

# Supramolecular and Nanochemistry

Edwin C. Constable\*, Catherine E. Housecroft\*, Marcel Mayor\*, Wolfgang P. Meier\*, Cornelia G. Palivan\*, Hermann A. Wegner\*, and Helma Wennemers\*

**Abstract:** The following contributions describe various research activities of the Department of Chemistry, University of Basel in the area of nanochemistry and supramolecular chemistry.

**Keywords:** Channel proteins · Gold nanoparticles · Membranes · Nanochemistry · Nanoreactors · Peptide libraries · Photoisomerization · Silver · Solar cells

## New Materials for Dye-Sensitized Solar Cells

Edwin C. Constable and Catherine E. Housecroft



The *Constable–Housecroft* group utilises metal–ligand interactions for the assembly of functional structures, lattices and devices. The favoured metal-binding motifs are 2,2'-bipyridine (bpy) and

2,2':6',2''-terpyridine (tpy) which have the advantage of being readily prepared with a wide variety of substituents and of forming metal complexes which are thermodynamically stable and possess varying kinetic properties (labile or inert).<sup>[1]</sup> The general aim of the research is to use these interactions in materials chemistry for the design of functional materials with a bias towards direct self-assembly within a device and the use of sustainable first row transition metals. This overview of the activity concentrates upon the materials chemistry programme which is complemented by fundamental research in metallosupramolecular chemistry.

The group recently described the concept of expanded ligands for the design of functional materials, in which a metal–ligand core serves as a spacer between functional groups which can bind additional metal centres.<sup>[2]</sup> Typical examples are seen in  $[M(\text{pytpy})_2]^{n+}$  complexes (pytpy = 4'-(4-pyridyl)-2,2':6',2''-terpyridine) which may be viewed as an expanded 4,4'-bipy-

ridine. The reaction of  $[M(\text{pytpy})_2]^{n+}$  with protons or additional metal ions at the pendant pyridine allows the designed synthesis of heterometallic one-dimensional materials in simple, self-assembly processes (Fig. 1a).<sup>[3–5]</sup> A simple extension of the concept leads to the ligand pymtpy which gives rise to two-dimensional structures in which both of the pyrimidine nitrogen atoms are coordinated to an additional metal centre (Fig. 1b).<sup>[6]</sup> The group is currently exploiting the redox and photophysical activity of the metal–ligand core to design novel functional materials.<sup>[7]</sup>

Molecular computing is one of the dreams of nanotechnology. In collaboration with Prof. Alberto Credi in Bologna, the group has been designing new photoactive metal complexes in which the emission characteristics may be modulated by the protonation state of basic substituents. The basic implementation using ruthenium or osmium complexes of pytpy allows the construction of truth tables corresponding to AND, OR or NOR logic operations, depending on the protonation of the pendant pyridyl groups. The basis of this behaviour is the difference in emission maximum and intensity in the three species  $[M(\text{pytpy})_2]^{2+}$

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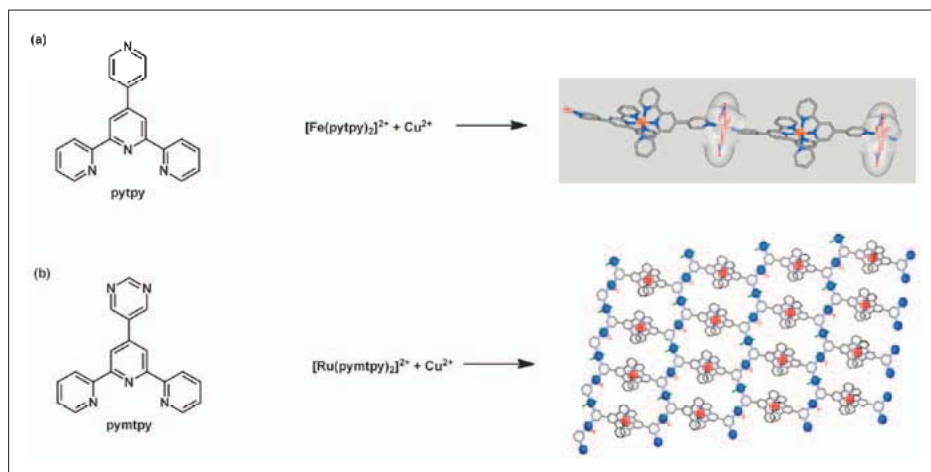


Fig. 1. The assembly of one- or two-dimensional networks from extended ligands based on (a) pytpy<sup>[4]</sup> or (b) pymtpy.<sup>[7]</sup>

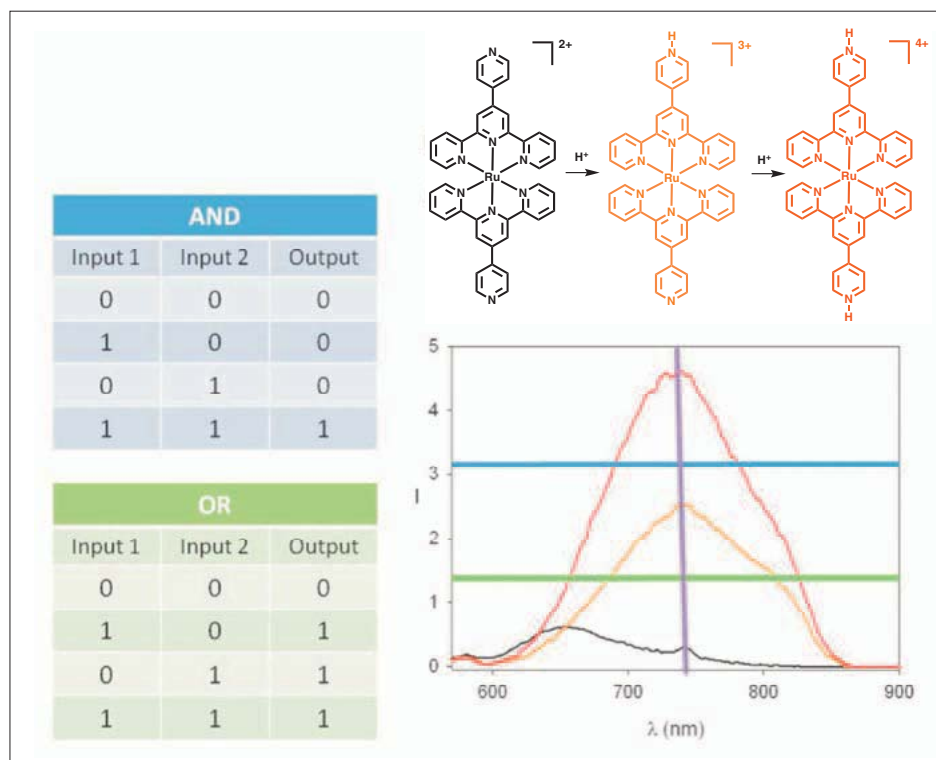


Fig. 2. The effect of protonation on the emission spectrum of  $[\text{Ru}(\text{pytpy})_2]^{2+}$  and a demonstration how different cut-off thresholds allow this simple system to exhibit two different logic operations (Acknowledgements to A. Credi and E. Dunphy for the artwork).

