SWISS SOFT DAYS

14th EDITION

BASEL

UNIVERSITY OF BASEL

DEPARTMENT OF CHEMISTRY

JUNE 6th, 2014

Organizing committee of SSD 14:

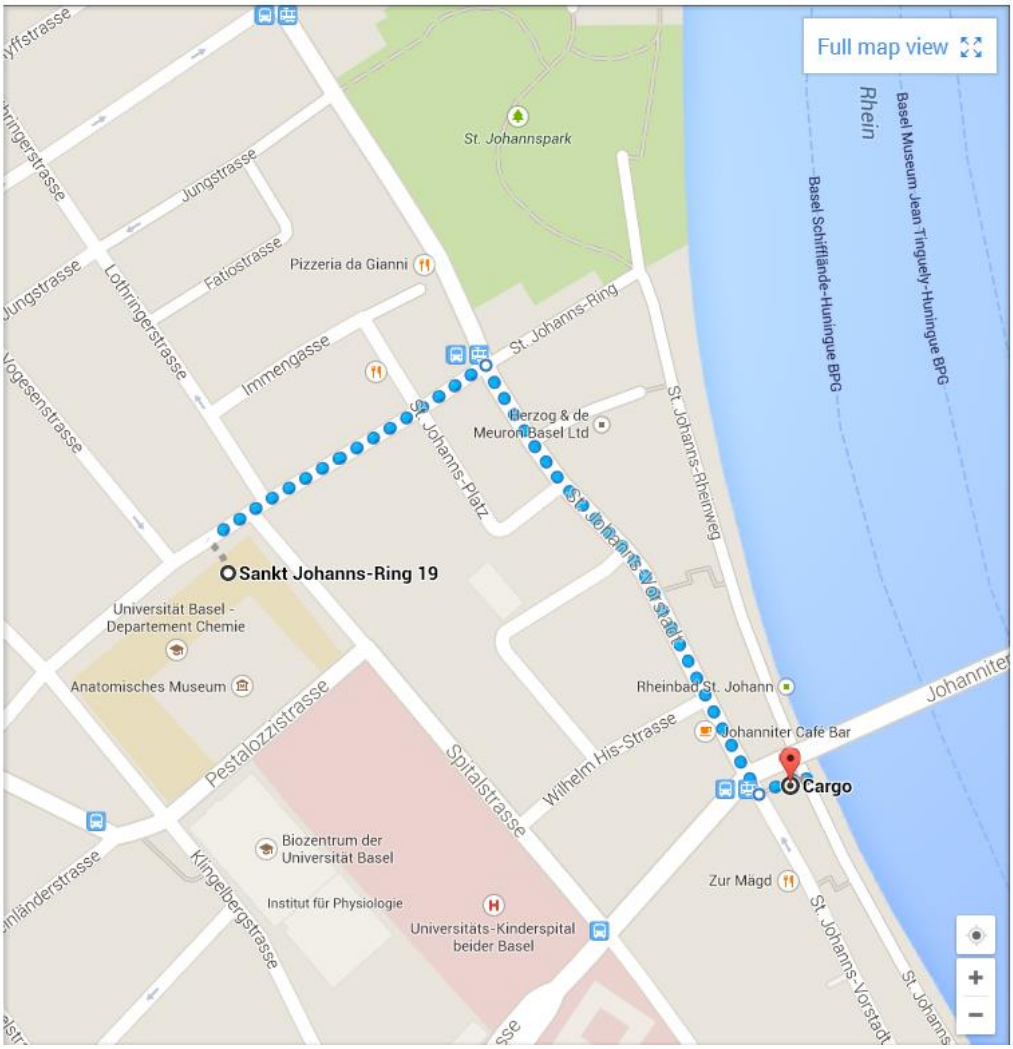
The groups of:

Prof. Wolfgang Meier,

Prof. Thomas Pfohl,

Prof. Cornelia Palivan

9:30-10:00	Arrival and Registration	
10:00-10:05	Opening Notes	
Session 1:Supramolecular assembly and nanostructure polymers		
10:05-10:45	Programming Precision Polymers for Biomedical Applications	Prof. Tanja Weil (Uni Ulm)
10:45-11:05	Poly(N-isopropylacrylamide-*co*-tris-nitrilotriacetic acid acrylamide) for a combined study of molecular recognition and distance constraints in protein binding and interactions	J.Liu (Uni Basel)
11:05-11:25	Effect of size polydispersity on the phase behaviour of soft microgel suspensions	A.Scotti (PSI)
11:25-11:45	Janus nanoparticles and nanobowls synthesis	F. Guignard (Uni Fribourg)
11:45-12:05	Mechanochemistry with metallosupramolecular polymers	D. W. R. Balkenende (Uni Fribourg)
12:05-13:40	**Lunch-Poster session I**	
Session 2:Smart materials and biological sytems		
13:40-14:00	Competence Centre TEDD and its activities	M. Rimann (Zürcher Hochschule für Angewandte Wissenschaften)
14:00-14:20	Interaction of Ni(II)-salophen complexes with G-quadruplex DNA	E. Prado (Uni Geneva)
14:20-14:40	Spectroscopic and mechanical analysis of single erythrocytes using whole human blood samples	M. Göllner (Uni Basel)
14:40-15:00	Label-free, Optical Sensing of the Supramolecular Assembly into Fibrils of a Ditryptophan-DNA Hybrid	J. Nixon Abraham (Uni Geneva)
15:00-15:20	Self-propelled particles driven by light	I. Buttinoni (ETH Zürich)
15:20-16:00	**Coffee break-Poster session II**	
Session 3:Polymer surfaces and advanced characterization methods		
16:00-16:15	i-net innovation networks and COLMAT a European network	R. Duempelmann (Uni Stuttgart)
16:15-16:35	Interplay of drainage and coalescence in SDS foams	D. Calzolari (Uni Fribourg)
16:35-16:55	Tracking the dynamics of ligand-induced conformational changes using nano-mechanical detection	P. Stupar (EPFL)
16:55-17:15	Supramolecular Polymers used as Stimuli-Responsive Reversible Adhesives	C. Heinzmann (Uni Fribourg)
17:15-17:35	Biomimetic membranes composed of synthetic block copolymers	G. Gunkel-Grabole (Uni Basel)
17:35-17:40	**Closing Remarks/End of SSD**	
Social Gathering at Cargo Bar		



Walk 550 m, 7 min

Use caution - may involve errors or sections not suited for walking

○ Sankt Johanns-Ring 19

4056 Basel, Switzerland

1. Head **northeast** on **St. Johanns-Ring** toward **Spitalstrasse**

200 m

2. Turn **right** onto **St. Johanns-Vorstadt**

300 m

3. Turn **left** onto **St. Johanns-Rheinweg**

Take the stairs

Destination will be on the right

33 m

◉ Cargo

Sankt Johanns-Rheinweg 46, 4056 Basel, Switzerland

ORAL ABSTRACTS

Programming Precision Polymers for Biomedical Applications

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Abstract

Proteins are sequence specific and geometrically defined macromolecules representing the central framework of all biological processes in Nature. Their precise physical architecture and consequent biochemical functions are unique and unrivalled in the synthetic world, providing an impetus for the incorporation of proteins into the development of contemporary hybrid materials. Unlike conventional polymers, their repertoire of chemical functionalities at discrete positions facilitates the grafting of designated synthetic moieties[1] to achieve a nanoscale construct with exceptional macromolecular definition.[2,3] Through these synthetic appendages, supramolecular polypeptides[4] and protein-polymer biohybrids[2,3], can be chemically programmed to possess new and improved physico-chemical properties while simultaneously exhibiting unique biological behavior.

We present our recent progress in the exquisite interplay of responsive supramolecular chemistry centering polypeptides in their two major structural forms, folded[5,6,7] and unfolded[2,3], with each concept exploring different strategies for the construction of responsive precision polymers.

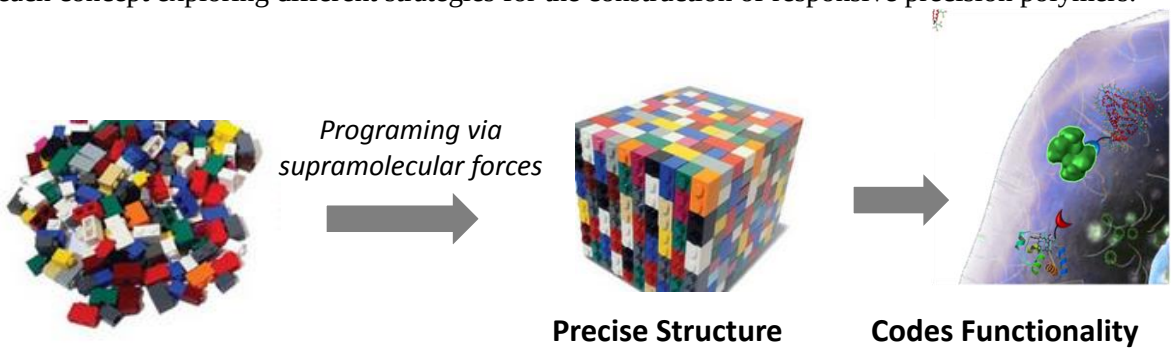

Fig. 1 Programed self-assembly into ordered architectures

1) T. Wang, A. Pfisterer, Y. Wu, O. Dumele, M. Lamla, K. Müllen and T. Weil, A Versatile and Bioorthogonal Approach for the Cross-Conjugation of DNA, Proteins and Peptides via the pH Switch, *Chem. Sci*. **2013**, 4, 1889-1894.

2) Y. Wu, G. Pramanik, K. Eisele, T. Weil *Biomacromolecules* 13, 6, 1890-1898, **2012** "Controlled synthesis of defined polypeptide copolymers from protein precursors.

3) Y. Wu, S. Ihme, M. Feuring-Buske, K. Eisele, M. Lamla, C. Buske, T. Weil, *Adv. Healthcare Mater.* **2013** 2, 6, 884-894. "Tailored albumin copolymers for high capacity loading and two-step release of doxorubicin with enhanced anti-leukemia activity."

4) M. Yolamanova, F. Arnold, O. Zirafi, J. Müller, D. Sauter, C. Goffinet, M. Reisser, V. Vas, H. Geiger, O. Lunov, T. Simmet, J. Bohne, K. Eisele, C. Meier, T. Weil, K. Schwarz, F. Kirchhoff, J. Münch, *Nature Nanotechnol.*, 8, 2, 130-6, **2013**. „Small amyloidogenic HIV-1 gp120 fragments boost retro-and lentiviral gene transfer".

5) D.Y.W. Ng, J. Fahrer, Y. Wu, S. L. Kuan, H. Barth, T. Weil, *Adv. Healthcare Mater.* **2013**, 2, 12, 1620-1629. "Supramolecular Dendronized Streptavidin Nanocarriers: A Versatile and Synergistic Strategy for the Delivery of Therapeutically Active Proteins into Human Cells.

6) S. L. Kuan, D.Y.W. Ng, Y. Wu, C. Förtsch, H. Barth, M. Doroshenko, K. Koynov, C. Meier, T. Weil, *J. Am. Chem. Soc.* **2013**. 135, 17254−17257. "pH Responsive Janus-like Supramolecular Fusion Proteins for Functional Protein Delivery."

7) D.Y.W. Ng, M. Arzt, Y. Wu, Seah Ling Kuan, M. Lamla, T. Weil, *Angew. Chem. Int. Ed.* 53, 1, 324–328, **2014**. "Constructing Hybrid Protein Zymogens through Protective Dendritic Assembly".

Poly (N-isopropylacrylamide-*co*-tris-nitrilotriacetic acid acrylamide) for a combined study of molecular recognition and distance constraints in protein binding and interactions

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University of Basel, Basel, Switzerland.

INTRODUCTION: Many biological processes require precise regulation and synergy of proteins activity, and consequently involve molecular recognition and spatial constraints between biomolecules. We synthesized a library of poly (N-isopropylacrylamide-*co*-tris-nitrilotriacetic acid acrylamide) (PNTs) that were complexed with Cu^{2+} in order to serve as models for investigation of the combined effects of molecular recognition and distance constraints in biomolecular interactions. The polymers serving as models for combined geometric topology with size requirements expected to show the real binding capacity of molecules to a complex targeting configuration, which mimics biological systems in important details.

METHODS: PNTs copolymers were synthesized by free radical polymerization. ^{1}H NMR and gel permeation chromatography (GPC) was carried out to characterise polymers. The coordination of Cu^{2+} to trisNTA pockets was characterized by Fourier transform infrared spectroscopy (FTIR), UV-vis spectroscopy, and electron paramagnetic resonance (EPR). Then, the binding of his-tagged molecules to trisNTA was analyzed by fast protein liquid chromatography (FPLC), FTIR, isothermal titration calorimetry (ITC) and EPR.

RESULTS: ^{1}H NMR and GPC results proved the successful synthesis of trisNTA functionalized polymers with a relatively narrow distribution. The distance between trisNTA pockets were varied from 2 nm to 13.3 nm by adjusting the trisNTA content in polymers. In contrast to poly(isopropylacylamide), PNT copolymers don't show any thermoresponsive behaviour at pH > 3. The coordination of Cu^{2+} to PNTs was investigated and a stoichiometry of 3:1 for Cu^{2+}: trisNTA on different polymers were determined, indicating that the copolymerization did not affect the accessibility of the trisNTA pockets to Cu^{2+}. Three his-tagged molecules, including hexahistidine (His_6), his-tagged enhanced yellow fluorescent protein (His_6-eYFP), and his-tagged collagenase (His_6-ColG), with a size varied from 1 to 11 nm were selected for the investigation of binding ability and binding affinity to PNT copolymers. As shown in Figure 1, the highest binding stoichiometry for both His_6-eYFP and His_6-ColG (0.87 and 0.47) was determined for PNT1 with the largest distance between trisNTA sites (13.3 nm). Decreasing the distance between triNTA-Cu^{2+} groups from 13.3 nm to 3.3 nm (PNT4) had no influence on the binding stoichiometry of His_6-eYFP, due to its relatively small size, but evidently reduced the binding stoichiometry of His_6-ColG from 0.47 to 0.36. When the distance between the binding sites was reduced, a decrease in K_D was observed for all his-tagged molecules, suggesting increasing interactions between his-tagged molecules, which helps the stabilization of the complexes.

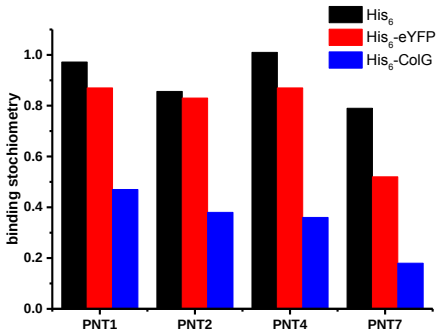

Fig. 1: Binding stoichiometry between trisNTA-Cu^{2+} groups in PNTs and His_6, His_6-eYFP and His_6-ColG.

DISCUSSION & CONCLUSIONS: A library of new poly (N-isopropylacrylamide-*co*-tris-nitrilotriacetic acid acrylamide) polymers containing multi-trisNTA binding sites with different average distances between them were synthesized.

Small molecular mass molecules (His_6), which are smaller than the smallest average distance between trisNTA sites on PNTs, exhibit high binding ability to all PNT polymers independent of the distance between the tris-NTA sites. His_6-eYFP only binds efficiently to PNTs when the distance between trisNTA binding sites is at least equal to its size.

ACKNOWLEDGEMENTS: We thank the Swiss National Science Foundation, and the University of Basel for financial support. J. L. thanks China Scholarship Council for supporting the fee to study abroad.

Effect of size polydispersity on the phase behaviour of soft microgel suspensions

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INTRODUCTION: No hard sphere crystals form at polydispersities higher than 12%. In contrast, soft microgel suspensions with a majority of small particles and a small fraction of big particles with about double size can form crystals without defects caused by the large particles. Due to the softness of microgel particles, the big particles can shrink to fit into the lattice formed by the small particles[1].

METHODS: We study the role of polydispersity in suspensions of fully swollen poly(N-isopropylacrylamide) (pNIPAM) microgel particles. The thermodynamic quantity that rules the phase behavior is the generalized volume fraction ζ. Phase behavior is studied by using series of 10 - 15 samples, which cover the ζ range of interest. Small-angle neutron scattering (SANS), small-angle X-ray scattering (SAXS) and dynamic light scattering are used to characterize particles. We observe crystallization in samples with a polydispersity as high as 17%.

RESULTS: Using SANS with contrast matching of the small particles, we have proven that the big particles shrink in suspension with $\zeta \geq 0.6$. We have blended a majority of small deuterated particles with 10.5% of big protonated ones. We see that the radii of the big particles decrease from 177 nm to 135 nm with increasing concentration as shown in Fig 1. Comparing the bulk modulus of our particles with the osmotic pressure of the samples we find that big particles deswell when the osmotic pressure is able to compress the fuzzy shell that surround the more cross-linked core[2]. Using SAXS we have been able to detect the nearest neighbor distance (nnd) in samples with increasing percentage of big particles, from 0.1% up to 80%. At low concentrations of big particles, the nnd of the mixed samples has the same value as the nnd in a sample made of small monodisperse particles in all the ζ range measured. Increasing the number of big particles we have found a ζ beyond which the nnd is separated from the characteristic value of nnd in a sample made of small monodisperse particles. At higher % of big particles the nnd of the mixed samples lies away from the value we observe for small particles, it is moving towards the value typical for a sample made of big monodisperse particles, Fig. 2.

