

17th WORKSHOP Fribourg 05.10.2015

Adolphe Merkle Institute, University of Fribourg Chemin des Verdiers 4, 1700 Fribourg

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Local Organizers

Véronique Trappe Andreas Zumbühl Marco Lattuada

Program

10.00-10.30	Registration / Coffee		
	Welcome: Marco Lattuada (U Fribourg)		
Chair: Andreas Zumbühl (U Fribourg)			
10.30-11.15	Invited Speaker: David Carrière (CEA) Dense intermediate states on the route from ionic solutions to nanocrystals		
11.15-11.35	Trefalt (U Geneva)	Interactions between Charged Surfaces in the Presence of Multivalent Coions	
11.35-11.55	Sassi (EPFL)	Kinetic model for the mechanism of RNA unwinding performed by DEAD-box proteins	
11.55-12.30		Introduction to posters	
12.30-14.00	Lunch/Coffee/Posters/Discussion		
Chair: Joachim Kohlbrecher			
14.00-14.20	Lesov (ETHZ)	Wetting of solid particles by liquid interfaces	
14.20-14.40	Nagy (PSI Villigen)	Correlation between Nano-Structure, Proton- Dynamics and Performance-Related Properties of Radiation-Grafted Proton-Conducting Membranes	
14.40-15.00	Juarez (ETHZ)	Biomechanical ordering and buckling due to microbial growth confined at oil-water interfaces	
15.00-15.20	Mueller (U Fribourg)	Targeted Drug Delivery based on Shear Sensitive Vesicles	
15.20-16.00	Coffee/Posters/Discussion		
Chair: Peter Fischer			
16.00-16.20	Gaitzsch (U Basel)	Stars at work: Controlling the surface topology of polymer vesicles	
16.20-16.40	Bruns (U Fribourg)	Photo-permeabilized Block Copolymer Vesicles as Nanoreactors for Enzymatic Reactions and Biocatalytic ATRP	
16.40-17.00	Sepe (U Fribourg)	Structure-Function Relationship in Photovoltaics	
17.00	Closing Remarks: Lucio Isa (ETHZ)		

Poster Contributions

1	Zhang (U Fribourg)	Structure of marginally jammed polydisperse packings of frictionless spheres
2	Nazzani (U Fribourg)	The quest for equilibrated super-cooled liquid phases: tuning relaxation and nucleation times in binary mixtures of charged colloids
3	Calzolari (U Fribourg)	Contributions to creep in colloidal gels
4	Ketari (Nestlé)	Characterization of oil migration in confectionery products
5	Pollard (U Fribourg)	ATRP of acrylamide catalyzed by Hemoglobin
6	Malinverni (EPFL)	Learning from evolution: Coevolutionary Analysis of Hsp70 chaperones
7	Grossman (ETHZ)	Bioinspired composites by vacuum assisted magnetic alignment
8	Fischer (U Fribourg)	Hierarchically structured materials for supercapacitors and batteries
9	Guignard (U Fribourg)	Janus Dumbbells: A flexible template for colloidal chemistry
10	Gunkel-Grabole (U Basel)	Self Assembly of Polymeric Nanoarchitectures and their Immobilization on Solid Surfaces
11	Vian (EPFL)	Production of mechanically robust capsules with thin shells
12	Hejazi (EPFL)	Tuning the wettability of surface
13	Isapour (U Fribourg)	Synthesis of Stimuli-responsive Microgels for the preparation of Color-changing Hydrogels
14	Neuhaus (U Fribourg)	Advanced Monolayer Studies for Fluorescent "Flippers"
15	Einfalt (U Basel)	Stimuli-triggered activity of nanoreactors by biomimetic engineering polymer membranes
16	Tanasescu (U Fribourg)	Cholesterol Interactions with an Artificial Phospholipid
17	Stalder (U Fribourg)	Addressing the temporomandibular joint disorder

Invited Lecture

Dense intermediate states on the route from ionic solutions to nanocrystals

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The synthesis of crystalline oxide nanoparticles by co-precipitation of ions in water and at room temperature is an industrially appealing method to produce functional nanomaterials. Yet, the development of functional materials from nanoparticles requires an optimal control over their crystallinity (quality and polymorph selection) and nanostructure (size, aggregation state). In the case of crystalline oxide nanoparticles synthesized at room temperature in water, a crucial bottleneck which hampers this control is the failure of the classical models to describe the nucleation processes which prelude the crystalline growth.

The acknowledged origin of the failure of the classical nucleation model is that it overlooks possible dense, disordered states prior to crystallization, *e.g.* (i) dense liquid phases that form even before any chemical reaction has occurred, and (ii) a possible succession of amorphous states that develop prior to crystallisation. The conceptual implications of the multi-step nucleation processes are to date poorly explored, partly because of a great experimental challenge to overcome: the characterisation of transient states from the Angstrom to the submicron scale, at reaction times significantly shorter than one millisecond.

Here, I will present recent progresses on the nucleation problematics obtained after selecting an *ad hoc* experimental model system, namely the synthesis in water of luminescent rare earth-doped vanadates nanoparticles (YVO₄:Eu). The emission properties of these nanocrystals provide a convenient probe which strongly supports other classical time-resolved, *in situ* structural characterization techniques (SAXS, WAXS, EXAFS). This quantitative approach supports progress not only on the understanding of nucleation processes, but also on the improvement of the specific synthesis YVO₄:Eu nanocrystals, which are used as luminescent biolabels and precursor for thin-film phosphors.



Interactions between Charged Surfaces in the Presence of Multivalent Coions

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Forces between charged polystyrene latex spheres across aqueous solutions were measured by colloidal probe technique. Salts containing multivalent *coions* were used for these measurements. Therefore the multivalent ions had the same charge as the surface and were consequently repelled from it. The behavior of such systems is completely different as compared to the multivalent *counterion* case, were ions adsorb strongly on the surface and the double layer repulsion is typically short-ranged and weak. In the coion case however, the forces are long-ranged and soft with an interesting sigmoidal shape. This characteristic shape can be explained by Poisson-Boltzmann theory and is a consequence of expulsion of multivalent *coions* from the area between the charged surfaces upon their approach, see Figure 1. At large separations the force-curves follow the far-field Debye-Hückel limit, whereas at small separations the near-field counterion-only limit is reached.



Figure 1. a) Schematic presentation of expulsion of the multivalent coions between the charged walls. b) Experimentally measured force curve in the presence of four valent coion together with the Poisson-Boltzmann prediction and far and near-field limits.

Kinetic model for the mechanism of RNA unwinding performed by DEAD-box proteins

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INTRODUCTION: In addition to its role in protein synthesis, RNA is involved in other biological tasks that are determined by its complex tertiary structure.

Proteins of the DEAD box family (Dbp) use ATP to stabilize the unstructured RNA with a mechanism that would not be possible in equilibrium. We provide a kinetic model in order to clarify this aspect and explain how the ATP hydrolysis is coupled to the RNA unwinding.