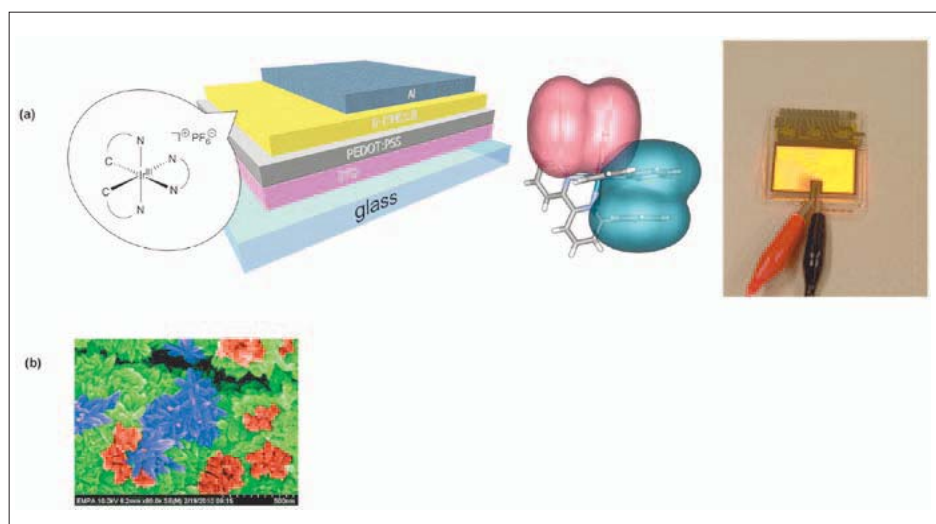


Fig. 3. (a) The general structure of an LEC, showing the generic structure of the iridium complex in the emitting layer and also showing an additional conducting polymer layer (PEDOT:PSS) to facilitate mobility; the p-stacking interactions important for obtaining long-lived devices and the emission of a typical device; (b) nanostructured haematite films obtained by hydrothermal synthesis and used for photoelectrochemical water-splitting. (Acknowledgements to H. Bolink and R. Costa for parts of Fig. 3a and A. Braun, D. Bora, T. Graule for Fig. 3b).

(Fig. 2),  $[\text{M}(\text{Hpytpy})(\text{pytpy})]^{3+}$  and  $[\text{M}(\text{Hpytpy})_2]^{4+}$ .<sup>[8]</sup> These complexes have then been coupled with other light or proton dependent reactions to produce prototype logical systems.<sup>[9,10]</sup> The disadvantage of the systems described to date is that they operate in solution and the group is actively involved in developing methods for the attachment of the functional units to innocent or functional surfaces.

The group has a long-standing and ongoing collaboration with that of Henk Bolink at the University of Valencia on the topic of light-emitting devices, including OLEDs and more particularly Light Emitting Electrochemical Cells (LECs). LECs are a very simple devices which in a prototype form comprise a single layer of electroactive material between two electrodes (Fig. 3). Upon applying a bias, holes and

electrons are injected, travel through the medium and combine to form an excited species which then decays to the ground state with emission of light. Real world devices are usually rather more complex as additional layers and blends are included to improve the mobility of the charge carriers. Until recently, LECs were viewed as a laboratory curiosity because the operating lifetime was very short, typically of the order of a few hours. In collaboration with Bolink, the group has demonstrated that by the careful design of iridium complexes containing cyclometallated ligands, such as the 2-phenylpyridine anion, devices with lifetimes long enough for commercialization may be prepared. The design of ligands which can control the properties of the excited state are critical to this approach and is predicated upon the observation that the excited states are antibonding with respect to ligand loss, which in turn is responsible for the low lifetimes of prototype structures. A strategy has been adopted in which intramolecular  $\pi$ -stacking is used to minimise excited state expansion and thus increase the lifetimes of the devices.<sup>[11–15]</sup> Current work centres upon determining the intrinsic and environmental factors which influence the lifetime, the brightness, the colour and the turn-on times of LECs, work involving the synthesis of a wide variety of redox and photoactive compounds for testing. The group is also involved in trying to elucidate the relationships between the three-dimensional crystal structures of the active layer materials and the structure of the material within the film. A new activity is the development of sustainable materials for use in OLEDs and LECs; whilst state-of-the-art devices are based upon iridium sensitizers or reactive layers, the price ( $\$22,820 \text{ kg}^{-1}$  on 16.08.10) and abundance (0.003 ppb in the Earth's crust) of iridium raises serious questions about the long-term viability of the technology and alternative complexes based upon copper ( $50 \text{ ppm}$ ,  $\$7 \text{ kg}^{-1}$ ) or zinc ( $75 \text{ ppm}$ ,  $\$2 \text{ kg}^{-1}$ ) are being investigated.

The group has long been involved in the design and optimisation of transition metal complexes as light absorbers for Dye-Sensitized Solar Cells (DSCs) and Constable was an author of the seminal paper describing dye-sensitization of single crystal  $\text{TiO}_2$ , and observation brought to exquisite success by the use of nano-particulate  $\text{TiO}_2$  in the Graetzel Cell. Briefly, the DSC works by matching the ground and excited states of a dye to the conduction band of the  $\text{TiO}_2$  semiconductor, such that excitation of the dye in the visible region leads to injection of an electron into the conduction band. The direct excitation of an electron from the valence band of the  $\text{TiO}_2$  would require UV light. The group is actively involved in the design of new materials

which tune the wavelength of absorption of the dye to utilise as much of the visible spectrum as possible, control the rates of the forward electron injection process and minimise the rates of back-electron transfer and which can be efficiently and rapidly regenerated. A key feature in the design is the incorporation of groups which bind the dyes to the surface of the  $\text{TiO}_2$  and in addition to the more conventional carboxylates, the group is actively investigating novel ways of utilising phosphonate linkers. Although state-of-the-art devices based on ruthenium dyes can achieve efficiencies of greater than 10%, the sustainability aspects relating to the abundance (1 ppb in the Earth's crust) and price ( $\$6100 \text{ kg}^{-1}$ ) of ruthenium may limit uptake of the technology and one of the major challenges for the Constable-Housecroft group is to establish efficient dyes based upon copper(I) complexes, which have similar photophysical properties to ruthenium compounds.<sup>[16,17]</sup> A prototype system has been described which has already reached efficiencies of 2–3% and newly designed complexes have proved to be even more efficient.<sup>[18,19]</sup>

In addition to the design of molecular dyes for DSCs, the group is also involved in novel methods for the preparation of metal oxide phases. In particular, in collaboration with Professor Uwe Pieleas at FHNW, flame spray pyrolysis methods are being investigated for the preparation of  $\text{TiFeO}_x$  materials and with Dr Artur Braun at EMPA solution-based methods are being utilised for the preparation of nanostructured haematite films. Hydrothermal processing and reforming of the haematite films results in the preparation of materials with beautiful nanostructures.

- [1] E. C. Constable, *Chem. Soc. Rev.* **2007**, *36*, 246.
- [2] E. C. Constable, *Coord. Chem. Rev.* **2008**, *252*, 842.
- [3] J. Beves, E. C. Constable, C. E. Housecroft, C. Kepert, D. J. Price, *Cryst. Eng. Comm.* **2007**, *9*, 456.
- [4] J. E. Beves, E. C. Constable, C. E. Housecroft, M. Neuberger, S. Schaffner, *Cryst. Eng. Comm.* **2008**, *10*, 344.
- [5] J. E. Beves, E. C. Constable, C. E. Housecroft, C. J. Kepert, M. Neuberger, D. J. Price, S. Schaffner, *Cryst. Eng. Comm.* **2007**, *9*, 1073.
- [6] J. E. Beves, E. C. Constable, S. Decurtins, E. L. Dunphy, C. E. Housecroft, T. D. Keene, M. Neuberger, S. Schaffner, *Cryst. Eng. Comm.* **2008**, *10*, 986.
- [7] E. C. Constable, E. L. Dunphy, C. E. Housecroft, M. Neuberger, S. Schaffner, F. Schaper, S. R. Batten, *Dalton Trans.* **2007**, 4323.
- [8] E. C. Constable, C. E. Housecroft, A. M. W. C. Thompson, P. Passaniti, S. Silvi, M. Maestri, A. Credi, *Inorg. Chim. Acta* **2007**, *360*, 1102.
- [9] S. Silvi, E. C. Constable, C. E. Housecroft, J. E. Beves, E. L. Dunphy, M. Tomasulo, F. M. Raymo, A. Credi, *Chem. Eur. J.* **2009**, *15*, 178.
- [10] S. Silvi, E. C. Constable, C. E. Housecroft, J. E. Beves, E. L. Dunphy, M. Tomasulo, F. M. Raymo, A. Credi, *Chem. Commun.* **2009**, 1484.
- [11] H. J. Bolink, E. Coronado, R. D. Costa, E. Ortí, M. Sessolo, S. Graber, K. Doyle, M. Neuberger,