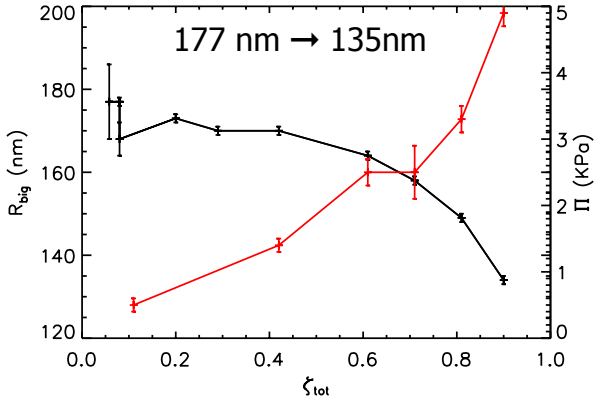

Fig. 1 Variation of the radius of the big particles with ζ is shown. The values of the osmotic pressure of the measured samples are shown in red.

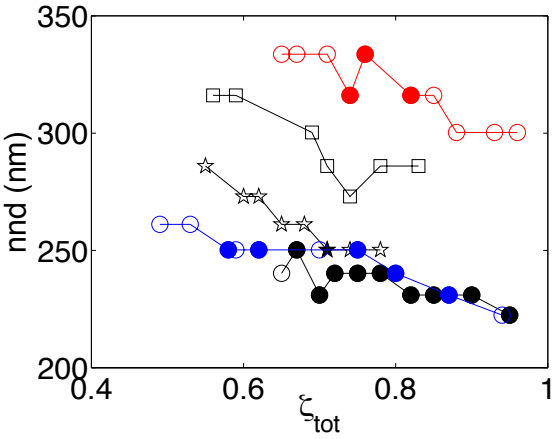

Fig. 2 nnd at different ζ for: monodisperse system made of small particles (O), monodisperse system made of big particles (O) and for three mixed samples (black) with 0.1% (O), 28% (★) and 78% (■). Closed symbols represent samples with crystals.

DISCUSSION & CONCLUSIONS: Our results show that the role of size-polydispersity in soft and deformable microgel suspensions fundamentally differs from that in hard spheres.

REFERENCES: [1] A. St. John Iyer and L.A.Lyon; **2009**; *Angew. Chem.*; 48: 4562-4566

[2] M. Stieger, W. Richtering, J.S. Pedersen and P. Lindner; **2004**; *J. Chem. Phys.*;120:6197-6206

Janus Nanoparticles and Nanobowls Synthesis

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INTRODUCTION: Over the last year, researchers dedicated many efforts to synthesize anisotropic materials. In the field of nanoscience, Janus nanoparticles are a topic of choice, as these nanoparticles possess properties which strongly differ from their isotropic counterparts.

RESULTS: Here, we report the synthesis of shape-anisotropic, asymmetrically functionalized polymer nanoparticles. These dumbbells have been synthesized via a multistep synthesis [1]. Monodispersed seeds polystyrene nanoparticles are first coated with a hydrophilic layer, which contains silane moieties coming from 3-trimethoxysilylpropylmethacrylate (MPS). Upon a second swelling step followed by polymerization, the newly formed polymer chains bulge out and give birth to a second hemisphere. The resulting dumbbells are not only shape anisotropic, but have also a different surface chemistry on the two lobes, as just the first one contains silane groups. This particular feature is of great importance, as it permits to perform selective reaction on one hemisphere only. [2]

One possible option is to use this asymmetrically functionalized dumbbels as template for silica nanobowls. In stöber-like conditions, a silica precursor like tetraethylorthosilicate (TEOS) can be hydrolyzed and condensed on the first hemispheres only. The polymeric template can be removed, giving birth to silica nanobowls bearing a clear defined hole. This is a consequence of the TEOS being only condensed on one hemisphere, and having the junction between the two lobes as the precursor for the nanobowls hole. Moreover, the composition of the inner wall of the nanobowls can be made different, depending on how the polymeric template is removed. By calcination at 550°C, all the polymer chains are burned, and the resulting nanobowls are made of pure silica. By dissolving the silica-coated dumbbells in tetrahydrofuran (THF), the polymer chains which are covalently bounded to the silica via the MPS molecule will remains, and a small hydrophobic polymer layer is therefore present on the inner wall of the nanobowls. The difference between the two type of nanobowls prepared has been analyzed by elemental analysis, thermogravimetry and spectroscopy techniques.

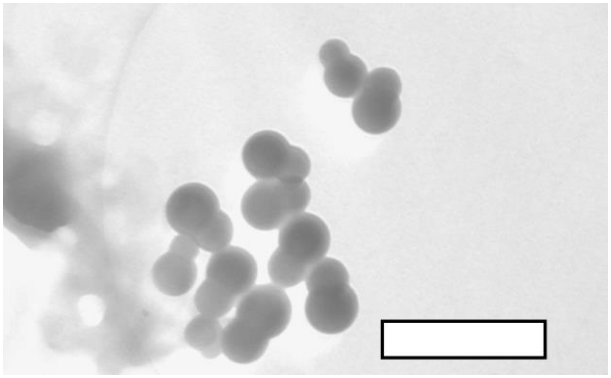

Fig 1: Transmission electron microscope image of polymer dumbbells used as template. Scale bar is 500 nm.

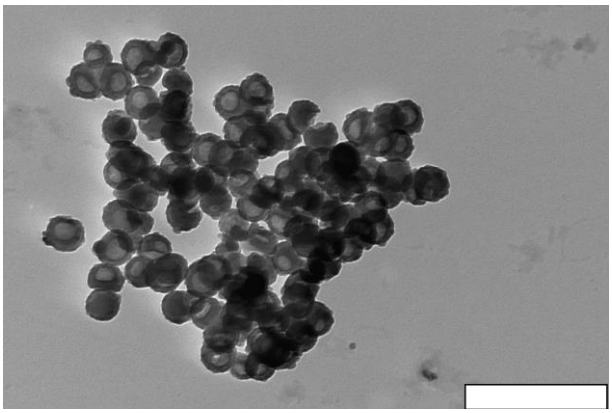

Fig. 2: Transmission electron microscope image of silica shells obtained by dissolution f the polymer template. Scale bar is 500 nm.

DISCUSSION & CONCLUSIONS: Silica nanobowls of different sizes have been synthesized by using a templated approach. They can bear a thin hydrophobic layer on the inner wall if the polymeric template is dissolved, while its calcination leads to purely hydrophobic silica.

REFERENCES

[1] Dufresne et.al, J. Am. Chem. Soc., 2010, 132, 5960-5961
[2] F. Guignard, M. Lattuada, Chimia (Polymer and Colloid Highlights), **67**, 829 (2013).

Mechanochemistry with metallosupramolecular polymers

D. W. R. Balkenende, S. Coulibaly, S. Balog, Y. C. Simon, G. L. Fiore & C. Weder

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INTRODUCTION: Many mechanochemical transduction processes that translate macroscopic forces into chemical reactions and enable essential functions occur in Nature. Typical weak covalent motives (mechanophores) utilized for polymers to achieve mechanochemical reactions are based on selective scission, extrusion of a small molecule, cycloreversion, isomerization and flex-activation [1]. Most of these mechanophores rely on the irreversible breaking of covalent bonds. Here, we demonstrate that reversible and irreversible mechanochemical reactions with metallosupramolecular polymers are possible, and can be used to impart these materials with new functions, such as the ability of being healed by exposure to ultrasound and mechanochromic behavior.

METHODS: Polymeric networks were prepared by coordinated of europium salts to poly(ethylene-co-butylene) polymer chains end-capped with 2,6-bis-(1′-methylbenzimidazolyl)pyridine (BKB) to afford $[Eu(BKB_{1.5})](ClO_4)_3$ (Fig 1a). The lanthanide ions serve as supramolecular crosslinks and a built-in optical sensor where the dynamics of the metal-ligand interactions upon ultrasonication can be monitored in situ using luminescence spectroscopy [2].

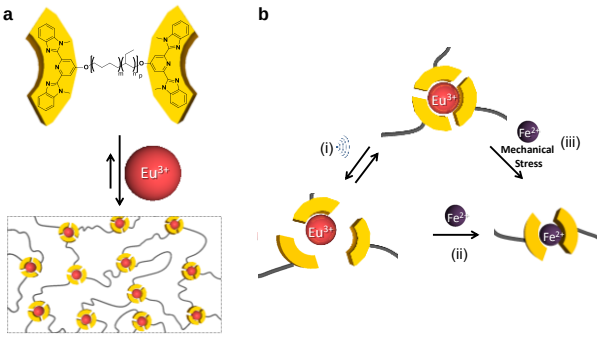

Fig. 1: Formation of $[Eu(BKB)_{1.5}](ClO_4)_3$ (a), and (b) reversible dissociation reaction of the Eu^{3+}-ligand complexes (i) upon ultrasonication irreversible metal exchange (iii) with Fe^{2+} ions in films imbibed with a $Fe(ClO_4)_2$ solution (ii) or application of other mechanical forces.

RESULTS & DISCUSSION: It was shown that the weak metal ligand interaction of $[Eu(BKB_{1.5})](ClO_4)_3$ (in $CHCl_3$) is reversible under exposure to ultrasonication. A low-molecular weight model complex $[Eu(MebipC_{12}H_{25})_{1.5}](ClO_4)_3$ did not show reversibility, suggesting that polymeric chains are necessary to generate the ultrasound-induced mechanochemical force required for ligand dissociation. Furthermore, temperature dependent measurements of $[Eu(BKB_{1.5})](ClO_4)_3$ gave additional conformation that the main mechanism for reversible metal ligand interaction is mechanochemical. Polymer films of $[Eu(BKB_{1.5})](ClO_4)_3$ were immersed in an acetonitrile solution of $Fe(ClO_4)_2$ for 5 d with no visible metal exchange (Fig 2a,2b). Upon ultrasonication an irreversible color change distinctive of the formation of $[Fe(BKB)](ClO_4)_2$ was observed (Fig 2c), demonstrating that solid-state mechanochemical activation is possible. Moreover, cut films of $[Eu(BKB_{1.5})](ClO_4)_3$ were welded upon exposure to ultrasonication, and the mechanical properties of the neat materials were recovered.

Fig. 2: Mechanically induced metal exchange in $[Eu(BKB)_{1.5}](ClO_4)_3$ films. Pictures of films before (a) and after (b) swelling in a solution of $Fe(ClO_4)_2$ in CH_3CN for 5 days, and after subsequent ultrasonication (c) for 60 min.

CONCLUSIONS: Our work demonstrates that metal ligand coordination in metallosupramolecular polymers can serve as versatile mechanophore as well in solution as in the solid state.

REFERENCES: [1] J. N. Brantley; **2012**; *Polym. Int;* 62:2-12; [2] F. S. Richardson; **1982**; *Chem. Rev.* 82:541-552.

ACKNOWLEDGEMENTS: This work was supported by the U.S. Army Research Office (W911NF-09-1-0288 and W911NF-06-1-0414), the Swiss National Science Foundation (Grant No. 200021_13540/1), the European Research Council (ERC-2011-AdG 291490-MERESPO), and the Adolphe Merkle Foundation.

Competence Centre TEDD and its activities

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Zurich University of Applied Sciences, Waedenswil, Switzerland

SUMMARY: It is accepted that standard two-dimensional (2D) monolayer cell culture does not represent cells' behavior in their natural 3D environment. Therefore, the use of biologically more complex cell models is gaining momentum especially in the fields of drug discovery and personalized medicine. Networks are emerging to join forces among basic and applied sciences, enabling technology providers, clinics and industry to promote the usage of organotypic tissue models for the direct benefit of man. In Switzerland, the Competence Centre TEDD (Tissue Engineering for Drug Development and Substance Testing) was founded in 2011 to foster the development and routine application of *in vitro* 3D cell culture. Only by combining diverse skills through integrative cooperation between biologists, chemists, material scientists, engineers, clinicians and industrial partners the technology can further progress.

One focus of the TEDD network is the development of new biomaterials for soft and hard tissue engineering to provide the cells a matrix to grow in 3D. With the advancement of the bioprinting technology suitable biomaterials so called "bioinks" are necessary. These biomaterials need to fulfill several criteria: i) fast polymerization, ii) cytocompatibility, and iii) (bio-) degradability. In our group we developed a BioInk that is suitable for skin bioprinting with primary cells. Furthermore, a current project is focusing on bioprinted muscle/tendon tissue for drug development. Despite the recent progress in bioprinting and development of novel bioinks, a thorough characterization of the material properties is still missing. Additionally, novel tailor-made biomaterials need to be developed that exactly match the cells/tissue requirements. In conclusion, the bioprinting technology is still in its infancy but bears a huge potential, which will also influence the field of regenerative medicine a soon as blood vessels can be reproducibly printed to produce entire organs. The bioprinting technology is the perfect example why networks such as TEDD are necessary to combine different skills.

INTERACTION OF NI(II)-SALOPHEN COMPLEXES WITH G-QUADRUPLEX DNA

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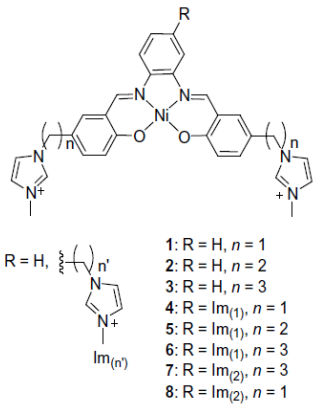
INTRODUCTION: G-quadruplexes are involved in several biological processes (including maintenance of telomeric regions). These thus represent interesting targets for the development of new anti-cancer therapies. However, the G-quadruplex can adopt different conformations that hampers the study of its interactions with ligands. We used a recently reported method based on Template Assembled Synthetic G-Quadruplex (TASQ) that allows precise control of G-quadruplex topography [1]. Using these mines, a test was developed by SPR to determine the affinity and selectivity of ligands for defined conformations of DNA quadruplexes and a DNA duplex system. A series of Ni(II) salophen complexes involving one, two, or three alkyl-imidazolium side-chains was prepared. The lengths of the side-chains were varied from one to three carbons. The binding constants of the complexes for parallel and antiparallel G-quadruplex DNA, as well as hairpin DNA, were measured, and the screening and optimization of molecular structure were achieved.

METHODS: Different biophysical techniques have been developed for investigating G-quadruplex DNA/ligand interactions [2]. An advantage of the SPR technique is that several oligonucleotide sequences can be evaluated and that experiments can be automated. The binding affinity of complexes **1-8** for G-quadruplexes and double-stranded DNA was investigated by SPR (Schema 1). The biomolecular system consists in an intermolecular-like G-quadruplex motif **A** d[TTAGGGT]$_4$, an intramolecular G-quadruplex **B** d(GGG(TTAGGG)$_3$TT), and a hairpin DNA **C** d(CGCGCGCGTTTTCGCGCGCG).

DISCUSSION & CONCLUSIONS: Each complex evaluated had K_D values in the 0.1 - 2 mM range for both inter- and intramolecular topologies A and B. It is significant that: i) the compounds with the lowest K_Ds measured by SPR are those that most significantly stabilized G-quadruplexes against heat denaturation and ii) each salophen derivative tested had a higher affinity for G-quadruplex DNA structures than for duplex DNA. The effect of the salophen substituents was evaluated by comparing the K_D values of the series of compounds for a given DNA structure.



Schema 1. Structures of complexes **1-8**.

Complexes with shorter alkyl-imidazolium side chains had higher affinity for G-quadruplexes than those with longer chains. When connected to the diaminobenzene ring a longer alkyl-imidazolium chain tends to increase the affinity of the complexes for G-quadruplexes, although this effect was rather small. Of note, the K_D values for G-quadruplex A are generally lower than those for G-quadruplex B, showing a certain degree of selectivity of the complexes for intermolecular-like structures. Finally, the high flexibility of the cationic arms in the salophen series favours their positioning into the grooves, in addition to p-stacking over the quartet.

REFERENCES:

[1] a) P. Murat, D. Cressend, N. Spinelli, A. Van der Heyden, P. Labbé, P. Dumy and E. Defrancq, *ChemBioChem* **2008**, *9*, 2588-2591; b) P. Murat, R. Bonnet, A. Van der Heyden, N. Spinelli, P. Labbé, D. Monchaud, M.-P. Teulade-Fichou, P. Dumy and E. Defrancq, *Chemistry – A European Journal* **2010**, *16*, 6106-6114.

[2] a) P. Murat, Y. Singh and E. Defrancq, *Chemical Society Reviews* **2011**, *40*, 5293-5307; b) J. Jaumot and R. Gargallo, *Current pharmaceutical design* **2012**, *18*, 1900-1916.

ACKNOWLEDGEMENTS: This work was supported by ANR QUARPDIEMS, Labex ARCANE, PRES Toulouse, Région Mydi-Pyrénées, Région Aquitaine grants, abd the Nanobio-ICMG platform.

Spectroscopic and mechanical analysis of single erythrocytes using whole human blood samples

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INTRODUCTION: Containing a wealth of information, human blood is the most used sample for diagnostic purposes. Microfluidics, with its unique advantages in performing analytical functions, has been increasingly used for whole blood and cell-based analysis. Single-cell studies using optical tweezers involve complex and expensive instrumentation to manipulate erythrocytes, which might be detrimental for easy application in medical diagnostics. Moreover, optical trapping shows photodamage causing difficulties with long-term and step-by-step analysis under reversible reaction control.

We developed a microfluidic setup in combination with optical and confocal Raman microscopy for single-cell assays starting with whole blood samples, which permits diffusion-controlled variation of the external environment without the need of optical tweezers for immobilizing the erythrocytes. Spectroscopic as well as mechanical properties like membrane elasticity, shape deformations and the full oxygenation cycle of individual erythrocytes under different osmolarities can be investigated

METHODS: Multi-height photolithography in combination with standard soft lithography is performed to produce the microfluidic system. The cured PDMS replica is further thermally aged[1] for 30 minutes at 150°C before it is covalently bound to a cover glass slide in order to generate permanently hydrophilic microchannels.

