Swiss **S**oft **D**ays

26th edition

6th of March 2020

University of Basel

Invited Speakers

Prof. Erik Reimhult, Universität für Bodenkultur, Vienna

Prof. Andreas Taubert, University of Postdam, Postdam

Industry Speakers

Dr. Wilfredo Yave, DeltaMem AG, Allschwill

Dr. Julien Iehl, Teoxane SA, Geneva

University of Basel

Swiss Soft Days

Local organizers

Prof. Cornelia Palivan and Prof. Wolfgang Meier

Contact

cornelia.palivan@unibas.ch

https://swisssoftdays.ethz.ch

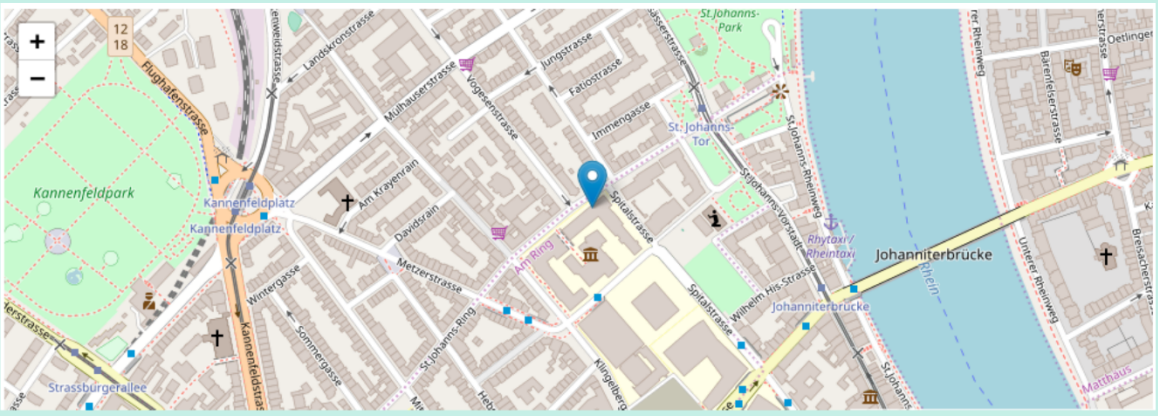
How to get there

Conference Venue

Department of Chemistry
University of Basel
St. Johanns-Ring 19
CH-4056 Basel, Switzerland

Talks: *Big lecture room OC, 1st floor*
Poster session: *OC foyer, ground floor*
Organic Chemistry building

Map



Directions: https://chemie.unibas.ch/en/department/sites-and-directions/site-st-johanns-ring/

By Plane
EuroAirport Basel-MulhouseMake sure that you take the exit to Switzerland (and not the one to France).
Public Transport: Take Bus 50 and exit at bus stop Kannenfeldplatz. Follow Metzerstrasse until you cross St. Johanns-Ring and follow St. Johanns-Ring to building no. 19.Alternatively, taxis are provided at the EuroAirport.

By Train / Bus
Station SBB (Schweizerischer Bundesbahnhof)
Leave the station at the main entrance and take tram line 11 with direction to St. Louis Grenze. Exit at tram station St. Johanns-Tor and follow St. Johanns-Ring until you reach building no. 19 on the left side.

Station Basel Badischer Bahnhof
Take bus line 30 and exit at bus station Kinderspital. Follow Schanzenstrasse (in the same direction as the bus you just exited) and turn right Klingelbergstrasse until you reach St. Johanns-Ring. Turn right again until you reach building no. 10 on the right side.

By Car
With direction from Switzerland or Germany
Leave the motorway at exit Basel Badischer Bahnhof and follow the signs to Universitätsspital. After crossing the bridge Johanniterbrücke turn right into Elsässerstrasse. At the town gate St. Johanns-Tor turn left into St. Johanns-Ring, building no. 19 is on the left side.

With direction from France
Leave the motorway at the border to Switzerland and follow the signs directing to Bahnhof SBB until you reach Kannenfeldplatz. Turn right into Metzerstrasse and then turn left into St. Johanns-Ring, building no. 19 is on the right side.

Program

09:00-09:50	**Registration and coffee**
09:50-10:00	**Welcome**
10:00-10:35	Tailoring responsive interactions of core-shell nanoparticles for biomedical applications, **Prof. Dr. Erik Reimhult BOKU Wien (keynote)**
10:35-10:55	Synthetic polymeric membranes: from lab to manufacture, **Dr. Wilfredo Yave DeltaMem AG (industry)**
11:00-11:20	**Coffee break**