- C. E. Housecroft, E. C. Constable, *Adv. Mater.* **2008**, *20*, 3910.
- [12] S. Graber, K. Doyle, M. Neuberger, C. E. Housecroft, E. C. Constable, R. D. Costa, E. Ortí, H. J. Bolink, *J. Am. Chem. Soc.* **2008**, *130*, 14944.
- [13] H. J. Bolink, E. C. Constable, E. Coronado, R. D. Costa, S. Graber, C. E. Housecroft, N. Lardiés, M. Neuberger, E. Ortí, S. Schaffner, M. Sessolo, *Chem. Commun.* **2009**, 2029.
- [14] H. J. Bolink, E. Coronado, R. D. Costa, N. Lardiés, E. Ortí, S. Graber, M. Neuberger, C. E. Housecroft, S. Schaffner, E. C. Constable, *Adv. Funct. Mat.* **2009**, *19*, 3456.
- [15] R. D. Costa, E. Ortí, H. J. Bolink, S. Graber, C. E. Housecroft, E. C. Constable, *Adv. Funct. Mater.* **2010**, *20*, 1511.

- [16] B. Bozic-Weber, E. C. Constable, E. Figgemeier, C. E. Housecroft, W. Kylberg, *Energy Environ. Sci.* **2009**, *2*, 299.
- [17] B. Bozic-Weber, E. C. Constable, C. E. Housecroft, M. Neuberger, J. R. Price, *Dalton Trans.* **2010**, *39*, 3585.
- [18] T. Bessho, E. C. Constable, M. Graetzel, A. Hernandez Redondo, C. E. Housecroft, W. Kylberg, M. K. Nazeeruddin, M. Neuberger, S. Schaffner, *Chem. Commun.* **2008**, 3717.
- [19] A. Hernandez Redondo, E. C. Constable, C. E. Housecroft, *Chimia* **2009**, *63*, 205.

## Nanoarchitectures and Molecular Devices

Marcel Mayor



The activities of the *Mayor* lab are geared towards tailor-made molecules for fundamental physical and physico-chemical investigations. Since its invention synthetic chemistry is focused on the design and the synthesis of molecules, tiny objects assembled with atomic precision and of nanoscale dimensions. Macromolecular oligomers with sizes of several nanometers can be synthesized from *bottom-up* with particular physical properties and intrinsic functions. From the other side, coming *top-down*, the same dimensional area is explored by experimental physicists by their recent improvements in experimental tools. At this fast developing interface between chemistry and physics a new scientific field emerged and was labelled according to the dimensions of interest 'nanotechnology'. Within the Mayor research team new scientific challenges and fundamental questions are identified in close cooperation with colleagues from physics and physical chemistry and molecular structures potentially providing answers are designed, synthesized, inte-

grated in the experimental set-up and investigated.

Since nearly one decade the group has explored the integration of single molecules as functional units in electronic circuits. While in the beginning their studies were limited to the comparison of solely two molecules differing in a structural property like *e.g.* symmetry<sup>[1]</sup> or the position of the anchor groups,<sup>[2]</sup> their recent investigations are based on entire families of molecules systematically varying in a single structural feature. The torsion angle  $\phi$  between both phenyl rings of the biphenyl skeleton was systematically varied within the series of cyclophanes displayed in Fig. 1 by varying the length of the second interlinking alkyl chain.<sup>[3–5]</sup> The delocalization of the biphenyl  $\pi$ -system depends on the torsion angle  $\phi$  which is reflected in numerous physical properties such as the electronic absorption properties,<sup>[3]</sup> the NLO efficiency<sup>[6]</sup> or the single molecule transport features.<sup>[4,5]</sup> Single molecule rectification was reported as an example of an electronic function as an intrinsic feature of the integrated molecule<sup>[7]</sup> and more recently even single molecule electroluminescence experiments became feasible with tailor-made molecular rods. Model compounds to explore the formation of intermolecular

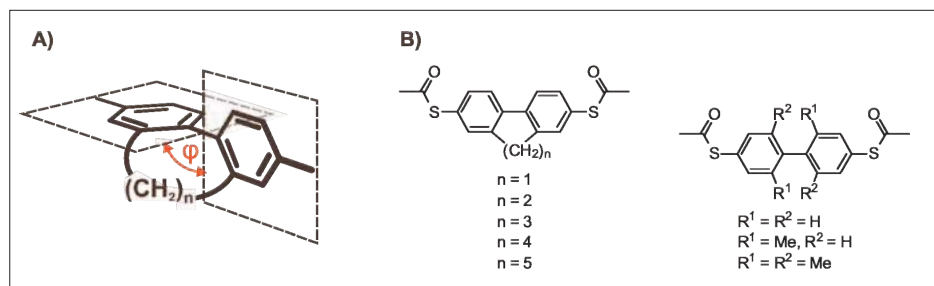


Fig. 1. A) Concept of tuning the interphenylring torsion angle  $\phi$  in a biphenyl cyclophane by adjusting the length of the interlinking alkyl chain. B) Series of synthesized biphenyl derivatives.

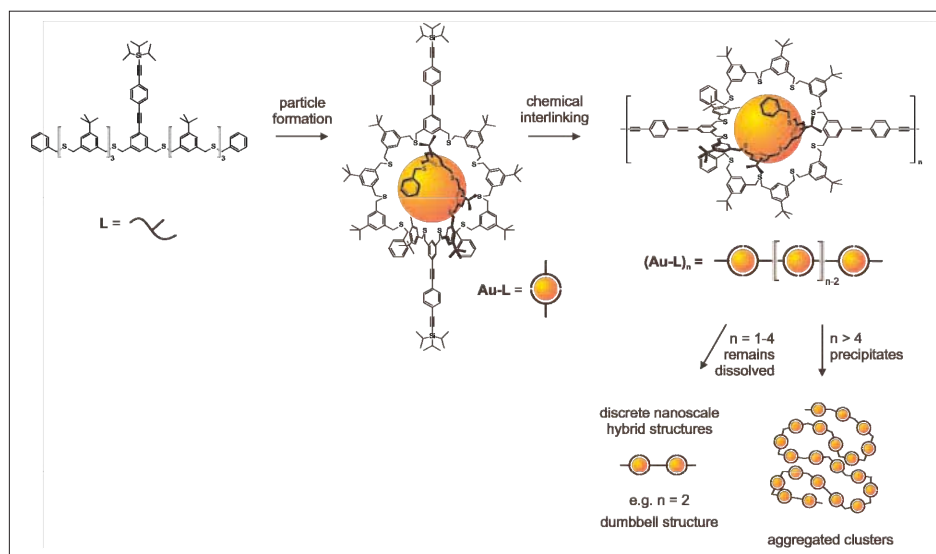


Fig. 2. The concept of controlling the formation and the surface functionalization of gold nanoparticles by oligomeric ligands. The integer number of surface functions allows the subsequent interlinking. The formation of either polymeric chains comprising nanoparticles or discrete hybrid structures can be tuned by the reaction conditions during interlinking.