Human adult blood, drawn from the fingertip of the healthy author is directly applied on the inlets of the microfluidic device, omitting the need of any preceding sample preparation. Therefore, filling of the microchambers with individual red blood cells (RBCs) is purely capillary force driven.

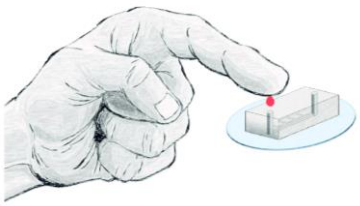

Fig. 1: Whole human blood is directly injected into the microfluidic device without the need of any preceding sample preparation.

Subsequently, the whole blood sample can be washed with various kinds of buffers. In addition, a solution of different concentration of sodium chloride can be applied to generate different osmotic pressure.

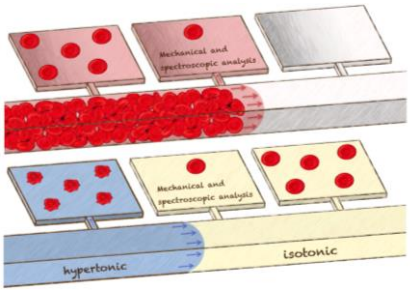

Fig. 2: Capillary force driven filling of microchambers with whole blood due to hydrophilic surface of PDMS (top). Applying two solutions with different sodium chloride concentration generates different osmotic pressure applied on the erythrocytes (bottom).

Confocal Raman microscopy (532 nm laser, 50 µm pinhole) is used to record resonant Raman spectra of the RBCs in the chambers.

RESULTS: Reversible photo-induced oxygenation cycles from oxyHb to deoxyHb of single RBCs were investigated, showing high susceptibility of oxyHb to photo-induced effects.

DISCUSSION & CONCLUSIONS: Previous studies using optical tweezers to immobilize RBCs are limited in terms of feasible integration time as well as for the lower limit of excitation power for Raman studies.[2] As a result, only mixtures of oxyHb and deoxyHb inside RBCs could be observed spectroscopically. Here, we demonstrate a method which opens the possibility of single cell analysis, e.g. for haemoglobin-related blood disorders, where it is crucial to omit any spurious effects introduced by the methodology of the experiment itself. Furthermore, our microfluidic system permits diffusion-controlled variation of the microenvironment, which allows manifold studies at the single cell level under entire control of reaction parameters.

REFERENCES: [1] D. T. Eddington *et al.*; **2006**; *Sensor Actuat B-Chem;* 114:170-172.
[2] K. Ramser *et al.*; **2005**; *Lab Chip;* 5:431-436.

Label-free, Optical Sensing of the Supramolecular Assembly into Fibrils of a Ditryptophan-DNA Hybrid

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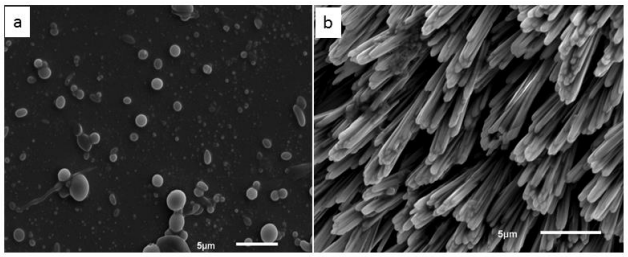
INTRODUCTION: The grafting of a short nucleic acid strand to ditryptophan dipeptide (WW) results in a peptide-DNA hybrid, which assembles into fibrils under controlled aggregation conditions and is evidenced by label free optical sensing owing to the intrinsic fluorescence of the dipeptide

METHODS: Grafting by conventional solid phase synthesis of the WW dipeptide to a model linear 5'-CTC TCT CTC TTT-3' synthetic single stranded nucleotide sequence (modified at the 5' end by an amino group) results in an amphiphilic, rod-coil peptide-DNA hybrid. Chemical characterization by HPLC and ESI-MS evidences the formation of the peptide-DNA hybrid in accordance with its chemical structure. The mechanism of controlled aggregation was determined by concentration and time dependent fluorescence spectroscopy. Scanning and transmission electron microscopy was performed to assess the morphological transitions depending on concentration and time.

RESULTS AND DISCUSSION: Owing to both chemical and physical incompatibility between the rigid hydrophobic dipeptide fragment and the water soluble flexible nucleotide sequence, the amphiphilic molecule organizes into spherical structures in dilute aqueous solution (**Figure a**). Depending on concentration and incubation time, fibrils of a thickness of 0.5-1 µm and length of several micrometres developed **(Figure b).**



As could be observed by TEM and SEM, direct dissolution in aqueous solution induced the spontaneous formation of spherical structures of about 300 nm size. An apparent hydrodynamic radius (230 nm) of the spherical structures assembled in the low concentration regime was determined by dynamic light scattering. These 230 nm size spherical structures would then act as seeds for nucleation polymerization. The peptide-DNA hybrid might therefore form the observed fibrils by both π-π stacking and hydrogen bonding according to a nucleation polymerization process comparable to the one that induces the formation of polypeptide fibrils. As described by Hamley, polypeptide fibril formation occurs by the interaction between the common main chain polypeptide backbone, whereas folding is due to specific interactions of the side chains. At low concentration, spherical structures formed by WW-DNA is induced by the chemical and physical incompatibility between the dipeptide and nucleic acid strands and stabilized by hydrogen bonding between the nucleotide sequences engaged in structure formation. These spherical structures at higher concentrations and under controlled aggregation (time and temperature) might develop into fibres by nucleation dependent polymerization.

CONCLUSIONS: In conclusion, we report in here on the successful coupling of the ditryptophan dipeptide to a synthetic nucleotide sequence. Of high interest is the intrinsic fluorescence of the dipeptide which enables the quantification of a critical aggregation concentration and the indirect evidence in a label-free optical mode that the WW-DNA hybrid organization is analogous to that of the nucleation polymerization of polypeptide fibrils, i.e. supported by both main chains π-π stacking of the dipeptide and side chains hydrogen bonding between the nucleic acid strands.

REFERENCES: a) K. B. Joshi and S. Verma, *Biophysical chemistry*, 2009, **140**, 129–32; b) S. Mondal, S. Ghosh, and S. Verma, *Tetrahedron Letters*, 2010, **51**, 856–859; (C) I. W. Hamley *Angew. Chem.* 2007, **46**, 8128–8147

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Self-propelled particles driven by light

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INTRODUCTION: Active Brownian particles are capable of using energy supplied by the environment to perform a directed motion; typical examples are chemotactic cells and bacteria. While the motion of single organisms has been extensively investigated in the past years, living active systems show, in complex environments, interesting phenomena which are only poorly understood. In order to obtain some fundamental understanding, we mimic similar processes in systems of artificial swimmers which have been already shown to exhibit striking similarities with biological systems.

METHODS: As microswimmers, we use Janus particles (Fig.1(a)), i.e. silica microparticles half-coated with a thin layer of gold. These particles are immersed in a critical water-2,6-lutidine mixture stabilized just below the critical temperature. Illumination of the particles leads to the heating of their golden side and to a local demixing of the critical mixture (Fig. 1(b)), which eventually results in the propulsion of the particle[1,2].

RESULTS: The spatial chemical concentration gradient that develops around the colloid due to the demixing is responsible for the particle's self-diffusiophoretic motion. The functionalization of the coated hemisphere determines what component of the binary mixture is preferentially adsorbed at the cap and therefore the swimming direction. Moreover, the strength of the propulsion can be easily controlled tuning the intensity of incident light.

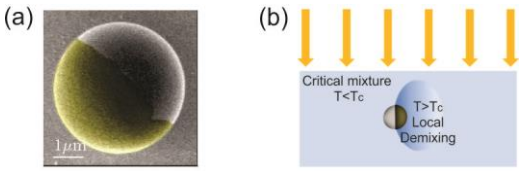

Fig. 1: (a) A scanning electron microscopy image of a colloidal particle with a 20 nm thick gold cap (highlighted). (b) Schematic explaining the self-propulsion mechanism: a Janus particle is illuminated and the cap is heated above Tc inducing a local demixing that eventually propels the particle.

DISCUSSION & CONCLUSIONS: By means of this novel active system we study the behavior of active particles across confinements and at high particle densities where we observe dynamical aggregation. We attribute the clustering to a simple self-trapping mechanism where two or more particles colliding head-on cannot free themselves because of the persistence of their orientation[3].

REFERENCES: [1] G. Volpe, I. Buttinoni, D. Vogt, H. Kümmerer and C. Bechinger. **2011**. *Soft Matter*, 7, 8810.

[2] I. Buttinoni, G. Volpe, F. Kümmel, G. Volpe and C. Bechinger. **2012.** *J. Phys.: Condens. Matter* 24, 284129.

[3] I. Buttinoni, J. Bialkè, F. Kümmel, H. Löwen, C. Bechinger and T. Speck. **2013**. *PRL*, 110, 238301.

i-net innovation networks and COLMAT a European network

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INTRODUCTION: i-net innovation networks is the public-private organisation of the four cantons AG, BL, BS and JU to foster innovation in Northwestern Switzerland. Due to former contacts i-net was asked to become partner in a Marie Sklodowska-Curie European Training Network COLMAT (systems as templates for materials). Project lead is by Prof. C. Stubenrauch, University of Stuttgart. In total COLMAT consists of 12 teams across Europe. Besides the scientific work a strong objective is training of next generation of colloid and interface researchers. The proposal has been submitted in April and project start would be January 2015 if granted. The role and motivation of i-net is to engage PhD students in short innovation studies and train them thereby in a broader entrepreneurial sense. Connection to related swiss-projects would be welcomed and appreciated.

DESCRIPTION OF COLMAT: The overall topic of the network is concerned with the ways in which colloidal systems can be used as templates for the synthesis of novel or newly structured materials. This is possible because colloidal science deals with a wide variety of length scales ranging from a few nanometers to many micrometers. Microemulsions (5-30 nm) and emulsions (a few µm) as well as foams (up to several hundreds of µm) will serve as templates for catalytically active nanoparticles, for polymer foams with different structures, as well as for ceramics.

The combination of formulation- and synthesis-based work with theoretical calculations is intended to greatly enhance the understanding of the decisive processes and mechanisms involved and thus to optimise process and reaction conditions.

Another important aspect of the scientific training programme is reflected in the fact that the characterization of both the templates and the synthesized materials requires a wide range of methods as the systems need to be examined on the very different length and time scales.

Finally, research-to-market activities are an integral part of the network which will lead to new concepts for the synthesis of energy-saving and bio-based materials, respectively.

WORKPACKAGES: the four work packages besides management, communication, recruitment and training are:

- Drying and/or sintering of foams and emulsions
- Polymerisation of foams & emulsions
- Nanoparticles via microemulsions
- Surface-modified nanoparticles

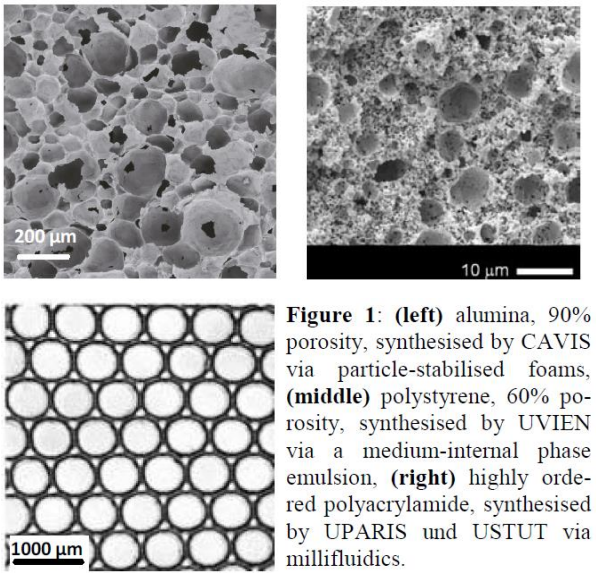

Figure 1: **(left)** alumina, 90% porosity, synthesised by CAVIS via particle-stabilised foams, **(middle)** polystyrene, 60% porosity, synthesised by UVIEN via a medium-internal phase emulsion, **(right)** highly ordered polyacrylamide, synthesised by UPARIS und USTUT via millifluidics.

PARTNERS:

- University of Stuttgart: C. Stubenrauch (leading), M. Buchmeiser, E. Klemm
- University of Cologne: D. Blunk
- European Synchroton Radiation Facility in Grenoble: T. Narayanan
- Inst. of Phys.Chemistry "Ilie Murgulescu" of Romanian Academy: D. Angelescu
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- I-net innovation networks (CH): R. Dümpelmann

CONCLUSION: COLMAT offers interesting possibilities – if granted. I-net could receive motivated PhD students for short innovation studies and the network in the area of soft matters and nanotechnology in Switzerland to other European groups is potentially facilitated too.

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Interplay of drainage and coalescence in SDS-foams

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We present ongoing investigations about the interplay of coalescence and drainage governing the instability of foams, using SDS-foams with a fixed initial liquid fraction of ε_0=0.25 and bubble size of a_0=25 μm. The foams are produced by the turbulent mixing of nitrogen and SDS-water-glycerol solutions with a fixed viscosity of η=45 mPa·sec that contain various amounts of NaCl. For these foams the coalescence rate can be directly observed at the top of the foam.

We find that liquid drainage and coalescence are directly correlated, both becoming faster with increasing NaCl content, as shown in Fig.1. The rather intuitive scenario that the screened electrostatic interactions determine the speed of film rupture and thus coalescence, which in turn determines the speed of the release of liquid, does not account for the observed behaviour.[1,2] Instead, these preliminary results support the idea that the decrease in the surface elasticity with increasing NaCl content allows for a faster drainage, which in turn entails a faster coalescence.[3-5].

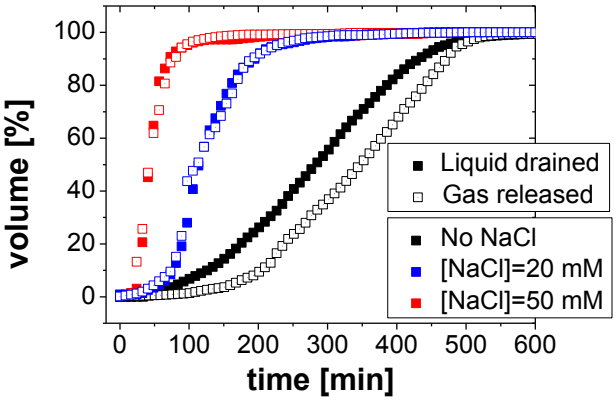

Fig.1 – Liquid drained at the bottom and gas released at the top of the foam (filled and empty symbols, respectively), both normalized by the respective final volumes, for increasing salt concentrations.

REFERENCES: [1] L. Wang, R.-H. Yoon, *Int. J. Miner. Process.* **85** 101–110 (2008); [2] V. Carrier, A.Colin, *Langmuir* **19** 4535-4538 (2003); [3] T. Tamura, Y. Kaneko, M. Nikaido, *J. Coll. Int. Sci.* **190** 61-70 (1997); [4] S. Sett, S. Sinha-Ray A.L. Yarin, *Langmuir* **29** 4934-4947 (2013), [5] L. Saulnier et al., *Soft Matter DOI: 10.1039/C3SM52433G* (2014).

Tracking the dynamics of ligand-induced conformational changes using nano-mechanical detection

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INTRODUCTION: The field of cantilever-based nano-mechanical sensing emerged around twenty years ago, and is still rising technology for label-free sensing [1], that involves the transduction of a (bio)molecular interaction to a measurable mechanical change in the cantilever, resulting from induced unbalanced surface stresses, added mass or the transfer of heat [2]. We recently developed a nano-mechanical sensor that can monitor protein conformation changes [3] as well as detecting antibiotic resistant bacteria [4].

METHODS: Briefly, proteins of interest were immobilized on a cantilever sensor, which was inserted into an analysis chamber, where its spontaneous oscillation deflections are recorded as a function of time, using the optical lever method. The deflection as a function of time was recorded and oscillations are quantified by measuring the signal's variance. The different working conditions are produced in the fluid cell by exchanging the liquids to modify the chemical environment.

RESULTS: We tested this detection system with numerous gram positive and negative bacteria and several proteins. The fact that the variance of the deflection signal increases with both the ligand and protein concentrations on the cantilever surface, strongly suggests that cantilever deflections directly measure the activity of studied proteins. In the other example, after the introduction of the bacteria, analysis of the variance of the deflection curves confirmed an increase, and this high level was maintained while they were still living. After the introduction of antibiotics, the variance dropped to very low values. Appropriate controls were used.

DISCUSSION & CONCLUSIONS: Up to now, the application of mentioned devices have been mostly limited to measurements of resonance frequency shifts, to determine the presence of very small masses or the static determination of the stress deflections induced by the presence of specific ligands. Moreover, the sensitivity of most of the techniques described in literature is greatly reduced in liquid environment. Here, we present a method to detect protein conformational movements within the physiological medium, after the introduction of their substrates. Furthermore, method has been used to characterize bacterial resistance to antibiotics. The sensitivity and the temporal resolution of this technique permit to predict its potential application to a vast number of fields, such as cellular and molecular biology, bacteriology, drug development, high-speed pharmaceutical evaluation or molecule conformational monitoring. However, there are still several fundamental questions to be addressed. For example, the origin of surface stress changes is still not fully understood. Also, change in stresses and resonant frequency are coupled phenomena and there is a need to study how these different mechanisms can be de-coupled.

