-2] The archetypal example of such a polymer is DNA, which stores genetic information in living organisms. However, DNA is not the only polymer that can contain molecular information. In principle, a string of information can be created in any copolymer using predefined monomer alphabets. For instance, binary information can be written in a polymer using two monomers defined intentionally as 0- and 1-bit. Yet, such polymers have to be monodisperse and perfectly sequence-defined. In addition, the message stored in their chains should be easily and rapidly read.

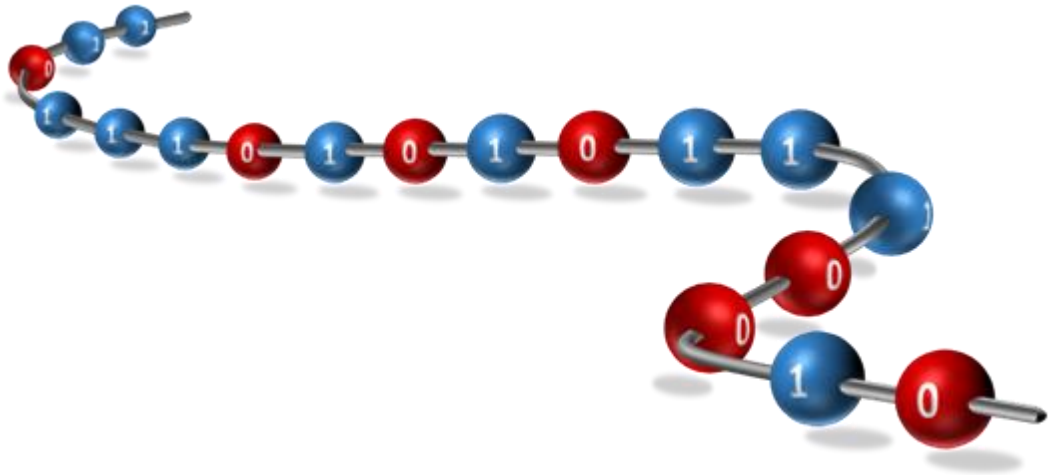

Figure 1. Schematic representation of an information-containing macromolecule that stores a monomer-encoded binary message. Blue and red spheres represent digital monomer units.

In this lecture, I will present recent achievements obtained in my laboratory for the synthesis of digital polymers. Recent progress in the field of sequence-controlled polymers allows synthesis of non-natural macromolecules with precisely controlled primary structures.[3-6] For example, uniform sequence-coded polymers, such as poly(phosphodiester)s, poly(triazole amide)s, poly(alkoxyamine amide)s, poly(alkoxyamine phosphodiester)s and polyurethanes can be prepared by solid-phase chemistry.[7] In addition, the sequencing of digital polymers by tandem mass spectrometry or using nanopores will be discussed. Examples of applications will be also presented in this lecture, for example the development of oligomer barcodes for traceability and anti-counterfeiting applications.

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Biomimetics for functional materials

Olli Ikkala

Aalto University, Department of Applied Physics, Molecular materials, P.O. Box 15100, FIN-00076 Aalto, Espoo, Finland

Structural materials of the Nature involve hierarchical self-assemblies from molecular scale to macroscale. Therein, the various structural components and interactions work in a balanced way to allow synergistic multifunctional properties. In this talk, biomimetic materials are described aiming at new functionalities. Cellulose nanocrystals (CNC) are colloidal rods of diameter of ca. 7 nm and length 100-200 nm with exciting mechanical properties. They assemble in cholesteric liquid crystals. We show that the inherent chiral twisting of the individual CNCs allow chiral plasmonics by templating gold nanoparticles [1]. Side chain brushes can be polymerized along the CNCs, and diblock copolymers can be bonded by interpolyelectrolyte complexation. Depending on the brush and block copolymer molecular weight, different surface topographies are observed, including screw-like patterns [2]. The side chain brushes can also be decorated by hydrogen bonding supramolecular groups to provide fracture toughness for the colloidal nanocomposite [3]. By contrast, if longer and entangled cellulose nanofibers (CNF) are used instead of the shorter CNCs, new property-combinations are obtained. CNF allows lightweight and porous aerogels. By selecting the processes, either deformable “sponge-like” materials or aerogel films with high tensile strength are obtained [4,5]. They can be modified with carbon nanotubes, allowing mechano-responsive conductivity or transparent conducting films. CNF can also be 3D-printed for fibers or meshes. CNF fibers are highly biocompatible, allowing even growing of stem cells and surgical fibers [6]. On the other hand, pearl of nacre is a prototypic material for strong and tough biological nanocomposites involving plate-like assemblies. We describe a method to construct bulk nacre-mimetic nanocomposites using nanoclay assemblies having fracture and crack deflection properties approaching that of nacre [7].

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Drug Delivery via Cell Membrane Fusion using Lipopeptide Modified Liposomes

Alexander Kros

Dept. Supramolecular & Biomaterials Chemistry, Leiden Institute of Chemistry, Leiden University, Einstenweg 55, 2333CC Leiden, The Netherlands

A.kros@chem.leidenuniv.nl

Efficient delivery of drugs to living cells is still a major challenge. Currently, most methods rely on the endocytotic pathway resulting in low delivery efficiency due to limited endosomal escape and/or degradation in lysosomes. Here, we report a new method for direct drug delivery into the cytosol of live cells *in vitro and vivo* utilizing targeted membrane fusion between liposomes and live cells. A pair of complementary coiled coil lipopeptides was embedded in the lipid bilayer of liposomes and cell membranes respectively, resulting in targeted membrane fusion with concomitant release of liposome encapsulated cargo including fluorescent dyes and the cytotoxic drug doxorubicin. Using a wide spectrum of endocytosis inhibitors and endosome trackers we demonstrate that the major site of cargo release is at the plasma membrane. This method thus allows for the quick and efficient delivery of drugs and is expected to have many in-*vitro, ex-vivo* and in-*vivo* applications.

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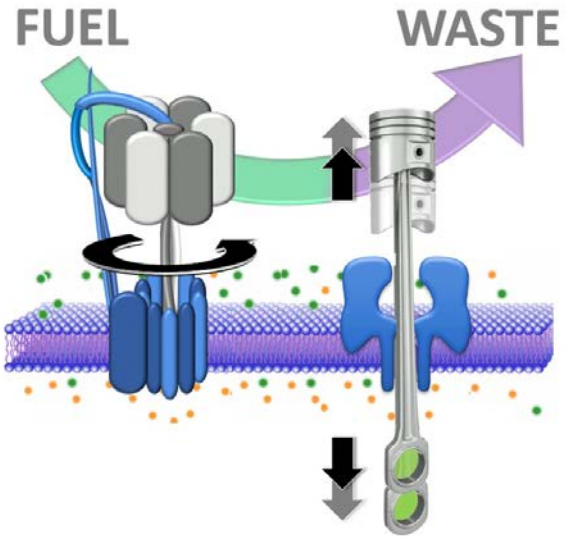
Transmembrane Nanopores: from Sensors to Logic Devices and Molecular Machines

Scott L. Cockroft, Matthew A. Watson, James A. Cooper, A. Bader

Scott L. Cockroft, University of Edinburgh, EaStCHEM School of Chemistry, Edinburgh, UK

scott.cockroft@ed.ac.uk

Membrane-bound channel proteins that undergo nanomechanical transitions to facilitate detection, communication and transportation are ubiquitous in nature. Similarly, such transmembrane proteins can also be exploited as components for the construction of nanoscale devices built to man-made specifications.[1] This talk will outline the evolution of nanopore-based approaches from sensor applications to the development of man-made molecular machines. The first part of the talk will illustrate how protein-based nanopores can be used as a sensor element for resolving supramolecular chirality[2] and the dynamics of nanomechanical translocation of DNA through the pore.[3] Taking inspiration from the ligand-gated acetylcholine receptors involved in biological neural responses, a man-made logic device that operates and provides logical-readouts on the single-molecule level will be introduced.[4] Finally, I will present a nanopore-based molecular machine that turns over fuel molecules to drive autonomous reciprocating (back-and-forth) nanomechanical motion and shares many characteristics with biological transmembrane pumps.[5]



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Assembly of Proteins into Cages and Tubes

Jeroen J.L.M.Cornelissen

Jeroen J.L.M. Cornelissen, Laboratory for Biomolecular Nanotechnology, MESA+ Institute for Nanotechnology, University of Twente, PO Box 217, 7500AE, Enschede, the Netherlands

j.j.l.m.cornelissen@utwente.nl

Protein cages are common structures in biology that can have profoundly different functional properties.The majority of these icosahedral organized particles is found in viruses, structures designed to hijack the molecular machinery of the host cell, while in a variety of bacteria these protein cages have organelle-like functions. In our group we aim to design and control the assembly of proteins into cages and tubes of well-defined dimensions, to use these e.g. as a nanoreactor and scaffold for functional materials. The novel properties introduced to these biological nanostructures combined with the enormous variety protein assemblies can form has led to the firm believe that new materials with interesting, chemical, physical and biological, properties are accessible.

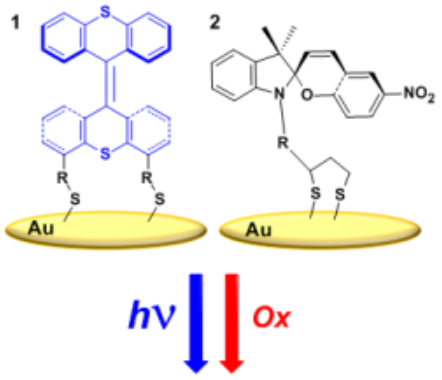
Photo- and Electrochemical switching at interfaces; challenges and opportunities

Wesley R. Browne

Wesley R. Browne, Molecular Inorganic Chemistry, Stratingh Institute for Chemistry, Faculty of Mathematics and Natural Sciences, University of Groningen

w.r.browne@rug.nl

Responsive surfaces built on functional molecular systems open up a myriad of opportunities in the development of smart surfaces – enabling chemical fine tuning and often reversible control of surface properties such as wetting, adhesion, catalytic activity. A central question arises however in immobilising molecular systems on surfaces as to how their properties are influenced by confinement. In this lecture the functionality of several molecular switches, in particular spiropyrans, in solution, in self assembled monolayers and in polymer films will be discussed. In particular, the methods applicable to explore its photochromic, thermal and electrochemical properties. I will focus on the well-known spiropyran motif, in which it will be demonstrated that the photo- and electrochemical properties are heavily influenced by both immobilisation and, critically, by the invasiveness of spectroscopic techniques used to characterise the functioning of the hybrid inorganic-organic devices formed[1,2,3]



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Light-controlled self-assembly of non-photoresponsive nanoparticles

Rafal Klajn, Martin Börner, Pintu K. Kundu, Ron Leizrowice, Debasish Manna, Baruch Margulis, Dipak Samanta, T. Udayabhaskararao, Hui Zhao

Department of Organic Chemistry, Weizmann Institute of Science, Rehovot 76100, Israel

rafal.klajn@weizmann.ac.il

The ability to guide the assembly of nanosized objects reversibly with external stimuli, in particular light, is of fundamental importance, and it contributes to the development of applications as diverse as nanofabrication and controlled drug delivery. However, all the systems described to date are based on nanoparticles that are inherently photoresponsive [1-3], which makes their preparation cumbersome and can markedly hamper their performance. In this talk I will describe a new methodology to assemble nanoparticles reversibly using light that does not require the particles to be functionalized with light-responsive ligands [4]. This strategy is based on the use of a photoswitchable medium that responds to light in such a way that it modulates the interparticle interactions. nanoparticle assembly proceeds quantitatively and without apparent fatigue, both in solution and in gels. Exposing the gels to light in a spatially controlled manner allowed us to draw images that spontaneously disappeared after a specific period of time. Recently, we have extended this methodology to aqueous environments, allowing us to interface our nanoparticles with biological systems [5].

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Molecular recognition using aromatic foldamers

Ivan Huc

CNRS-Univ. Bordeaux, European Institute of Chemistry and Biology

2 rue Escarpit, 33600 Pessac (France)

i.huc@iecb.u-bordeaux.fr

Aromatic amide oligomers constitute a new, distinct, and promising class of synthetic foldamers – oligomers that adopt stable folded conformations. Single helical structures are predictable, show unprecedented conformational stability, and constitute convenient building blocks to elaborate synthetic, very large (protein-sized) folded architectures. They possess a high propensity to assemble into double, triple and quadruple helices, or to fold into sheet-like structures. Cavities can be designed within such synthetic molecules that enable them to act as artificial receptors and molecular motors. Water soluble analogues of these foldamers show promise in nucleic acid and protein recognition (Fig. 1). This lecture will give an overview of the molecular recognition properties of these functional molecular architectures.[1-6]

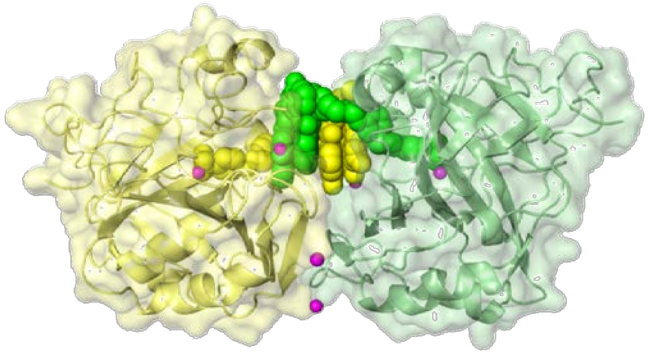

Figure 1. Crystal structure of a protein-foldamer complex.

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Functional, bio-inspired supramolecular polymeric materials – the interplay between covalent and non-covalent bonds

Olga J.G.M. Goor, Maxime O. Grillaud, Peter P.K.H. Fransen, Maarten H. Bakker, Patricia Y.W. Dankers

Eindhoven University of Technology, Institute for Complex Molecular Systems, and Department of Biomedical Engineering, Laboratory of Chemical Biology, Laboratory for Cell and Tissue Engineering, Eindhoven, The Netherlands
p.y.w.dankers@tue.nl

Full integration of synthetic materials into living tissues requires the interplay between synthetic and living materials in a spatiotemporal way, i.e. the process of dynamic reciprocity plays an important role. Bio-inspired materials based on supramolecular units intrinsically show this dynamic behavior. However, the development of materials with stable bioactivity presentation and with good mechanical properties demands for the incorporation of covalent bonds. Inspired by nature we have combined supramolecular bonds based on hydrogen bonding, pi-pi stacking and hydrophobic interactions, with covalent bonds in order to incorporate (bio)functionality on supramolecular thermoplastic elastomers, and to introduce robustness in supramolecular hydrogel systems. Reactive additives have been supramolecularly incorporated in thermoplastic elastomers that can be covalently post-modified with reporter molecules and/or proteins. Importantly we showed that the application of in depth 3D ToF-SIMS profiling resulted in elucidation of the bulk and surface composition of such polymeric materials. Furthermore, the introduction of additional chemical crosslinks in supramolecular hydrogel systems has shown to improve the mechanical properties while self-healing behavior is still displayed. In this way the control of both biological and mechanical properties in synthetic polymeric materials is regulated in a comparable way as natural polymers in the extracellular matrix control these properties; en route to synthetically meet nature's complexity.