METHODS: We modelled a system of RNA and Dbp with the kinetic cycle shown in Fig. 1. Such a cycle has been obtained with a simplification from a more complex cycle, where the ATP state is taken into account explicitly. We assumed that the Dbp is able to unwind the RNA when it is in the ADP state. Moreover, we assumed the chaperones to be in excess with respect to the RNA. In equilibrium, namely when there is no hydrolysis of ATP, the detailed balance must be satisfied and the final yield of unfolded RNA cannot be increased in the presence of Dbp with respect to the case of spontaneous unwinding reaction. However, if such a reaction is slow, Dbp can in principle accelerate the process, leading the system to reach faster the steady state.

On the contrary, if there is energy consumption because of the hydrolysis of ATP, the system is driven out of equilibrium and, in this case, the unfolded state can be significantly stabilized with respect to the native state.

RESULTS: We associated a system of Master equations to the kinetic cycle shown in Fig 2. By solving this system numerically, we obtained the fraction of native RNA as a function of time. As we can see in Fig. 2, the fraction of native RNA in the stationary state decreases as we increase the concentration of Dbp. Moreover, for the first time, it has been possible to relate directly the flux of hydrolysis, and therefore the energy consumed per unit time, to the stabilization of unfolded RNA.



Fig. 1: Kinetic cycle used in our work. The two states in the bottom represent the RNA in unfolded (left) and native (right) conformation. On the bottom the RNA is bound with Dbp in the ADP state.



Fig. 2: The fraction of structured RNA is lower in a system with Dbp and ATP (red, [Dbp]=20 μ M and blue, [Dbp]=10 μ M) than in a system where the DEAD box protein is absent.

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Wetting of solid particles by liquid interfaces

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INTRODUCTION: The wetting of solid particles on fluid interfaces has been widely studied in the fields of colloid and materials science. Its importance is related to the long-term stability of emulsions and foams, as well as the preparation of novel two- and three-dimensional materials such as anti-reflective coatings and photonic crystals.

There is a limited number of methods for measuring the particles wettability at liquid-liquid interfaces¹. Even further, all the methods available work in a different timescale and comparison between them is often scarce or completely missing.

METHODS: In the current study, we present a systematic comparison between some of the most popular and simplest methods for contact angle measurement of the particles: atomic-force microscopy²; gel-trapping technique³, freeze-fracture shadow casting cryo-SEM⁴, cyanoacrylate fuming⁵ and macroscopic measurement of sessile droplets.

RESULTS: We show that in most cases there is an excellent agreement between the experimental methods but some limitations may apply (e.g. for highly hydrophilic particles). Additionally, we examine some aspects of the particles roughness on the contact angle assessment (see Figure 1).



Figure 1: Micron-sized silica particles with predesigned surface roughness.

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Correlation between Nano-Structure, Proton-Dynamics and Performance-Related Properties of Radiation-Grafted Proton-Conducting Membranes

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INTRODUCTION: Polymer electrolyte fuel cells using hydrogen can serve as clean and efficient energy converters. One of the crucial components of these electrochemical cells is the proton conducting membrane. The proton conductivity, mechanical stability and durability of these membranes are strongly affected by the phase segregation found on the nanoscale, a topic extensively studied with various methods [1-2] such as small-angle neutron scattering, an ideal technique for this class of materials [3].

METHODS: We combined the structural characterization tools of small-angle neutron (SANS) and X-ray scattering (SAXS), the energy dispersive X-ray analysis (EDX), dvnamic experimental methods of nuclear magnetic resonance (NMR) spectroscopy [4] and quasielastic neutron scattering (QENS) to gain insight into the fuel-cell relevant properties of membranes synthesized via radiation grafting. For the preparation of the membranes we used a commercially available base film (ETFE, poly(ethylene-*alt*-tetrafluoroethylene)) grafted with polystyrene, sulfonated subsequently.

RESULTS: We found structural and/or dynamic variations of the membranes upon changing the following parameters: basefilm manufacturer (DuPont/Saint-Gobain), level of grafting, radiation grafting protocol and sulfonation. We also revealed how the structural and dynamic parameters vary along different directions in the membrane. Structural studies were facilitated by the development of a sample environment allowing measurements at different membrane orientations and humidity conditions. The obtained results were correlated with membrane performance relevant measurements, such as membrane conductivity, and with macroscopic characteristics, such as dimensional changes.

DISCUSSION & CONCLUSIONS: These results allow us to better understand the correlation between synthesis, structure, (proton) dynamics, and functionality of radiation grafted membranes, which will lead to the development of membranes with improved performance.



Fig. 1: Small-angle neutron scattering signal of DuPont (top) and Saint-Gobain (bottom) base films with the machining (MD) and transverse (TD) directions marked.

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Biomechanical ordering and buckling due to microbial growth confined at oil-water interfaces

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INTRODUCTION: Marine microbes are key players in the mitigation of crude oil pollution in ocean environments. Fundamentally, this occurs through physical interactions at the microscale between individual cells and liquid-liquid interfaces in a dynamic fluid and physical environment. Because bacteria are a micron in size, they are considered environmental colloids that spontaneously attach and self-assemble at liquid-liquid interfaces. Once attached to the oilwater interface, microbes transform the carbon rich substrate into biomass which leads to growth and the production of new cells.

METHODS: Through experiments using microfluidic chambers and time-lapse microscopy, we directly visualized the interactions between marine bacteria and crude oil droplets of different diameter ranging from 1 to 300 microns.

RESULTS: Here, we present results on the growth dynamics of individual rod-shaped bacteria confined to finite oil-water interfaces of varying curvature. We find that active oil-water interfaces spontaneously form when bacteria are confined to grow on an oil droplet. We study the formation of macroscopic structures observed as adsorbed bacteria grow, divide, and self-assemble in a nematic phase due to biomechanical interactions. The continued growth at the interface leads to a jammed monolayer of cells, which then causes the interface to buckle and undergo large wrinkling deformations including and tubulation (Fig 1). The growth dynamics and non-equilibrium structures are closely coupled with the initial diameter of the oil droplet.



Fig. 1: Time-lapse montage of a 100 micron crude oil droplet that is being colonized. The continued growth of cells confined at the interface over the course of 24 hours leads to the self-assembly of a jammed monolayer which buckles and undergoes large deformations.

DISCUSSION & CONCLUSIONS: These observations highlight the interplay between physical environment, such as confinement and interface curvature, and active biological processes, such as growth, at the scale of individual agents and shape our understanding of processes microbial macroscale such as degradation of oil in the ocean.

Targeted Drug Delivery based on Shear Sensitive Vesicles

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INTRODUCTION: Temperature, ultrasound, enzymes, pH-changes, redox-reactions as well as photo-reactions are well known as trigger for cargo release from phospholipid liposomes.¹ A new approach in targeted drug delivery is shearsensitivity; recently our group described the first mechano-sensitive phospholipid, the artificial 1,3diamidophospholipid Pad-PC-Pad (1).^{2,3}



Scheme 1: The artificial 1,3-substituted phospholipid Pad-PC-Pad (1).

METHODS: In order to understand the mechanosensitivity of Pad-PC-Pad (1) vesicles SAXS and WAXS were used to determine the membrane thickness and organization, whereas cryo-TEM imaging and tomography were used to specify the shape of large unilamellar vesicles of 1.