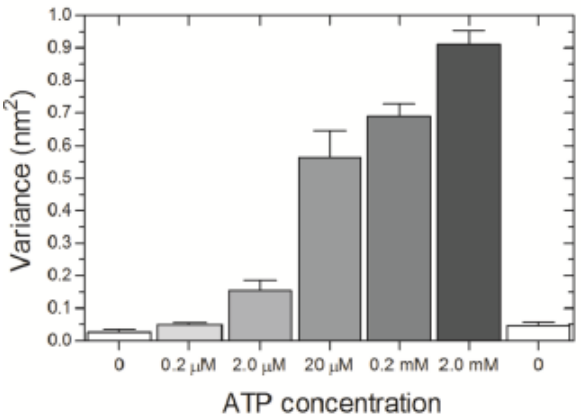

Fig. 1: Variance of the cantilever deflection data, corresponding to Topo II protein used to functionalize the cantilever upon adding the ATP. The variance data was collected from three independent experiments.

REFERENCES: [1] Boisen Anja et al.; **2011**; Reports on Progress in Physics 74. [2] Tamayo Javier et al.: 2013; Chemical Society Reviews 42; 1287–1311. [3] Sarduy, Livan Bladimir Alonso; 2012; EPFL; PhD diss. [4] Longo, G. et al.; 2013; Nature Nanotechnology 8; 522–26.

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Supramolecular Polymers used as Stimuli-Responsive Reversible Adhesives

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INTRODUCTION: Adhesives with switchable adhesive properties are not only useful for temporary bonded joints, but can also be helpful for easy reparation. Debond on demand features already exist, but most often are irreversible. Supramolecular polymers offer full reversibility and are stimuli-responsive. These features were used to synthesize stimuli-responsive, reversible supramolecular adhesives.

Two supramolecular motifs (hydrogen bonding and metal coordination) were used to functionalize a telechelic polyethylene-*co*-butylene (PEB) polymer on the chain ends. The hydrogen bonding system is based on a ureidopyrimidinone (UPy) derivative (UPy-PEB-UPy), and the metal coordination system uses 2,6-bis(1′-methylbenzimidazolyl)-pyridine (Mebip) ligands in combination with a zinc salt ([$Zn_{0.8}$Mebip-PEB-Mebip]$(NTf_2)_{1.6}$). [1-3]

In earlier publications [2,3] both supramolecular polymers showed switchable mechanical properties at elevated temperatures. It was also known, that UPy-PEB-UPy can adhere to objects, and [$Zn_{0.8}$Mebip-PEB-Mebip]$(NTf_2)_{1.6}$ is UV light responsive. This knowledge was used to create the first UV light switchable supramolecular adhesives, which could be bonded, rebonded after failure, and debonded on command.

METHODS: Polymer films were produced by compression molding under elevated temperatures and pressure. Adhesive properties were investigated using a Zwick/Roell Z010 tensile tester. Single lap joints were prepared with quartz glass, regular glass, and stainless steel. A Hönle Bluepoint 4 Ecocure UV lamp was used as a light source (λ = 320-390 nm, 900-950 mW/cm^2) for the UV-light bonding/debonding experiments. For more detailed description, please see reference 1.

RESULTS: The mechanical data of both synthesized supramolecular polymers were investigated by DMTA and adhesive (shear test) measurements. UPy-PEB-UPy showed a storage modulus of 7 MPa (at 25 °C), a shear strength of 1 MPa when thermally bonded, and around 1.2 MPa when bonded by UV-light. [$Zn_{0.8}$Mebip-PEB-Mebip]$(NTf_2)_{1.6}$ revealed a storage modulus of 100 MPa (at 25 °C), a shear strength of 2.5 MPa when thermally bonded, and 2 MPa when bonded by UV light. Both polymers could be rebonded after the shear test, with the original shear strengths restored. Additionally, both polymers could be debonded under exposure to a stimulus (UV light or heat), which drastically lowered the adhesive strength.

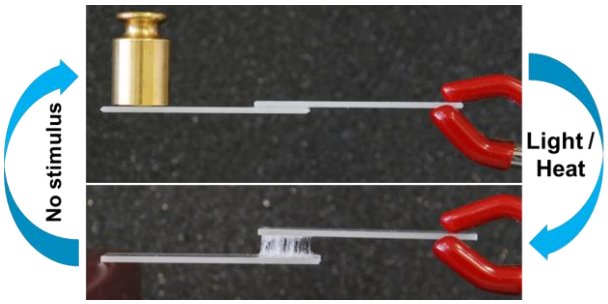

Fig. 1: Adhesive properties can be changed reversibly under exposure of a stimulus (UV light or heat) and go back to their original properties when the stimulus is removed.

DISCUSSION & CONCLUSIONS: It was the first time, that a supramolecular polymer was used as a light-responsive, reversible adhesive. Under ambient conditions the material displays rubbery properties, whereas under irradiation of UV light or exposure to heat, both the metal-coordinate and the hydrogen bonding based polymers liquefy, enabling the bonding of two substrates. This change of states can be reapeated almost infinitely, resulting in a supramolecular adhesive, which can be bonded, debonded and rebonded on demand.

REFERENCES: [1] C. Heinzmann, G. L. Fiore, C. Weder *et al.*; **2014**; *ACS Appl. Mater. Interfaces*; 6 (7):4713-4719. [2] E.W. Meijer *et al.*; **2001**; *Chem Rev.*; 101:4071-4097. [3] G.L. Fiore, C. Weder *et al.*; **2011**; *Nature*; 742:334-337.

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Biomimetic membranes composed of synthetic block copolymers

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INTRODUCTION: Amphiphilic block co-polymers can form structures that resemble those of naturally occurring cell membranes. These polymeric membranes mimic their natural counterparts and add beneficial properties such as increased stability and robustness. Further, they give access to new properties through the variety of polymers with specific functionalities available for assembling polymeric membranes. Special characteristics can be introduced upon interaction with active biomolecules. Importantly, naturally occurring channel proteins can be integrated into the biomimetic membrane to obtain the specificity of biological systems, combined with the advantageous properties of synthetic polymers. Potential areas for applications of the systems described here range from medicine to catalysis and environmental sciences.

METHODS: Polymeric membranes on planar solid support can be formed by different techniques. The main methods that were used are the Langmuir-Blodgett/Schäfer film formation technique, vesicle spreading and grafting of the polymer chains. The properties of the resulting polymeric membranes, such as thickness and morphology were characterized thoroughly, e.g. by spectroscopic ellipsometry and atomic force microscopy. Furthermore biological membrane proteins have been successfully integrated into polymeric membranes through exploiting their preference of a hydrophobic environment. The successful insertion and preservation of the biological function of membrane proteins is probed with methods suited to the particular protein of interest.

RESULTS: Different block copolymers composed of polyoxazoline and polydimethylsiloxane or polybutadiene and polyethylene oxide have been used to form biomimetic polymer membranes. The methods for their formation (see schematically in Figure 1) and the characteristics of the resulting membranes will be discussed. In addition, naturally occurring membrane proteins like α-hemolysin or aquaporins were successfully integrated into these membranes, which can be probed by changes in the membrane conductance.[2] In addition, it was studied in detail that the natural channel proteins preserve their function, i.e. only allowing transport of specific species, after integration into the polymeric membrane.

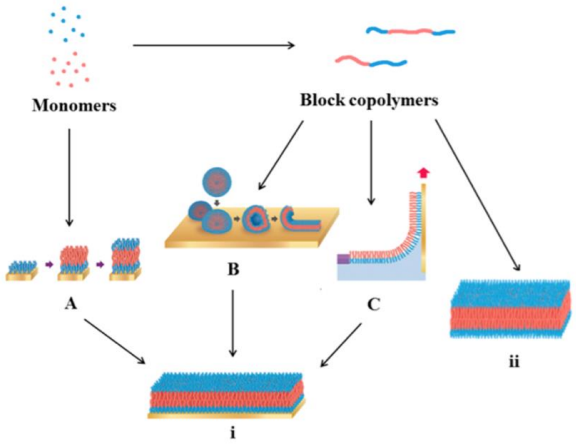

Fig. 1: Overview of methods used in the formation of planar polymeric membranes based on amphiphilic block copolymers, from Kowal & Zhang et al.[1]

DISCUSSION & CONCLUSIONS: These results show the successful formation and detailed investigation of planar polymeric membranes on solid support materials. Further, their application as biomimetic membranes is highlighted, which was demonstrated by the insertion of functional membrane proteins. The results presented here underline the potential of biomimetic polymer-based membranes in a range of applications.

REFERENCES: [1]Kowal, J., Zhang, X., Dinu, I. A., Palivan, C. G., Meier, W.; **2013**; *ACS Macro Letters*; 3:59–63. [2]Zhang, X., Fu, W., Palivan, C. G., Meier, W.; **2013**; *Scientific Reports*; 3:2196.

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POSTER ABSTRACTS

Dynamic Depolarized Light Scattering of Small Round Plasmonic Nanoparticles: When Imperfection is only Perfect

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INTRODUCTION: Although small round plasmonic nanoparticles (PNPs) possess only a small degree of shape anisotropy, they support localized surface plasmon resonances and exhibit intrinsic optical anisotropy. These inherent features promote depolarized light scattering, whose temporal fluctuations carry information about rotational Brownian dynamics, and thus can be used to describe the size distribution of round PNPs.[1] We demonstrate that through depolarized dynamic light scattering, this allows for a much more accurate determination of particle size and polydispersity - especially when compared to standard particle sizing with light scattering.

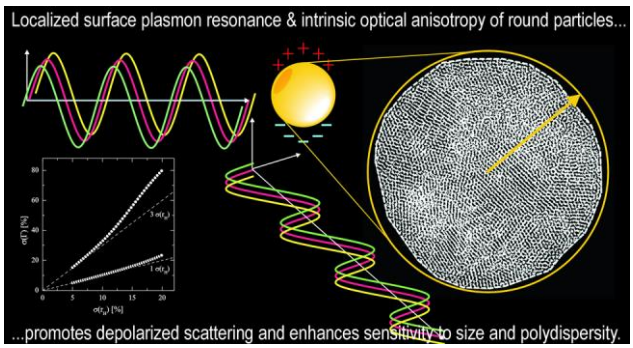

Fig. 1: Dynamic depolarized light scattering of small round plasmonic nanoparticles: imperfections provide access to a very precise and sensitive characterization of particle size.

METHODS: Citrate-stabilized Au NPs ([Au] = 0.5 mM) were synthesized as reported by Turkevich et al. Aqueous solutions (3.4×10^{-3} mM) of thiolated methoxy- (PEG-CH_3, M_w = 5000 g/mol) poly(ethylene glycol) were sonicated for 15 min, subsequently mixed with 100 mL of Au NP suspension and left to react at 25 °C for 24 h. This mixing ratio is expected to provide approximately 10 molecules for each nm^2 of particle surface. The PEGylated particles were centrifuged twice for 1h at 10^4g to remove excess polymers, and then re-dispersed in 10 mL water. Finally, the particles were transferred to a phosphate buffer (10 mM sodium phosphate monobasic/disodium phosphate hydrogen, pH 7).

UV-Vis spectra of the samples were recorded at 25 °C using a Jasco V-670 spectrophotometer, using 10-mm-path-length quartz cuvettes.

Micrographs of the Au NPs were taken with a Tecnai F20 transmission electron microscope (FEI), operating at 200 kV. High-resolution images were recorded with an UltraScanTM 1000 CCD sensor (Gatan, Inc.) with an image resolution of 2048 times 2048 pixels. To prepare the sample, the suspension was spin-coated and dried on carbon-film square mesh copper grids (Electron Microscopy Sciences, CF-300-Cu). The size distribution of the NPs was obtained from these micrographs by using ImageJ particle analysis software (National Institutes of Health NIH, USA).

Light scattering measurements were performed at constant temperature (21°C) using a commercial goniometer instrument (3D LS Spectrometer, LS Instruments AG, Switzerland). The primary beam was formed by a linearly polarized and collimated laser beam (HeNe, 632.8 nm, 21 mW), and the scattered light was collected by single-mode optical fibers equipped with integrated collimation optics. The collected light was coupled into two high-sensitivity APD detectors (Perkin Elmer, Single Photon Counting Module), and their outputs were fed into a two-channel multiple-tau

correlator (Correlator.com). The signal-to-noise ratio was improved by cross-correlating these two channels. With respect to the primary beam, depolarized scattering was observed via cross-polarizers. The instrumental depolarization was controlled by measuring a suspension of Fetal Bovine Serum (FBS, Invitrogen, Switzerland) diluted in phosphate buffer (10% Vol./Vol.).

RESULTS:

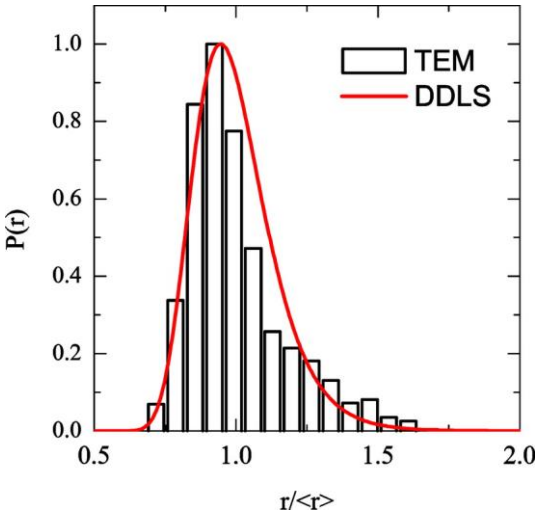

Fig. 2: Comparison of the Au NP size distributions obtained by TEM and DDLS. Both datasets are normalized according to the amplitude, and plotted around their respective average value. The TEM histogram is built from counting and classifying 1775 Au NPs (average = 7.5 nm and SD = 1.3 nm). The number-weighted distribution of the hydrodynamic radius is obtained via DDLS.

REFERENCES: [1]S. Balog *et al.*, Dynamic depolarized light scattering of small round plasmonic nanoparticles: when imperfection is only perfect, *under review*

ACKNOWLEDGEMENTS: S. Balog, L. Rodriguez-Lorenzo, Christophe A. Monnier, B. Michen, B. Rothen-Rutishauser and A. Petri-Fink are grateful for the financial support of the Adolphe Merkle Foundation. L. Rodriguez-Lorenzo acknowledges the financial support from the L'Oreal Switzerland and UNESCO's fellowship program "For Women in Science 2013". The authors would like to thank Herbert Schaffer for the expertise and assistance in HRTEM. The support of the Dr. Alfred Bretscher Fund is gratefully acknowledged, and access to TEM was kindly provided by the Microscopy Imaging Centre of the University of Bern. P. Schurtenberger acknowledges financial support from the Swedish Research Council VR through the Linnaeus Center of Excellence on Organizing Molecular Matter. The authors also acknowledge financial support from the European Commission under the Seventh Framework Program by means of the grant agreement for the Integrated Infrastructure Initiative N. 262348 European Soft Matter Infrastructure (ESMI).

DWS: A Modern Light Scattering Technique to Characterize Mixtures/Soft Matter Systems

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Diffusing Wave-Spectroscopy (DWS) is a modern light scattering technique that allows the quantitative measurement of microscopic motion in soft mater systems, from which the rheological properties can be extracted via the so-called microrheology approach.

DWS applies to highly turbid media such as concentrated particle suspensions or emulsions. In such opaque mixtures, the light is scattered multiple times by solid or liquid particles. These particles perform Brownian motion, which makes the intensity of scattered light fluctuate over time. The measurement and the correlation of the temporal intensity fluctuations of the multiply scattered light then enables, within the diffusion approximation for light propagation, the mean square displacement (MSD) of the particles to be obtained [1]. Moreover, the rheological properties of the medium, namely the storage (G') and loss (G'') moduli, can be derived from the particle MSD by applying the Generalized Stokes-Einstein Relation [2]. Microrheology represents the main application of DWS, and can be also carried out in initially transparent (non-scattering) systems after addition of tracer particles ("Tracer microrheology").

Another application of DWS is particle sizing, which uses the particle MSD and the standard Stokes-Einstein relation to calculate the mean hydrodynamic radius of particles in Newtonian fluids [3].

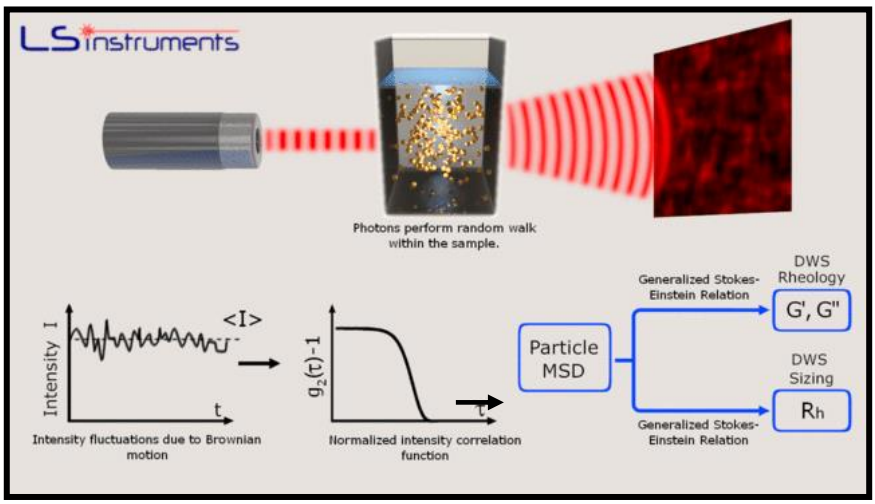

Figure 1 Microrheology and particle sizing based on diffusing wave spectroscopy (DWS).

In this presen
basic fundam
Next, we wil
systems including mixtures (suspensions and emulsions) on which microrheology has been successfully applied. In particular, we will show the abilities of our commercial product, namely the DWS RheoLab II, in this field. Finally, we will succinctly demonstrate how the DWS RheoLab II can accurately measure the mean hydrodynamic radius of solid or liquid particles in turbid mixtures.

REFERENCES: [1] Weitz, D. A.; Pine, D.J. *Diffusion Wave Spectroscopy*. In Dynamic Light Scattering; Brown, W., Ed.; Oxford University Press: New York, 652-720 (1993).