Molecules that Generate 'Fingerprints': A New Class of Fluorescent Probes for Chemical Biology and Cryptography

David Margulies

David Margulies, Department of Organic Chemistry, Weizmann Institute of Science, 76100 Rehovot, Israel

david.margulies@weizmann.ac.il

Our group has recently developed a new class of molecular sensors, termed 'combinatorial fluorescent molecular sensors', which mimic the function of cross-reactive sensor arrays (the so-called chemical "noses/tongues").[1-3] In this talk I will explain how these pattern-generating probes can be used to analyze specific populations of proteins in complex mixtures and within live cells. In addition, I will show how secret messages can be concealed within the emission spectra of these unimolecular analytical devices.[4]

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Poster Abstracts

Transducing Light Energy Giant Vesicles

Altamura E.,* Milano F., Trotta M., Stano P., Mavelli F.

*Via Orabona 4, 70126, Dipartimento di Chimica, Università "Aldo Moro" Bari-Italy

emiliano.altamura@uniba.it

The photosynthetic reaction center (RC) is a transmembrane pigment-protein complex that plays a major role in the photochemical conversion of light into chemical energy in plants, algae and photosynthetic bacteria[1,2]. It couples light-induced electron transfer to the generation of a proton concentration gradient across a lipid membrane, via reactions involving a quinone molecule that binds two electrons and two protons at its active site. The so-obtained electrochemical gradient can be harnessed to synthesize ATP[2]. In a previous work[3] it has been shown that the reconstitution of functional, but randomly oriented, RC is possible in conventional (diameter 50-100 nm) lipid vesicles typically obtained by the detergent depletion method[4]. Following a bottom-up approach thanks to the droplet transfer method for giant lipid vesicles (1-100 µm) preparation, here we show that synthetic protocells, embedding a highly oriented reaction center, are capable of generating a photo-induced proton gradient across the membrane. Under constant illumination, protocells generate 0.06 pH gradient units in one minute, contributing to a proton motive force of 3.4 mV per minute.

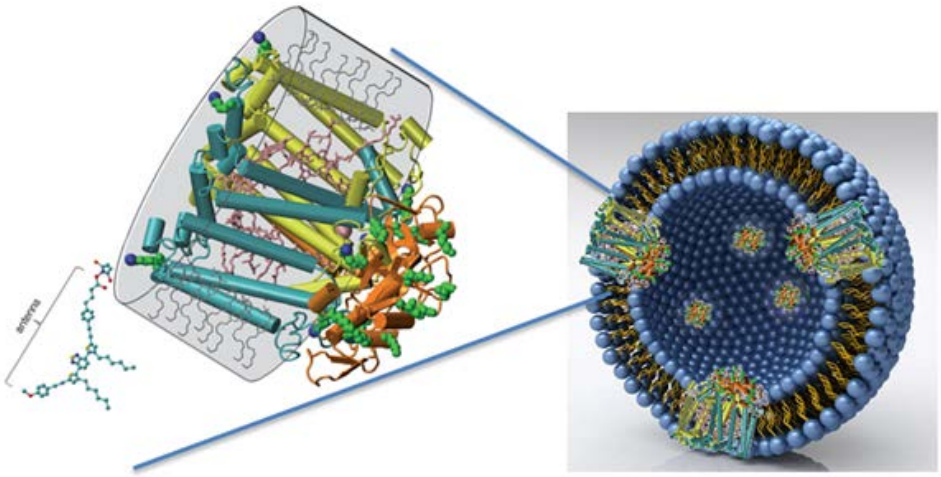

Fig. 1. Highly oriented photosynthetic RCs within the GV membrane.

Remarkably, the facile assembly of the sophisticated reaction center into the synthetic lipid membrane, as obtained by the droplet transfer method5, paves the way to the construction of novel and more functional protocells for synthetic biology.

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Template Assisted Emergence of Self-Replicators from Dynamic Combinatorial Libraries

Yiğit Altay, Sijbren Otto

University of Groningen, Center for Systems Chemistry, Stratingh Institute of Chemistry, Nijenborgh 4, 9747 AG, Groningen The Netherlands

y.altay@rug.nl

One of the most fundamental questions at the interface between biology and chemistry is what constitutes the minimal molecular basis of life. There is a big gap in our knowledge considering the early steps of the formation of evolvable life. Systems chemistry, and dynamic combinatorial chemistry in particular, is a promising approach to address this intriguing question.

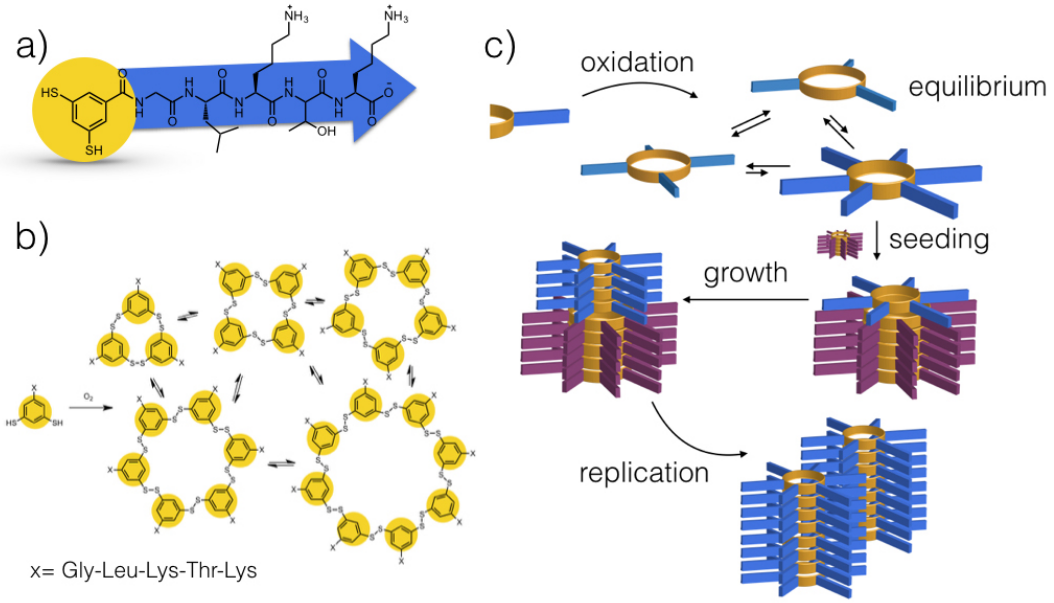

Fig. 1. a) Chemical structure of Thr containing peptide. **b)** Formation of different sized macrocycles in a dynamic combinatorial chemistry. **c)** Schematic representation of template assisted emergence of self-replicators.

Self-replicators, constructed from β-sheet prone peptide building blocks, emerges from a dynamic combinatorial libraries that is under thermodynamic control[1]. If the energy profile of the system is shallow enough, various parameters such as ionic strength, co-solvent[2], and use of template would allow us to access different sized replicators made out of the same building blocks. In this study, we demonstrate template assisted emergence of a new self-replicator using threonine (Thr) containing peptide building block which by itself only forms trimers and tetramers that do not show any replication behaviour. Upon seeding of the very library with different sized replicators (hexamers and octamers), we observed the emergence of hexamer replicator of Thr peptide only when it is seeded with an octamer replicator. This result is the first example of access to a novel replicator using another replicator as a template.

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From Adaptive to Surface-Confined Self-Assembly

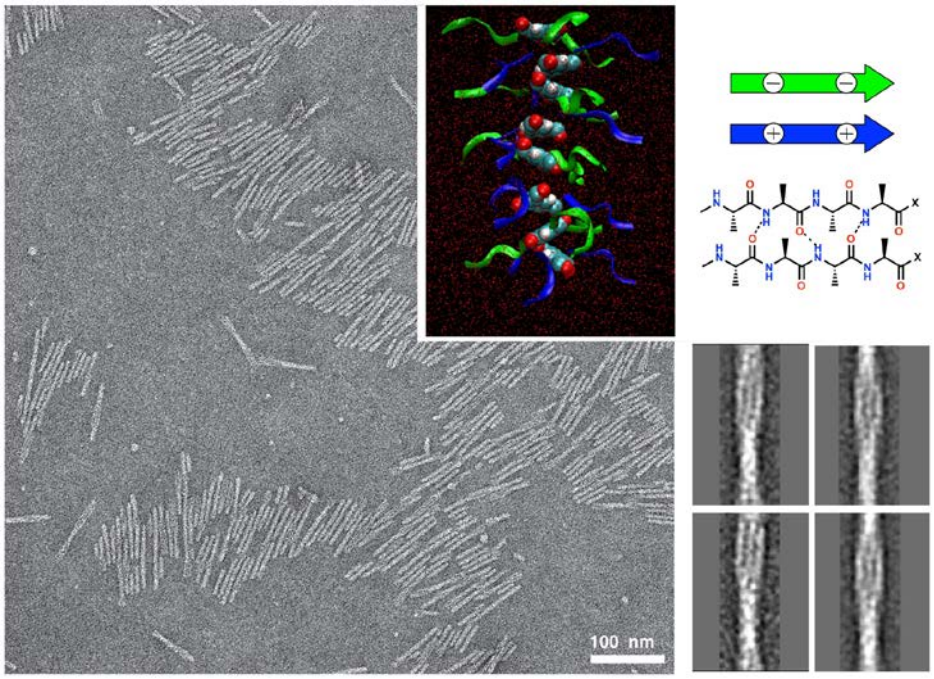
Pol Besenius, Patrick Ahlers, Hendrik Frisch, Daniel Spitzer

Institute of Organic Chemistry, Johannes Gutenberg-Universität Mainz

besenius@uni-mainz.de

Self-assembly of molecular building blocks into ordered architectures, polymers and materials opens exciting avenues for fundamental developments in nanoscience and applications in biomedical technologies, optoelectronics and catalysis. Our young group designs supramolecular building blocks for controlling dynamic self-assembly processes in water and off surfaces. I will discuss our efforts in controlling adaptive supramolecular polymerisations through a variety of strategies, including recent work on surface confined growth of chiral supramolecular polymers (*Angew. Chem.* **2016**).

Inspired by protein functionality in their biological setting, we have designed *electrostatic- and pH-regulated supramolecular polymerisations* in water *(Angew. Chem.* **2013***, Chem. Eur. J.* **2015***, Polym. Chem.* **2015***).* The synthons are based on β-sheet encoded anionic and cationic peptides that form supramolecular alternating copolymers with a nanorod-like morphology. The materials have been designed for on-off polymerization in response to pH triggers. The self-assembly is switched on at a physiologically relevant pH value and can be switched off by increasing or decreasing the pH value. The pH at which the transition occurs can be tuned by the design and reactivity of the supramolecular comonomer, behaviour that is in agreement with the self-assembly of protein based morphologies and virus particles.
In a second strategy we use *frustrated self-assembly*, that describes the balance of positive non-covalent interactions with repulsive forces. This has allowed us to control and manipulate the size, shape and stability of supramolecular nanorods in water. (*J. Mater. Chem B* **2013**, *Org. Biomol. Chem.* **2015**, *Chem. Eur. J.* **2015**). In view of recent reports that anisotropic shapes in the design of biomedical carrier materials outperform conventional isotropic structures, our designs will have implications for applications in imaging and therapy.



Core-shell Rare Earth-YVO_4@SiO_2 Nanocomposites and their Functional Hybrids for Fluorescence Imaging of Prostate Cancer Cells

M.S. Bernardo,[1] V. Mirabello,[2] H. Ge,[2] D. G. Calatayud,[2,3] L. Alcaraz,[4] P. Arevalo,[4] J. Isasi,[4] T. Jardiel,[3] A.C. Caballero,[3] M. Peiteado,[1]* S. I. Pascu[2]*

1. POEMMA-CEMDATIC, ETSI Telecomunicación (UPM), 28040, Madrid, Spain

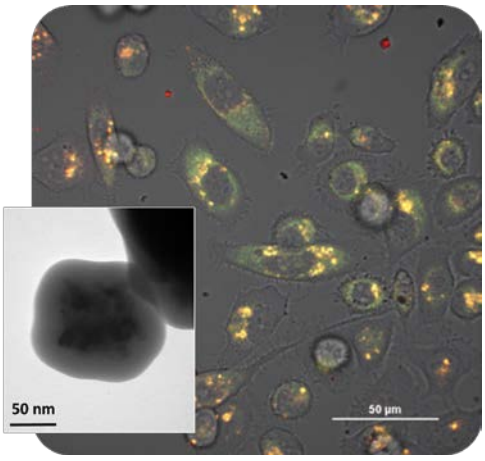
2. Depart. of Chemistry, University of Bath, Claverton Down, BA2 7AY, Bath, UK

3. Depart. of Electroceramics, Instituto de Cerámica y Vidrio (CSIC), 28049 Madrid, Spain

4. Depart. of Inorganic Chemistry I, Universidad Complutense de Madrid, 28040, Madrid, Spain

dgcalatayud@icv.csic.es, s.pascu@bath.ac.uk, marco.peiteado@upm.es

The main advantages of optical imaging compared with other imaging modalities are: superior sensitivity, low energy radiation, the capacity to monitor multiple independent optical biomarker reporters simultaneously, and relatively simple imaging hardware. There is a necessity of developing highly sensitive imaging tools which involve the medical applications of luminescent nanoparticles, enabling highly sensitive *in vivo* optical detection.[1,2] The luminescent core-shell nanostructures composed by rare-earth doped transition metal oxides (group IV and V) cores and encapsulated in a silica shell have been synthesized using a soft-processing approach based on hydrothermal synthesis and the Stober process. As such, novel luminescent ceramic nanoparticles, based on core-shell structures composed of rare-earth (RE) doped yttrium vanadate and silica, RE-YVO_4, RE-YVO_4@SiO_2, have been synthesized, functionalised with organic tags and tested as promising candidates for luminescence imaging in cells. The synthetic conditions were optimised to achieve highly homogeneous core-shell structures with spherical morphology and fluorescent properties suitable for *in vitro* imaging. Moreover, the variation of the synthesis parameters enables to modify the size and aqueous media dispersibility of the emerging core-shell nanoparticles. To evaluate the potential application of these compounds as luminescent probes for cell imaging, epi- and fluorescence confocal microscopy studies were carried out in living cells, using a prostate cancer (PC-3) cell line for proof of concept. These results showed that such core-shell nanoparticles are taken-up by the cells and can be successfully used for *in vitro* bio-imaging. The authors would like to thank ERC Consolidator grant scheme (O2SENSE to Dr. Sofia I. Pascu).



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Covalent functionalization of SWNT for the imaging of prostate cancer cells

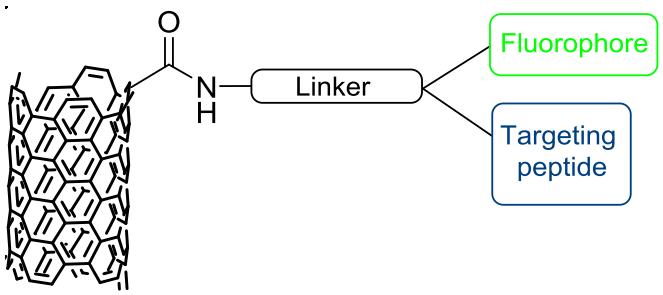
Fernando Cortezon-Tamarit, Haobo Ge, Vincenzo Mirabello and Sofia I. Pascu*

Fernando Cortezon-Tamarit, Department of Chemistry, University of Bath, Claverton Down, Bath, BA2 7AY, United Kingdom

fctc20@bath.ac.uk, sp350@bath.ac.uk

Prostate cancer is the second most common cancer in men and one of the principal causes of mortality.[1] The targeted imaging of prostate cancer has consequently attracted much interest as it allows to detect and delineate prostate cancer tumors.[2] In parallel, the application of carbon nanomaterials to biomedical imaging has showed great promise because of the large surface area and ability to enter into cells. Thus, it became a challenge to discover the most effective way towards converting these platforms into ideal vectors for imaging agents or drug delivery.[3][4] Here, we present the development of an imaging nanoprobe supported on pristine, shortened single-walled carbon nanotubes (SWNT). The SWNT were covalently functionalized *via* two strategies and aliphatic linkers introduced to improve the stability in solution of the nanomaterial which is key to reduce the possible toxicity. In addition, a bifunctional BODIPY fluorophore was synthesized and conjugated to the [7-13] fragment of bombesin, a peptide that targets prostate cancer cells. The fluorophore-peptide conjugate was finally included in the nanoprobe.