RESULTS: With SAXS and WAXS a length of 0.80 nm for the headgroup region and 1.92 nm for the tail region was determined.



Fig. 1.: Schematic view of leaflet interdigitation of the lipids forming the bilayer (head group region green and tail region blue).

Cryo-TEM micrograph and tomogram are showing developed surfaces and dForm shaped vesicles of Pad-PC-Pad (1).



Fig. 2: Left: Cryo-TEM image of Pad-PC-Pad (1) vesicles; scale bar is 200 nm. Right: cryo-tomography image of Pad-PC-Pad (1) vesicles; scale bar is 50 nm.

DISCUSSION & CONCLUSIONS: The measured distance d of the tail region in the vesicle is 1.92 nm. As a single tail has a length of 1.90 nm a fully interdigitation could be estimated. The observed leaflet interpenetration stiffens the membrane in the lateral direction, resulting in non spherical, dForm shaped, liposomes as shown by cryo-TEM imaging and tomography. A dForm is a developable surface of two ellipses which are turned 90 ° to each other and connected with one continuous edge.

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Stars at work: Controlling the surface topology of polymer vesicles

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INTRODUCTION: Polymer vesicles. or polymersomes, have taken considerable steps in the past years. They can now incorporate a wide range of functionalities and come close to mimicking natural vesicles. [1] In this respect it is important to note that biological surfaces are never plain, but always show a patterned, or patchy, structure. Patchy polymersomes are also known and are generally produced by mixing 2 different amphiphilic block-copolymers. However, they demix on the polymersome surface until they eventually separate completely. [2]. One way to prevent the demixing and thus produce stable surface patterns would be the use of a miktoarm star polymer as lineactant. The chemical links of the blocks in the star would prevent the demixing. In addition, the patch size could be regulated by the amount of lineactant added to the mixture.

METHODS: Our synthetic approach utilises a dibromomaleimide core with an azide handle. This molecule is readily used in peptide chemistry but has not been used in polymer chemistry. [3] Both bromine atoms can be displaced by thiols and result in a more stable link than the traditional sulphide-maleimide link. Thanks to the azide handle, a third functionality can be added using traditional azide-alkyne click chemistry. (Fig. 1, top) The final vesicles can then be imaged using TEM with selective staining to proof the formation of polymersomes with stable and regulated patches.

RESULTS: We have successfully synthesised the miktoarm star terpolymer starting from the trifunctional maleimide core described above. The methacrylic polymers PMPC and PDPA (Fig. 1, top) contained a disulphide moiety which was then cleaved in situ while attaching it to the core in clean successive reactions. PEG was attached afterwards using the CuAAC reaction (Fig. 1 top), which posed some unexpected challenges. [4]

The miktoarm star was then mixed with a linear PMPC-PDPA block-copolymer and did indeed induce the formation of a stable patterned surface on the polymersomes. Our established method of selective staining proved the presence of the patches in TEM. [4] (Fig.1, bottom, incl. cartoon)



Fig. 1: A miktoarm star polymer is constructed in efficient reactions from a dibromo-maleimide core. If mixed with a diblock copolymer, they induce a stable and controllable pattern on polymer vesicles.

DISCUSSION & CONCLUSIONS:

We hence succeeded in the synthesis of the amphiphilic miktoarm star terpolymer with efficient reactions. In addition, the the final molecule also suited the purpose intended when self-assembled with a linear block-copolymer into polymersomes. With stabilising and regulating the surface topology of polymersomes we have taken them another step forward to mimic natural vesicles.

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Photo-permeabilized Block Copolymer Vesicles as Nanoreactors for Enzymatic Reactions and Biocatalytic ATRP

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INTRODUCTION: Nanoreactors provide confined reaction spaces with dimensions on the nanoscale [1]. Carrying out chemical reactions within nanoreactors allows controlling their pathways in unique ways and opens routes to novel nanostructures. Polymersomes, i.e. vesicles that form by the self-assembly of amphiphilic block copolymers, are often used as nanoreactors for enzymatic reactions. To this end, their membrane has to be permeable for substrates and products. Such permeability can be achieved by reconstituting membrane proteins into the block copolymer membranes, or by using polymers that form porous membranes [1]. However, these methods require expensive biomolecules or specialty polymers, so that they are not feasible for technical applications.

RESULTS: We found that the UV-induced reaction of an α -hydroxyalkylphenone with polymersomes renders them permeable for organic molecules, independent of the chemical nature of the block copolymers (Figure 1) [2]. Thus, a broadly applicable and easy to perform method to permeabilize polymersomes was developed. The used vesicles were as nanoreactors for biotransformations. Moreover, enzymatic ATRP [3, 4] was carried out within the aqueous lumen of these polymersomes [5]. The polymerization was spatially confined into these nanoreactors and resulted in polymer-filled polymersomes. They are intriguing nanostructures that can be regarded as simple cell mimics and that could find applications biocatalytic systems in demanding as environments, such as organic solvents.



Fig. 1: Photoreaction of block copolymer vesicles with an α-hydroxyalkylphenone makes the vesicle membrane permeable for enzyme substrates, monomers and other organic compounds. Reprinted with permission from [2]. Copyright 2013 American Chemical Society.

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Structure-Function Relationship in Photovoltaics

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INTRODUCTION: The extension and further development of photovoltaics is essential to reduce the carbon footprint of industrialized nations by 2050. This implies that all forms of harvesting solar energy must be exploited. Since there is no in clear front-runner low-cost alternative photovoltaic devices, it is important to pursue all possible avenues. Organic solar cells have many advantages and therefore have the potential to supplement energy production of silicon based solar cells. Polymer containing solar cells have reached power conversion efficiencies above 10%, they thus remain a promising technology. Similar to many new alternative photovoltaic concepts, the scientific basis of polymer-based photovoltaics is weak. Despite more than a decade of research, highly performing organic photovoltaic devices (OPVs) are optimized by "trial-and-error" processing. In particular, detailed knowledge on how the processing of device ingredients determines materials assembly and how different material assemblies affect electronic properties is Trial-and-error approaches, currently missing. while often effective, have the disadvantage that a change in parameters or the discovery of new materials requires the renewal of often-lengthy device optimization protocols. Scientifically the lack of deterministic models is frustrating [1].

RESULTS: Our research focuses on two promising polymer-based OPV technologies with the goal of unravelling the way in which structure formation during processing affects device performance in (i) all organic systems, encompassing conjugated polymer blended with C₆₀ derivatives and polymer-polymer blends, this is then extended to (ii) the more recent hybrid polymer - nanocrystal quantum dot (NCQD) devices [2]. The final aim is to gain a fundamental understanding of the formation of mesoscopic morphologies within the photoactive layers, as well as their formation kinetics. Our study resulted in a fundamental understanding of structural and functional properties of semiconducting polymers, blended with different classes of fullerenes, conductive polymers and NCQDs. The principally employed techniques encompass a range of advanced synchrotron scattering methods. Furthermore, the large amount of data acquired by the extensive use of these methods requires the implementation of automatized computational

frameworks addressing the Big Data analysis and modelling issue, the development of which is also part of our research.