[2] Mason, T. G.; Weitz, D. A. *Optical Measurements of Frequency-Dependent Linear Viscoelastic Moduli of Complex Fluids*, Physical Review Letters **74**, 1250-1253 (1995).

[3] Scheffold, F. *Particle Sizing with Diffusing Wave Spectroscopy*, Journal of Dispersion Science and technology **23**, 591-599 (2002).

Flow-directed assembly of colloidal particles

Ahmet Faik Demirörs, Complex Materilas, ETH Zürich

Interest in assemblies of colloidal particles has long been motivated by their applications in photonics, electronics, sensors and microlenses. Existing assembly schemes can position colloids of one type relatively flexibly into a range of desired structures, but it remains challenging to produce multicomponent lattices, clusters with precisely controlled symmetries and three-dimensional assemblies. A few schemes can efficiently produce complex colloidal structures, but they require system-specific procedures. Here, we report a new method which uses flow field of the dispersing solution for assembling the colloids.

pH and photo-responsive polymers: Toward gene delivery platform

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INTRODUCTION: Considerable attention has been dedicated to the development of stimuli responsive charged polymers in the last few years [1-3]. Among them, positively charged polymers have the ability to interact with negatively charged molecules (e.g. dyes, pDNA or siRNA), but they showed a high level of toxicity with the increase of charge density. Therefore, the design of new polymer systems with low toxicity and high delivery efficiency presents a new challenging field in pharmacotherapy [1-3]. In this context, two different delivery systems based on pH- and photo-responsive amphiphilic poly(dimethysiloxane)-*b*-poly(2-(dimethylamino)ethyl methacrylate) (PDMS-*b*-PDMAEMA) block copolymers have been designed.

METHODS: Amphiphilic block copolymers were synthesized by atom transfer radical polymerization starting from a hydrophobic PDMS-Br macroinitiator and by using DMAEMA as hydrophilic co-monomer. Furthermore, the copolymers were converted into photo-responsive copolymers having pendant quaternary ammonium groups by chemical modification with photo-cleavable o-nitrobenzyl-carboxymethyl groups. The chemical structure and polydispersity of block copolymers were established by ^{1}H-NMR and GPC. The self-assembly of both stimuli responsive systems was investigated by DLS and TEM, and the positive charge on the surface of nanoparticles was determined by zeta potential. The interaction of positively charged nanoparticles with small molecules like anionic dyes (SRB) as well as their release has been analyzed by UV/Vis and FCS.

RESULTS:

PDMS-*b*-PDMAEMA diblock copolymers with hydrophilic blocks having different lengths were successfully designed. The characteristics of the non-modified amphiphilic block copolymers, as measured by ^{1}H-NMR and GPC, are summarized in *Table 1*.

Table 1. ^{1}H-NMR and GPC data of PDMS-b-PDMAEMA block copolymers.

Sample code	M_n (g/mol) ^{1}H-NMR	M_n (g/mol) GPC	PDI
AB5	6300	7400	1.08
AB13	7600	7800	1.16
AB22	9000	10800	1.15

PDMS is a non-toxic and biocompatible polymer, while cationic PDMAEMA exhibit a certain level of cytotoxicity. Therefore, the effect of pristine and modified amphiphilic diblock copolymers on the viability of HeLa cells was evaluated with an MTS assay (*Fig. 1*).

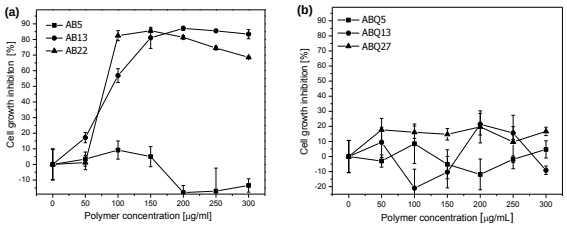

Fig. 1: HeLa cell growth inhibition versus polymer concentration for the non-modified (a) and quaternized (b) block copolymers after 24 h of incubation.

DISCUSSION & CONCLUSIONS:

Due to the tertiary amine groups present as pendant groups within the PDMAEMA blocks, which can be protonated by pH variation, these copolymers can act as pH release systems. The photo-triggerable block copolymers were able to undergo, upon UV irradiation, a transformation from cationic to zwitterionic form at physiological pH. The modified copolymers were non-toxic after self-assembly in PBS even with extended hydrophilic chain lengths, as it can be seen in *Fig. 1(b)*.This could be due to the steric hindrance of the quaternary charges leading to decrease interaction of the positive charges with the cell membrane. The strong interaction between the positive charges of photo-triggerable copolymers and anionic charges of SRB has been proven by UV/Vis measurements. The release of the dye upon irradiation has been shown by FCS. In conclusion, new responsive systems have been designed to interact with anionic species and improve release and toxicity. Further analysis is being performed for possible plasmid DNA delivery.

REFERENCES:

[1]J. Zhang, X. Li; **2012**; *Prog. Polym. Sci.;* 37:1130-1176.

[2]A. Sinclair, T. Bai, L.R. Carr, J.-R. Ella-Menye, L. Zhang, S. Jiang; **2013**; *Biomacromolecules;* 14:1587−1593.

[3] P. Sobolciak, M. Spírek, J. Katrlík, P. Gemeiner, I. Lacík, P. Kasák; **2013**; *Macromol. Rapid Commun.;* 34: 635−639.

Towards nanofluidic devices for biomolecules

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INTRODUCTION: Trapping and manipulating of nano-objects in solution is of great scientific and technological interest in a wide range of field such as soft matter, biophysics and clinical medicine. Although several methods have been developed such as optical and magnetic tweezers, electro and dielectrophoresis, stable trapping of nanometer-sized particles remains challenging.

METHODS: Our approach of trapping charged nano-objects is "geometric induced electrostatic trapping". Therefore nanofluidic channels containing finer nanostructures (traps) are etched into a silicon dioxide layer on a silicon chip. The chip is finally bound to a cover glass that provides optical access to the inside of the channels. Obtaining higher repulsion in the nano-channels due to the electrostatic potential of the silicon dioxide surfaces in aqueous solution, single negatively charged particles are forced into the finer nanostructures and trapped for several minutes.

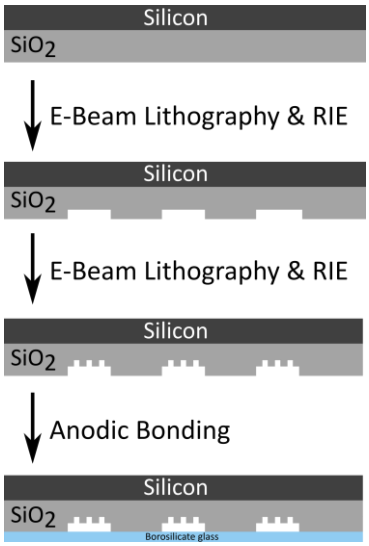

Fig. 1: Fabrication of the nanofluidic trapping devices

RESULTS: In this poster we show trapping events of 80 nm-gold particles without any externally applied forces using interferometric scattering detection (iSCAT) microscopy. It is shown that the decreasing of the pocket diameter reduces the confinement of the nano-particles.

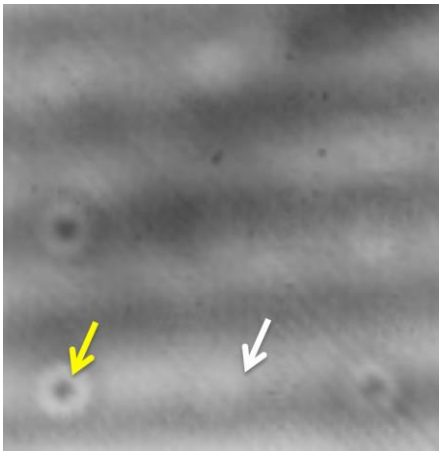

Fig. 2: 80 nm gold particles trapped in 250 nm wide pockets (yellow arrow) and unoccupied pockets (white arrow).

DISCUSSION & CONCLUSIONS: Negatively charged nano-objects can be passively confined by geometric-induced trapping. By altering the surface topology of the nano-channels the trap stiffness can be controlled. In future, we plan to extend this method to trap and track biological macromolecules using fluorescence microscopy. Since biological operations naturally need higher salt concentrations, the surface charges of the channels are getting screened. By adapting the geometry of the device and increasing the surface charge of the channels, we want to overcome this challenge.

REFERENCES: [1] S. Köster, D. Steinhauser and T. Pfohl, Brownian motion of actin filaments in confining micro-channels, J. Phys.: Cond. Matt. 17 (2005), pp. S4091.
[2] M. Krishnan, N. Mojarad, P. Kukura and V. Sandoghdar, Geometry-induced electrostatic trapping of nanometric objects in a fluid, Nature 457 (2010), 692-695

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DEVELOPMENT OF A MOLECULAR HOOVER

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INTRODUCTION: The emerging field of synthetic biology aims for the creation of novel devices with functionalities not found in nature. The NANOCELL project targets at the creation of a light-driven device which resembles a molecular hoover. Over the last decade, several artificial devices have emerged in research functioning as nanoreactors. Nevertheless, the transport of molecular compounds into their reaction compartment was achieved by passive diffusion. By reconstitution of light-driven proton pumps together with transport proteins which utilize the proton gradient, a fully controllable device would be achieved.

Building Blocks & Assembly: Block copolymers are like lipids able to self-assemble into vesicular structures. Due to their increased molecular weight they offer a higher mechanical robustness compared to common lipid membranes. Additionally, they are flexible enough to allow insertion of membrane proteins[1]. The first light-driven proton pump discovered was bacteriorhodopsin (BR). Proteorhodopsin (PR) exhibits similar structural and functional characteristics as BR, but is easily producible in common biotechnological systems and open for protein engineering[2].

The assembly relies on the subsequent solubilization of preformed vesicles with increasing amounts of detergent. Upon increase of the detergent concentration, the lipid membrane gets saturated in the first regime. With further increase, the membrane starts to dissolve leading finally to complete solubilization of the membrane. The protein is added at defined concentration and the reconstitution is carried out by removal of the detergent. The resulting proteoliposomes are subsequently characterized regarding their physical properties and functionality[3].

RESULTS: The fluorescent dye NTA-Atto 647 binds specifically to the His tag of PR. By using fluorescence autocorrelation spectroscopy the diffusion time of the tagged protein can be determined and the results indicate that PR is attached to the membrane when using 0 to 17.2 mM of the detergent n-Octyl-β-D-Glucopyranoside (OG) during reconstitution.

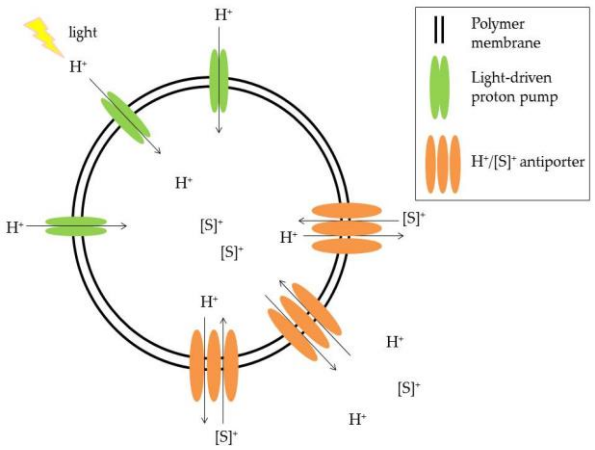

Fig. 1: ***Schematic view of the molecular hoover*** *Light induces the transport of H^+ into the NANOCELL, building up a gradient. The $H^+/[S]^+$ antiporter uses the gradient to transport the substrate $[S]^+$ into the NANOCELL in exchange for a proton.*

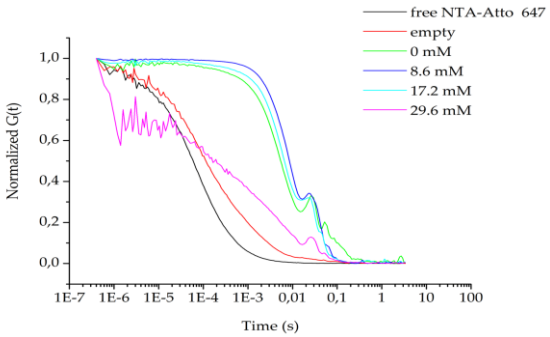

Fig. 2: Normalized correlation functions of the specific binding of NTA-Atto 647 to PR, indicating succesful delivery to the membrane.

DISCUSSION & CONCLUSIONS: Current approaches from membrane protein reconstitutions in liposomes appear to be applicable to polymersomes. Due to the asymmetric charge distribution of the N- and C-terminus at different pH it appears to be possible to direct PR during reconstitution via opposite charges on the membrane[4].

REFERENCES: [1] J.-F. Le Meins, O. Sandre, S. Lecommandoux, TheEuropeanPhysicalJournalE 2011, 34, 1.

[2] M. Grote, M.A. O'Malley, FEMSmicrobiologyReviews 2011, 35, 1082.

[3] J.-L. Rigaud, D. Lévy, in Liposomes,PartB (Ed: N. Duzgunes), Academic Press2003, 65.

[4] R. Tunuguntla, M. Bangar, K. Kim, P. Stroeve, C.M. Ajo-Franklin, A. Noy, BiophysicalJournal 2013, 105, 1388.

A REAL-TIME DRUG-ASSAY ON MOTILE SINGLE CELLS

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The protozoan flagellates called *Trapanosoma* are not only causative agents of the sleeping sickness and the Chagas' disease, but they are also a model organism for motility. They live in the bodily fluids of their hosts, especially in the blood stream. And the blood vessels are a world of microscopic dimensions – a world at low Reynolds numbers – where our everyday macroscopic strategies of self-propulsion just do not work. To counter that, Trypanosomes show off their fascinatingly complex patterns of motility.

To analyse these patterns, we present a simple microfluidic device in which diffusion controlled concentration changes can easily be induced together with a versatile new method to measure their impact on living and motile eukaryotic cells. By combining microfluidic devices with optical tweezers and the motile protozoan flagellate *Trypanosoma brucei brucei* we can directly assess how drugs and other chemicals influence cells and their motility.

Our results show that our device can be used for a quick and easy assay for the effect of almost any water-soluble drug on motile cells, even protozoa that are normally not that easy to permanently investigate.

Fig. 1: Scheme of the method:

Motile cells and medium are introduced from the left inlet into the main channel (I.). Using an optical trap, motile cells are placed into a microchamber (II.), where they are released and their motility is recorded (III.). Then, from the right inlet, drug-laden solution is introduced, diffuses into the chamber and the changes in motility are recorded (IV.) and later analysed.

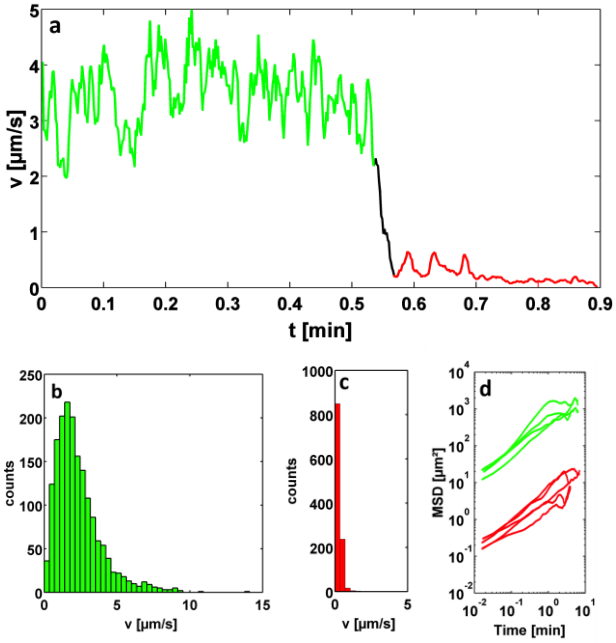

Fig. 2: In situ cell fixation:

(a) velocityplot (smoothed) of one exemplary trypanosome, (b,c) velocity histograms and (d) MSDs of an ensemble of trypanosomes in confinement before (bright green) and after (red) fixation with glutaraldehyde

ABC Amphipilic Triblock Copolymers: Effect of Hydrophobicity on Nanoparticle Formation

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INTRODUCTION: Asymmetric amphiphilic triblock copolymers (ABC) can self-assemble into nanoparticles and provide a preferable orientation of membrane proteins [1]. Orientation of asymmetric copolymers mainly depends on the nature and length of hydrophilic parts. However, to the best of our knowledge, influence of hydrophobicity of the central hydrophobic block on the nanoparticle formation has never been studied. In this work, we investigated two asymmetric triblock copolymers: $mPEG_{45}$-b-$PMCL_{110}$-b-$PDMAEMA_{37}$ (*I*) and $mPEG_{45}$-b-$PPhCL_{100}$-b-$PDMAEMA_{30}$ (*II*). The crucial difference in the structures is the presence of more hydrophobic phenyl group in case of *II* (*Fig. 1*). The self-assembly behavior of these polymers has been investigated using DLS and TEM. Both methods have shown formation of larger particles in case of polymer *II*, which has a more hydrophobic central block.

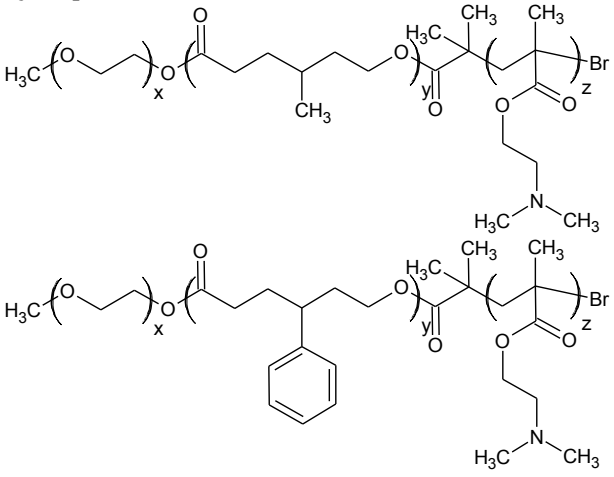

Fig. 1: Structures of copolymer I (top) and II (bottom).