junctions<sup>[8]</sup> and molecule-based switching mechanisms are in the current focus of the research group too.<sup>[9–13]</sup>

Our research interests are not only geared towards the integration of single molecules but also towards monomolecular layers investigated by scanning probe methods. Cyclophanes comprising two naphthalenediimides were synthesized in order to provide one chromophore to steer the lateral self-assembly while the second one remains decoupled from the surface.<sup>[14]</sup> While the variation of the core substituents allowed the optical features to be adjusted,<sup>[15]</sup> these model compounds turned out to be of interest as anion binders as well.<sup>[16]</sup> New approaches to assemble oligomeric macromolecules by a protection group-based masking of the reactivity on the substrate<sup>[17]</sup> or rigid star-type structures tailored to form porous networks based on fluorine–hydrogen bonds were reported.<sup>[18]</sup>

In another approach the group tries to combine the self-assembly potential of organic structures with the improved stability features of inorganic nanoparticles by synthesizing organic/inorganic hybrid materials. Organic ligands able to stabilize gold nanoparticles of a particular size were synthesized<sup>[19]</sup> and used to functionalize the particle surface with an integer number of reactive groups.<sup>[20]</sup> The concept is displayed in Fig. 2 and provided molecule-like particles addressable by wet chemical procedures.

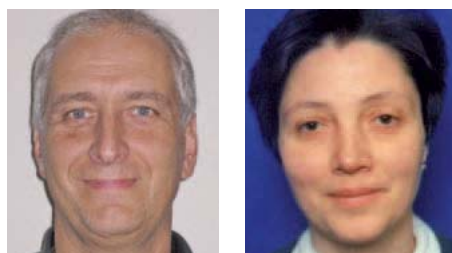
By tailoring physical-chemical properties the group is synthesizing macromolecular model compounds for molecular interferometry experiments in order to explore the transition between quantum and classical mechanics.<sup>[21,22]</sup> Recently an intrinsic molecular feature – namely its

susceptibility – was distinguished in an interference experiment. For that purpose two sublimable constitutional isomers with different polarizability were designed and synthesized.<sup>[23]</sup>

- [1] J. Reichert, R. Ochs, D. Beckmann, H. B. Weber, M. Mayor, H. v. Löhnneysen, *Phys. Rev. Lett.* **2002**, *88*, 176804.
- [2] M. Mayor, H. B. Weber, J. Reichert, M. Elbing, C. von Hänisch, D. Beckmann, M. Fischer, *Angew. Chem. Int. Ed.* **2003**, *42*, 5834.
- [3] D. Vonlanthen, J. Rotzler, M. Neuburger, M. Mayor, *Eur. J. Org. Chem.* **2010**, 120.
- [4] D. Vonlanthen, A. Mishchenko, M. Elbing, M. Neuburger, T. Wandlowski, M. Mayor, *Angew. Chem. Int. Ed.* **2009**, *48*, 8886.
- [5] A. Mishchenko, D. Vonlanthen, V. Meded, M. Bürkle, C. Li, I. V. Pobelov, A. Bagrets, J. K. Viljas, F. Pauly, F. Evers, M. Mayor, T. Wandlowski, *Nano Lett.* **2010**, *10*, 156.
- [6] J. Rotzler, D. Vonlanthen, A. Barsella, A. Boeglin, A. Fort, M. Mayor, *Eur. J. Org. Chem.* **2010**, 1096.

## Polymeric Membranes

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Cell membranes serve as an interface that controls interactions and communication within a cell and between a cell and the environment. In addition, they provide (in-

- [7] M. Elbing, R. Ochs, M. Koentopp, M. Fischer, C. von Hänisch, F. Weigend, F. Evers, H. B. Weber and M. Mayor, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 8815.
- [8] S. Wu, M. T. González, R. Huber, S. Grunder, M. Mayor, C. Schönenberger, M. Calame, *Nature Nanotech.* **2008**, *3*, 569.
- [9] G. Pace, V. Ferri, C. Grave, M. Elbing, C. von Hänisch, M. Zharnikov, M. Mayor, M. A. Rampi, P. Samorì, *Proc. Nat. Acad. Sci. USA* **2007**, *104*, 9937.
- [10] V. Ferri, M. Elbing, G. Pace, M. D. Dickey, M. Zharnikov, P. Samorì, M. Mayor, M. A. Rampi, *Angew. Chem. Int. Ed.* **2008**, *47*, 3407.
- [11] J. M. Mativetsky, G. Pace, M. Elbing, M. A. Rampi, M. Mayor, P. Samorì, *J. Am. Chem. Soc.* **2008**, *130*, 9192.
- [12] S. Grunder, R. Huber, V. Horhoiu, M. T. González, C. Schönenberger, M. Calame, M. Mayor, *J. Org. Chem.* **2007**, *72*, 8337; S. Grunder, R. Huber, S. Wu, C. Schönenberger, M. Calame, M. Mayor, *Eur. J. Org. Chem.* **2010**, 833.
- [13] N. Weibel, A. Mishchenko, T. Wandlowski, M. Neuburger, Y. Leroux, M. Mayor, *Eur. J. Org. Chem.* **2009**, 6140.
- [14] S. Gabutti, M. Knutzen, M. Neuburger, G. Schull, R. Berndt, M. Mayor, *Chem. Commun.* **2008**, 2370.
- [15] S. Gabutti, S. Schaffner, M. Neuburger, M. Fischer, G. Schäfer, M. Mayor, *Org. Biomol. Chem.* **2009**, *7*, 3222.
- [16] R. E. Dawson, A. Hennig, D. P. Weimann, E. Emery, V. Ravikummar, J. Montenegro, T. Takeuchi, S. Gabutti, M. Mayor, J. Mareda, C. A. Schalley, S. Matile, *Nature Chem.* **2010**, *2*, 533.
- [17] S. Boz, M. Stöhr, U. Soydaner, M. Mayor, *Angew. Chem. Int. Ed.* **2009**, *48*, 3179.
- [18] Z. Mu, L. Shu, H. Fuchs, M. Mayor, L. Chi, *J. Am. Chem. Soc.* **2008**, *130*, 10840.
- [19] T. Peterle, A. Leifert, J. Timper, A. Sologubenko, U. Simon, M. Mayor, *Chem. Commun.* **2008**, 3438.
- [20] T. Peterle, P. Ringler, M. Mayor, *Adv. Funct. Mater.* **2009**, *19*, 3497.
- [21] S. Gerlich, L. Hackermüller, K. Hornberger, A. Stibor, H. Ulbricht, M. Gring, F. Goldfarb, T. Savas, M. Müri, M. Mayor, M. Arndt, *Nature Physics* **2007**, *3*, 711.
- [22] S. Gerlich, M. Gring, H. Ulbricht, K. Hornberger, J. Tüxen, M. Mayor, M. Arndt, *Angew. Chem. Int. Ed.* **2008**, *47*, 6195.
- [23] J. Tüxen, S. Gerlich, S. Eibenberger, M. Arndt, M. Mayor, *Chem. Commun.* **2010**, 4145.