DISCUSSION & CONCLUSIONS: We focused on the development of more efficient and environment friendly photovoltaic cells, aiming at replacing fossil energy generation. Our results made a significant contribution to this initiative, paving the way to low-cost solar cells devices that can be processed at low temperatures, and making use of established printing processes. We have thus laid the scientific groundwork for a range of polymer based devices [3], in fact despite the research of polymer maturity of based photovoltaics, the structure-function relationship in these devices is not well known. We have further extended the fundamental understanding on the structural properties and thermodynamics of NCQDs, which are indispensable to further develop hybrid solar cells into a new concept with low fundamental losses [2]. Organic and related hybrid materials progressed rapidly from exotic niche materials to vital players in the arena of future photovoltaic materials, our research is thus focusing on unravelling the interplay of the respective components in the photoactive layer. Further understanding the interplay between structural and electronic properties will open new ways towards self-assembled nano-morphologies in solar cells. The application of NCQDs in combination with polymers has proven to be extraordinarily effective and further advances in overall efficiency are expected by extending the electronic functionalities through the fundamental understanding of the structural properties of NCQDs and broadening this concept to the organic semiconductors, with a high impact within the energy field and relevant technological implications.

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Structure of marginally jammed polydisperse packings of frictionless spheres

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FIG. 1. Three-dimensional imaging of jammed emulsions droplets with an average droplet radius $\bar{a} = 1.05 \mu m$. (a) Raw image of a plane in the bulk of the sample obtained by laser scanning confocal microscopy of light emitted by the fluorescent dye Nile-red at $\lambda = 595$ nm. The droplets are marginally jammed and the volume fraction is $\phi \simeq 0.646 \pm 0.014$. (b) Three-dimensional reconstruction of the droplet positions using the sphere matching method (SMM). The lines show the Voronoi radical tessellation around the droplet centroids. The total dimensions are $51.2\mu m \times 51.2\mu m \times 20.1\mu m$. One corner is cut out to reveal the internal structure of the jammed system.

We model the packing structure of a marginally jammed bulk ensemble of polydisperse spheres. To this end we expand on the granocentric model [Clusel et al., Nature **460**, 611 (2009)] explicitly taking into account rattlers, rather than considering only particles in contact. Then we consider the influence of size correlations[1] between particles and their shell, previously neglected [2]. Next we address the distribution $G_s(s)$ of surface-to-surface separations s = r - 2a. We can use the scaling of the excess number of contacts $\Delta Z \sim \sqrt{\bar{Z}_J - 6}$ to derive $G_{sJ}(s) \sim s^{-1/2}$ [3]. For the rattlers we take the simple *ad-hoc* assumption that their neighbors are distributed uniformly $G_{sR} = const.$

The eGCM can be evaluated numerically and we can obtain statistical information directly from the model. We compare the model predictions with experiments on micron scale emulsion droplets under marginal jamming conditions. High resolution images (Figure 1) of the individual droplet positions are obtained using 3D laser scanning confocal microscopy (A1R, Nikon, Japan). 3D-images of size $512 \times 512 \times 201$ pixels are recorded with a resolution of 100nm/pixel in all spatial directions. To track the position of the polydisperse droplets we implement the sphere matching methods (SMM) algorithm. A Voronoi radical tessellation is applied and particles with adjacent cell walls are identified as neighbors.

From an extensive comparison with experimental data and packing simulations, we demonstrate that our extended granocentric approach can deliver accurate predictions for a bulk ensemble of marginally jammed particles covering the full range of polydispersities of practical interest. The observed quantitative agreement opens the path towards a full structural characterization of jammed particle systems for imaging and scattering experiments.

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The quest for equilibrated super-cooled liquid phases: tuning relaxation and nucleation times in binary mixtures of charged colloids

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Super-cooled liquid states in colloidal suspensions can be obtained by shear rejuvenating systems that in equilibrium are crystalline. However, a super-cooled liquid needs to be equilibrated to be defined as such; i.e. the system needs to be able to re-configure several times without interference of crystallization. This requires that the relaxation time τ_{α} is short compared to the nucleation time τ_N .

We explore this interplay of relaxation and nucleation in binary colloidal suspensions that contain two different microgels. Both microgels are similar in size but significantly differ in their effective charge. At quasi-deionized conditions this difference leads to distinct behavior. At a given number concentration of $N=7.07 \ \mu m^{-3}$ the system containing the microgels with the lower effective charge S2 is a stable liquid, characterized by fast diffusive dynamics. By contrast, the microgels with the higher effective charge S1 display at the same number concentration a very slow α -relaxation and crystallize almost immediately after rejuvenation.

By combining the two systems in mixtures with varying fractions of S1, X, both the nucleation and the relaxation time vary over several decades. At very high X the nucleation time never exceeds the relaxation time, and the temporal evolution of τ_{α} after rejuvenation is not stationary before crystallization occurs. By contrast, in the lower X range we find that τ_{α} is smaller than τ_N and the dynamics is stationary before nucleation occurs. The transition between both types of behavior occurs when τ_{α} exceeds the free diffusion τ_{0} by a factor of 10⁴. We define this point as the transition between the super-cooled state and the unstable glassy state.

Contributions to creep in colloidal gels

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The response to an external stress displayed by both, hard and soft materials, are qualitatively very similar: the material deforms instantaneously due to elasticity and then slowly creeps at a decaying rate. In crystalline materials such as metals the decay of the creep rate is generally attributed to a hardening process that impedes plastic deformation. By contrast, a decaying creep rate in soft matter systems is often interpreted as due to the slowing down of the structural relaxation processes during aging.

In this contribution we explore the creep behavior of a colloidal gel and show that the creep response is here governed by a combination of several processes: a time dependent storage process, a hardening process and a dissipative process. We find that both hardening and dissipation relate to aging, while the time dependent storage process does not. We tentatively propose that the origin of this storage process relates to the heterogeneous configuration of the gel. A definite explanation, however, has yet to be found.

Characterization of oil migration in Confectionery products.

Abstract

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Oil migration between different phases in composite confectionery products, such as filled chocolate bars, is a common yet poorly understood phenomenon. It is of great concern to food manufacturers as fat migration leads to visual and sensory defects making the product unacceptable for the consumer. [1] In fact, migration from a highly oil-rich phase to a crystalline fat-rich phase, i.e. oiling out, is becoming more and more relevant since the liquid lipid fraction is constantly increased in order to achieve a better product nutritional profile. However, current interpretation of actual mechanisms are mostly speculative even though the triacylglycerol (TAG) chemical potential (μ_{TAG}^{Oil}) gradient implies that there will be some net diffusive flux. Migration will continue until thermodynamic equilibrium between solid and liquid phases is reached. [2]

This study laid meticulous foundations for further elucidation of the driving forces behind oil migration but also to assess some kinetic factors. The first approach, i.e. oil uptake experiment, consisted in measuring the weight increase of thin milk chocolate tablets in direct contact with authentic fillings (similar to those used in factory). Typical mass uptake results showed a linear dependence between the average weight gain against square root of time. The migration of 22% of high oleic sunflower oil (HOSFO), i.e. filling fat, in milk chocolate after seven days did not lead to blooming. The second approach was based on assessing handmade chocolate coated bars during an accelerated shelf life test. It consisted of temperature cycles of sixteen hours at 18°C followed by eight hours at 24°C, through visual and sensory tasting. After three months under these conditions all the samples did not show any bloom even though other critical features appeared, i.e. such as severe softening of chocolate edges. These observations were confirmed, for both approaches, by the calorimetric curves that highlighted no significant shift of melting peaks, i.e. no recrystallization of cocoa butter crystals at chocolate surface.