METHODS: The copolymers were synthesized according to [2] (synthesis of mPEG-PMCL diblock) and [3] (synthesis of triblock). Nanoparticles were prepared using the co-solvent method. To remove bigger aggregates, the samples were extruded. After extrusion the particles were characterized by DLS, and their morphology was observed by TEM.

RESULTS: In the present work, the ability of two asymmetric triblock copolymers mPEG-b-PMCL/PPhCL-b-PDMAEMA has been studied. Both polymers assemble into nanoparticles by co-solvent method. Copolymer *I* has longer hydrophobic B block (110 vs. 100 units) and hydrophilic PDMAEMA C block (35 vs. 30 units) compared to copolymer *II*. Nevertheless, DLS data and TEM images show that copolymer *I* forms smaller nanoparticles compared to copolymer *II* (*Fig. 2, Table 1*).

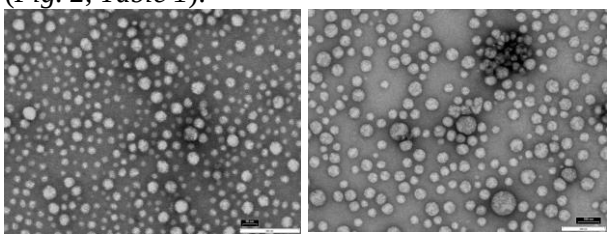

Fig. 2: TEM images of particles formed by copolymer I (left) and II (right). Scale bar represents 200 nm.

Table 1. Comparison of diameter of nanoparticles by DLS and TEM.

Polymer	D_h, nm	D_{TEM}, nm
I	59±3	10-40
II	80±2	40-100

DISCUSSION & CONCLUSIONS: We investigated the self-assembly behavior of two asymmetric triblock copolymers with different hydrophobic groups in the central block (mPEG-b-PMCL/PPhCL-b-PDMAEMA). Both DLS and TEM data show formation of bigger particles in case of polymer *II*, which contains more hydrophobic groups. Thus, hydrophobic nature of the central block plays a crucial role in the self-assembly process of asymmetric mPEG-b-PMCL/PPhCL-b-PDMAEMA copolymers.

REFERENCES: [1] R. Stoenescu, A. Graff, and W. Meier; **2004**; *Macromol Biosci*; 4:930-5.
[2] M.A. Petersen, L. Yin, E. Kokkoli, and M.A. Hillmyer; **2010**; *Polymer Chemistry*; 1:1281-1290.
[3] Y. Matter, R. Enea, O. Casse, C.C. Lee, J. Baryza, and W. Meier; **2011**; *Macromolecular Chemistry and Physics*; 212:937-949.

ACKNOWLEDGEMENTS: We thank Mrs. Gabriele Persy (University of Basel) for TEM measurements. Financial support from SNF is gratefully acknowledged.

Functional Solid-Supported Membranes Based on Amphiphilic Block Copolymers

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INTRODUCTION: Development of artificial membranes is today of great interest, because they are representing a simplified membrane models, which can be used for investigation and understanding of processes taking place in the cell membrane. Amphiphilic block copolymers have been already successfully used for preparation of vesicles, which find applications as drug carriers and nanoreactors, as well as preparation of planar membranes.[1, 2] We present one step further in domain of functional biomaterials by introducing a membrane protein into solid-supported membrane based on amphiphilic block copolymer.

METHODS: The membranes based on poly(dimethylsiloxane)-*block*-poly(2-methyl-2-oxazoline) (PDMS-*b*-PMOXA) amphiphilic diblock copolymers were prepared on three various substrates, i.e. silica, gold, and glass. Polymer bilayers were prepared through Langmuir-Blodgett and Langmuir-Schaefer transfer techniques, which allow preparation of highly ordered films on substrates of unrestricted sizes. We introduced a new approach for biomolecule insertion into the solid-supported polymer membrane by usage of Bio-Beads. This method allows for gentle protein and membrane destabilization by detergent removal, which triggers molecule incorporation.

RESULTS: Atomic force microscopy (AFM) measurements showed the membrane to be smooth and homogeneous. Thickness of the bilayer was approximately 12 nm, as determined by ellipsometry. For insertion experiments we used the nucleotide modulated potassium channel from the bacterium *Mesorhizobium loti*.[3] The successful protein incorporation was established by means of confocal laser scanning microscopy (CLSM), while the electric conductance measurements showed that after insertion the potassium channel stays functional.

DISCUSSION & CONCLUSIONS: We have introduced a new method for engineering functional surfaces by protein insertion into solid-supported polymer membranes. The advantage of this method for engineering functional surfaces is that it can be achieved on solid substrates of unrestricted size, which represents an advance for technological applications.

REFERENCES:

1. J. Kowal, X. Zhang, I. A. Dinu, C. G. Palivan and W. Meier, *ACS Macro Letters*, **2014**, 3, 59-63.
2. X. Y. Zhang, P. Tanner, A. Graff, C. G. Palivan and W. Meier, *J Polym Sci Pol Chem*, **2012**, 50, 2293-2318.
3. J. Kowal, M. Chami, P. Baumgartner, M. Arheit, P.-L. Chiu, M. Rangl, S. Scheuring, G. F. Schröder, C. M. Nimigean and H. Stahlberg, *Nature Communications*, **2014**, 5, 3106.

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Design of a K^+ and Na^+-responsive nanoreactor

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INTRODUCTION: Ion transport across cellular membranes plays an important role in the shrinkage or enlargement of the cellular volume, which are key factors for the control of apoptotic cell death or cell proliferation [1]. Additionally, ion channels drive the transmembrane flux of ions, functions which can be exploited in the design of synthetic spherical nanoarchitectures for the control of ionic gradients. Our approach was to use a monovalent cation selective ion channel, gramicidin A, to permeabilize polymeric membranes for this type of ions. Moreover, the ion sensitive molecules are shown to maintain their activity *in situ* [2], while they are protected by the polymeric membrane (Figure 1).

METHODS: Two monovalent cation-sensitive (Na^+ and K^+ - sensitive) fluorescent dyes were individually encapsulated in the cavity of polymersome. Polymeric vesicles were characterized by dynamic light scattering (DLS), as well as transmission electron microscopy (TEM). Fluorescence correlation spectroscopy (FCS) was used to test the encapsulation efficiency of both dyes. Insertion of gramicidin into the membrane and the Na^+ and K^+ influx was demonstrated based on fluorescence measurements.

RESULTS & DISCUSSION: Polymersomes with a diameter ranging from 100 to 200 nm, were observed in TEM and DLS. The diffusion times of the free dyes were measured by FCS and average diffusion times of *26-30 μs* were determined. These values were compared with the average diffusion times of *2220-2943 μs*, obtained for the vesicles containing dyes. This confirmed that the dyes were entrapped inside polymersomes. By controlling the intra- or extra-vesicular cation concentration, it was possible to evaluate the changes in fluorescence intensities of the dyes, in the protective vesicle lumen, and to prove the successful reconstitution of the ion channel in the polymeric membrane, which was permeabilized towards monovalent cations.

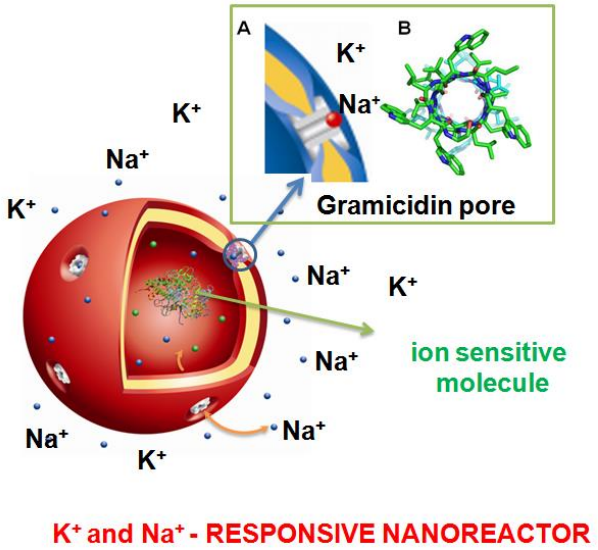

Fig. 1: Conceptual design of a K^+ and Na^+-responsive nanoreactor.

CONCLUSIONS: The encapsulation of Na^+ and K^+ - sensitive cation-sensitive fluorescent dyes and the functional reconstitution of gramicidin A, enabled us to prove the passage of Na^+ and K^+ ions through the polymeric membrane and the design of a simple, but highly sensitive Na^+ and K^+-responsive nanoreactor. In the future, polymeric vesicles containing entrapped enzymes activated by monovalent cations [4] could act as artificial organelles, able to detect and equilibrate sodium and potassium concentration disturbances inside cells.

REFERENCES:

[1] F. Lang; **2007**; *Methods in Enzymology - Osmosensing and Osmosignaling;* 428:209-225.

[2] C.G. Palivan; **2012**; *Chemical Society Reviews*; 7:2800-23.

[3] W. Jing; **1998**; *Electrochimica Acta*; 44:99-102.

[4] E. Di Cera; **2006**; *J. Biol. Chem.;* 281:1305-8.

ACKNOWLEDGEMENTS: We acknowledge G. Persy, University of Basel, for TEM measurements. This work would not have been possible without the funding support from the Swiss Nanoscience Foundation.

A novel setup for measuring solvent permeability in lubricating polymer-brush coatings

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INTRODUCTION: Research on polymer brushes, grafted polymer chains densely grown on a surface, has enjoyed growing attention in recent years due to their enormous potential for friction reduction in industrial as well as medical applications. Well-designed polymer-brush coatings, with thickness in the nanometer range, possess the ability to reduce friction beyond theoretically expected values.[1] However, the details of the lubrication mechanisms and the interplay with the confinement of liquid within the polymer-brush system, are yet to be fully explained.[2] The aim of this project is to shed light on these phenomena by investigating the role of confined fluids in the lubrication mechanisms via the measurement of the permeability of the viscous fluid flow through polymer-brushes.

METHODS: A novel experimental microfluidic setup is currently being developed. The aim is to derive the permeability value from the pressure drop across micrometric channels filled with the polymer brushes, as a function of flow rates.

$$\kappa = v\,(\mu * \Delta x)/(\Delta P) \qquad (1)$$

Following Darcy's law (1), when able to control the dimensions (Δx) of the fluid cell precisely, using a specialized microfluidic pump and flow sensor to apply ΔP and measure v accurately, one can derive a value for the permeability of the system under investigation. The viscosity value μ depends on to the solvent used during the experiments.

RESULTS: Currently the fabrication of the microfluidic device is pursued. Having tested production methods including PDMS casting and microparticle sintering techniques, the concept of using photolithography in order to produce a cell of precise dimension has turned out to be the most promising option. A sketch of the setup can be seen in Figure 1 below, indicating the cell in dark grey, the polymer-brush coated glass counter surface in pink and the piping system in white.

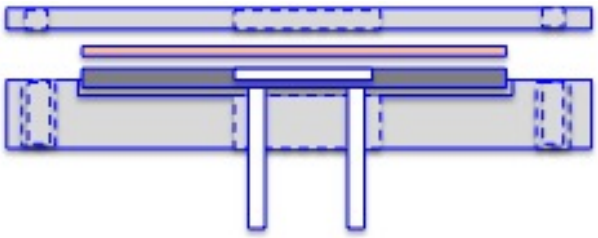

Fig. 1: Schematic of the fluid cell setup inside the holder. In white the in- and outlet show the space provided for the fluid to penetrate a polymer brush layer coated on the pink coloured glass surface.

DISCUSSION: Varying the solvent quality as well as the polymer brush grafting density will elucidate the interaction between fluid and the brush. Furthermore, brush permeability in squeeze flows will be characterized by means of AFM indentation experiments and will be compared to the outcome of the microfluidics experiments.

REFERENCES:

[1] Bielecki, R. M., Crobu, M. & Spencer, N. D. Polymer-Brush Lubrication in Oil: Sliding Beyond the Stribeck Curve. *Tribology Letters* 49, 263–272 (2012)

[2] Espinosa-Marzal, R. M., Bielecki, R. M. & Spencer, N. D. Understanding the role of viscous solvent confinement in the tribological behavior of polymer brushes: a bioinspired approach. *Soft Matter* 9, 10572–10585 (2013)

ACKNOWLEDGEMENTS: We thank Petra Burkhard, Maria Leibinger and Sandro Losli of the FIRST Center for Micro- and Nanoscience as well as Lauriane Alison and David Moore of the Laboratory for Complex Materials for their support. Special thanks go to Rebecca Huber of the Laboratory for Surface Science and Technology for many fruitful discussions.

STM characterization of binary self-assembled monolayers on gold nanoparticles

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Gold nanoparticles are typically coated with a self-assembled monolayer (SAM) of ligand to prevent coalescence and impart certain bio-chemical properties. The particles can also be functionalized with multiple types of extend their functionalities. It was found that binary SAMs of thiolated ligands on gold nanoparticles undergo nano-phase separation into patterned structures. The structure details have been challenging to characterize. Scanning tunneling (STM) microscopy imaging has been used to show an existence of stripe-like domains with a characteristic spacing of ~1nm in a number of binary SAMs on gold nanoparticles. We present quasi-molecular resolution STM images that have been achieved recently and a newly developed power spectral density approach to confirm the consistency of stripe features in large datasets of STM images.

References:

Q. K. Ong, J. Reguera, P. J. Silva, M. Moglianetti, K. Harkness, M. Longobardi, K. S. Mali, C. Renner, S. De Feyter and F. Stellacci, *ACS Nano*, 2013, **7**, 8529-8539.

F. Biscarini, Q. K. Ong, C. Albonetti, F. Liscio, M. Longobardi, K. S. Mali, A. Ciesielski, J. Reguera, C. Renner, S. De Feyter, P. Samorì and F. Stellacci, *Langmuir*, 2013, **29**, 13723-13734.

M. Moglianetti, Q. K. Ong, J. Reguera, K. M. Harkness, M. Mameli, A. Radulescu, J. Kohlbrecher, C. Jud, D. I. Svergun and F. Stellacci, *Chem Sci*, 2014, **5**, 1232-1240.

Aging properties of human red blood cells

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INTRODUCTION: Red blood cells in healthy subject live 120 days. There are cases when it is important to determine the age of RBC. At present bio labelling is used, but it is a slow method, because the results can be obtained only in 120 days (that is the normal lifespan of human RBC [1]). It is inefficient and sometimes even not possible to wait that time therefore a reliable and instant RBC aging test is needed and our group is working on development for such test.

METHODS: In ex vivo studies it was shown that RBC changes their size during the aging process due to small particles (micro particles) that forms from cell membrane. As a result – RBC becomes smaller and stiffer. The size difference between young and old RBC is about 20%. [2] We are using that property to develop aging test for RBC. To separate RBC by size, we are using micro fluidic device with complex channel system (Fig. 1). RBC that are pumped through the system behaves differently because of difference in size and that behaviour can be measured as cell deflection from its original streamline.

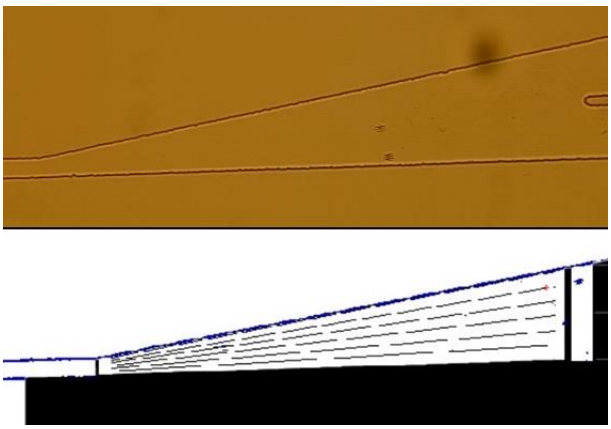

Fig. 1: One of the channel systems in our experiment. Deflection in degrees from cells original streamline is measures when it exists the channel.

RESULTS: Results contains statistics of RBC that pass through our channel system and during their way does not interact with each other or does not stick to the channel walls or anything else.

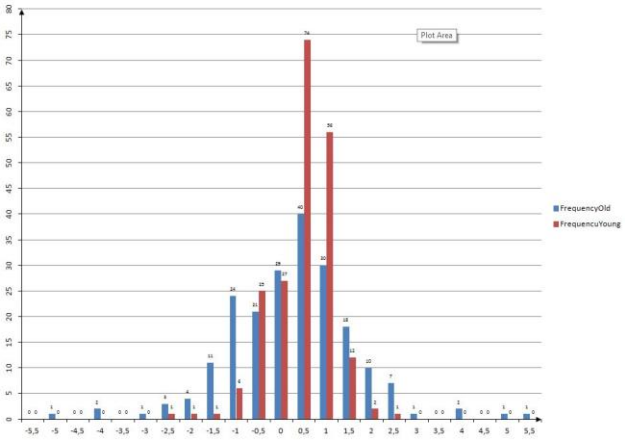

Fig.2: Graph, where distribution of deflections away from streamlines are plotted for young (6 days old) and old (41 days old) RBC

DISCUSSION & CONCLUSIONS: Results shows that there is difference in distribution between young and old RBC samples. Old RBC tent to spread more away from their corresponding streamlines and while the maximal angle for old RBC is about +/- 5 degrees, young cells deflects only +/- 2 degrees away from their streamlines. These results proves the theory about deflection and leads to further work on this method.