ternal) compartmentalization that permits spatial control of different functions. Artificial membranes and vesicles are the subject of increasing interest as model systems that mimic biomembranes and organelles or even whole cells. In particular, in recent years membranes and vesicles from amphiphilic block copolymers have raised considerable attention.<sup>[1a–d]</sup> Amphiphilic block copolymers can generally be regarded as higher molar mass homologues of conventional lipids or surfactants that form similar self-assembled superstructures in selective solvents. However, as a result of

higher molar mass, they frequently form larger aggregates with lower dynamics. Membrane structures from amphiphilic block copolymers may be up to ten times thicker than those of natural bilayer-forming phospholipids, therefore displaying considerably higher mechanical stability. Additionally, they can be stabilized and 'frozen' by crosslinking polymerization of reactive block copolymers. The mechanical properties of block copolymer membranes are primarily controlled by their hydrophobic domain and their 'phase behaviour' (e.g. fluid or glassy). The complexity of the artificial membranes can also be increased by mixing different block copolymers, or lipids and block copolymers. This combination was recently used to control the average membrane thickness<sup>[2]</sup> or even to induce formation of polymeric and/or lipid rafts that result from the very limited miscibility of the different components within the membranes.<sup>[3]</sup> In amphiphilic ABC triblock copolymers with two chemically different hydrophilic blocks, the incompatibility of different polymers induces the formation of asymmetric membranes<sup>[4a,b]</sup> that – in certain cases – seem to be able to undergo pH-induced 'breathing'<sup>[5]</sup> or membrane inversion.<sup>[4a,6]</sup> Interestingly, the broken symmetry of ABC triblock copolymer membranes also induces a directional insertion of molecules and proteins, and hence a directional functionality across membranes.

Different aspects of block copolymer vesicles and membranes have recently been summarized in various reviews<sup>[1b–d,7a,b]</sup> that provide a good overview of the current state of the art. Therefore, in the following we will primarily focus on certain selected aspects and newer developments in this field.

**Meiers'** group is interested in the design of new biomimetic membrane structures, *i.e.* spherical vesicles and planar membranes.<sup>[4a,8]</sup> Depending on their chemical composition, polymer membranes have been designed to be symmetric or asymmetric, with a variety of hydrophobic and hydrophilic block lengths and ratios thereof. This permits a variety of morphologies or the fulfillment of complex requirements when combined with biological molecules, such as enzymes or membrane proteins. Vesicles formed by self-assembly of amphiphilic copolymers can be designed to show 'stealth' properties, to be non-toxic, and biodegradable.<sup>[9]</sup> They can be designed with high loading capacities<sup>[10]</sup> and, due to their compartmentalized structure, to allow for simultaneous delivery of hydrophilic and hydrophobic drugs.<sup>[11]</sup>

More recently, research has been directed toward the preparation of solid-supported amphiphilic block copolymer membranes. Such structures are particu-

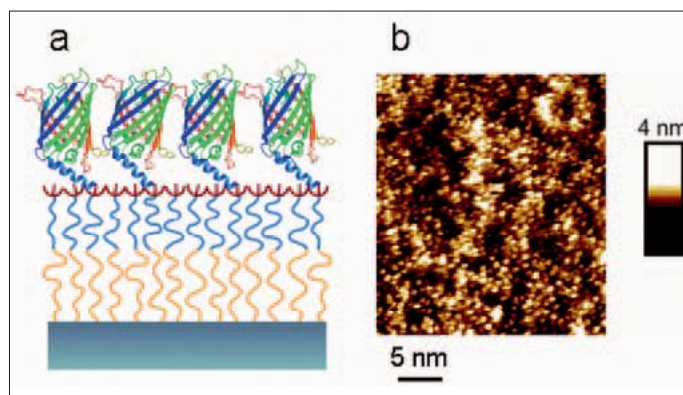


Fig. 1. a) Schematic representation of proteins binding to metal-functionalized copolymer films, b) height AFM images of the copolymer film after protein incubation.

larly interesting as model systems for the development of robust biosensor devices. The first biomimetic, polymer-based membrane was prepared by a 'grafting from' approach, *i.e.* a surface-initiated atom transfer radical polymerization of amphiphilic triblock copolymers with a hydrophilic-hydrophobic-hydrophilic sequence on gold and silicon surfaces.<sup>[12]</sup> Furthermore, 'grafting to' approaches have also been applied successfully as an alternate technique for preparing solid-supported block copolymer membranes by fusion of positively charged polymer vesicles on negatively charged SiO<sub>2</sub> and mica<sup>[13]</sup> or successive Langmuir-Blodgett transfer of thiol-modified block copolymer monolayers to gold surfaces.<sup>[14]</sup> Preliminary experiments indicate that supported block copolymer membranes conserve their structural integrity even upon drying, thus opening a potential route to air-stable biosensor systems.

Polymer membranes are quite tolerant of chemical modification as a result of the macromolecular nature of the basic building blocks. This has recently been exploited for the coupling of specific ligands and/or receptors, such as biotin, polyguanylic acid, or Ni-NTA, allowing for molecular recognition at block copolymer membrane surfaces (Fig. 1a). In recent years we and others have applied this concept successfully to study cell targeting and/or binding of block copolymer vesicles to surfaces.<sup>[9,15a,c]</sup>

An interesting aspect arises from the densely packed, hydrophilic polymer brushes at the surface of block copolymer membranes that allow for the engineering of ligand–receptor interactions: the length of the hydrophilic block of the polymers can be used to sterically control access by ligands to larger receptors at the membrane surface.<sup>[15b,c]</sup> By designing membrane surfaces appropriately, however, Ni-NTA groups at the surface of poly(butadiene)-*b*-poly(ethylene glycol) vesicles show binding affinities for oligohistidine residues of proteins in the micromolar range.<sup>[15b]</sup> This value is in good agreement with literature data, thus indicating that the polymer chains in this case did not affect protein

binding. Recent experiments indicate that protein binding to Ni-NTA functionalized block copolymer membranes can induce the formation of densely packed and ordered protein arrays (Fig. 1b).<sup>[16]</sup> A particularly interesting feature of polymer membranes and monolayers arises from high compressibility, which conveniently allows the adaptation of the density of binding sites at their surfaces to the dimensions of a particular protein. This opens a new route to induce two-dimensional crystallization of proteins or to develop new types of biosensors.

Remarkably, despite their thickness and mechanical stability, synthetic block copolymer membranes permit functional insertion of membrane proteins, enabling additional interactions and providing, for example, controlled permeability.<sup>[17]</sup> This clearly indicates that block copolymer membranes can serve as a robust, versatile model of natural biomembranes that enables unprecedented control of membrane parameters such as intramembrane and transmembrane processes.<sup>[18a,b]</sup> Surprisingly, recent model investigations with the antimicrobial peptide alamethicin indicated that block copolymer membranes may even be more compatible with this peptide than are natural lipid bilayers.<sup>[19]</sup> This seems to be the result of extremely high flexibility and conformational freedom inside the polymer membranes. Computer simulations confirmed that transmembrane proteins can be incorporated into polymer membranes, even with a large thickness mismatch; the origin of this approach lies in the exceptionally high compressibility of the polymer membranes together with the polydispersity of the polymers.<sup>[20]</sup> For example, transmembrane transport has been demonstrated to be mediated by successfully incorporating pore proteins LamB, OmpF, maltoporin, and aquaporin in polymer membranes (Fig. 2a). Such systems offer new possibilities for bioconversion, development of artificial organelles, filter devices, virus 'traps', *etc.*<sup>[21]</sup>

Since membrane proteins are usually very difficult to purify from associated phospholipids of biological membranes,

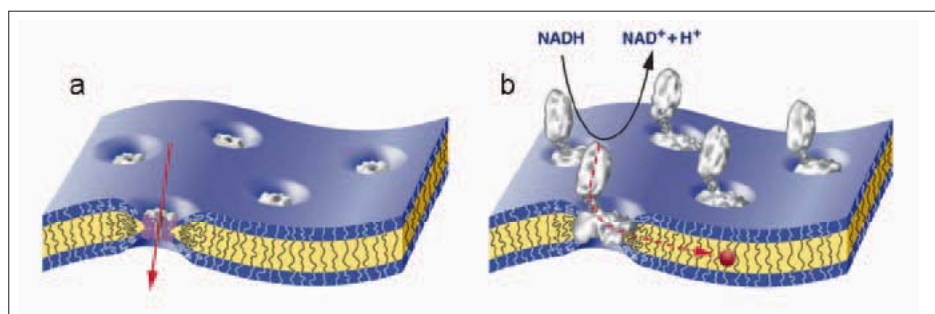


Fig. 2. Schematic representation of insertion in a polymeric membrane of a) channel proteins, and b) membrane proteins.