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Figures:



Figure 1: (a) Typical filling recipe used during the oil uptake experiment within this study. (b) Picture showing the handmade chocolate coated bars. Each bar was half coated and the other one "naked" to observe the effects of oil migration on chocolate but also on the wafer.



Figure 2: Calorimetric curves (2°C/min) during the first heating step, i.e. from room temperature to 60°C, highlighting the melting peaks obtained from the (a) first approach and (b) second approach experiments.

ATRP of acrylamide catalyzed by Hemoglobin

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INTRODUCTION: Among controlled polymerization techniques, atom transfer radical polymerization (ATRP) is the most popular one since it is versatile, tolerant toward functional groups and yields halogen-terminated polymer chains¹. To extend furthermore the scope of ATRP, the transition metal catalyst can be replaced by metalloenzymes, so called ATRPase².

RESULTS: To demonstrate the improvement encompassed by this system, acrylamide polymerization, known to be difficult to control under ATRP conditions³, was carried out. Hemoglobin which has already proven to be an efficient catalyst for the controlled polymerization of water-soluble monomers⁴ was used to control the polymerization of acrylamide. Polymers with very narrow polydispersity were obtained as shown in Figure 1 and the kinetics of the polymerization were characterized by NMR, GPC and MALDI-TOF-MS.



Fig. 1: MALDI TOF MS of polyacrylamide

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Learning from evolution: Coevolutionary Analysis of Hsp70 chaperones

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INTRODUCTION: Hsp70s are a class of highly conserved ubiquitous and molecular chaperones playing a central role in the regulation of proteostasis in the cell. Hsp70s assist a miriad of cellular processes by binding unfolded or misfolded substrates during a complex biochemical cycle involving large-scale structural rearrangements. Here we show that an analysis of coevolution at the residue level fully captures the characteristic large-scale conformational transitions of this protein family, and predicts an evolutionary conserved, and thus functional, homo-dimeric arrangement.

METHODS: The Hsp70 family proteins were analysed using the recently developed Direct Coupling Analysis (DCA)¹ technique. DCA is based on the analysis of a large Multiple Sequence Alignment of the protein family. By identifying pairs of residues that display strongly correlated mutations, protein contact maps can be inferred (Fig.1). To study the phylogenetic origin of a particular set of contacts, we introduced a sequence-reweighting scheme, which allows observing the difference in evolutionary conserved contacts between eukaryotes and bacteria.



Fig. 1: Schematic view of the DCA method. Pairs of positions displaying above average correlated mutations are indicative of spatially proximal residues. Results are reported as predicted contact maps.

RESULTS: Due to the high conservation and ubiquitous nature of the Hsp70 proteins, a high number of sequences is available, resulting in high quality DCA predictions (Fig.2). By comparing the DCA predictions with the available structures of the two known conformers of Hsp70, we could identify a set of contacts strictly not explainable by

the available crystallographic structures of the Hsp70 monomers. These contacts, however, resulted in being compatible with a homo-dimeric complex observed, previously thought to be a crystallographic artefact. The evolutionary conservation of these dimeric contacts indicate a functional role of a multimeric form of Hsp70s. By reweighting bacterial and eukaryotic sequences, we could observe that the dimeric signal is stronger in bacterial sequences, possibly contributing an evolutionary explanation to the absence of the Hsp110 subfamily cochaperones in bacteria².



Fig. 2: DCA predicted contacts overlaid on the union of the contact maps of the two known conformers of Hsp70. In green (resp. red) are true (resp. false) positive predictions. The region highlighted in blue corresponds to dimeric predictions.

DISCUSSION & CONCLUSIONS: Evolutionary coupling analysis, and particularly DCA, allows for the effective use of the large sequence datasets to infer structural information for large protein families. DCA predicts contacts encoding structure, allostery as well as oligomerization. The rapid growth of sequence databases forecasts the growing predictive power of such methods.

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BIOINSPIRED COMPOSITES BY VACUUM ASSISTED MAGNETIC ALIGNMENT

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INTRODUCTION: The rational design of high strength composites with high fracture toughness is a major challenge in materials science because the molecular origins of strength and toughness are in conflict. However, biology demonstrates that is possible to create composite materials which avoid molecular level conflicts between strength and fracture toughness by creating interconnected hierarchical meso-structures, separating stiffening toughening mechanisms into and different hierarchical levels and modulating their interactions with structural control. In order to materialize an example of fracture-toughening meso-structure in a high strength composite, we build composites that structurally mimic nacre, a.k.a. mother-of-pearl. Nacre has a brick and mortar structure of close packed mineral microplatelets networked by nano-scale mineral bridges and interlocking surface asperities and percolated with a minor phase soft organics. This work presents a process for producing aligned ceramic scaffolds with a nacre-like brick and mortar structure and controlled interfacial nano-structure, and characterizes the mechanical properties of epoxy-infiltrated-scaffold composites.

METHODS: Nacre-like ceramic scaffolds were synthesized from commercially available Titania-coated Alumina micro-platelets, as illustrated in Fig. 1. After magnetization¹, platelets were dispersed in aqueous suspension and transferred to



Fig. 1: Schematic of vacuum assisted magnetic alignment and sintering process

a Buchner funnel inside a rotating magnetic field. Platelets instantaneously aligned with the magnetic field and vacuum filtration was used to consolidate them into brick and mortar structure. Green bodies were then dried and partially sintered in a ceramic hot press. Infiltration with epoxy forms the final composite.

RESULTS: During the sintering process Titania de-wets the alumina surface forming networks of mineral contacts. By varying the sintering temperature, the structure and strength of the contacts between platelets can be modulated; resulting in a series of composites with the same chemistry and mineral density, yet very different mechanical properties. (Fig. 2) Scaffolds with stronger mineral contacts produce brittle composites, however composites built from scaffolds with weaker contacts display pseudoductile behavior, allowing them to be loaded at much higher strains before failing by stable crack propagation.



Fig. 2 Variation of Titania surface morphology as a function of sintering temperature

CONCLUSIONS: This model suggests that optimizing the strength and structure of connections between reinforcement elements is key to maximizing fracture toughness in hard composites.

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Hierarchically structured materials for supercapacitors and batteries

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INTRODUCTION: Amphiphilic blockcopolymers are known to form well-ordered structures on the 10nm length-scale. Such nanostructures have been utilized to increase the performance of solar cells¹ and supercapacitors² among other applications. By confining sol-gel chemistry to one of the blocks of the copolymer these structures can be transferred to various functional inorganic materials.