The molecular probes and nanoprobes were characterized in detail and the behavior *in vitro* in PC-3 and LNCaP cells evaluated by single-photon confocal microscopy and fluorescence lifetime imaging. The results indicate that the conjugate effectively targets prostate cancer cells and the nanoprobe results in a good platform for the optical imaging of prostate cancer cells and a promising candidate for multimodal imaging through radiolabeling of the fluorophore or the SWNT.



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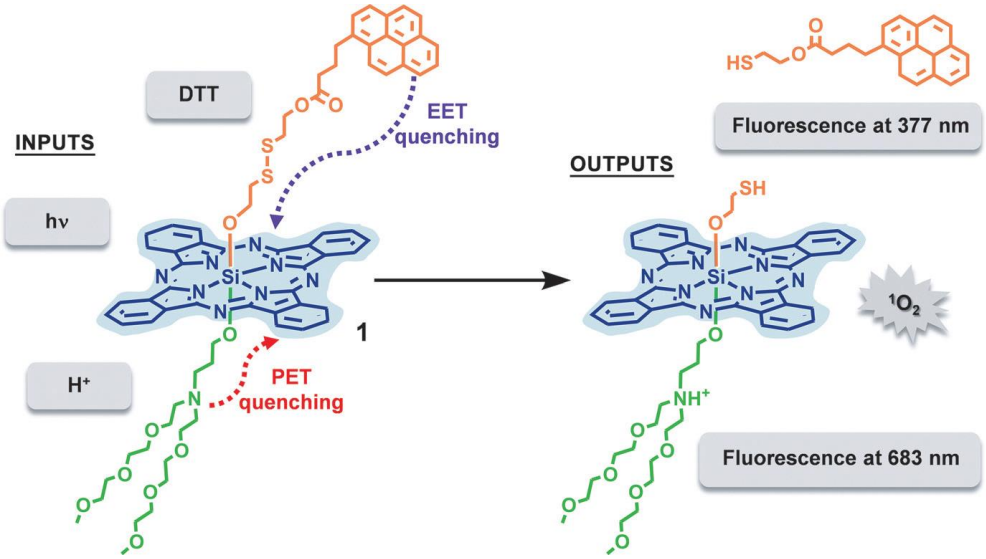
Multifunctional Logic in a Photosensitizer with Triple-Mode Fluorescent and Photodynamic Activity

Andrés de la Escosura, Eveline van de Winckel, Tomás Torres

Organic Chemistry Department, Universidad Autónoma de Madrid, Campus de Cantoblanco, Madrid (Spain)

andres.delaescosura@uam.es

We describe a photosensitizer[1,2] (PS) with the capacity to perform multiple logic operations based on a pyrene-containing phthalocyanine (Pc) derivative. The system[3] presents three output signals (fluorescence at 377 and 683 nm, and singlet oxygen ($^1O_2$) production), which are dependent on three inputs: two chemical (concentration of dithiothreitol (DTT) and acidic pH) and one physical (visible light above 530 nm for $^1O_2$ sensitization). The multi-input/multioutput nature of this PS leads to single-, double-, and triple-mode activation pathways of its fluorescent and photodynamic functions, through the interplay of various interrelated AND, ID, and INHIBIT gates. Dual fluorescence emissions are potentially useful for orthogonal optical imaging protocols while $^1O_2$ is the main reactive species in photodynamic therapy (PDT). We thus expect that this kind of PS logic system will be of great interest for multimodal cellular imaging and therapeutic applications.



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Studying self-assembling bionanostructures using computational techniques

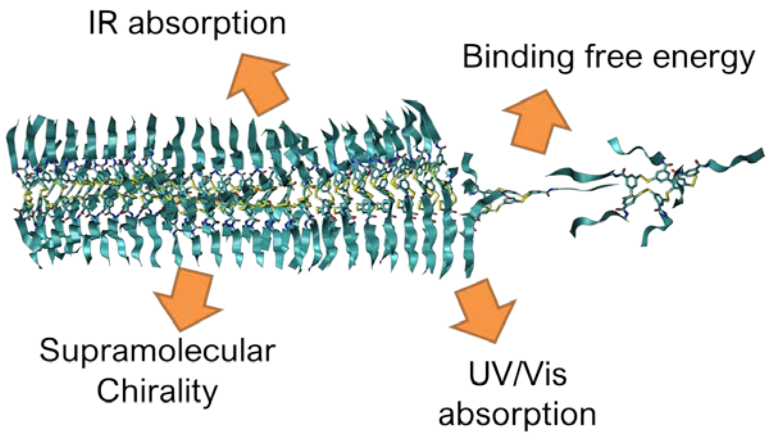
Pim W.J.M. Frederix, Siewert-Jan Marrink, Sijbren Otto

Molecular Dynamics, Groningen Institute for Biomolecular Sciences and Biotechnology, University of Groningen, p.w.j.m.frederix@rug.nl

Several small peptides and their derivatives have been found to spontaneously self-assemble into nanostructured materials such as hydrogels. These materials are starting to find their way to the commercial market in applications such as cell culture scaffolds and additives in food or cosmetics as a consequence of their inherent biocompatibility. However, their structure and function are often very sensitive to environmental conditions and there are no experimental techniques that have enough resolution to determine their molecular packing in realistic environments. This impairs the discovery of new peptidic nanostructures, but also the general understanding of the self-assembly process.

Computational techniques based on Molecular Dynamics (MD) are ideally suited for solving this problem: modern computational resources allow us to monitor molecular motions and packing within self-assembled nanostructures.[1] The steps we take to understand and predict the properties of peptidic nanostructures will be outlined. A combination of multiple levels of theory is used, i.e. coarse-grain MD, atomistic MD, semi-empirical quantum chemical calculations and DFT, to link nanoscale properties directly to experimental observables.

Self-replicating peptide macrocycles[2] are a particularly interesting case study for these methods. Specifically, we have simulated their nanoscale architecture and computed building block binding free energies, supramolecular circular dichroism spectra and infrared absorption spectra and compared these to experimental results.



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Dynamic Disulfide Metathesis Induced by Ultrasound

Urs Fabian Fritze, Max von Delius*

Urs Fabian Fritze, Ulm University, Institute of Organic Chemistry and Advanced Materials,

Albert-Einstein-Allee 11, 89081 Ulm, Germany

fabian.fritze@uni-ulm.de

Dynamic disulfides play an important role in biological systems, most notably in protein chemistry. Over the last decade, dynamic disulfide exchange has also become one of the most powerful tools in dynamic combinatorial chemistry (DCC).[1]

In nature and most man made systems, disulfide exchange is based on an S_N2-type mechanism. Therefore basic conditions, reducing agents and long equilibration times are needed. We report that disulfide metathesis can be initiated simply by sonicating the starting materials in appropriate solvents.[2]

Mechanistic studies revealed that the sonolysis of the solvent ($CHCl_3$) initiates a radical chain reaction, which results in a statistical mixture of products. Although it is possible to carry out the reaction in a conventional ultrasonic bath, the use of a sonotrode leads to remarkably short equilibration times (1 h or less).

This new method for generating dynamic mixtures could be a practical alternative to existing protocols, particularly in scenarios where short equilibration times, base-free reaction conditions or a new vector for dynamic covalent orthogonality are needed.

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Application of new functional carbon based nanomaterials for biomedical imaging

Haobo Ge[1], Stan Botchway[2], Rex Tyrrell[1], Sofia Pascu[1]*

[1]*University of Bath, Claverton Down, Bath, BA2 7AY, United Kingdom*

[2]*Research Complex at Harwell (RCaH), Rutherford Appleton Laboratory, Harwell Oxford, Oxon, OX11 0FA, United Kingdom*

h.ge@bath.ac.uk, s.pascu@bath.ac.uk

Here we present the assembly of a highly selective drug delivery system with the potential to act as hypoxia cancer bioimaging probe. A novel synthetic strategy was developed to generate a boronic acid-based fluorescent sensor. Such fluorophore was tagged with biotin as biomarkers that can be functionalised onto the surface of β-D-glucan-wrapped single walled carbon nanotubes (SWNTs) *via* interaction between boronic acid and hydroxyl groups (scheme 1-1). [1] Such device was successively studied in various healthy cell lines like, CHO cells and FEK4 cells, or cancerous cell lines, such as cervical cancer (HeLa) cells, breast cancer (MCF-7) cells, prostate cancer (PC-3) cells, LnCap cells and EMT6 cells under normoxia and hypoxia conditions. The bio-distribution of the complex was investigated by one- and two-confocal fluorescence microscopy. Cytotoxicity of the complex was tested *via* 3-(4, 5-Dimethyl-2-thiazolyl)-2, 5-diphenyl-2H-tetrazolium bromide (MTT) and lactate dehydrogenase (LDH) assays. Fluorescence-lifetime imaging microscopy (FLIM) was employed to investigate the kinetic stability of the probe and the nature of the interactions between SWNTs, fluorophore and cellular environment. We also explored new strategies for incorporating metal ions from aqueous media, such as Cu^{2+} and Zr^{4} within SWNTs [2] and we investigated the uptake and release efficacy of SWNTs as small molecules and radiolabelled metal ions delivery system. Such internally functionalised SWNTs were characterised by transmission electron microscopy (TEM), scanning electron microscope (SEM), atomic force microscope (AFM) and Raman spectroscopy. Finally, we report the application of such SWNTs for *in vivo* positron emission tomography (PET) imaging studies in a rodent model.

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Rationalizing the impact of subtle structural differences on the properties of hydrogen-bonded assemblies

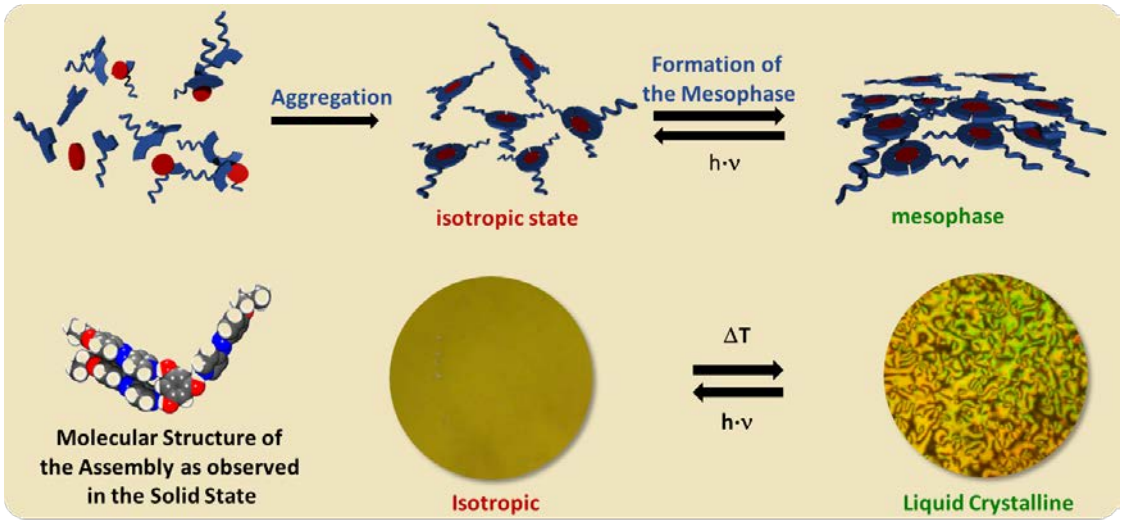
Michael Giese, Michael Pfletscher

Michael Giese, University of Duisburg-Essen, Institute of Organic Chemistry

michael.giese@uni-due.de

In the recent years, Supramolecular Chemistry turned to a powerful tool to create novel functional materials.[1] Employing non-covalent forces provides many advantages compared to conventional methods and facilitates fabrication, processing and recycling.[2] Simple mixing of pre-tailored building blocks at room temperature yields highly functional aggregates via self-assembly and allows dynamic response to external stimuli or damages (self-healing/-repair). By following a modular approach[3] our goal is to systematically investigate the structural parameters and their influence on the liquid crystalline properties of hydrogen-bonded assemblies in order to develop novel functional materials[4] with tailor-made properties.

Our initial study yielded a series of photo-responsive liquid crystals based on the hydrogen-bonded assemblies of phloroglucinol and azopyridine derivatives. In order to create novel materials based on a rational design a deeper understanding of the structure-property relationship is crucial. Therefore, we are currently investigating a series of hydrogen-bonded assemblies based on mono-, di or tri-hydroxybenzene derivatives and correlating the observed structural features of the crystal structures with their mesomorphic behavior.



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pH-Switchable Building Blocks With Quaternary Amines

A. Heimann, C. Schmuck*
Anja Heimann, Institute of Organic Chemistry, University of Duisburg - Essen, anja.heimann@uni-due.de

Supramolecular chemistry is a modern branch of organic chemistry and deals with reversible association of molecules by non-covalent interactions for example ionic-, ππ-interactions and hydrogen bonds.
Building blocks which use ionic interactions have to possess both charges within one molecule to be a self-complementary system.
A zwitterionic unit, which combines ionic interactions and hydrogen bonds in a molecule, is the guanidiniocarbonylpyrrole carboxylate-zwitterion (Fig. 1). One special feature of this molecule is that its self-aggregation can be reversibly switched on and off by pH adjustments. These zwitterions can be connected to a linker or a spacer to create more binding sites within the molecule.
In our working group we had connected four zwitterions with a flexible core.[1] Due to the high flexibility, the molecule shows supramolecular polymeric properties only at higher concentration. Furthermore the connection of the four zwitterions directly with a rigid core leads reduces the solubility significantly. To increase the solubility we want to synthesize a building block with quaternary amines and flexible spacer. The molecule should have also an aromatic systems to get more rigidity.