REFERENCES: [1] Robert S Franco; **2012**; *Transfus Med Hemother;*39:302-307. [2]You-Xiong Huang et al **2010**; *J. Cell. Mol. Med. Vol 15, No12 2011 pp. 2634-2642.*

ACKNOWLEDGEMENTS: We are grateful for the Blood Transfusion Center in Lausanne to provide us blood sample to analysis.

WORM-LIKE micelles of polymerizable surfactant as a template for polymerization

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INTRODUCTION: The use of self-assembled materials as templates in materials synthesis is a rapidly growing area. However, the subset of work that focuses on rodlike and wormlike self-assembled micelles for polymerization of organic solution is under-utilized given the potential of these systems for synthesizing anisotropic materials. The use of particles with anisotropic shape is of significant interest since it allows fabrication of structures with special symmetries and degree of packing, as well as with anisotropic properties. Rod-like polymer particles could have interesting properties and could find many practical applications; however, few methods for the production of such particles are available.

METHODS: In this work we introduced and investigate a method for synthesis of a new class of polymeric nanorods and nanofibrils based on emulsion polymerization using wormlike polymerizable micelles as template. Wormlike micelles, are elongated and semiflexible aggregates of surfactant molecules. The equilibrium and dynamics of the micellar structures, however, are determined by a delicate balance of intermolecular forces that can be easily disrupted. In the current study it has been observed that addition of oils or polymers typically reduces the average micelle length and results in a dramatic decrease of the solution viscosity on the microstructure and loss of the highly elongated and entangled micelles. Solubilization and polymerization of styrene in different Cetyl trimethyl ammonium Tosylate (CTAT) wormlike solutions at various concentrations, temperatures and initiator systems have been performed, and have been showed to preferentially form spherical particles. This is explained as follows: during the polymerization process, the viscosity is reduced by several orders of magnitude to a water-like value, and no viscoelasticity can be observed either visually or rheometrically. These data suggest a transition from rodlike to spherical micellar aggregates. In order to overcome the problem, a polymerizable surfactant, cetyltrimethylammonium 4-vinylbenzoate (CTVB), containing a polymerizable counterion, has been prepared and investigated with the purpose of "locking in" the micellar structure over the oil polymerization so that the template is less sensitive to environmental changes.

RESULTS: Elongated particles and long polymer fibrils have been formed depending on cross linker concentration used, partially preserving the structure of the parent micelle upon polymerization. Therefore, the presented approach represents a possible method for the production of anisotropic particles, with the purpose of studying their assembly for the preparation of nano- and microstructured material.

Protein-polymer conjugates hosting linear or dendritic polycations for nucleic acid delivery

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INTRODUCTION: Protein cages are hollow nano-structures, which can be genetically modified and be used to perform chemical reactions within their cavity. The thermosome (THS) from *Thermophilum acidophilum* is a cage, that is composed of two hemispheres and each hemisphere is assembled from alternating α- and β-subunits. A genetically modified variant with accessible cysteines on the inside of every β-subunit was used. Thiol-specific ATRP initiators were attached to cysteines in order to polymerize 2-(Dimethylaminoethyl)methacrylate (DMAEMA) within that cavity under ARGET ATRP conditions resulting in a protein cage-polymer conjugate with linear polymer chains. In a second approach the dendritic poly(amidoamine) (PAMAM) was conjugated into the THS. Since poly(DMAEMA) and PAMAM are cationic polymers at physiological pH, they can electrostatically bind negatively charged oligonucleotides[2]. Thus the protein cage-polymer conjugates were used for entrapment of siRNA and its delivery to cells. In addition, the protein cage-polymer hybrid protects siRNA from degradation by RNAses and the protein cage shields cells from positive charges of polycations.

METHODS: THS-poly(DMAEMA) was synthesized in a glovebox under argon atmosphere. 1,1,4,7,10,10-Hexamethyltriethylenetetramine was used as ligand and sodium ascorbate as reducing agent. Quenching of reaction and purification of synthesized conjugates was performed by spin diafiltration (MWCO: 100kDa, AMICON, Millipore). THS-PAMAM was synthesized by conjugation of hydrazine-modified PAMAM G4 to aldehyde modified cysteins of β-subunits. Conjugates were analysed by gel electrophoresis (BN-PAGE & SDS-PAGE).

RESULTS: We could show polymerisation of DMAEMA inside of THS. This protein cage-polymer is able to bind siRNA, and the binding capability depends on the polymer length. THS-PAMAM conjugates showed, besides siRNA binding, also protection of siRNA degradation.

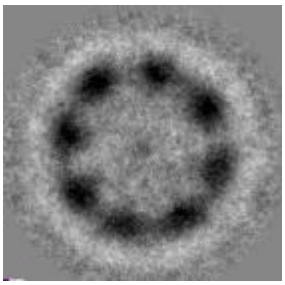

Fig. 1: Cryo-TEM image (single particle analysis) of top view of the thermosome .

DISCUSSION & CONCLUSIONS: Protein-polymer conjugates based on THS promises to represent a novel platform for nucleic acid delivery. The ability of external modification of THS with targeting ligands and cell-penentrating peptides enables to target and transfect cells. Experiments are on the way to elucidate such cell-targeting and siRNA delivery.

REFERENCES: [1] N.Bruns et al.; **2009**; *Angew. Chem.; 121*:5776-5779.

[2] P. van de Wetering et al.; **1999**; *Bioconjugate Chem.; 10*:589-597.

ACKNOWLEDGEMENTS: We would like to thank the Holcim Stiftung Wissen, the SNSF and the SNI for financial support, as well as Dr. Mohamed Chami (C-CINA, Basel) for the Cryo-TEM analysis.

Self-Assembly of Chitosan-g-ssDNA in aqueous solution

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INTRODUCTION: The self-assembly of amphiphilic molecules is attracting considerable attention since it can yield ordered structures with a wide range of morphologies, including spheres, cylinders, lamellae, vesicles in dilute aqueous solution[1] as well as several others complex hierarchical assemblies[2]. To achieve bioactive structures, the conjugation of nucleotide sequences with biocompatible segments has thus become a topic of intense research[3].

We report herein on the self-assembly of chitosan-grafted-ssDNA hybrids (C-g-ssDNA) were synthesized through covalent binding between the amine bearing chitosan and the carboxylic acid-functionalized ssDNA (HOOC-ssDNA) at a 1:1 molar grafting ratio. The self-assembly of C-g-ssDNA in aqueous solution results in nucleotide sequence decorated spherical structures.

METHODS: Grafting of chitosan to single stranded DNA (C-g-ssDNA) was realized by conventional solid phase synthesis.

To induce self-assembly, the chitosan-grafted-ssDNA copolymer was dissolved in acetonitrile/water and further dialyzed against water. Mass spectrometry (MALDI-TOF) evidences the successful coupling between the natural chitosan biopolymer and the ssDNA, while two main imaging technics, i.e., atomic force microscope (AFM) and transmission electron microscope (TEM) were used to characterize the self-assembled structures.

RESULTS:

Mass spectrometry (MALDI-TOF) was used to evidence the successful coupling between the natural chitosan and the ssDNA at 8250 Da.

Morphological characterizations and height profiles achieved by AFM reveal the presence of spherical homogeneous structures, of 50 nm size. From figure 2, TEM imaging is in good agreement with AFM.

DISCUSSION & CONCLUSIONS: The self-assembly behavior of theses hybrids is unique, since the hydrophobic to hydrophilic weight balance differs from that of conventional amphiphiles. Due to the chemical incompatibility between the water soluble DNA fragment and the poor water solubility of the chitosan polymer, Chitosan-grafted-ssDNA probably self-assembles into vesicular structures, as might be evidenced by ongoing investigations by cryo-TEM.

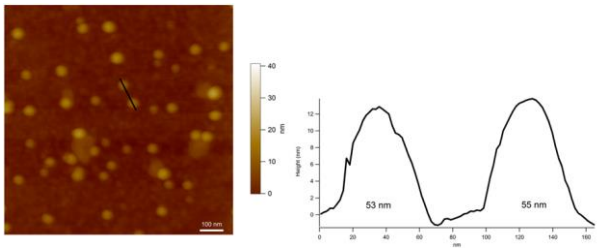

Fig. 1: AFM imaging of self-assembled chitosan-g-ssDNA deposited on silica.

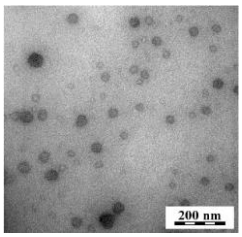

Fig.2: TEM imaging of self-assembled chitosan-g-ssDNA,

REFERENCES:

1 Frank S. Bates and Glenn H. Fredrickson, "Block Copolymers—Designer Soft Materials," Physics Today **52** (2), 32 (1999).

2 Yiyong Mai and Adi Eisenberg, "Self-assembly of block copolymers," Chemical Society reviews **41** (18), 5969-5985 (2012).

3 Amit Patwa, Arnaud Gissot, Isabelle Bestel, and Philippe Barthelemy, "Hybrid lipid oligonucleotide conjugates: synthesis, self-assemblies and biomedical applications," Chemical Society Reviews **40** (12), 5844-5854 (2011).

ACKNOWLEDGEMENTS: We especially thank Pr. Nicolas Winssinger, Prof. Michal Borkovec (Uni. Geneva),) for experimental facility supports. The University of Geneva and the SNSF (PPOOP2-128380) are greatly acknowledged for financial support

ATRP conducted in PDMS-PMOXA polymersomes

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INTRODUCTION: Atom transfer radical polymerization (ATRP) is one of the most powerful tools in obtaining well defined polymers by radical means. [1-2] The catalytic cycle in ATRP involves reversible switching between two oxidation states of a transition metal (especially Cu- used mostly as catalyst), but such catalysts are mildly toxic, and difficult to remove from the polymer product.[2] A more environmentally friendly and biocompatible alternative is using enzymes to replace the copper catalyst. We recently reported that horseradish peroxidase (HRP) and hemoglobin (Hb) can catalyze ATRP of vinyl-monomers such as poly(ethylene glycol) methyl ether acrylate (PEGA) .[3] Encapsulation of biocatalysts inside of semipermeable nanoreactors offers the advantages of protecting the biocatalyst from the destructive action of various degrading agents, and of increasing the catalysts performance due to the confinement of a reaction into a small volume.[4] Here we present enzyme-catalyzed ATRP inside of polymersome nanoreactors and investigate the effect of the confined volume on the control of the polymerization and therefore the polydispersity of polymers.

METHODS: The dimensions of the extruded vesicles were determined by dynamic and static light scattering (DLS, SLS). The morphology as well the size of the formed polymersomes was characterized by transmission electron microscopy (TEM) on a Philips EM400 electron microscope. UV-Vis spectroscopy was measured on a Specord 210 plus spectrometer (Analytik Jena, Germany). Gel permeation chromatography (GPC) was used in order to determine the polymers' number average molecular weight M_n and polydispersity index (PDI). ^{1}H-NMR spectra were recorded on a Bruker DPX-400 spectrometer operated at 400.140 MHz in $CDCl_3$ and processed with MestReNova software.

RESULTS: HRP is able to catalyse the ATRP of PEGA in phosphate buffer at pH 7.4 in a ratio of [Monomer]:[Initiator]:[HRP] of 80 to 1 and 1. The reaction show a first order kinetic and a final PDI 0f 1.7. HRP was encapsulated by film rehydration method in PDMS-PMOXA polymersomes, and both TEM and LS data showed spherical hollow structure, before and after encapsulation. The polymersomes, impermeable to small molecular weight molecules, were permeabilized by photo-treatment with MPP-OH that did not influence the morphology or size of the vesicles (as indicated by LS and TEM). In a last step HRP loaded polymersomes permeabilized were used for the polymerization of PEGA in conditions similar with those used in bulk. The conversion of PEGA after diffusing into the nanoreactors was followed for 24 hours.

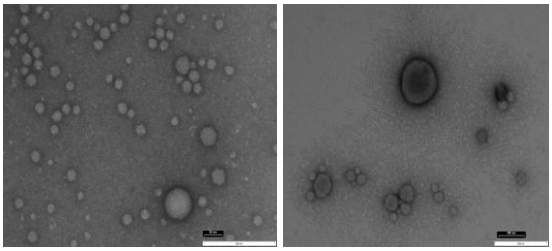

Fig. 1: TEM micrographs showing HRP loaded vesicles after 24 h ATRP reaction Left: PDMS-PMOXA-HRP, Right: PDMS-PMOXA-MPP-OH-HRP.

DISCUSSION & CONCLUSIONS: HRP is able to catalyse the ATRP of PEGA both in bulk and in the confined space of the permeabilized polymersomes. The conversion is much higher in bulk, reaching 25% after 24 h, but presents a better reaction control (M_n = 6000 g/mol and PDI 1.04 compairing with M_n = 8150 g/mol for the reaction in buffer PDI 1.6).

REFERENCES: [1] W. A. Braunecker et al., **2007**; *Progress in Polymer Science*, *32*, 93-146.

[2] K. Matyjaszewski et al., **2012**; *Macromolecules*, *45*, 4015-4039.

[3] T. B. Silva, et al., 2013, *Biomacromolecules*, *14*, 2703-2712..

[4] M. Spulber et al., **2013**; *J. Am. Chem. Soc.*, 135(24): 9204-9212.

PHOSPHATE TEST 2.0

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The determination of the phospholipids concentration in liposomal suspensions is a key step in phospholipids science. Standard phosphate tests date back several decades and require extended hands-on time. The procedures consist in a chemical digestion step where the phosphodiester moiety of the phospholipid is oxidized to an orthophosphate. This step is often carried out by heating the phospholipid suspension in the presence of a strong acid or oxidizing agent in a open vessel. Evaporation of solutes calls for an extra, time consuming volumetric step. The orthophosphate is the detected colorimetrically as a metallo complex. Many coloring agents can be used mainly molybdenum compound such as vanadomolybdophosphoric acid, molybdenum blue or phophomolybdenum-malachite green complex[1].

The use of microwave assisted chemical digestion allows skip the volumetric step as no solvent is evaporated during the oxidation of the phospholipids. Vanadomolybdophosphoric acid has a maximum absorption wavelength (402 nm) close to the standard 405 nm filter found on almost every plate reader. The plate reader allows to analyze several samples in parallel with a high number of replicates. The new phosphate test method has proven to be efficient even for low concentration suspensions (2 µM to 200 µM of phosphate).

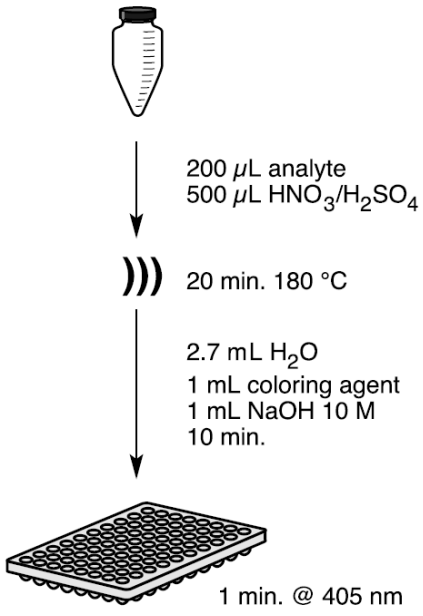

Fig. 1: Flow diagram of the microwave assisted chemical digestion of liposome suspension followed by colorimetric analysis.

REFERENCES:[1]Etienne Stalder, Andreas Zumbuehl, CHIMIA International Journal for Chemistry, 67, (**2013**), 819-82.

ACKNOWLEDGEMENTS: The authors thank the Swiss National Science Foundation (PP00P2_138926/1), the University of Fribourg and the NCCR Chemical Biology for financial support.

Development of pH-Triggered Delivery Platform

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INTRODUCTION: Amphiphilic block-copolymers, particularly those containing pH and thermo responsive blocks, play an important role in novel delivery system design. Their ability to self-assemble into various hierarchical structures in solution makes them interesting for diverse biomedical applications. For example, micelles have emerged as one of the most promising nanocarriers in cancer therapy[1]. They are an excellent system for drugs with poor water solubility and less effective in delivery of hydrophilic cargo[2]. Hence, the development of colloidal particles with the ability to encapsulate hydrophilic therapeutics is very challenging. However, by tuning the block copolymers composition and optimization of self-assembly conditions vesicular structures can be prepared. Vesicles (polymersomes) are very desirable because they possess an internal cavity available for encapsulation of hydrophilic drugs (*e.g.* peptides).

The development of new delivery systems is always associated with potential *in vivo* applications. Therefore, the biocompatibility and toxicity of these systems need to be addressed. With this aim in mind we are developing block copolymers based on poly-(2-methyloxazoline) (PMOXA) and different pH responsive acrylate blocks.

The final goal of our project is to develop a pH-responsive protein delivery platform which will contain the correspond requirements needed in successful delivery of hydrophilic therapeutics *in vivo*.

METHODS: The amphiphilic diblock copolymers based on poly-(2-methyloxazoline) PMOXA and poly(2-dimethylaminoethyl methacrylate) (PMDAEMA) and n-butyl methacrylate (BMA), were synthesized from a PMOXA macroinitiator by atomic transfer radical polymerization (ATRP). Block copolymers were characterized with ^{1}H-NMR and GPC. For self-assembly studies light-scattering and TEM were used.

RESULTS: The optimization of the synthesis was carried out by kinetic studies and different ratio of monomers. ^{1}H-NMR analysis of one type of block copolymer is depicted in Fig.1. Further self-assembly studies are currently under investigation.