METHODS: We combine sol-gel chemistry and block-copolymer self-assembly to synthesize and examine nanostructured electrodes of different chemical composition and morphology. The materials under investigation are either already used in lithium-ion-batteries or supercapacitors, or are likely candidates for the next generation of energy materials.

We further aim to incorporate this approach into the fabrication of hierarchically structured materials. By blending the sol-gel precursor/blockcopolymer mixture with a sacrificial homopolymer, macropores can be introduced into the mesoporous electrode structure, offering further performance enhancements.

RESULTS: The resulting well-defined morphologies (cf. figure 1) provide huge internal surface areas while at the same time facilitating efficient ionic and electronic conductivities due to their well-defined mesoporosity and the potential to carbon-coat these structures, respectively.

Furthermore, hierarchical electrodes have been fabricated, consisting of accessible mesopores and different types of macroporosity.

Realizable structures include mesoporous microspheres, bicontinuous frameworks and graded films.



Fig. 1: Different ordered mesostructures of TiO2, obtained by combining sol-gel chemistry with block-copolymer self-assembly.

DISCUSSION & CONCLUSIONS:

The presented strategy provides a scalable approach, an important feature when trying to introduce these concepts on an industrial scale.

Hierarchical structures are envisioned to allow for high ionic conductivity, fast ion-intercalation reactions and good electronic conductivity. The combination of these factors is crucial for optimizing current and future battery technologies, having applications in consumer electronics, electromobility and large-scale energy storage.

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INTRODUCTION: The recent development of nanotechnology led to an increased amount of scientist working on nanoparticles worldwide. However, most of the studies are focusing on spherical isotropic nanoparticles, which are the easier to prepare. We used a described procedure to prepare shape-anisotropic, asymmetricallyfunctionalized dumbbells nanoparticles covering a good range of size and aspect ratio. We then used the presence of silane groups on one hemisphere of the dumbbells only to selectively functionalize the nanoparticles [1], creating different types of hybrids

RESULTS: The hydrolysis and condensation of a silane precursor covered one bulb with a thin layer of silica. Upon removal of the polymeric template, we prepared silica nanobowls bearing a well-defined opening in their shell. Calcination of the template at 550 °C led to purely hydrophilic silica nanobowls, while the dissolution of the template in THF gave birth to Janus nanobowls having a thin polymer layer on their inner side. We proved the different reactivity of the inside and outside surfaces by selectively binding oppositely-charged silica nanoparticles. They selectively adhered outside the Janus nanobowls, while they were present both inside and outside the nanobowls prepared by calcination [2].

Magnetic anisotropic nanoparticles were prepared attaching either by negatively charged Superparamagnetic Iron Oxide Nanoparticles (SPIONS) on dipolar dumbbells, or by preparing dumbbells with commercially available magnetic beads as seed nanoparticles. In both cases, we obtained asymmetric dumbbells with magnetic nanoparticles only on one side. We then studied the impact of shape-anisotropy on the directed self-assembly of these nanoparticles in the presence of an external magnetic field. We showed that it is possible to change the type of chain-like structures obtained by tuning the aspect ratio of the dumbbells.

Using the same dipolar dumbbells, we prepared Janus nanomotors by selectively attaching citratecoated platinum nanocrystals on one hemisphere. The resulting nanoparticles can undergo selfpropulsion when placed in a solution containing hydrogen peroxide fuel. The catalytic decomposition of the fuel is only taking place on one side of the dumbbells, generating a gradient which leads to effective propulsion.

Finally, we made the dumbbells temperatureresponsive by growing some polv-Nisopropylacrylamide brushes on one hemisphere. We first attached an initiator to the dumbbells by silane chemistry, and then used a surface initiated atom transfer radical polymerization (ATRP) to grow the PNIPAM chains. This renders the dumbbells hydrophilic below 32 °C (PNIPAM LCST), and amphiphilic above. We showed that it is possible to induce aggregation between the dumbbells by hydrophobic interactions above LCST. These stimuli-responsive nanoparticles have also been used to prepare multiple Pickering emulsions

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Self Assembly of Polymeric Nanoarchitectures and their Immobilization on Solid Surfaces

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INTRODUCTION: Polymeric nanoarchitectures represent functional units with a large potential for future applications in biomedicine, particularly for therapeutic intervention at specific target sites.¹ Oftentimes control over the localization and the environment of these nanoarchitectures is essential optimize functionality for the specific application in mind. This is very challenging to achieve for free structures in solution, but can be addressed elegantly by immobilizing the nanoarchitectures on solid substrates as we present here.



Figure 1: Schematic illustration of surface immobilized hollow polymer nanoarchitectures.

METHODS: The nanoarchitectures used in this study are formed by self-assembly in aqueous solution using biomimetic, amphiphilic triblock copolymers composed of polyoxazoline and polydimethylsiloxane. The solid substrates are functionalized with amino groups and PEG spacers to facilitate the nanoarchitecture immobilization reactions. A biocompatible thiol-ene reaction is employed to covalently attach the self-assembled structures solid substrates. to The nanoarchitectures are characterized thoroughly by several different methods including electron microscopy, light scattering and atomic force microscopy.

RESULTS & DISCUSSION: The amphiphilic triblock copolymers used for the nanoarchitecture formation are decorated with functional end-groups to facilitate surface immobilization by a biocompatible thiol-ene click reaction.² Importantly, several analytical techniques are employed to ensure their structural integrity also after the immobilization process. Different strategies of surface modification have been

exploited to allow the best control over the density of immobilized nanoarchitectures. The immobilization reaction can be followed in realtime using the quartz crystal microbalance and the functionalized surfaces are comprehensively atomic studied and imaged using force microscopy, making our approach a well characterized and controlled system tunable to a number of applications.



Figure 2: Atomic force microscopy image of polymeric nanoarchitectures covalently attached to a silicon wafer surface (contact mode in buffer).

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Production of mechanically robust capsules with thin shells

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INTRODUCTION: Polymersomes are vesicles formed with a bilayer of amphiphilic block copolymers, they can be used for encapsulation of hydrophilic components in the core or hydrophobic components in the membrane. The membrane mechanical properties and thickness can be tuned by the chemical structure of the block copolymer used to form the membrane.

METHODS: We use water / oil / water double emulsion droplets as a templates to assemble the polymersomes. Block copolymers assemble into two monolayers, one at eachliquid-liquid interface. Then the oil phase is removed to form the bilayer membrane of the vesicle.

To remove the oil we push those double emulsion drops through a micro channel containing a constriction as shown in fig 2.

We studied the influence of the flow rates and the wettability of the channels on the efficiency of oil removal.

DISCUSSION & CONCLUSIONS: Double emulsion drops were used as templates to make capsules with thin shells produced using microfluidics as this method allows high encapsulation efficiency, good control over the size and composition of the capsules and polymersomes. Those double emulsions were used as templates for the production of capsules with thin shells. We decreased the shell thickness of he double emulsion droplets by mechanically confining thems; this results in a partial removal of the oil from the shell. We are further optimizing this procedure to completely remove the oil from the shell.

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Fig. 1: Schematic of the production of monodisperse polymersomes. First a double emulsion is formed using microfluidics. The amphiphilic copolymers dissolved in the oil adsorb at the liquid-liquid interface to form one monolayer at the outer interface of the double emulsion. Finally the oil is removed from the shell to form a bilayer.