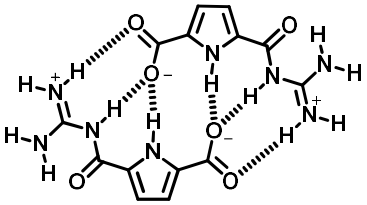

Fig.1: dimer of the guanidiniocarbonylpyrrolecarboxylate-zwitterion

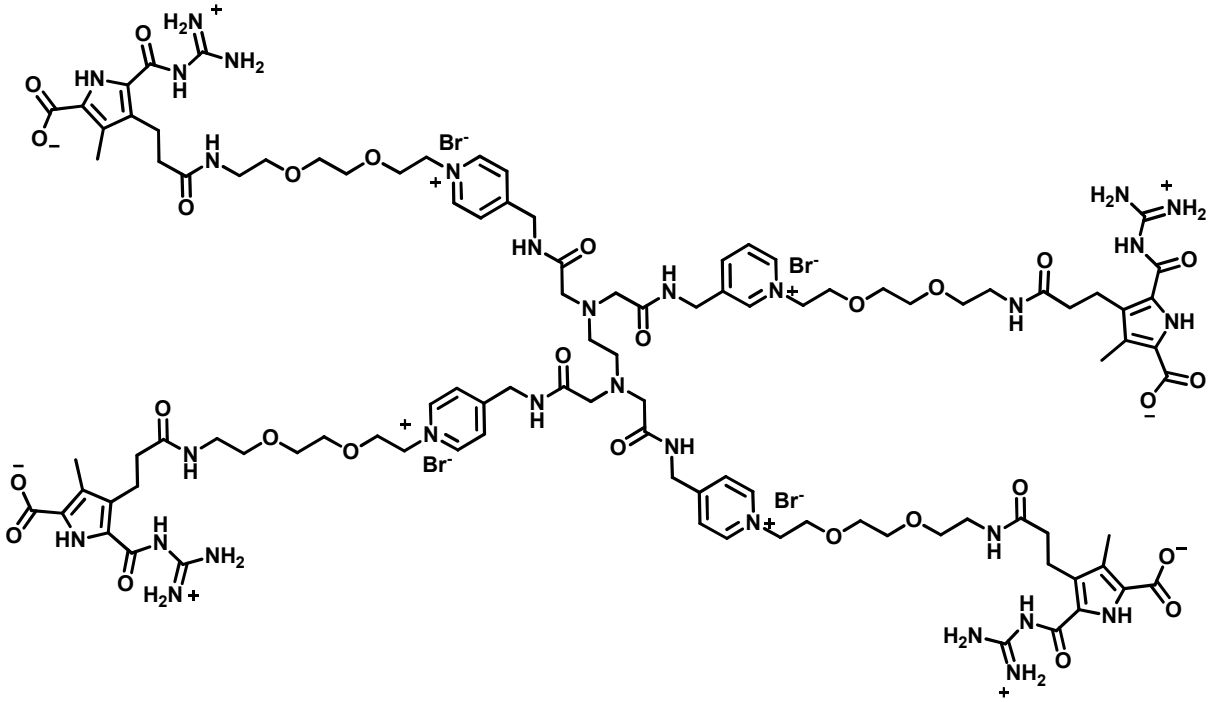

Fig 2: molecule with four zwitterion binding sites and four quaternary amines

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Replication in an out-of-Equilibrium System

Andreas S. Hussain, Shuo Yang and Sijbren Otto

University of Groningen, Centre for Systems Chemistry, Stratingh Institute, Nijenborgh 4; 9747 AG Groningen, The Netherlands
a.s.hussain@rug.nl

In Darwinian evolution species that are better adapted to their environment win the competition for common resources from less well-adapted competitors. Thus, in such competition scenarios the nature of the environment may dictate the outcome of the competition. We wondered to which degree these biological principles acting at the level of species extend to the molecular level into systems based on fully synthetic self-replicating molecules.

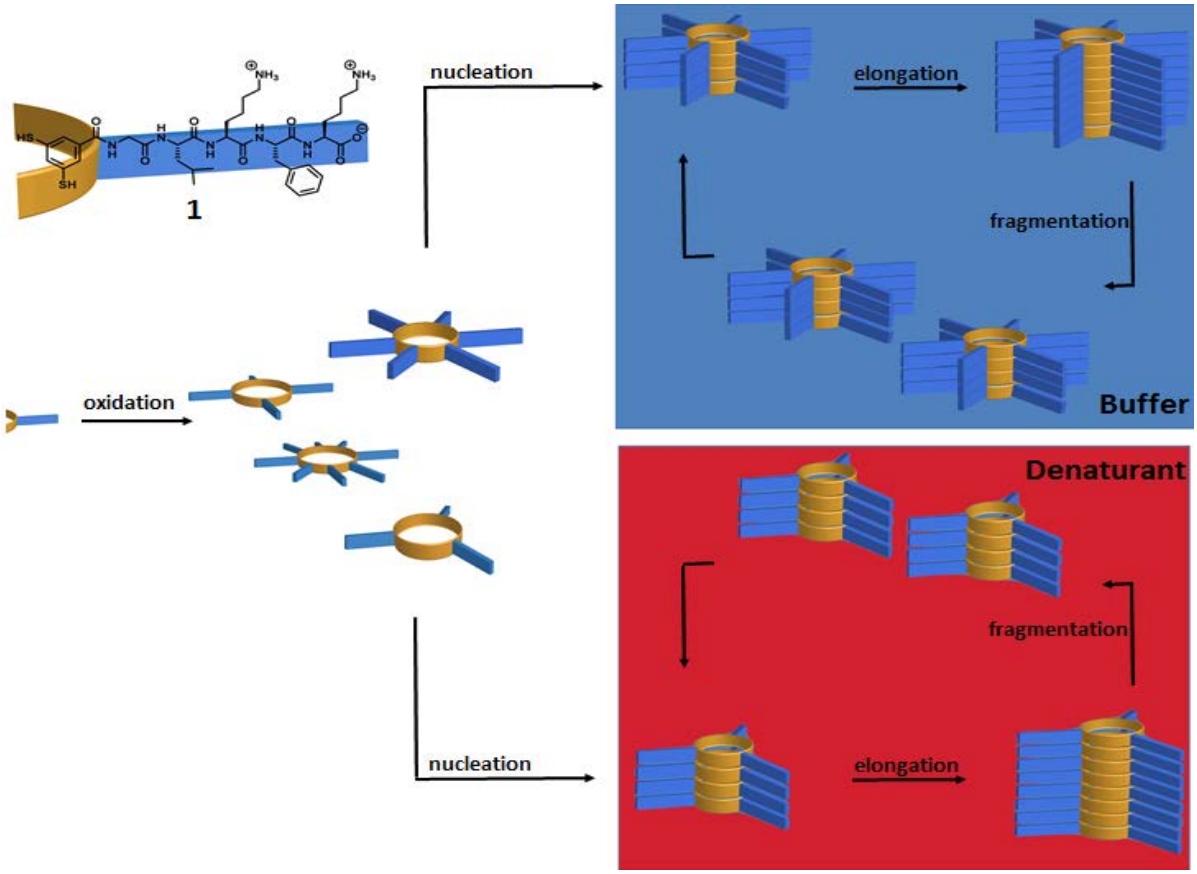

Fig. 1: In a dynamic combinatorial approach self-replicating molecule **1** is able to form different replicating species in different environments.[1,2]

Here we show how fully synthetic replicators can survive and correspond to a dynamic environment change by adding a denaturant under far-from-equilibrium conditions with use of simple continuous-flow setups.

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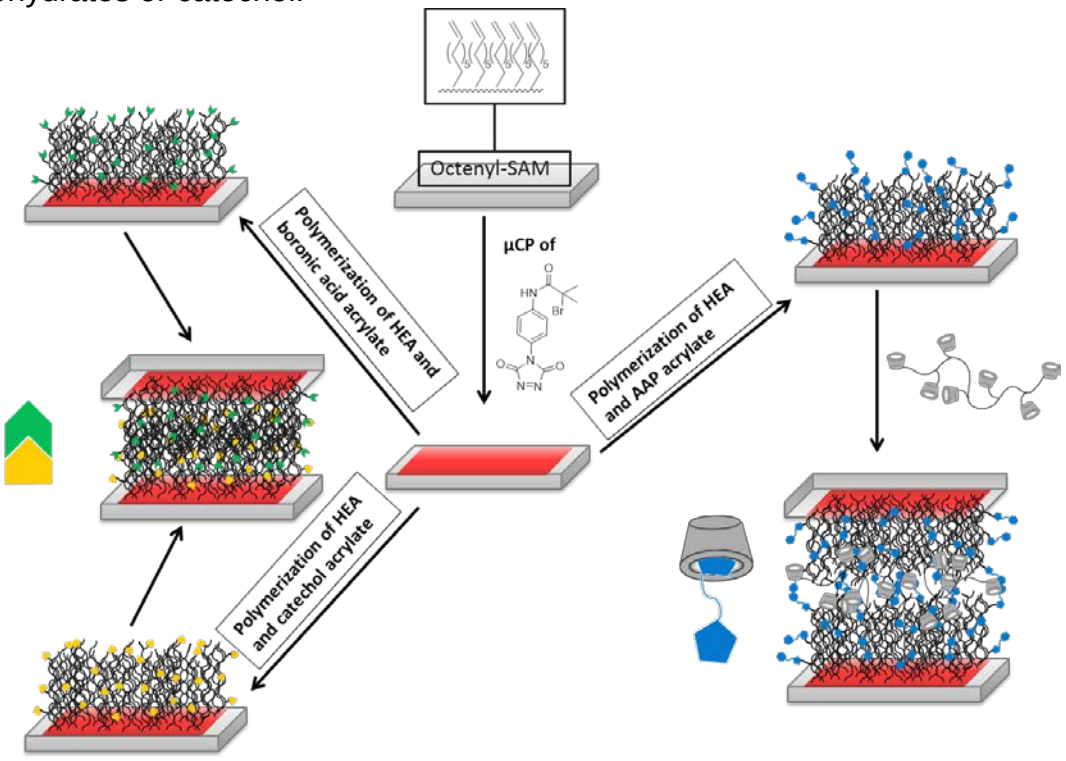
Innovative Adhesives Based on Supramolecular Host-Guest Interactions and Dynamic Covalent Bonds

Sebastian Lamping, Lucas Stricker, Tobias Otremba and Bart Jan Ravoo

Sebastian Lamping, Organic Chemistry Institute, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149 Münster, Germany

s_lamp03@uni-muenster.de

Adhesives find broad application in various sections, e.g. in offices, construction areas, car industry or medicine. Most commonly used adhesives are based on a covalent bonded polymer backbone for good cohesion properties and various functional groups for adhesion. Due to the strong covalent bonds in the back bone almost all glues can be used only once, as for loosing of the glued objects enormous forces must be applied, which destroy either the covalent bonds or the adhesive interactions. Often those separated objects can't be glued together again. Therefor we synthesized two different types of adhesives, which are reusable and investigated in a gentle way to loose the objects after gluing. Furthermore, we encapsulated an arylazopyrazole[1] in our surface bound polymer, which is light-switchable and can bind to cyclodextrins with non-covalent host-guest interactions.[2] In addition we make use of the dynamic covalent behaviour of boronic acids and 1,2-diols, such as carbohydrates or catechol.[3]



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Hydrogel Particles of Defined Shapes using Superhydrophobic-Hydrophilic Micropatterns

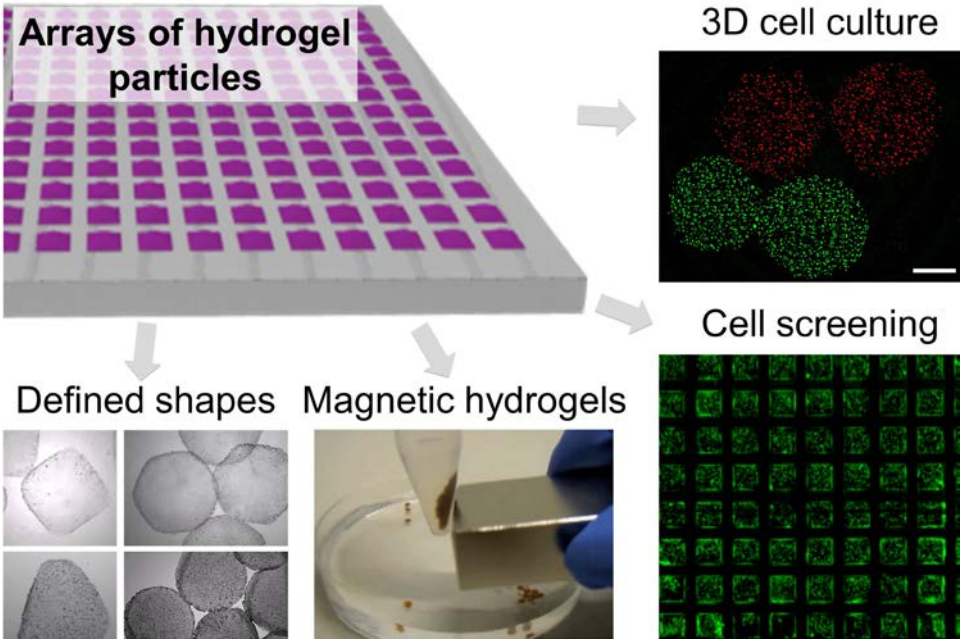
Ana I. Neto, Konstantin Demir, Anna A. Popova, Mariana B. Oliveira, João F. Mano and Pavel A. Levkin

Pavel Levkin, Karlsruhe Institute of Technology (KIT)

Institute of Toxicology and Genetics, Germany

levkin@kit.edu, www.levkingroup.com

Hydrogels are hydrated three-dimensional cross-linked polymers resembling natural extracellular matrix that provide soft support for cellular growth and tissue formation. Due to their unique properties such as high porosity, permeability for gases, nutrients and metabolites, as well as their compatibility with physiological conditions, hydrogels have been extensively studied as material support for 3D cell culture. The limitations of bulk hydrogels are that they usually lack the hierarchical architecture of in vivo tissues and suffer from slow diffusion of nutrients and other biological signaling molecules.



Here we describe a method for the rapid fabrication of alginate hydrogel particles of defined sizes and shapes using the effect of discontinuous dewetting on superhydrophobic-hydrophilic microarrays. We applied this method in three demonstrations: (1) preparing an array of hydrogel particles and free-standing hydrogel particles with distinct geometries and sizes defined by the photomask features; (2) examining the in situ viability of cells encapsulated into free-standing hydrogel particles, and (3) constructing magnetic responsive hydrogel particles for modular tissue engineering and shape-coded free-standing hydrogels of distinct cell types.

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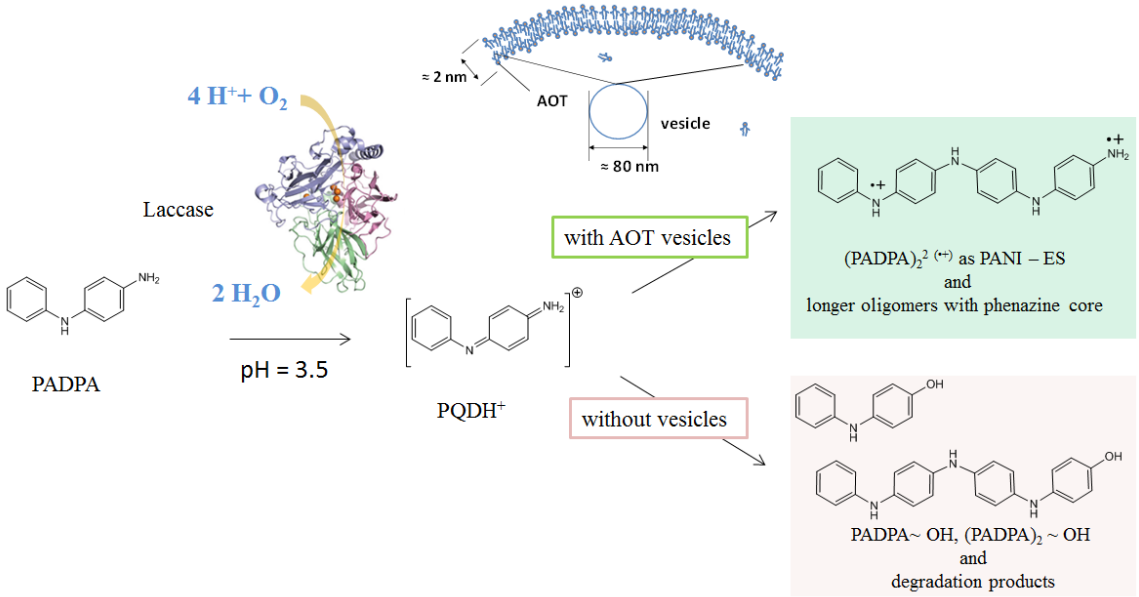
Enzymatic oligomerization in AOT vesicle membranes

Sandra Luginbühl, Martin Willeke, Louis Bertschi, Lukas D. Schuler, Takashi Ishikawa, Peter Walde

Sandra Luginbühl, Polymer Chemistry, Department of Materials, ETH Zurich, Switzerland

sandra.luginbuehl@mat.ethz.ch

The oxidation and oligomerization of the aniline dimer, *p*-aminodiphenylamine (PADPA), with *Trametes versicolor* laccase and O_2 in an aqueous solution is positively influenced by negatively charged vesicles formed from AOT (= sodium bis(2-ethyl-hexyl) sulfosuccinate): a product resembling polyaniline in its emeraldine salt form (PANI-ES) is obtained under optimal conditions [1]. Without vesicles, no such product is formed. In order to understand this observation, HPLC − MS analysis of all reaction mixtures in combination with isotope labelling were conducted [2]. We found that there are two reaction routes in the presence of vesicles. The primary route leads to the formation of the main product in an overall yield of ≈ 50 %, which is the N-C *para* coupled PADPA dimer. It is soluble in organic solvents and is the shortest possible aniline oligomer which possesses PANI-ES characteristics (unpaired electrons, electrical conductivity, redox active). Without vesicles, multiple hydrolysis products were found. Molecular dynamics simulations show that PADPA and its main intermediate oxidation product are embedded within the vesicle membrane, where the water content is very low. We propose that this microenvironment *inter alia* protects PADPA and its products from hydrolysis. Furthermore, cryo-TEM images show that the AOT vesicles undergo fusion after PADPA is added to the suspension; a complex process which can be followed using a stopped-flow apparatus.