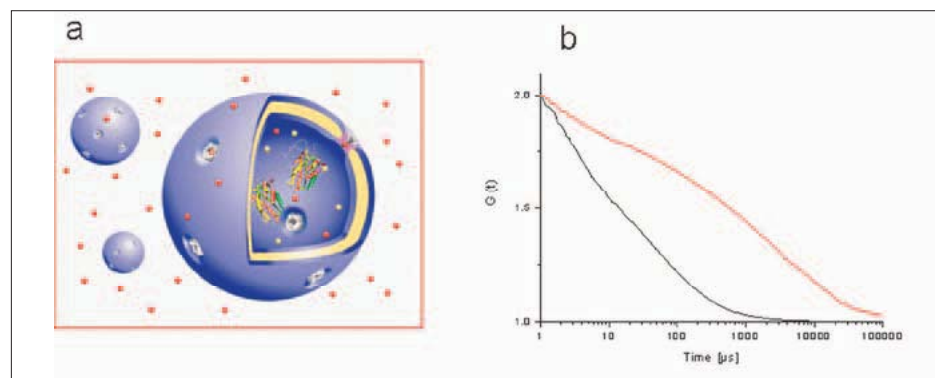


Fig. 3. a) Schematic representation of a polymeric nanoreactor with channel proteins inserted in the membrane to allow passage of substrates/products from and to its environment; b) FCS autocorrelation curves indicating that superoxide dismutase was successfully encapsulated inside the nanoreactor.

one might speculate that such lipid ‘islands’ in the polymer membranes are responsible for protein activity in polymer membranes. In an important basic experiment, Meier and Palivan recently demonstrated that delipidized NADH-ubiquinone oxidoreductase is reactivated in polymer membranes, thus clearly proving that pure block copolymer membranes also provide an environment that allows membrane proteins to adopt an active conformation. In addition, the molecular composition of the polymer membranes can be used to control their activity.<sup>[22]</sup> NADH-ubiquinone oxidoreductase mediates an electron transfer across polymer membranes. This could potentially be exploited for the design of biomimetic batteries or fuel cells or to perform specific chemical reactions inside or across polymer membranes (Fig. 2b).

Reconstituted channel proteins can be used to prepare polymer membranes with controlled permeability. Recently, the group used this concept to develop new, highly selective, water-permeable polymer membranes by inserting the water channel, Aquaporin Z, from *E. Coli*.<sup>[23]</sup> Permeability measurements were performed with block copolymer vesicles that were exposed to osmotic shock by dispersing them in a buffer of high osmolarity. The resulting osmotic pressure gradient drove the encapsulated

water out of the vesicles and induced their shrinkage. The rate at which the shrinkage occurs can then be used to calculate the water permeability coefficients. Although the resulting hybrid membranes have not yet been optimized with respect to density of inserted channel proteins, they exceed the water permeability of conventional, reversed osmosis membranes by more than an order of magnitude.

Some years ago Meier’s group introduced the concept of so-called polymer nanoreactors that makes use of polymer vesicles with encapsulated enzymes as nanometer-sized reaction compartments. Achieving persistent, continuous reactions requires selective permeability on the part of nanoreactor walls in order to exchange substrates and products with the environment. Typically, this requires a certain membrane porosity that can be created by using appropriately designed block copolymers<sup>[24]</sup> that form nanoporous membranes, or by inserting channel proteins into the vesicle walls (Fig. 3a).<sup>[18b,25]</sup> Recently, such channel-equipped nanoreactors were selectively immobilized on glass surfaces and successfully applied as nanometer-sized compartments to directly monitor the formation of a fluorescent product in their interiors.<sup>[26]</sup> These systems can be regarded as ideal models to investigate the effect of confined geometries on reac-

tion kinetics. A relatively large fluctuation in the number of reactants is inherent in systems that contain a small number of interacting species. Therefore, the partitioning of reagent species into small volumes and the low number of species present in each compartment make it difficult to apply classical chemical kinetics to describe the temporal course of individual reactions within restricted geometries. Similar conditions are found in highly compartmentalized biological cells.

An interesting alternative to ‘porous’ membranes has recently been introduced by designing the wall-forming membranes of the nanoreactors such that substrates are readily soluble in their hydrophobic parts and, hence, are able to permeate efficiently. For example, Palivan developed antioxidant nanoreactors, inside of which superoxide dismutase or its mimics were both shielded from the outside environment and were able to act *in situ*.<sup>[27a,b]</sup>

The mild procedure of vesicle generation in the presence of the enzyme allowed its encapsulation, as established by fluorescence correlation spectroscopy (Fig. 3b). In addition the metal-binding region, which represents the catalytic active site of the enzyme/mimics<sup>[28]</sup> was not affected, thus the enzyme/mimics were completely functional inside the nanoreactor. Here, the chemical constitution of the polymeric wall was designed to allow optimum permeation of superoxide radicals and related oxygen species.<sup>[10]</sup>

A particularly interesting aspect arises from the high stability and inertness of the wall-forming block copolymers. Recent experiments have shown that enzyme-loaded nanoreactors that were modified with specific ligands on their outer surfaces can selectively be taken up by macrophages *via* receptor mediated endocytosis. Surprisingly, the intact nanoreactors were able to escape from the lysosomes and accumulated inside the cytoplasm of the living cells, where they preserved their activity over several days and actively exchanged substrates and products with their environment. Such ‘artificial organelles’ hold great potential as a new concept for prodrug therapy or to analyse the response of living organisms on a persistent perturbation induced by locally producing bioactives at a subcellular level.

In order to develop new strategies to create materials with a high level of complexity and functionality in the lab, a deeper understanding is required on how self-organization and the resulting structures and interfacial patterns are controlled by the molecular architecture of the building blocks. A detailed understanding of such behaviour requires multi-disciplinary strategies combining concepts from chemistry, biology and physics. Biomimetic block

copolymer membranes, vesicles and nanoreactors provide an ideal tool to reduce the complexity of biological systems and to systematically investigate individual aspects, such as interactions at membrane surfaces or reactions in confined media. For the latter in particular, the robustness of the polymeric systems together with the possibility of combining them with biological building blocks opens a route for transferring concepts from biology to technical applications.