Fig. 2: Optical microscope images showing the squeezing of double emulsion drops. Scalebar is $100\mu m$, flow rate is $Q=500\mu L/h$.

Tuning the wettability of surfaces

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INTRODUCTION:

The ability to tune the wettability of surfaces is crucial for many applications for example in the biomedical field and for coatings. The wettability is determined by the chemistry and roughness of surfaces. We design surfaces with a hierarchical roughness and a well-defined chemistry. We introduce a roughness in the micrometer length scale by arranging 100 µm diameter microparticles with a narrow size distribution to surfaces. We introduce a roughness in the nanometer length the microparticles scale by coating with nanometer-sized silica particles. We control the surface chemistry by coating the silica particles with different types of silanes.

METHODS:

We use a microfluidic millipede device to produce monodisperse emulsion drops at a high throughput

Microparticles with a narrow size distribution are made from emulsion drop templates.

We produce drops from an aqueous solution containing 20 wt% polyethylene glycol diacryalate (PEGDA, Mw = 700).

We convert the drops into microparticles through UV-initiated polymerization.

We functionalize silica nano particles with propyl methacrylate trimethoxysilane to covalently bind it to the microparticle surface and Trichloro(1H,1H,2H,2H-perfluorooctyl)silane to increase the

affinity of the nanoparticles to the liquid-liquid interphase of the water drops that are dispersed in a perfluorinated oil.

Finally we assemble the microparticles on surfaces and tune their assembly by controlling the rate of solvent removal.

RESULTS:

We produce monodisperse PEGDA microparticles, coated with functionalized silica nano-particles on the surface and then we assemble this microparticles on the surface.

Due to the surface functionalization of silica nanoparticles with silane we achieve a high surface coverage of nano-particle on the surface of PEGDA microparticles.

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Synthesis of Stimuli-responsive Microgels for the preparation of Color-changing Hydrogels

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INTRODUCTION

Smart microgels have attracted great attention in soft matter studies for various applications such as drug delivery and sensors. Their ability to respond to a variety of physical and chemical stimuli, such as temperature and pH makes them interesting systems for a variety of applications in both material science and biomedical engineering. Poly N-isopropylacrylamide (PNIPAM) with a lower critical solubility temperature (LCST) of ~ 32 °C and poly methacrylic acid (PMAA) with $pK_a \sim 5.5$ are among the most studied polymers with responsive behaviour, temperature and pН respectively. Colloidal crystals of monodisperse microgels made of these polymers can show iridescent structural colour. The stimuli responsiveness, on top of this, provides them the ability of changing their size and therefore their spacing in colloidal crystals, which results in colour change. Incorporating organic or inorganic dyes in the particles combine with the stimuli responsiveness further allows one to enhance/tune the colour-changing pattern within the system. In order to maximize the colour change effects, microgels with a strong size change in response to a stimulus need to be prepared.

METHODS

For this work, water-based free radical polymerization method¹ at temperature of about 70 °C was used to prepare PNIPAM and P(NIPAMco-MAA) particles. Polymerizations were initiated with V-50(2,2'-Azobis(2 and stabilized methylpropionamidine)dihydrochloride) and CTAB (Hexadecyltrimethylammonium bromide) respectively for PNIPAM systems, and with KPS (Potassium persulfate) and SDS (sodium dodecyl sulfate) respectively for P(NIPAM-co-MAA) particles. Both systems were crosslinked with MBA (N,N'-methylenebisacrylamide). Fluorescein o-acrylate ($\lambda ex = 489 \text{ nm}$, $\lambda em = 512 \text{ nm}$) was used fluorescent comonomer as dve in the polymerization reaction. Dynamic Light Scattering (DLS) and UV-Vis spectrophotometer were used to measure size and absorbance of particles by changing the temperature. Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) were imaged the particles when they dry up. Confocal Laser Scanning

Microscope (LSM) was used to observe fluorescent particles.

RESULTS:

The synthesised PNIPAM particles have a narrow size distribution, and the fluorescent ones show and eightfold size decrease, compared to the nonfluorescent fivefold size decrease, as the temperature is increased well above the LCST of PNIPAM. SEM showed similar morphologies for both particles.



Fig. 1: Change of average hydrodynamic radius $(R_{h ave})$ and colour of the PNIPAM particle suspension (left), SEM image of particles (right).

Dually monodisperse responsive particles prepared with P(NIPAM-co-MAA) showed about a sevenfold size change at pH 9 and much smaller size change at pH 2 (Fig. 2), as the temperature is increases above the LCST of PNIPAM.



Fig. 1: Temperature response of P(NIPAM-co-MAA) particles in terms of average hydrodynamic radius ($R_{h ave}$) at two pH values below and above pK_a

DISCUSSION & CONCLUSIONS The Synthesis parameters were tunes to prepare monodisperse particles with very strong and sharp temperature and/or pH response.

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Advanced Monolayer Studies for Fluorescent "Flippers"

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INTRODUCTION: Recently, Matile *et.al.* introduced a new kind of mechanosensitive fluorescent probes for biomembrane analytics. These so called "Flipper" molecules consist of two independent chromophores which can twist relatively to each other. If a lateral pressure is applied to the molecules the two chromophores can align and form a conjugated chromophore, which therefore has different spectroscopic properties compared to the two unaligned chromophores.[1]



Fig. 1: Dithienothiophene - derived push-pull system, so called Flipper (1), for membraneanalytics (left). Working-principle of the Flipper molecules (right).

The properties of the "Flipper" molecules were determined by fluorescence spectroscopy in vesicles with two different membrane-compositions and showed a change in excitation spectra between L_d and S_o phase.[1]

This work gave more spectroscopic data, correlating the surface-pressure of a monolayer and the spectroscopic properties of the probe.

METHODS: A fluorescence microscope mounted on a Langmuir-Pockels-trough was used containing ultrapure water as subphase (20 °C), the air-temperature was kept constant at 22 °C. As detector a wide-spectrum microscope camera Leica DFC7000 T was used. The video-data was processed with MatLab[®]. **RESULTS:** Fluorescence-analysis correlated to the surface pressure of a monolayer of **1** shows a significant change in hue (digital value for colour in the HSV-colour-model) beginning at a surface-pressure of 25 mNm⁻¹ (Fig. 2).



Fig. 1: Hue to surface-pressure correlation of **1** *on a monolayer at the air-water interface.*

This change in colour is due to the conjugation of the two independent chromophores to one enlarged chromophore.

DISCUSSION & CONCLUSIONS: For the first time, it was possible to correlate the lateral surface-pressure on a monolayer to the spectroscopic properties of a fluorescent probe.

The observed change in spectroscopic properties could be utilised for surface-pressure analytics in natural or artificial membranes for drug-research or biochemical assays.

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Stimuli-triggered activity of nanoreactors by biomimetic engineering polymer membranes

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INTRODUCTION: We introduce here the engineering of synthetic polymer membranes equipped with channel proteins so that they are stimuli-responsive. Polymersome nanoreactors with triggered activity were designed by simultaneously encapsula1ng an enzyme inside polymer nano-compartments, and inserting protein "gates" in the membrane to allow controlled passage of substrates/products of the in situ reaction.