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Effect of a beta-breaker moiety in tripeptide self-assembly

Ana M. Garcia, M. Melchionna, R. De Zorzi, S. Kralj, S. Marchesan

University of Trieste, Chem. Pharm. Sc. Dept., Via L. Giorgieri 1, 34127, Trieste, Italy

agarcia@units.it

Self-assembling tripeptides are being exploited as innovative systems in the medicinal field, deserving special attention as they possess several advantages over longer peptides or other molecules of higher chemical complexity.[1] The incorporation of unnatural D-amino acids in the tripeptide sequence can lead to unexpected effects on peptide conformation, self-assembly behavior and even therapeutic activity.[2] In this context, the diphenylalanine (Phe-Phe) motif is an extremely versatile self-assembling building block, and subtle changes introduced to its chemical structure are sufficient to obtain different nanomorphologies that are generally based on beta-sheet conformations.[3]

In this work, we couple the beta-sheet forming Phe-Phe motif with the beta-breaker amino acid proline to evaluate the contrasting effects on self-assembly, whilst adding in the chiral factor given by all combinations of amino acid stereochemistry. Each compound identity and purity was confirmed by ESI-MS, ^{1}H- and ^{13}C-NMR. Peptide conformation was assessed by circular dichroism and ATR-IR. The superstructures formed by each of these tripeptides at physiological pH have been studied both by atomic force and transmission electron microscopy, revealing discrete nanomorphologies of interest. Current studies based on single-crystal XRD structures and molecular dynamics are highlighting complex or simple architectures depending on the tripeptide stereochemistry, thus adding valuable information to unravel the role of chirality for the rise of hierarchical organization. This structural information will be exploited towards function. Due to the presence of the beta-breaker proline, it is anticipated that these compounds will have interesting effects on the fibrillogenesis of pathological peptide aggregation associated with amyloidoses.

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Bromination of 2,7′-bi-indolyls and quinazolin-7-ones as a key step in the synthesis of macrocyclic tetra-indolyls

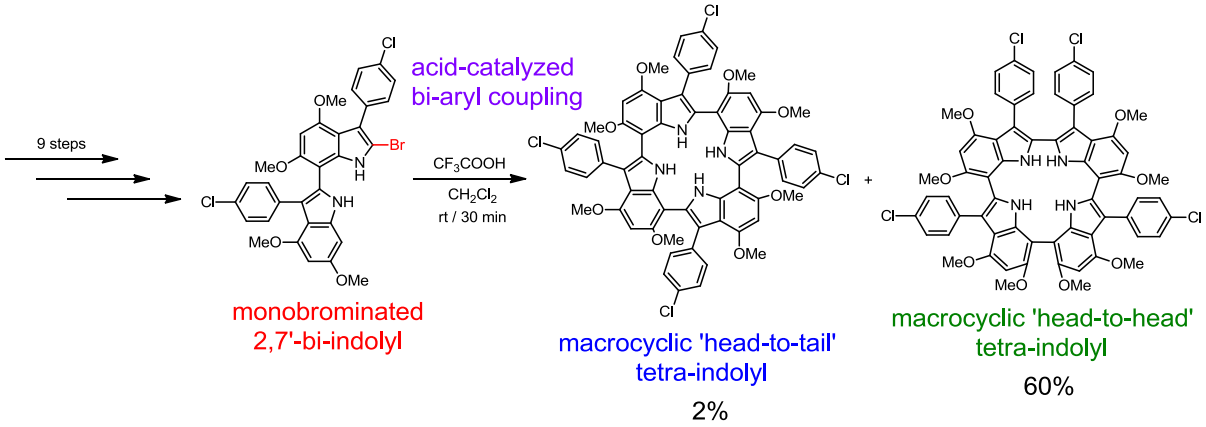
Marcin Mielczarek [a], Mohan Bhadbhade [b], Rui Chen [c], Naresh Kumar [c] and David St. C. Black [c]

[a] *Department of Chemistry, Faculty of Science, University of Burgos, 09001 Burgos, Spain*
e-mail: mmielczarek@ubu.es

[b] *X-Ray Diffraction Laboratory, Solid State & Elemental Analysis Unit, Mark Wainwright Analytical Centre, UNSW Australia, Sydney, NSW 2052, Australia*

[c] *School of Chemistry, Faculty of Science, UNSW Australia, Sydney, NSW 2052, Australia*

Our previous research resulted in the discovery of the synthesis of macrocyclic tetra-indolyls *via* oxidative coupling of 2,7′-bi-indolyls by *p*-benzoquinone in the presence of concentrated hydrochloric acid as a catalyst.[1] Following this outcome further work was undertaken in order to elaborate an alternative method for the synthesis of the tetra-indolyl-based macrocycles involving brominated 2,7′-bi-indolyls. Efficient regioselective procedures for bromination of 2,7′-bi-indolyls and quinazolin-7-ones using molecular bromine and *N*-bromosuccinimide were developed to afford a wide range of novel mono-, di-, tri- and tetrabrominated derivatives with various substitution patterns. Protection of the nitrogen atoms in the 2,7′-bi-indolyl scaffold by acetyl, benzenesulfonyl and carbonyl groups was investigated. Stability of 2,7′-bi-indolyls in the presence of strong bases was explored to discover formation of imines followed by the unusual ring opening reaction. Single crystal X-ray crystallography and NMR spectroscopy were employed in order to assign structural isomers of the dibrominated quinazolin-7-ones. A new method for the synthesis of macrocyclic tetra-indolyls *via* acid-catalyzed coupling of 2′-bromo-2,7′-bi-indolyl is reported and a possible mechanism of the reaction presented.[2]



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Fluorogenic Composite Materials of Thermally Reduced Graphene Oxide with Naphthalenediimides Chromophores for Prostate Cancer Bioimaging

Vincenzo Mirabello[a]*, James Tyson[a], David C. Calatayud[b], Gabriele Kociok-Köhn[a], Haobo Ge[a], Stanley Botchway[c], G. Dan Pantoș[a], Sofia I. Pascu[a]*

[a].*Department of Chemistry, University of Bath, Claverton Down, BA2 7AY, United Kingdom*
[b].*Department of Electroceramics, Instituto de Cerámica y Vidrio (CSIC), 28049 Madrid, Spain*
[c].*Central Laser Facility, Rutherford Appleton Laboratory, Research Complex at Harwell, STFC, Didcot OX11 0QX, UK*

v.mirabello@bath.ac.uk, s.pascu@bath.ac.uk

Graphene-based fluorogenic composite materials (GFCM) have focused considerable interest over recent years and become highly promising functional materials with several applications in biosensor, electronic, photovoltaic and composite materials.[1] Thermally reduced graphene oxide (TRGO) has been of interest lately as it has been employed to bypass those difficulties surrounding the lab-scale availability of functional graphenes. Furthermore, naphthalenediimides (NDI) are a class of fluorescent organic compounds with wide utility in the area of bioconjugation particularly when biocompatible appendages are included.[2]

We report our advances towards the assemblies of novel ground- and photo-excited nanohybrid materials formed between TRGO or a model small molecule, coronene and a series of new halogenated α-amino acid tagged NDI chromophores.[3] We hypothesise that the functionalization of graphene-like systems with NDI chromophores can be monitored due to the Föster resonance energy transfer (FRET) and the photoinduced electron transfer takes place and leads to the formation of new GFCM.

Confocal fluorescence microscopy studies show that our nanocomposites are internalised in PC-3 cells suggesting their potential as prostate cancer bioimaging agents. MTT assays suggest that the deliberate functionalization of the surface of TRGO and coronene with phenylalanine-NDIs significantly improves the biocompatibility of such graphene-like nanocomposites with respect to the pristine TRGO and coronene.

The authors would like to thank ERC Consolidator grant scheme (O2Sense to Sofia Pascu).

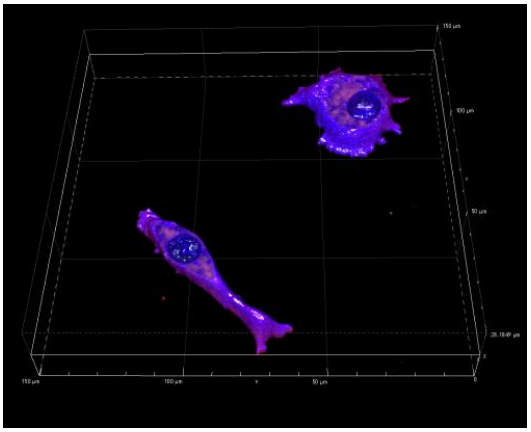

Figure. 3-dimentional render of Single-photon laser-scanning confocal fluorescence Z-stack series of PC-3 cells incubated at 37°C for 15 minutes with bromophenylalanine-NDI-TRGO nanohybrid (50μM, in 5 : 95 DMSO : serum free medium). λ_{ex} = 405, 488, 561 nm. λ_{em} = 417-477, 500-550, 570-750 nm.

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One-Pot Synthesis of Combinatorial Library of Stimuli Responsive Transfection Vectors and Highthroughput Screening for Nonviral Gene Delivery

Mijanur Molla

Mijanur Molla, Karlsruhe Institute of Technology (KIT)
Institute of Toxicology and Genetics, Germany, bk7754@partner.kit.edu

In recent past, gene therapy has been of great interest to treat wide variety of human diseases ranging from viral infections to hereditary disorder and cancers. The primary challenge in gene therapy is developing safe and effective delivery method. In the recent scenario, although most of the gene delivery therapeutics in clinical trials is based on viral vectors, safety issues and manufacturing costs are the major concerns of this approach. On the other hand, synthetic vectors offer greater flexibility, more facile manufacturing and safer delivery platform. Cationic lipids are one of the most well studied families in the synthetic vector based gene delivery approach. Synthetic difficulties of those lipids introduced limitations in the possibility of fast structural optimization for an efficient transfection vector. Currently, lipid-like materials called "lipidoids" are synthesized using very simple synthetic technique for gene delivery applications. But their transfection efficiencies are still lesser than the viral based delivery systems. So, it is necessary to search for synthetic vectors with high transfection efficiency. Ease of synthesis and opportunity for high-throughput screening of libraries of compounds motivated us designing and synthesizing lipidoids using combinatorial synthetic approach. This can produce large quantities of structure-activity data which will significantly increase the probability of finding a potential candidate for efficient gene delivery.

In this work, we followed a facile synthetic approach to synthesize a library of stimuli responsive lipid like materials (lipidoids) by using thiolactone ring opening reaction in a one-pot fashion. Since there is the opportunity of varying head groups and hydrophobic tail of a lipidoids, a library of 288 lipidoids were synthesized in very short time using this one-step method. The simplicity of this approach makes it expedient for accelerated synthesis of library of lipidoids for gene delivery applications. Lipidoids were screened for transfection activity by delivering eGFP plasmid into HEK293T cells in culture. We have investigated the produced library in a high-throughput cell transfection screen and analyzed structure-activity relationship of the lipidoids with respect to transfection efficiency. To aid high-throughput screening, all transfections were performed using multichannel pipette and serial dilution in a 96 well plate format. At first, liposomes were prepared using sodium acetate buffer (pH = 5). Plasmid DNA was mixed with liposome and incubated for 20 minutes to form lipoplex. Therefore, the cells were exposed to lipoplex and incubated for 48h. The cellular GFP expression was examined using flow cytometry analysis and the GFP expression was calculated by dividing the mean fluorescence intensity of treated cells to that of untreated controls. The efficiency of GFP expression using lipidoids was compared with the commercial gene transfection reagent screenfect A.

Near-Infrared Photoswitching of Cyclodextrin-Guest Complexes Using Lanthanide-doped $LiYF_4$ Upconversion Nanoparticles

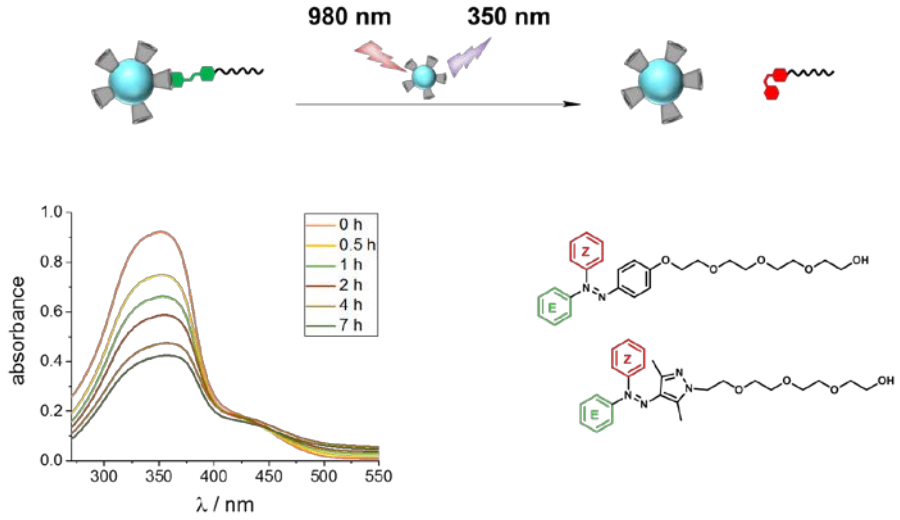
Nadja Möller, Tim Hellwig, Lucas Stricker, Carsten Fallnich, Bart Jan Ravoo

Nadja Möller, Westfälische Willhelms Universität Münster,

Organic Chemistry Institute, Corrensstr. 40, 48149, Germany

nadja.moeller@uni-muenster.de

Light responsive molecules are particularly promising in host-guest interactions due to a reversible, photochemical control over the formation of inclusion complexes. [1] However, in most cases the use of UV light is inevitable for photoswitching processes, becoming problematic in biological applications as UV light causes damage to those tissues. Therefore the use of low energy irradiation – such as near-infrared light – would be desirable and could be achieved by using such light sources in combination with upconversion nanoparticles. The advantage of those nanoparticles is their remarkable property of showing the *anti*-Stokes effect, converting low energy photons into high energy ones. Herein, a new type of supramolecular cyclodextrin-guest complexes using α- and β-cyclodextrin acid@$LiYF_4$: Yb^{3+}, Tm^{3+}, Gd^{3+}-upconversion nanoparticles as host and azobenzene derivatives as guest molecules is presented. The water-soluble nanoparticles were synthesized in a ligand exchange reaction and are able to isomerize azobenzene derivatives by irradiation at 980 nm and a very low light intensity of 0.22 W/cm^2. For β-cyclodextrin the recently by our group introduced class of arylazopyrazole was used.[2] The nanoparticles were fully characterized by fourier transform infrared spectroscopy (FTIR), transmission electron microscopy (TEM), X-ray diffraction (XRD), emission spectroscopy and thermal gravimetric analysis (TGA). The presented hybrid materials offer a biocompatible, photochemical control over host-guest interactions and provide the opportunity for bio-applications.