- [1] a) D. E. Discher, A. Eisenberg, *Science* **2002**, *297*, 967; b) A. Mecke, C. Dittrich, W. Meier, *Soft Matter* **2006**, *2*, 751; c) K. Kita-Tokarczyk, J. Grumelard, T. Haefele, W. Meier, *Polymer* **2005**, *46*, 3540; d) D. E. Discher, F. Ahmed, *Annu. Rev. Biomed. Eng.* **2006**, *8*, 323.
- [2] K. P. Davis, T. P. Lodge, F. S. Bates, *Macromolecules* **2008**, *41*, 8289.
- [3] D. A. Christian, A. Tian, W. G. Ellenbroek, I. Levental, K. Rajagopal, P. A. Janney, A. J. Liu, T. Baumgart, D. E. Discher, *Nature Mater* **2009**, *8*, 843.
- [4] a) R. Stoescu, W. Meier, *Chem. Commun.* **2002**, 3016; b) R. Stoescu, A. Graff, W. Meier, *Macromol. Biosciences*, **2004**, *4*, 930.
- [5] S. Yu, T. Azzam, I. Rouiller, A. Eisenberg, *J. Am. Chem. Soc.* **2009**, *131*, 10557.
- [6] E. G. Bellomo, M. D. Wyrsta, L. Pakstis, D. J. Pochan, T. J. Deming, *Nature Mater.* **2004**, *3*, 244.
- [7] a) J. Du, R. K. O'Reilly, *Soft Matter* **2009**, *5*, 3544; b) O. Onaca, R. Enea, D. W. Hughes, W. Meier, *Macromol. Biosci.* **2009**, *9*, 129.
- [8] C. Nardin, T. Hirt, J. Leukel, W. Meier, *Langmuir* **2000**, *16*, 1035.
- [9] P. Broz, S. M. Benito, C. L. Saw, P. Burger, H. Heider, M. Pfisterer, S. Marsch, W. Meier, P. Hunziker, *J. Controlled. Release* **2005**, *102*, 475.
- [10] O. Onaca, D. W. Hughes, V. Balasubramanian, M. Grzelakowski, W. Meier, C. W. Palivan, *Macromol. Biosci.* **2010**, *10*, 531.
- [11] P. Broz, N. Ben-Haim, M. Grzelakowski, S. Marsch, W. Meier, P. Hunziker, *J. Cardiovascular Pharm.* **2008**, *51*, 246.
- [12] E. Rakhmatullina, A. Mantion, T. Bürgi, V. Malinova, W. Meier, *J. Polym. Sci. A, Polym. Chem.* **2009**, *47*, 1.
- [13] E. Rakhmatullina, W. Meier, *Langmuir* **2008**, *24*, 6254.
- [14] S. Belegriou, J. Dorn, M. Kreiter, K. Kita-Tokarczyk, E.-K. Sinner, W. Meier, *Soft Matter* **2010**, *6*, 179.
- [15] a) D. A. Hammer, G. P. Robbins, J. B. Haun, J. J. Lin, W. Qi, L. A. Smith, P. P. Ghoroghchian, M. J. Therien, F. S. Bates, *Faraday Discussions* **2008**, *139*, 129; b) R. Nehring, C. G. Palivan, O. Casse, P. Tanner, J. Tüxen, W. Meier, *Langmuir* **2009**, *25*, 1122; c) P. Rigler, W. Meier, *J. Am. Chem. Soc.* **2006**, *128*, 367.
- [16] R. Nehring, C. G. Palivan, S. Moreno-Flores, A. Mantion, P. Tanner, J. L. Toca-Herrera, A. Thünemann, W. Meier, *Soft Matter* **2010**, *6*, 2815.
- [17] W. Meier, C. Nardin, M. Winterhalter, *Angew. Chem., Int. Ed.* **2000**, *39*, 4599.
- [18] a) C. Nardin, J. Widmer, M. Winterhalter, W. Meier, *Eur. Phys. J. E* **2001**, *4*, 403; b) A. Graff, M. Sauer, P. van Gelder, W. Meier, *Proc. Acad. Sci. USA* **2002**, *99*, 5064.
- [19] T. Haefele, K. Kita-Tokarczyk, W. Meier, *Langmuir* **2006**, *22*, 1164.
- [20] V. Pata, N. Dan, *Biophys. J.* **2003**, *85*, 2111.
- [21] V. Malinova, S. Belegriou, D. B. Ouboter, W. Meier, in 'Polymer Membranes/Biomembranes', Ed. W. Meier, K. Knoll, Springer, Heidelberg, Germany, *Adv. Polym. Sci.* **2009**, *224*, 113.
- [22] A. Graff, C. Fraysse-Ailhaas, C. G. Palivan,

- M. Grzelakowski, T. Friedrich, C. Vebert, G. Gscheidt, W. Meier, *Macromol. Phys. Chem.* **2010**, *211*, 229.
- [23] M. Kumar, M. Grzelakowski, J. Zilles, M. Clark, W. Meier, *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 20723.
- [24] S. F. M. Van Dongen, M. Nallani, J. J. L. M. Cornelissen, R. J. M. Nolte, J. C. M. Van Hest, *Chem. Eur. J.* **2009**, *15*, 1107.
- [25] M. Nallani, A. Graf, A. O. Onaca, M. Lindemann, M. Winterhalter, W. Meier, U. Schwaneberg, *J. Biotech.* **2006**, *123*, 50.
- [26] M. Grzelakowski, O. Onaca, P. Rigler, M.

- Kumar, W. Meier, *Small*, **2009**, *5*, 2545.
- [27] a) F. Axthelm, O. Casse, W. H. Koppenol, T. Nausner, W. Meier, C. G. Palivan, *J. Phys. Chem. B* **2008**, *112*, 8211; b) V. Balasubramanian, O. Onaca, F. Axthelm, D. Hughes, M. Grzelakowski, W. Meier, C. G. Palivan, *J. Optoelectronics & Adv. Mat.* **2009**, *1*, 1083.
- [28] C. Palivan, V. Balasubramanian, B. A. Goodman, *Eur. J. Inorg. Chem.* **2009**, *31*, 4634.

## Switchable Materials

Hermann A. Wegner



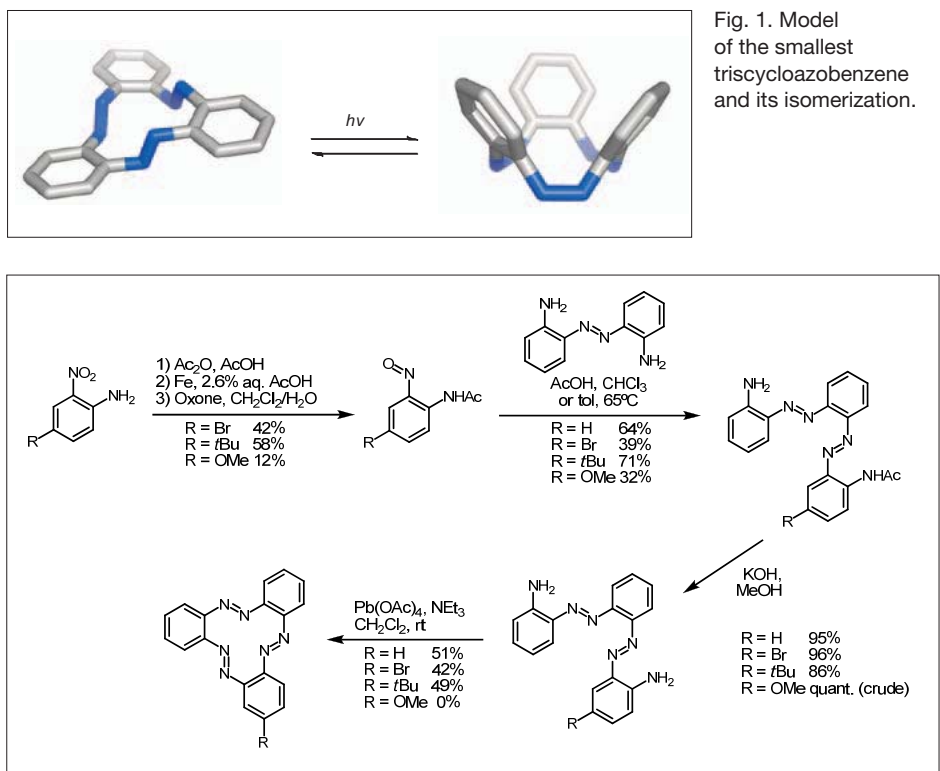
The group of **H. A. Wegner** is interested in new multi-photochromic structures such as the conjugated, cyclic oligo-azobenzenes. These molecules can be reversibly photo-switched undergoing a controlled change of molecular geometry from the *E*-configured planar to the *Z*-configured bowl-shaped structure (Fig. 1). These molecular properties render cyclic oligo-azobenzenes interesting to modify the surface of nanoparticles or act as molecular grippers.