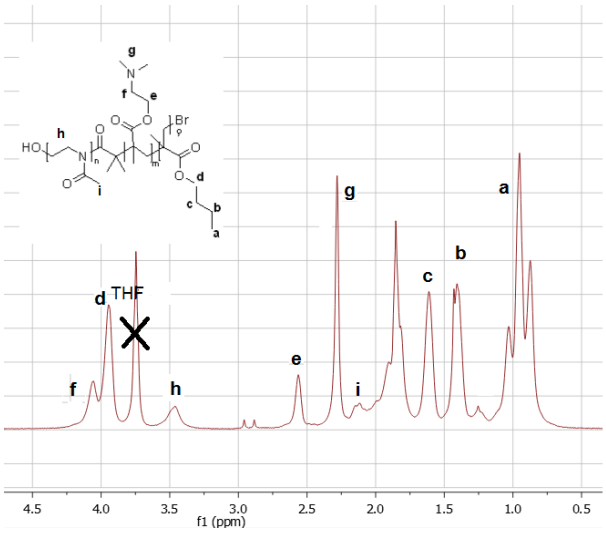

Fig. 1: ^{1}H-NMR spectra of diblock copolymer in $CDCl_3$.

DISCUSSION & CONCLUSIONS: The syntheses of block copolymers were successfully performed. Polymers in solution assembled into spherical nanoparticles showing pH responsiveness. Detailed structure and understanding of the delivery system is still under detailed investigation.

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REFERENCES:

[1] N. Nishiyama, K. Kataoka, *Pharmacology & Therapeutics* **2006**, *112*, 630-648.

[2] S. Kim, Y. Shi, J. Y. Kim, K. Park, J.-X. Cheng, *Expert Opinion on Drug Delivery* **2010**, *7*, 49-62.

Long-term stable immobilization of nano-particles on the surfaces

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INTRODUCTION: The use of nanotechnology in the food industry has increased over the last years. The development of active packaging, which is able to improve or preserve the food's quality, is very relevant. Such packaging is often based on migration of bioactive compounds from the nanoscaled size films deposited on packaging into the food. To preserve the migration in the food they should be chemically attached to the processing surfaces.[1]

There are different possibilities to immobilize the compounds on the surface via covalent bonding. However, the stability of such attachments and the toxicity of the system are crucial parameters for the development of active packaging.

The aim of our project is to develop a method for long-term stable immobilization of nano-particles, such as vesicles or nanoreactors, which can be successfully used for food industry applications.

METHODS: The hydroxyl groups of an amphiphilic poly(2-methyloxazoline)-*b*-poly(dimethylsiloxane)-*b*-poly(2-methyloxazoline) (PMOXA-*b*-PDMS-*b*-PMOXA) triblock copolymer were modified to aldehyde groups. The formed vesicles were covalently attached to the glass surfaces via the hydrazone bond.

For characterization of self-assembled vesicles, TEM and dynamic light scattering were used. The immobilized vesicles on the glass surface were characterized via contact angle, FTIR and AFM.

RESULTS: The self-assembly of amphiphilic triblock copolymers is represented in *Fig.1*.

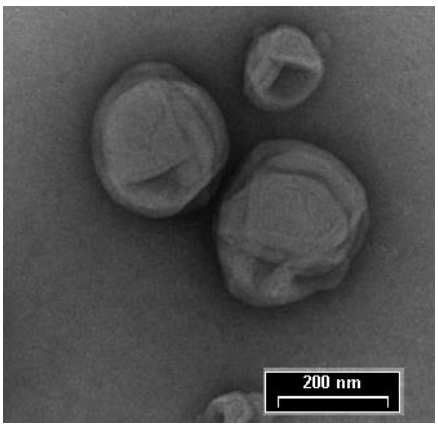

Fig. 1. TEM image of self-assembled vesicles.

Vesicles with a size of around 200 nm were successfully immobilized on the glass surface via hydrazone bond. The AFM image of attached vesicles is represented in *Fig.2*.

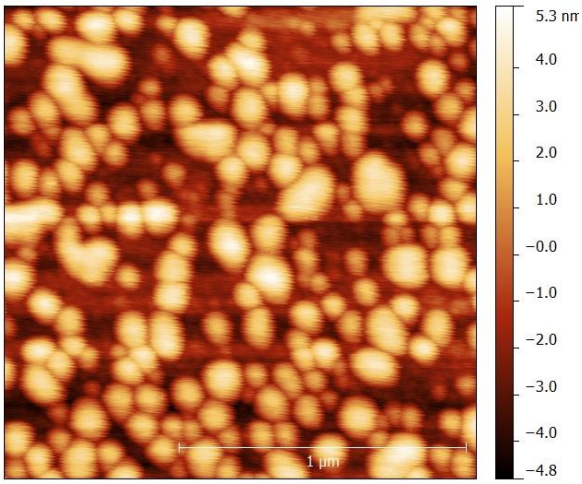

Fig. 2. AFM image of vesicles immobilized on the glass surface.

The reaction conditions are currently under optimization.

DISCUSSION & CONCLUSIONS: The immobilization of vesicles on the glass surface was successful performed.

The chemical bond between the vesicles and glass surface remains intact at 5 weeks after preparation and is being further monitored. Further testing includes the modification of other surfaces, such as PET and LDPE, and testing the stability of the system under other storage conditions.

REFERENCES:

[1] J. M. Goddard, J. H. Hotchkiss, *Progress in Polymer Science* **2007**, *32*, 698-725.

In situ release of DNA from artificial gene carriers

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INTRODUCTION: In chromosomes DNA exists in a highly organized state, wrapped around histones, forming a composite material called chromatin. Decondensation of DNA plays an essential role in gene expression and cell division. In both processes DNA must be unpacked and physically accessible. Our goal is to discover the real-time dynamics of the release of DNA from artificial gene carriers (poly-amidoamine dendrimers PAMAM). The impact of heparin and salt concentrations as well as pH on the disintegration of DNA/PAMAM G6 complexes can be analyzed in a temporal manner.

METHODS: In our studies, we use PAMAM G6, because its size and charge is compatible to histone core proteins. We employ a newly developed soft lithography-based microfluidics reaction device in combination with a lab source X-ray instrument. Using SAXS and SAXD (small angle X-ray scattering and diffraction), we can study the nanostructural evolution of the involved processes. Negatively charged heparin competes with negatively charged phosphate groups of DNA to interact with positively charged amines of PAMAM G6.

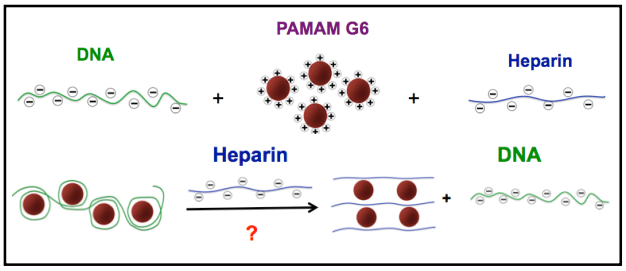

Fig. 1: Schematic representation of charge induced electrostatic interaction of DNA/PAMAM G6 and heparin.

RESULTS: Results are presented that are derived from bio-mimetic investigations of a straightforward DNA compaction model system containing dendrimers (PAMAM G6)[1], which can be viewed as uniformly charged cationic nanospheres and DNA. Mixtures of PAMAM G6/DNA/heparin with different heparin concentrations are analyzed, where by increasing the amount of heparin structural changes are observed. Further heparin is discovered as a decompaction agent of the formed PAMAM G6/DNA complexes.

DISCUSSION & CONCLUSIONS: Heparin is highly negatively charged compound and it competes with negatively charged DNA to form complexes with positively charged PAMAM G6. In mixtures of PAMAM G6/DNA/heparin already at 10% of heparin, DNA is completely released. Heparin can be used as a decompaction agent to unwrap DNA from PAMAM G6.

REFERENCES: [1]R. Dootz; **2011**; *Soft matter;* 7: 8343-8351.

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Impact of confinement on interacting actin polymers

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INTRODUCTION: Composed mainly of three classes of protein fibers, the cytoskeleton forms the foundation of mechanical stability within cells. The dynamic and multifunctional nature of the cytoskeleton is defined by passive and active mechanical behavior, which is highly heterogeneous in space and time and closely connected with various biological functions. In an attempt to piece together mechanics of the entire network, *in vitro* assemblies of independent cytoskeletal units can serve as a compromise between experimental simplicity and substantially complex results. Filamentous actin is an important semi-flexible module of the cytoskeleton, its physical properties playing a crucial role in the deformation and the resistance of the cell to mechanical triggers. Actin filaments are generally geometrically confined within cells, thus the range of physical dynamics exhibited by biopolymers in response to internal confinement is linked to our comprehension of the cellular framework.

METHODS: Using a microfluidic platform, we have studied the effects of varying confinement areas on actin filaments. We are able to study the polymerization of actin filaments *in vitro* within diffusion-controlled micro-confinements, subject to various geometric parameters. Observations of single-filament and multiple-filament fluctuations are correlated and the interactions between filaments are analyzed.

RESULTS: The segment distribution of one, two and multiple actin polymers inside a 2 μm channel reveals different scaling. For a single filament the segment distribution scales as $z^{2/3}$, which is in agreement with previous experiments[1], however the exponent is increased as more filaments are introduced into the channel. Upon closer examination of two interacting filaments, there can be seen a dampening of the lateral center of mass diffusion as two filaments begin to interact. The lateral motion of each filament can be further divided into three regimes: i) separated filaments ii) interacting filaments and iii) synchronized filament movement (Fig. 1). Investigating these phases separately we can determine diffusion coefficients for each filament, which decrease as they progress through the three phases mentioned. According to this data, a critical crossover length L^* (~4-5 μm) can be defined as the maximum lateral overlap length between the two polymers before they become trapped in a synchronous state.

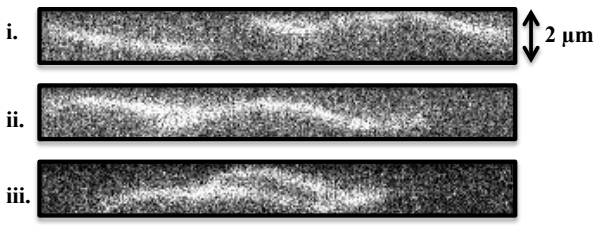

Fig. 1: Images of two fluorescent actin filaments shown during each phase of lateral motion described: i) separated, ii) interacting, and iii) synchronized

DISCUSSION & CONCLUSIONS: Based on the segment distribution scaling, we observe distinct dynamics depending on the number of filaments present in the channel, which we explain as an increase of hydrodynamic interactions. Furthermore, in narrow confining channels the lateral motion of two filaments is progressively dampened due to the hydrodynamic interactions that take place as they move closer together, eventually leading to their synchronization.

REFERENCES: [1] S. Köster, J. Kierfeld, T. Pfohl; **2008**; *European Physical Journal E;* 25:439-449.

Immobilization of biomimetic block copolymer membranes on solid supports

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INTRODUCTION: The functionalization of surfaces through biomimetic block copolymer membranes aims at developing smart surfaces for biotechnological applications such as biosensing. Amphiphilic block copolymer membranes were chosen instead of lipid membranes as mimics of biological membranes because of their properties, such as thickness, chemical and mechanical stability, lower permeability, fluidity, mobility, etc. Upon insertion of membrane proteins, these systems could allow for the preparation of mechanically and chemically robust and air-stable biosensor devices.

METHODS: Surface-initiated atom transfer radical polymerization (ATRP) provides a good control of the brush thickness by controlling polymer molecular weight and by initiating polymerization of a second monomer from the chain end of the first. Poly(2-hydroxyethyl methacrylate)-b-poly(n-butyl methacrylate)-b-poly(2-hydroxyethyl methacrylate), PHEMA-b-PBMA-b-PHEMA block copolymers were synthesized with the first PHEMA block anchored to a self-assembled monolayer on the gold surface while the other PHEMA block exposed to the outer surface. To this end, a self-assembled monolayer of ($BrC\text{-}(CH_3)_2COO(CH_2)_{11}S)_2$) initiator was formed through a covalent binding of disulfides to gold. Then, HEMA monomer was polymerized by ATRP. The first PHEMA block initiated the polymerization of BMA. Subsequently, the second PBMA block again initiated HEMA polymerization, thus resulting in a triblock copolymer membrane anchored to the gold substrate. Block copolymer brushes were prepared with different block lengths and characterized on the gold surfaces using different characterization methods.

RESULTS: The formation of the self-assembled monolayer was successfully characterized by AFM, contact angle- and X-ray photoelectron spectroscopy (XPS), providing information on the presence of chemical elements and their binding energies, and therefore on the structure of the initiator on the surface. Contact angle, ATR-FTIR, and AFM measurements were taken to monitor the ATRP synthesis. PHEMA brushes render the surface smoother and more hydrophilic, whereas PBMA brushes result in a rougher, more hydrophobic surface. The thickness was measured layer by layer by surface plasmon resonance (SPR), with an overall thickness of 12 nm.

DISCUSSION & CONCLUSIONS: The thickness was well-tuned in order to obtain a suitable model for the use as biomimetic membrane. Moreover, to predict a suitable model, the grafting density was varied by mixing the ATRP initiator with a molecule inert to ATRP reaction. It was shown that lowering the grafting density contributes to decrease the layer thickness. Therefore, a grafting density > 70% of the brushes on surfaces can be used as models for further protein insertion experiments. The polymer brushes with a hydrophilic-hydrophobic-hydrophilic sequence can be regarded as the first example of solid supported, biomimetic block copolymer membranes prepared by a "grafting-from" approach.

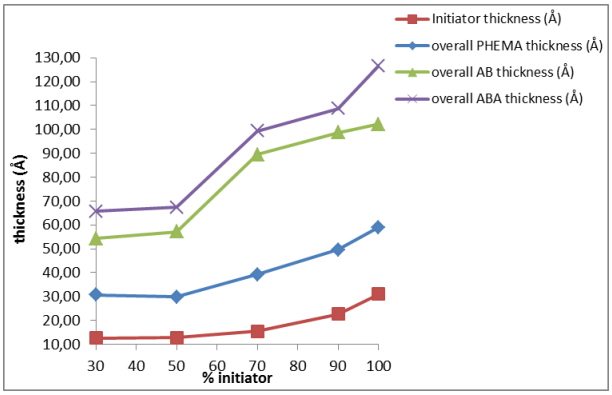

Fig. 1 : Relationship between the brushes thickness and the grafting density using neutron reflectometry.

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Silica Particles Interactions across Ionic Liquids and Ionic Liquid-Water Binary Systems.

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INTRODUCTION: Ionic liquids (ILs) are pure salts with melting point below 100°C. During the past years they attracted considerable interest on account of their unique physicochemical properties and their tuneability through systematic variation of cation's and anion's structure and combination. For these reasons they appeared to be suitable for different applications, among which colloidal systems (as dispersant or solvent for nanoparticles synthesis) or at the interface with a solid material (fuel cells, batteries) [1]. Our work is addressed to characterize forces between surfaces in pure ILs, and in the whole dilution range of IL-water mixtures, giving a qualitative and eventually quantitative interpretation of the data acquired.

METHODS: Forces between surfaces have been measured using the Atomic Force Microscopy (AFM) by mean of the colloidal probe technique [2]. Silica particles of 5 μm diameter, have been attached on tipless AFM cantilevers and glass substrates via sintering (1050°C, 2 h), allowing the direct measurements of forces between single pairs of colloids.

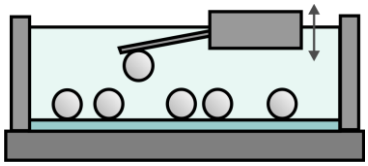

Fig. 1: Schematic representation of the experimental set-up.

Four different imidazolium based ILs with different anions have been investigated: 1-butyl-3-methylimidazolium thiocyanate (BMIM SCN), 1-butyl-3-methylimidazolium tetrafluoroborate (BMIM Cl), 1-butyl-3-methylimidazolium dicyanamide (BMIM DCA) and 1-butyl-3-methylimidazolium chloride (BMIM Cl).

RESULTS: For IL-water mixtures, at very low concentrations, forces are electrostatic in nature, where the double layer repulsion decreases with the IL concentration and can be predicted quantitatively with Poisson-Boltzmann theory. Increasing the IL's concentration above 50 mM, the double layer is completely screened and the interaction is attractive, due to dispersion forces.

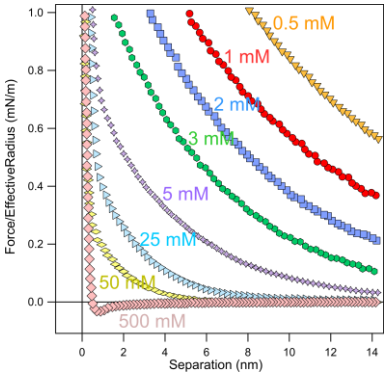

Fig. 2: Force curves in BMIM SCN-water mixtures.

In pure ILs step-like force profiles are observed (3-4 layers were most likely be detected for each IL), showing layering of ILs molecules on the surface, whose order decreases going from the surface to the bulk. For each force curve the height (force required to disrupt the layer) and the position (layer thickness) of the steps have been recorded and a statistical analysis has been performed.

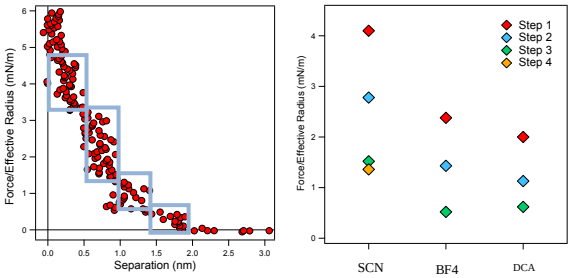

Fig.3: Force profile in pure BMIM SCN (left) and statistic for force related to each steps for the ILs investigated (right).

DISCUSSION & CONCLUSIONS: All the ILs investigated show qualitatively and quantitatively similar features for the IL-water binary systems, while for the pure IL, BMIM SCN shows a higher degree of ordering at the interface than the others investigated.

REFERENCES: [1] N. V. Plechova; **2008**; *Chem. Soc. Rev.;* 123-150. [2] W.A. Ducker; **1991**; *Nature; 239-241.*

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