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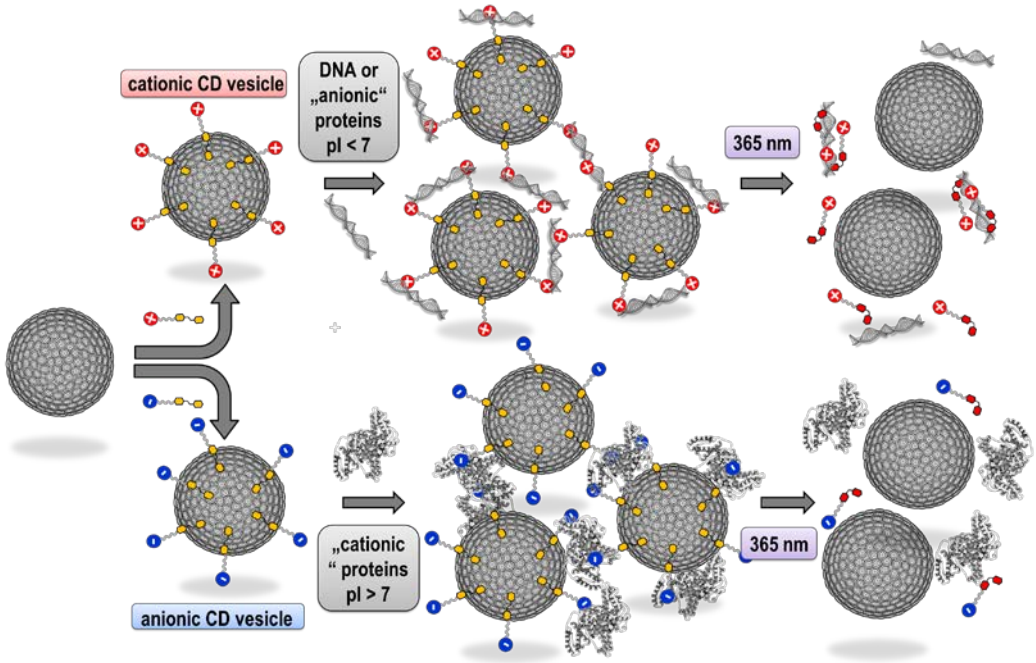
Light-Controlled DNA Transfection with Supramolecular Complexes

Johanna Moratz, Sabine Hüwel, Andrea Rentmeister, Bart Jan Ravoo

Johanna Moratz, University of Münster, Organic Chemistry Institute, Corrensstr. 40, 48149 Münster (GER)

Johanna.moratz@uni-muenster.de

Light-induced binding and release of proteins and DNA was achieved, combining host-guest chemistry and electrostatic attraction. [1] Vesicles of 100 nm were obtained from amphiphilic cyclodextrin (CDV), self-assembling into supramolecular complexes of 1 µm size in the presence of a bifunctional linker and target biomolecules. The linker molecules comprise an azobenzene moiety, forming photo-switchable host-guest inclusion complexes with CDV, and a charged functionality, thus inducing orthogonal aggregation of either negatively or positively charged proteins or DNA. It was validated that irradiation with ultraviolet light causes complex dissociation, based on the transition between a modus of multivalent electrostatic interactions and a low-affinity monovalent state.
Currently we are investigating this systems capacity to serve as a transporter for biomolecules. The cell uptake and biocompatibility of supramolecular complexes containing DNA or RNA were confirmed by fluorescence microscopy. The complexes are stable enough to protect the RNA from degradation. Confocal microscopy revealed that the release of RNA inside the cells can be influenced with light. Future focus will lie on studying and optimizing the release of DNA.



Multivalent capture and photo-induced release of biomolecules in colloidal complexes. [1]

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Bioinspired / Biohybrid Nanomaterials: From Multimodal Therapeutics to Precision Membrane Technology

David Y.W. Ng, Andreas Riegger, Sean Harvey, Tanja Weil

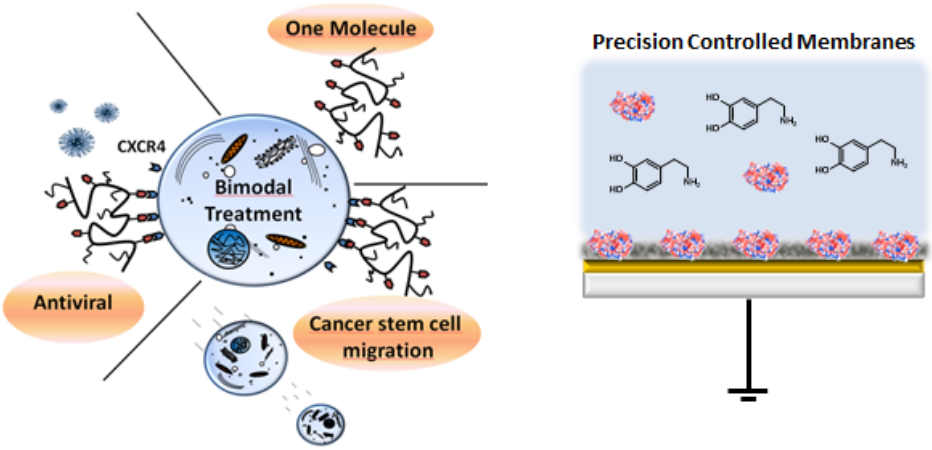
Max Planck Institute for Polymer Research

david.ng@mpip-mainz.mpg.de

Polymer science has seen its evolution as conventional materials into state-of-the-art nanotechnology and a platform for macromolecular engineering. Primarily, the transformation in the field arises as we discover more intrinsic truths from Nature and upon the realization that biomacromolecules may very well be the future of polymer design. Even though these biopolymers are the epitome of polymer chemistry, the synthetic world can still provide exceptional tools to achieve new frontiers.

In one aspect, the construction of hybrid materials, in general, employ the prospect that the properties of synthetic polymers can act complementarily to grafted biological entities (e.g. peptides, proteins, DNA etc.). Such strategies have been implemented widely but for the material to exhibit broad therapeutic effects that target two very different classes of diseases, it is rarely seen. We show herein a polymer-peptide conjugate that is able to halt HIV entry into mammalian cells as well as the capability to prevent the migration of cancer cells that is typical in metastasis.

Beyond macromolecular design, the precision level of biomaterials can also be tuned as well using synthetic methods. Polydopamine is a mussel-inspired material that spontaneously forms adhesive coatings around most materials. However, the control of this process is often very challenging due to its polymerization mechanism and supramolecular interaction of the oligomers. Through electrochemistry, we report that the film formation and thickness can be precisely controlled in the low nanometer scales. In addition, proteins can be incorporated into the film matrix and have shown that their activity remains intact through the polymerization process.



Synthesis and application of chiral bisphosphates based on 1,1´-binaphthyl units

Frescilia Octa-Smolin, Raja Mitra, Jochen Niemeyer

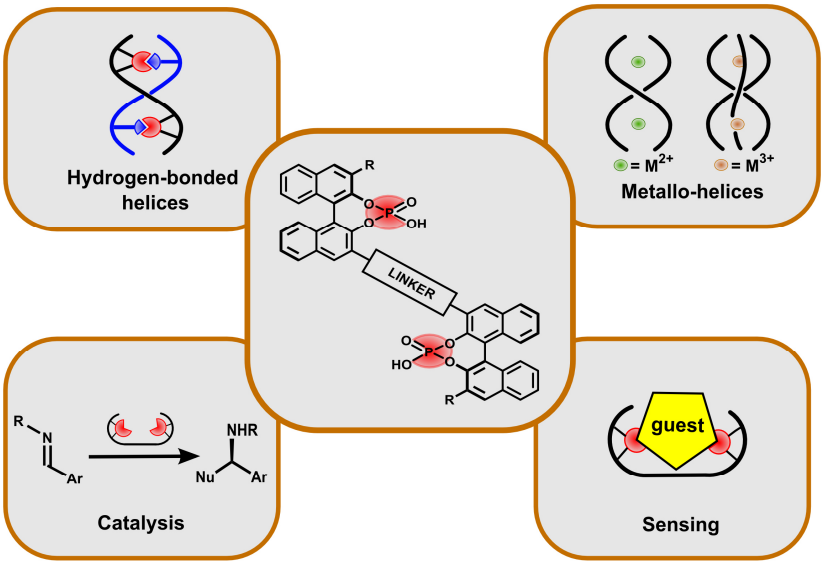
Institute of Organic Chemistry, University of Duisburg-Essen

Universitätsstrasse 7, 45117 Essen

Email: frescilia.octa-smolin@uni-due.de

The double-helical structure of DNA has inspired chemists to design and synthesize artificial helical molecules for decades. Although numerous helical polymers have been reported since the 1950s,[1] the formation of well-defined supramolecular double-helices has only been achieved more recently.[2] Due to their close resemblance to DNA; such supramolecular double-helices have gained increased attention ever since.

We have synthesized a series of chiral *bis*-binaphthyl-phosphates using different linkers to control the distance between the phosphate units. These bisphosphates will be used to generate self-assembled supramolecular double-helices, allowing for a control of the helix-chirality by the chiral binaphthyl-backbones. On one hand, we are envisaging the use of complementary *bis*-guanidine-structures to generate hydrogen-bonded double-helices and on the other hand we will employ suitable metal ions to generate the corresponding metallosupramolecular double- and triple-helices. In addition to this, we are also planning for the use of the chiral bisphosphates in sensing and in enantioselective organocatalysis.[3]



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Stimuli Responsive Aggregation through Combinations of Orthogonal Switchable Binding Sites on a PBI Scaffold

C. Schlütting, C. Schmuck

C. Schlütting, University of Duisburg-Essen, Universitätsstraße 7, 45141 Essen, Germany

Christian.schluetting@uni-due.de

The combination of orthogonal switchable supramolecular binding motifs with one scaffold offers the possibility to build up more dimensional switchable aggregates. There are some multi stimuli responsive interactions that might be interesting to combine e. g. metal-ligand coordination, ππ-stacking and ionic interactions. We combined three switchable binding sites based on these interactions in one molecule. Namely a PBI molecule which has interesting optical properties and is able to form ππ-stacks, a terpyridine which forms highly stable metal complexes and our guanidiniocarbonyl pyrrole carboxylate zwitterion which forms very stable dimers ($K_{ass} > 10^{10}$ M^{-1} in DMSO).[1] One possible combination of these binding motifs within one molecule which we have synthesized is shown in Figure 1a. This molecule shows a pH depended aggregation behavior. In the zwitterionic state it is able to form network like structures and further aggregation is achieved through the addition of metal ions. A schematic representation of the possible effect of switching two parameters is shown in figure 1b.

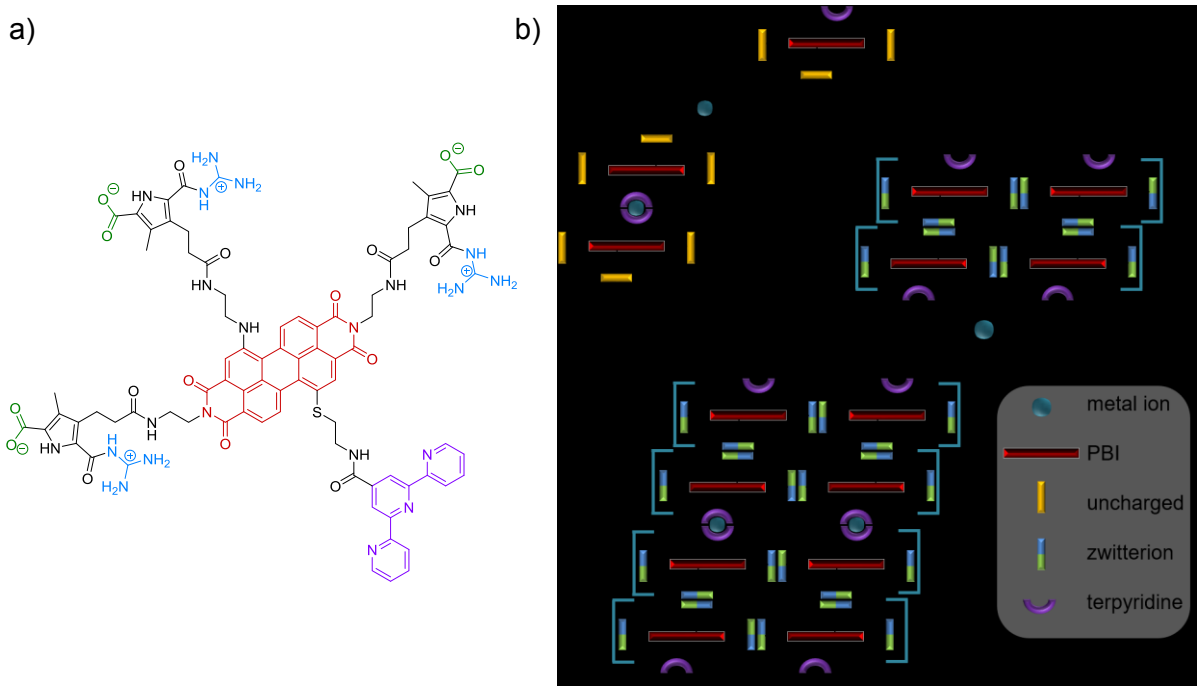

Figure 1: (a) Synthesized target molecule, (b) possible switchability by adjusting the pH value and adding or removal of metal ions.

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Supramolecular Sequenced Poly(phosphodiesters)

Christopher J. Serpell

Dr. Christopher J. Serpell, School of Physical Sciences, Ingram Building, University of Kent, Canterbury, Kent, CT2 7NH, UK

c.j.serpell@kent.ac.uk

Specifically sequenced polymers are integral to all life. The information coded into the nucleobase sequence within DNA strands contains much of the blueprint for each organism. This information is communicated *via* RNA, another sequenced polymer, and translated in the production of proteins. The amino acid sequence determines protein folding and self-assembly, giving structures capable of catalysing reactions, enabling intracellular motion and compartmentalisation, creation of electrical gradients, and modulation of energy flows. In nature, polymers are active agents: functional, finely detailed, monodisperse, and acting largely as unitary species; control of sequence is central to these processes. In contrast, synthetic polymers are typically simple, often consisting of a single repeated monomer; inherently disperse, rarely dynamic, and put to use as aggregates or in the bulk. These properties have not prevented polymers becoming one of the most important classes of materials in day-to-day life thanks to their tuneable physical properties and processability. Nonetheless, control over sequence is expected to yield major new technologies.