Session 1: ***Physical properties and characterization of soft materials***

11:20-11:35	Complex-shaped cellulose composites made by wet densification of 3D printed scaffolds, **R. Libanori ETHZ**
11:35-11:50	Developing a fluorescence force probe: peptides interacting with polydiacetylene, **J. Nuck UNIGE**
11:50-12:05	Phase separation of active Brownian disks in the presence of alignment, **E. Sesse Sansa EPFL**
12:05-12:20	Delayed elastic storage in foams, **F. Lavergne Uni Fribourg**
12:20-13:20	**Lunch**
13:20-13:55	Gels and gel surfaces for bioinspired composites, **Prof. Dr. Andreas Taubert Uni Potsdam (keynote)**
13:55-14:15	Chemical Crosslinking of Hyaluronic Acid-Based Filler: The Importance of Rheological Parameters, **Dr. Julien IEHL Teoxane Laboratories (industry)**

Session 2: ***Micro & Nano self-assembly of soft materials***

14:15-14:30	Directed-assembly of Colloidal Shuttles and Micromachines for Programmable Cargo Delivery, **A. Demirörs ETHZ**
14:30-14:45	Co-assembly of block copolymer and nanoparticles: nanoparticle anisotropy and (ultra)thin films, **J. Diaz EPFL**
14:45-15:00	Continuous and on-scale production of polymeric nanoparticles for drug delivery, **G. Bovone ETHZ**
15:00-15:15	Immobilizing different types of drops in microfluidic devices, **M. Kessler EPFL**

Session 3: ***Poster Pitches***

15:15-15:20	Incorporation of bone cell mimics within electrospun fiber scaffolds, **F. Itel EMPA**
15:20-15:25	Hydrogel-filled microfluidic valves for isolating, retaining, and studying bacteria, **D. Rackus ETHZ-DBSSE**
15:25-15:30	Guiding macrophage phagocytic efficiency through particle mechanics, **A. Lee University of Fribourg**
15:30-15:35	Rheological Tuning of Granular Hydrogels, **B. Emiroglu ETHZ**
15:35-15:40	Gelation of tuneable bioinspired telechelic hydrogels, **A. Charlet EPFL**
15:40-16:30	**Poster session - coffee break**

Session 3: ***Soft materials at the interface with biological systems***

16:30-16:45	Polymersome clusters for advances nanotheranostics, **C. Meyer UNIBAS**
16:45-17:00	Continuous production of acoustically aligned cells within hydrogel fibres for musculoskeletal tissue engineering, **D. Deshmukh ETHZ**
17:00-17:15	Basicle: Giant lipid vesicles as culture vessels for E. coli, **Y. Schmid ETHZ-DBSSE**
17:15-17:30	Bioinspired molecular factories with architecture and in vivo functionalities as cell mimics, **T. Einfalt UNIBAS**
17:30-17:40	***Closing***

List of Posters

01	Chemical Networks for Time-Domain Programming of Soft Materials	G. Panzarasa	ETH Zurich
02	Fungal melanin-based electrospun membranes for heavy metal detoxification of water	A. N. Tran-Ly	ETH Zurich, Empa
03	Characterization of the dispersion of silica nanoparticles in epoxy-based microstructures using FIB-SEM tomography	P. Yajan	University of Fribourg
04	Capillary-Assisted Deposition of Bacteria as a Tool for Studying Population Heterogeneity	C, Boggon	ETH Zurich
05	Engineered nano-carrier ink platform for additive manufacturing of precision biomaterials	E. A. Guzzi	ETH Zurich
06	Adaptive multifunctional composites of inorganic nanoparticles and bio-inspired intrinsically disordered proteins	U. C. Palmiero	ETH Zurich
07	Lipid droplet biogenesis is driven by liquid-liquid phase separation	V. Zoni	University of Fribourg
08	Acceleration of an Enzymatic Reaction in Liquid Phase Separated Compartments Based on Intrinsically Disordered Protein Domains	Küffner A.M	ETH Zurich
09	A numerical investigation of active nematic liquid crystals in a channel with hybrid alignment at the walls	C. Rorai	EPF Lausanne
10	Engineered bioactive single cell niches to study cell function in 3D	O. Y. Dudaryeva	ETH Zurich
11	Organic deposits in methanation catalyst Ru/C	U. Gasser1	PSI
12	A microfluidic platform for characterizing the structure and rheology of biofilm streamers	G. Savorana	ETH Zurich
13	Capillary deposition of microorganisms for the study of cells in spatially controlled environments	R. Pioli	ETH Zurich
14	Model-free Determination of Interaction Potentials from Small-angle Scattering Data	P. Campomanes	University of Fribourg
15	Bacterial Biofilms as Soft Materials	S. Geisel	ETH Zurich
16	The role of solvent effects on the aggregation of mixed-monolayer - protected gold nanoparticles	E. Petretto	University of Fribourg