METHODS: The outer membrane protein F (OmpF) porin served as a model protein, which was chemically engineered to act as a "gate" by a hydrazone based pH-responsive binding molecular cap (Cy5-hydrazide) to carbonylated lysine residues inside the pore. Once the chemically modified OmpF was reconstituted this produced a pH-driven molecular flow through the amphiphilic block copolymer (poly(2 methyloxazoline)-block-poly(dimethylsiloxane)-(PMOXA₆block-poly(2-methyloxazoline) PDMS₄₄-PMOXA₆) polymersome membrane.

RESULTS: Control of in situ enzymatic activity inside the nanoreactors was established by enzyme activity activity assays. After reducing the pH to 5.5, the activity of nanoractors equipped with OmpF-CA-Cy5 increased to 74% in one hour. This indicates a successful pore opening, which allowed a significant increase in the influx of substrates (Fig. 1).



Fig. 1: Triggered activity was evaluated by Amplex red conversion kinetics of nanoreactors equipped with different OmpFs: OmpF-CA-Cy5 (blue), OmpF-CA (grey), Ompf-WT (black), and unpermeabilised nanoreactors (orange) at pH 5.5, at time 0 (a) and after 1 hour (b).

TEM and cryo-TEM micrographs were preformed to evaluate the structure and stability of nanoreactors. The results indicate the formation of spherical structures, with radii around 70 nm at pH = 7.2 and 5.5, both after self-assembly of PMOXA₆–PDMS₄₄–PMOXA₆ copolymers, and after reconstitution of OmpF and encapsulation of HRP in the polymer nanoarchitectures correspondingly (Fig 2). No change in structure was observed after the nanoreactors were exposed to acidic environments.



Fig 2. A.: Cryo-TEM of nanoreactors without OmpF B.: Cryo-TEM of nanoreactors with reconstituted OmpF C.: Cryo tem of nanoreactors with reconstituted modified OmpF-CA-Cy5. Scale bar 200nm.

DISCUSSION & CONCLUSIONS: Modulation of enzyme activity inside nanoreactors was successfully executed by inserting chemicallymodified channel proteins to act as pH-controlled "gates" in the membrane of enzyme-loaded polymersomes. Together with a preserved of the polymersomes, architecture the decrease/blocking of the flow of substrates through the membrane at neutral pH, and its unblocking at a lower pH resulted in very efficient stimulusdriven active nanoreactors. Through the encapsulation of therapeutic enzymes, such an approach opens new possibilities for therapeutic or diagnostic applications of nanoreactors.

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Cholesterol Interactions with an Artificial Phospholipid

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INTRODUCTION: Phospholipid vesicles are versatile and offer biocompatible drug carriers. Today, 13 liposomal drug formulations for in human use have the FDA's approval.[1]

We have reported on the use of mechanosensitive vesicles as concept for purely physics-based targeted drug delivery.[2] Pad-PC-Pad, an artificial phospholipid, forms a so called "d-form" (Fig. 1) shaped unilamellar vesicles (LUV) that release their content when exposed to shear stress but not at rest.

METHODS: Langmuir-Pockels trough in combination with Brewster angle microscopy and grazing incidence X-Ray diffraction were used in monolayer experiments.

Cryo transmission electron microscopy, differential scanning calorimetry as well as small angle and wide angle X-ray scattering were used in bilayer experiments.

RESULTS: Bilayer studies show that mechanosensitivity is induced by membrane interdigitation. Monolayer experiments support this hypothesis, showing high fluidity at air/water interface whereas cryo transmission electron micrographs show non-round, d-form like LUVs. Clearly, membrane interdigitation is brought by an additional force present in bilayers but absent in monolayers.

Here, we report the influence of cholesterol on Pad-PC-Pad bilayers and monolayers. Cholesterol addition reduces the stiffness of the bilayer by inserting itself in the membrane thus disrupting the interdigitation, and leading to spherical vesicles. The bilayer's main phase transition is completely removed by the addition of \geq 35 mol% cholesterol which leads to a liquid-ordered membrane organization. In comparison, DPPC:cholesterol mixtures still maintain their phase transition even after the addition of 40 mol% cholesterol.[3]

DISCUSSION & CONCLUSIONS: Pad-PC-Pad monolayers are condensed to almost the size of a cholesterol molecule by the addition of the latter. In bilayers, cholesterol disturbs the interdigitation thus eliminating the mechanosensitivity.

Overall, cholesterol dominates the forces between Pad-PC-Pad and itself.



Fig. 1: (Top) Developable surface of two ellipses rotated by 90° and glued together with one continuous edge. The developable surface D-form. Picture taken from paulbourke.net. (Bottom) Electron density profile of the Pad-PC-Pad membrane depicting the complete interdigitation below the main transition temperature; the length of a C_{15} chain is 19.25 Å.

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Addressing the temporomandibular joint disorder

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INTRODUCTION: The temporomandibular joint (TMJ) is the joint connecting the mandible to the skull and regulating the action of the mandible. Temporomandibular joint disorder (TMD) is a generic term designating the dysfunction of the TMJ. TMD is caused by a broad range of causes, injuries of the jaw or the TMJ, disc displacement, osteoarthritis, rheumatoid arthritis, teeth grinding are some of them. Current treatment range from physical therapy to surgical replacement of the ioint. the most current one being the administration of painkiller with all the known side effects.¹ The idea of the work presented here is to design and study an in situ crosslinking mechanoresponsive hydrogel containing liposomes able to locally release a painkiller over a mid to long term time period to and to replace the parental and/or oral administration of the painkiller.

METHODS: Periodate oxidized dextran undergoes a Schiff base formation reaction with both an amine bearing liposome (*i.e.* containing DPPE) and polyethyleneimine (PEI). We have developed an *in situ* crosslinking hydrogel using these three components: PEI, liposomes, and oxidized dextran. Following the crosslinking, the rheological behavior of a wide range of hydrogel components was studied as well as the release profile of rhodamine B from the hydrogels.

RESULTS: Dextran with different degrees of oxidation degree was synthesized and its rheological behaviour were studied (Figure 1). The influence of the presence and composition of vesicles were also studied (Figure 2).



Fig. 1: Time sweep measurement of different hydrogel. DextCHO¹⁰(blue), DextCHO⁸(green), DextCHO⁵(red) and DextCHO^{1.5}(black), depicting that the degree of oxidation of the dextran has a significant influence on the rheological behavior of the hydrogel.



Fig. 1: Time sweep measurement of different hydrogels made of DextCHO⁵ and PEI (blue), DextCHO⁵ and PEI and DPPC liposome (green), DextCHO⁵ and PEI and DPPC/DPPE liposomes (red), showing that the presence of non-reactive vesicles fluidifies the hydrogel and that reactive vesicles stiffens it.

DISCUSSION & CONCLUSIONS: Preliminary rheological studies show an important influence of the liposome composition (Figure 2), giving a first indication of the reaction between the vesicles and the hydrogel network.

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