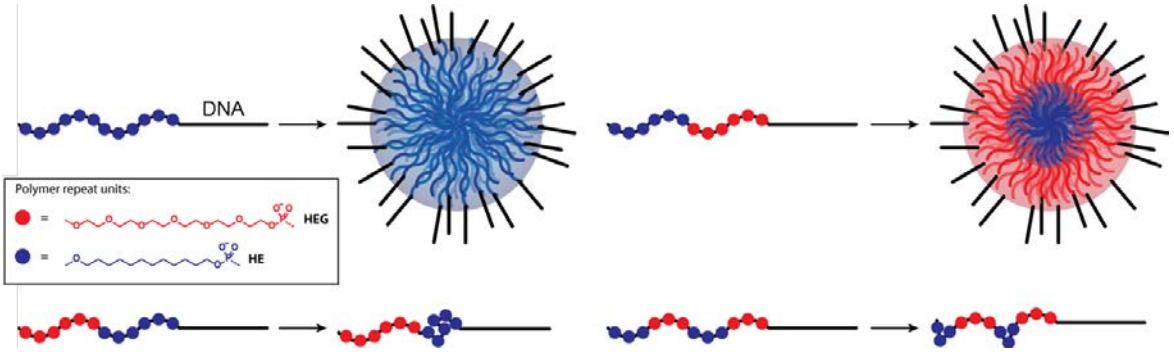

Figure. 1. Control over self-assembly and single chain folding using polymer sequence.

We have developed a method for the creation of sequence defined polymers of macromolecular length based upon the phosphoramidite chemistry used for solid phase DNA synthesis, and shown that alteration of the sequence of hydrophobic and hydrophilic units can be employed to control self-assembly and single chain folding of DNA conjugates (Fig. 1).[1] Subsequent work by ourselves[2] _ENREF_2 and others[3] has illustrated the versatility of this method. We are now investigating the integration of a wider range of supramolecular motifs into these phosphodiester polymers to provide yet finer control of folding, molecular recognition, looking towards the functions embodied by biological sequence polymers.

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Self-assembly and adaptive behavior of orthoester cryptates

Oleksandr Shyshov, René Brachvogel, Prof. Dr. Max von Delius

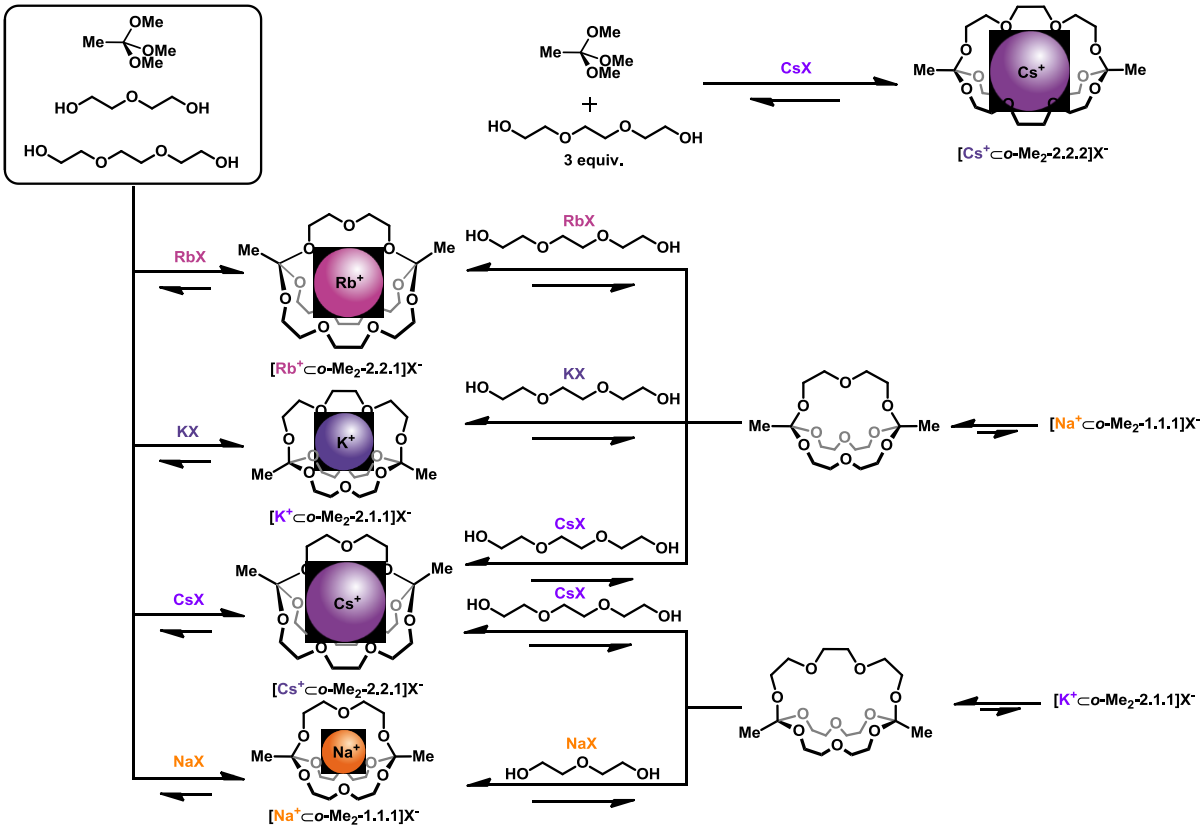
Oleksandr Shyshov, Ulm University, Department for Organic Chemistry II and New Materials

Albert-Einstein-Allee 11

Oleksandr.shyshov@uni-ulm.de

Dynamic orthoester exchange was introduced to the toolbox of dynamic covalent chemistry (DCC) by R.-C. Brachvogel and M. von Delius in 2015.[1] Later on, the same authors showed that sodium ions can serve as templates for the self-assembly of orthoester-bridged coronates and cryptates,[2]

Herein we report on the K^+,- Rb^+- and Cs^+-templated dynamic self-assembly of orthoester cryptates.[3] All new compounds have been extensively characterized by NMR and single crystal X-ray analyses. The dynamic behavior of the cryptands was studied and the ammonium ion was found to be a particularly interesting template. We could show that dynamic orthoester cryptands are highly adaptive by changing their structure in response to subtle changes of the system composition (addition of cationic guests and ethyleneglycols).



We believe that orthoester architectures represent a versatile platform for systems chemistry, due to the pronounced thermodynamic differences between competing cages.

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How to synthesize a monodisperse, sequence controlled Polydimethylsiloxane-*graft*-BTA

Marcin L. Ślęczkowski, Anja R.A. Palmans, E.W. Meijer

Institute for Complex Molecular Systems, Laboratory of Macromolecular and Organic Chemistry, Eindhoven University of Technology,

De Rondom 70, 5612 AP Eindhoven, The Netherlands

m.sleczkowski@tue.nl

The field of single chain polymer nanoparticles (SCPNs) recently attracted significant attention in the scientific community. SCPNs are linear polymers folded into nanometer-sized objects due to the intramolecular interactions between the functional grafts. The nature of these interactions can be divided into covalent, dynamic covalent and noncovalent. From a bottom-up approach point of view, in which the responsivenes to external stimuli is a crucial feature, directional noncovalent interactions are of great interest. In recent literature, a number of supramolecular motifs has been explored with 2-ureidopyrimidinone (UPy), thymine-diaminopyridine and benzene-1,3,5-tricarboxyamide (BTA)[1] as the most prominent examples. Unfortunately, due to the constraints in current state of knowledge in polymer chemistry, no reliable method for a monodisperse and fully sequence-controlled polymer was developed. In this research we want to apply an interative strategy in order to ultimately control the primary structure. Being inspired by nature, we believe that we can translate the full control of a primary structure of a polymer into the control of its tertiary structure via self-assembly processes (**Figure 1)**. As a well-studied supramolecular motif, BTA is a perfect candidate to be implemented into well defined polymers. Recently we explored a synthetic method for a monodisperse oDMS-bl-oLA[2], now we want to develop this to graft polymers. Extraordinary physicochemical properties of pDMS open new possibilities in supramolecular chemistry. Significant ionic character of Si-O bond and p_{π}-d_{π} interactions contribute to exceptionally low energy barrier for rotation of the organic groups linked to the silicon atom, resulting in high flexibility of the polymer.[3] The physicochemical intertness of PDMS towards majority of organic compounds, will be a driving force for a phase seggregation between the BTA helical stack and the polymer backbone, giving extra stability to formed SCPNs.

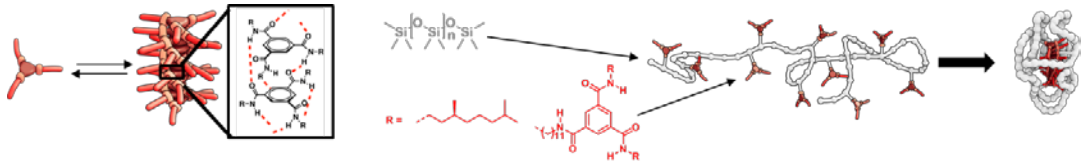

Figure 1: *Helical stack-driven folding of the pDMS-graft-BTA into SCPN*

Herein we present our recent results in the synthesis and self-assembly studies of synthesized to-date BTA-siloxane conjugates.

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Multi-Responsive Coordination Polymers Utilising Metal-Stabilised, Dynamic Covalent imine Bonds

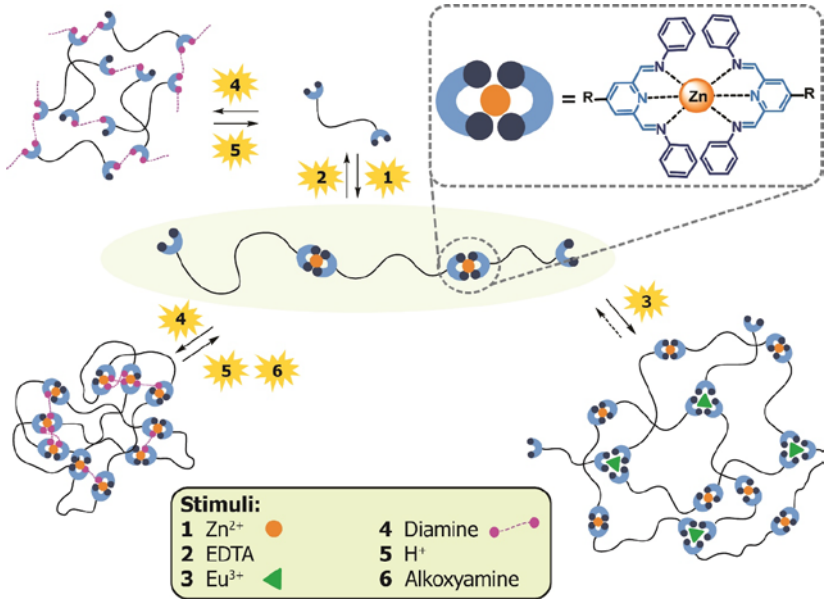
Fátima García, Janis Pelss, Han Zuilhof, and Maarten M. J. Smulders

Maarten Smulders, Laboratory of Organic Chemistry, Wageningen University

Stippeneng 4, 6708WE Wageningen, NL

maarten.smulders@wur.nl

The incorporation of reversible bonds in covalent polymers has enhanced polymer materials to become adaptive, leading to 'smart' materials that are, *e.g.*, self-healing or stimuli-responsive. Next to non-covalent interactions, more recently also dynamic covalent bonds have been employed to prepare such smart polymer materials, as this type of bond combines intrinsic reversibility with the robustness of covalent bonds.
Herein, we extend the use of dynamic imine bonds to the construction of hydrolytically stable, multi-responsive coordination polymers. To this aim we combine imine bonds and metal-ligand (M–L) bonds to obtain dynamic covalent polymer materials that are responsive *via* their imine and their M–L bonds, as well as through both types of interactions in concert.[1]
As key binding motif we rely on a tridentate pincer ligand bearing a 2,6-diiminopyridine moiety, which is known to coordinate to octahedral metal ions in a 2:1 fashion (see figure). As such, this pincer can be considered as the dynamic covalent structural analogue of the classic terpyridine ligand.



We show by various techniques (including NMR, DOSY, UV/vis and viscometry) that selective end-functionalisation of macromonomers with this motif leads to the formation of stable polymers that are sensitive to a range of stimuli. This approach yielded a stable, multi-responsive main-chain coordination polymer: the resulting polymer material was found to be responsive to a range of stimuli (choice of metal: Zn^{2+} versus Eu^{3+}; addition of metal scavenger; transimination by a diamine or an alkoxyamine; addition of acid; see figure), giving access to five different macromolecular states with distinct material properties.

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Arylazopyrazoles as Superior Photoswitch in Supramolecular Systems

Lucas Stricker, Sven Sagebiel, Sabrina Engel, Bart Jan Ravoo

Organic Chemistry Institute (Corrensstraße 40, Westfälische Wilhelms-Universität Münster, 48149 Münster, Germany)

l.stricker@wwu.de

The formation of light-responsive host-guest inclusion complexes of azobenzenes and cyclodextrins (CDs) are well known. While the rod-like *E*-isomer forms a stable inclusion complex with α- and β-CD the more polar and bent *Z*-isomer does not fit in either CD cavity.[1] Despite their extensive use as light-responsive switch, azobenzenes exhibit considerable disadvantages. For example, as a result of the overlapping absorbances of both isomers incomplete photoswitching is observed for azobenzenes. The photostationary state (PSS) for common azobenzenes is about 80% for the *E*→*Z* and 70% for the *Z*→*E* isomerization. In particular in highly multivalent systems this drawback can limit a complete switching since a large fraction of remaining *E*-isomer can still dominate the properties of the material.[2]
Therefore, we recently explored arylazopyrazoles (AAPs) as a new light-responsive motif in those systems. Compared to azobenzenes, AAPs offer nearly quantitative photoisomerzation in both directions.[3] Derivatives of AAPs, varying in their substitution pattern, were readily synthesized in high yields enabling easy post-functionalization and water solubility. The excellent photophysical properties were confirmed by UV/Vis- and NMR spectroscopy. The formation of a host-guest complexes with CDs were investigated by isothermal titration calorimetry (ITC) revealing binding constants comparable to normal azobenzenes. Afterwards, AAPs were applied in CD-based supramolecular systems composed of cyclodextrin vesicles (CDV) and/or CD decorated (nano)particles.

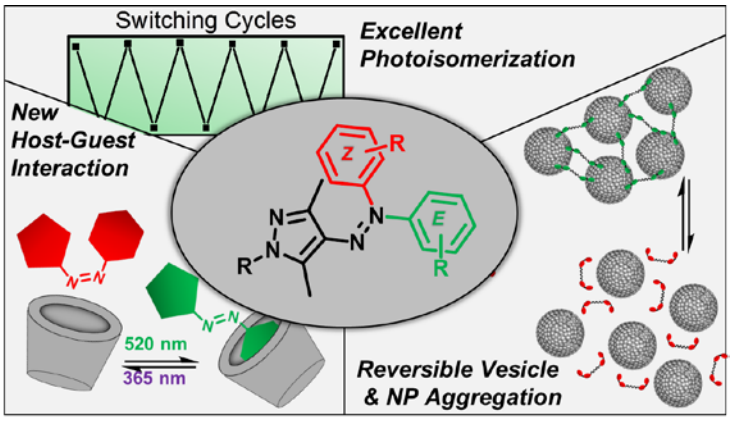

Figure 1: Schematic illustration of arylazopyrazole based supramolecular systems.

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Regulating autocatalytic kinetics using supramolecular interactions

Abraham J. P. Teunissen, Tim F. E. Paffen, Ivo W. Filot, Roy J. C. van der Haas, Menno D. Lanting, Tom F. A. de Greef and E. W. Meijer

Abraham J. P. Teunissen, University of Technology Eindhoven

a.j.p.teunissen@tue.nl

Feedback in biochemical networks embodies the essence of complex behavior and forms the basis of cellular regulatory mechanisms. However, it is still rare in synthetic systems and hereby hampers the advancement of life-like synthetic chemical networks. Here, we report a system in which the non-covalent interactions between two phase-transfer-catalysts are used to tune reaction kinetics from bimolecular to strongly autocatalytic, which is investigated in more detail using a computational model. The simplicity of the building blocks and mild operating conditions allow easy modification and provide a platform to construct complex reaction networks that mimic the complexity of intracellular signaling pathways.