The access towards derivatives of **1** has been reported by Dreiding<sup>[1]</sup> albeit in low yields. Hence, more efficient strategies were developed based on modifications

of the Mills reaction.<sup>[2]</sup> Finally, a new efficient route to various substituted triscyclo-ortho-azobenzenes could be established (Scheme 1).<sup>[3]</sup> Also different ring sizes are accessible. These azomacrocycles are currently being investigated for their photochemical properties.

Based on the improved protocol for the efficient assembly of azobenzenes novel functional scaffolds based on the azobenzenes structure are accessible. This will be applied for the preparation of useful devices, e.g. molecular grippers or multi-photochromic units.

- [1] H. Hilpert, L. Hoesch, A. S. Dreiding, *Helv. Chim. Acta* **1985**, *2*, 325.
- [2] C. Mills, *J. Chem. Soc.* **1895**, 67, 925.
- [3] R. Reuter, N. Hostettler, M. Neuenburg, H. A. Wegner, *Eur. J. Org. Chem.* **2009**, 5647.



Scheme 1. Preparation of cyclotrisazobenzenes.

Fig. 1. Model of the smallest triscyclo-ortho-azobenzene and its isomerization.

# Peptides as Templates for the Controlled Formation of Ag-Nanoparticles

Helma Wennemers



Silver nanoparticles (NPs) are becoming more and more important for manifold applications ranging from molecular electronics, catalysis and imaging, to antimicrobial coatings.<sup>[1]</sup> They are typically prepared by chemical reduction or irradiation with visible light of aqueous solutions of Ag<sup>+</sup>-salts in the presence of additives such as polymers or surfactants that induce the formation of Ag-NPs and stabilize the NPs. The properties of Ag and other metal NPs depend largely on their size and shape.<sup>[1]</sup> As a result, a lot of research has focused on the development of additives and conditions that allow for the controlled formation and stabilization of Ag-NPs. Peptides are promising additives<sup>[2]</sup> due to the large structural and functional diversity that can easily be accessed by linking different amino acids to a simple tripeptide. However, the rational design of a suitable peptidic additive is not trivial due to the still limited understanding of the factors that are required for controlling the defined formation of Ag-NPs. To address this challenge, the Wennemers group developed a screening method that allows for the identification of compounds that enable for the gen-

eration and stabilization of AgNPs among the members of combinatorial split-and-mix libraries.<sup>[3]</sup> The distinct coloration of AgNPs which depends on their size and shape provided for an easy tool to identify active library members. Using a library in which the amino acids serine (Ser), aspartate (Asp), histidine (His) and tyrosine (Tyr) were linked by both rigid as well as flexible spacer molecules, peptides were identified that control the formation of Ag-NPs from Ag<sup>+</sup>-ions either in the presence of light or sodium ascorbate (NaAsc) as a reducing agent (Fig. 1).

Moreover in the assay using NaAsc to reduce the Ag-ions different peptides were identified that generate Ag-NPs in distinctly different sizes.<sup>[3]</sup> This is qualitatively indicated by the different coloration of the beads ranging from yellow to dark red in the combinatorial assay (Fig. 1) and verified by SEM analysis. For example, peptides such as His-Ahx-Asp were on the red beads and induce the formation of Ag-NPs with an average diameter of ~50 nm which can agglomerate to larger assemblies of ≤200 nm. Ag-NPs on the yellow-colored beads bearing peptides such as Ser-Ahx-Tyr are significantly smaller with an average diameter of ~10 nm. These studies demonstrate that short-chain peptides are highly attractive additives to not only control the generation but also the size of AgNPs.<sup>[3]</sup>

- [1] For reviews see: a) I. Pastoriza-Santos, L. M. Liz-Marzán, *J. Mater. Chem.* **2008**, *18*, 1724; b) C. J. Murphy, A. M. Gole, S. E. Hunyadi, J. W. Stone, P. N. Sisco, A. Alkilany, B. E. Kinard, P. Hankins, *Chem. Commun.* **2008**, 544.
- [2] For examples see: a) C.-L. Chen, N. L. Rosi, *Angew. Chem. Int. Ed.* **2010**, *49*, 1924; b) M. B. Dickerson, K. H. Sandhage, R. R. Naik, *Chem. Rev.* **2008**, *108*, 4935.
- [3] K. Belsler, T. Vig Slenters, C. Pfumbidzai, G. Upert, L. Mirolo, K. M. Fromm, H. Wennemers, *Angew. Chem. Int. Ed.* **2009**, *48*, 3661.

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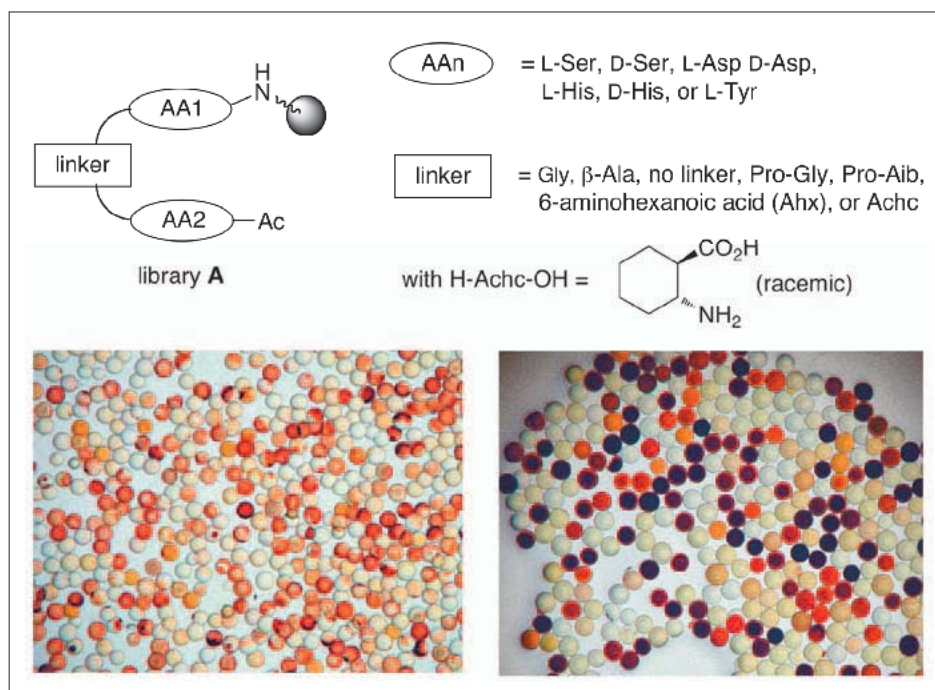


Fig. 1. AgNP formation within the assay of library A complexed to Ag<sup>+</sup>-ions and reduction with light (left) and NaAsc (right).