Extremely Robust and Post-Functionalizable Gold Nanoparticles Coated with Calix[4]arenes

Hennie Valkenier, Ludovic Troian-Gautier, Alice Mattiuzzi, Ivan Jabin, Corinne Lagrost, Yann R. Leroux, Gilles Bruylants

Hennie Valkenier, Engineering of Molecular NanoSystems, Université Libre de Bruxelles, Avenue F.D. Roosevelt 50, CP165/64, B-1050 Brussels, Belgium

Hennie.Valkenier@ulb.ac.be

Gold nanoparticles (AuNPs) can be functionalized with various ligands to tailor their stability and other properties for a wide range of applications, from medicine to electronics. Thiols are most commonly used for the functionalization of AuNPs. The dynamic nature of the Au-S bond allows the facile formation of a dense self-assembled monolayer on gold, but also limits the stability of this layer. More robust organic layers are formed when aryl diazonium compounds are used to form Au-C bonds, though control of this process is limited.[1]

We will present the use of a calix[4]arene-tetra-diazonium salt (Fig 1a)[2] to form an extremely robust organic protection layer on AuNPs (Fig 1b). The robustness of our calixarene-coated AuNPs is demonstrated by drying the AuNPs into a gold-colored film or by precipitating them at pH 1, followed by their resuspension in an aqueous solution of NaOH to obtain a stable red suspension (Fig 1c). Dispersions of these AuNPs are also stable in the presence of physiologically relevant concentrations of NaCl or phosphate buffer. Even upon addition of fluoride, a stable red suspension is maintained for AuNPs coated with calixarenes, whereas AuNPs stabilized with citrate, alkanethiols, or decylbenzene (via Au-C bonds) aggregate as soon as fluoride is added (Fig 1d).

The carboxylate functional groups on the small rim allow post-functionalization of the AuNPs. We envision the use of mixtures of differently functionalized calix[4]arenes for the design of mixed binary monolayers[3] on gold nanoparticles, with controllable levels of post-functionalizable groups.

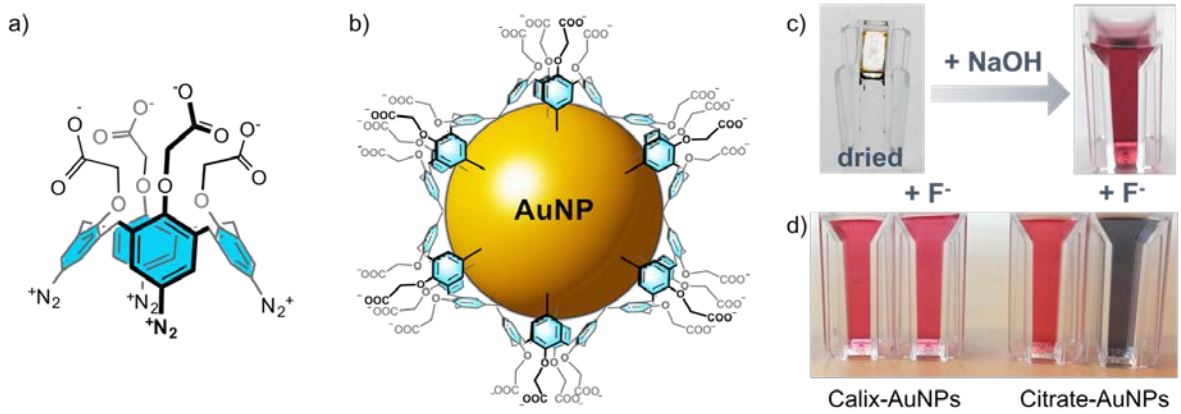

Figure 1 (a) Structure of calix[4]arene-tetra-diazonium salt used to prepared calixarene-coated AuNPs (b), which can be resuspended after drying (c), and are stable in the prescence of fluoride (d).

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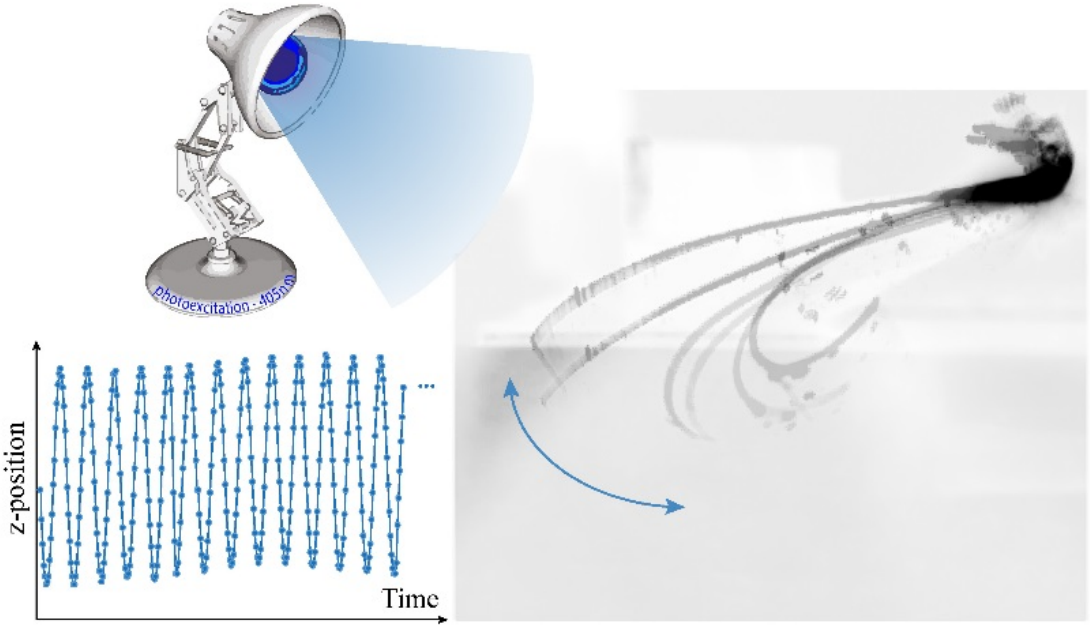
Light induced self-oscillation of hydrazone-based liquid-crystal networks

G. Vantomme, A. H. Gelebart, D. J. Broer, E. W. Meijer

Ghislaine Vantomme, Institute of Complex Molecular Systems, Laboratory of Macromolecular and Organic Chemistry, Eindhoven University of Technology

g.vantomme@tue.nl



Creating materials able to self-oscillate under (sun)light is regarded as a real challenge in the field of adaptive and stimulus-responsive materials. Smart materials that can convert light into mechanical energy are emerging as powerful devices.[1] Although light-responsive polymers that adapt their shapes and properties have been reported, materials that work under out-of-equilibrium conditions remain challenging[2] and hold promise for intriguing applications in energy harvesting and micro-robotics. We describe here the use of hydrazones as photo-switching units to obtain continuous motion into liquid crystal polymer network.[3] We demonstrate photo-induced unidirectional bending/unbending of colorless transparent films by hydrazone E to Z isomerization[4] into spatially confined aligned network. By incorporation of hydrazone with a fast thermal Z to E relaxation in the polymer network, we accomplish self-oscillations into the material in the form of large amplitude oscillations under continuous, unpolarized, monochromatic light irradiation.

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Facile Thioethers as Novel Class of Luminophors with Aggregation Induced Emission Properties

Jens Voskuhl[a], Steffen Riebe

[a] *Institute of Organic Chemistry, University of Duisburg-Essen, Universitätsstrasse 7, D-45117, Essen (Germany), jens.voskuhl@uni-due.de*

The need of novel efficient fluorophors for the recognition and labeling of biomolecules such as proteins enzymes and cells is one of the most challenging disciplines in modern biosupramolecular chemistry. Our group uses a phenomenon called aggregation induced emission.[1] Molecules with this ability show fluorescence, contrary to normal fluorophores, when aggregated or in the solid state. Recently we found a novel class of facile thioethers with this remarkable characteristic. Our system can be easily modified and was used for the detection of proteins and bacteria.[3] Furthermore we investigated the formation of fluorescent micelles using hydrogen bonding.[2] Currently 15 different compounds were investigated concerning their fluorescence properties. A range of emission in the visible region was found ranging from 430 to 590 nm. Interestingly delayed fluorescence was observed for specific compounds leading to the assumption, that and intersystem crossing to a triplet state occurs leading to a long lived fluorescence state, termed phosphorescence.

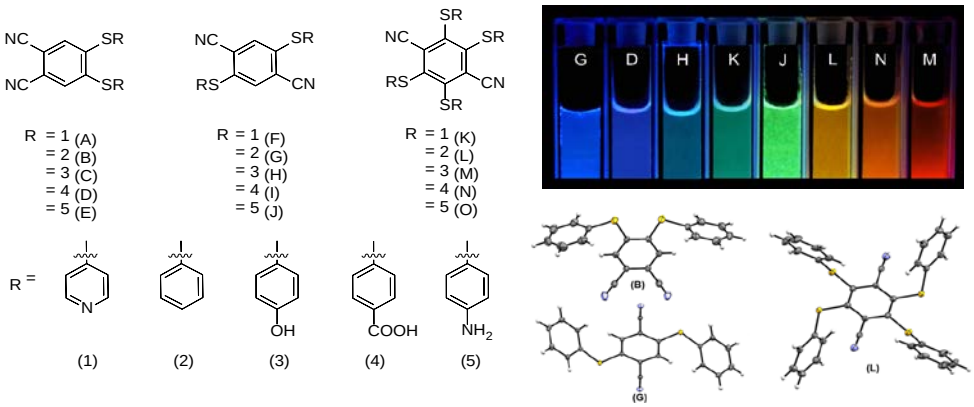

Fig.1: Molecular structures of the investigated molecules, photograph of selected compounds, when dispersed in water under UV-light irradiation and X-ray structures of compounds B, G and L.

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Stimulus-Responsive Nanocontainers with Functional Surface Modification by Use of Self-Assembled Templates

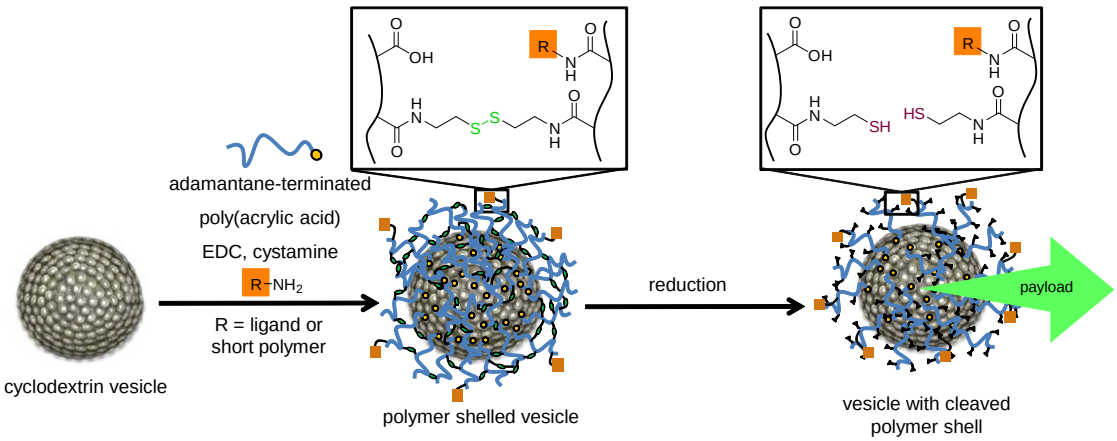
Wilke de Vries, M. Tesch, D. Grill, V. Gerke, A. Studer, B. J. Ravoo

Wilke de Vries, Oranic Chemistry Institute, Westfälische Wilhelms-Universität,

Corrensstr. 40, 48149 Münster, Germany.

W.deVries@uni-muenster.de

Synthetic vesicles allow the development of biomimetic soft materials, drug delivery systems and microreactors.[1,2] Previously, we reported on highly stable polymer shelled vesicles based on self-assembled templates of amphiphilic cyclodextrin derivatives. Adamantane-terminated poly(acrylic acid) was anchored on cyclodextrin vesicles *via* host-guest recognition followed by crosslinking of carboxylic acid groups.[3]
In this project a stimulus-responsive release of a hydrophilic payload from polymer shelled vesicles is realized by using reductively cleavable cystamine linker for crosslinking. The release of cargo is studied in reducing environments by fluorescence spectroscopy. Moreover it is shown that the surface of these stimulus-responsive nanocontainers can be functionalized easily within the crosslinking step. By using several ligands or short polymers a facile engineering of surface properties is possible. The immobilization of ligands enables highly specific recognition of proteins at the nanocontainer surface, which can be followed in aggregation experiments and by immobilization of the containers on protein-decorated surfaces. Currently we are investigating the capacity of these nanocontainers as a delivery system for hydrophilic cargo into cells.



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Dynamic control of anion binding affinity and selectivity

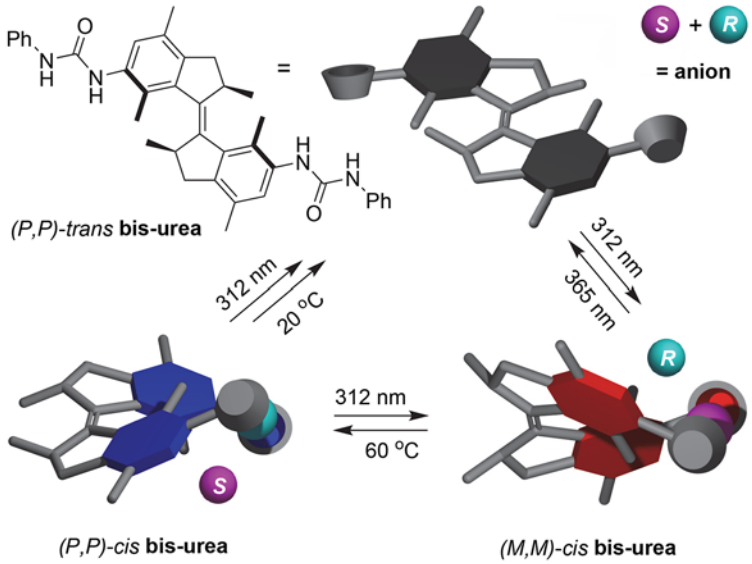
Sander J. Wezenberg, Matea Vlatković, Ben L. Feringa

Stratingh Institute for Chemistry, University of Groningen,

Nijenborgh 4, 9747 AG, Groningen (The Netherlands)

s.j.wezenberg@rug.nl

Anionic species play important regulatory roles in many essential biological processes (e.g. osmosis, recognition and signal transduction). Therefore, a tremendous effort is put into the development of artificial anion receptors that are able to facilitate transmembrane transport.[1] However, where biological anion transport systems alternate between low- and high-affinity states, the dynamic regulation of binding affinity in artificial receptors is extremely rare.[2]
We have developed a light- and heat-responsive anion receptor through the equipment of an overcrowded alkene-based molecular motor with two urea binding motifs (see Scheme).[3] This receptor can be switched between three isomers that possess different anion binding properties. Furthermore, The two possible *cis*-isomers hold opposite enantioselectivity in the binding of chiral phosphates.[4] Hence, the anion binding affinity can be controlled in a unique three-step process and, for the first time, it is demonstrated that the enantioselectivity of a receptor can be inverted dynamically in response to external stimuli. Potential applications of our system are foreseen in, for example, photocontrolled drug delivery and transmembrane anion transport.



Scheme: Isomerization and coordination behavior of the responsive bis-urea receptor.

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