17	Efficient Asymmetric Synthesis of Carbohydrates by Aldolase Nano-Confined in Lipidic Cubic Mesophases	T. Zhou	ETH Zurich
18	Metal Reinforced Carboxymethyl Cellulose Methacrylate/Poly(Acrylic Acid) Hydrogels	M. Hirsch	EPF Lausanne
19	Alignment and differentiation of myoblasts in hydrogel fibers	N. Pasquero	ETH Zurich
20	Surface Stress of Soft Solids under Strain	K. Smith-Mannschott	ETH Zurich
21	Quantitative mechanochromism of polydiacetylenes on the nanoscale	L. Juhasz	University of Geneva
22	Development of a high throughput assay for screening peptide cooperative effects based on polydiacetylene	J. Zhao	University of Geneva
24	Double emulsion templated polymer GUVs for studying compartmentalized enzymatic cascade reactions	E. C. dos Santos	University of Basel
25	Porphyrin containing polymersomes: ROS generation and biological evaluation in mammalian cells	M. Kyropoulou	University of Basel
26	Synthesis and Complex Self-Assembly of the Amphiphilic PEO-b-PEHOx polymers into Multicompartment Micelles, Pseudo-Vesicles and Yolk/Shell Nanoparticles	D. Daubian	University of Basel
27	Novel Cancer-Targeted Nanoparticles	S-L. Abram	University of Basel
28	PBO-b-PG Self-Assemblies: Towards the Effect of Tacticity in Amphiphilic Diblock Copolymers	R. Wehr	University of Basel
30	Self-Assembled Peptide Nanoparticles for Safe and Efficient Gene Delivery	S. Tarvirdipour	University of Basel
31	Bioactive catalytic nanocompartments integrated into cell physiology and their amplification of cGMP signaling cascade	A. Belluati	University of Basel

Keynotes

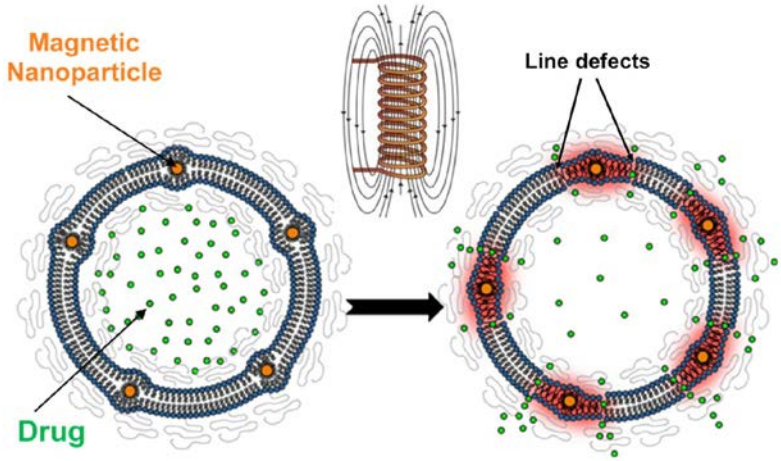
Tailoring responsive interactions of core-shell nanoparticles for biomedical applications

Erik Reimhult

Department of Nanobiotechnology, Universität für Bodenkultur Wien, Austria

Nanoparticles grafted with polymers are used and developed for a multitude of biomedical and biotechnological applications (Figure 1), such as imaging contrast agents, hyperthermia treatment drug delivery, separation, and purification. Unique functions can be achieved for these applications by using nanoscale inorganic cores, such as nanoplasmonic metal cores or superparamagnetic oxide cores, combined with responsive, organic coatings.

We will present our work on the design of monodisperse superparamagnetic iron oxide nanoparticles grafted with various sorts of polymer brushes. The influence of design parameters such as grafting, polymer chemistry, core size, molecular weight, and polymer topology on the performance of responsive nanoparticles will be discussed. In particular, we will introduce examples of how polymer- and membrane-embedded particles can use the antenna-like function of nanoparticles to trigger functional changes in the embedding matrix of the next generation of smart biomedical materials.



Gels and gel surfaces for bioinspired composites

Andreas Taubert

Institute of Chemistry, University of Potsdam, Germnay

Surfaces and gels that are suited for applications in the biomaterials field have been a subject of intense research. Largely, this is due to the fact that good biomaterials provide tremendous business opportunities but also pose fascinating scientific challenges. The presentation will highlight some of our own approaches towards hybrid materials, mostly calcium phosphate composites, using soft matter strategies. These include polymer surfaces that have been tailormade to contain certain chemical groups supporting mineral formation, but also hydrogels or hydrogel thin films that are excellent growth media for both an inorganic mineral phase and bone cells. Moreover, the presentation will also introduce initial experiments involving 3D printed scaffolds and their surface modification along with first data on how ionic liquids can be used for the fabrication of biocompatible soft and hard materials, especially materials from starting materials that are hard to process otherwise such as silk.

Industry

Synthetic polymeric membranes: from lab to manufacture

Wilfredo Yave, Luigi Leva

Research and Development laboratory, DeltaMem AG, Allschwil, Switzerland

Modifying or tailoring the physical and chemical property of polymers, today we are able develop endless products, including synthetic membranes that have a wide range of industrial applications. In recent years, the research and development activities at DeltaMem AG are more focused on fundamental understanding of polymers to improve the existing products and to develop novel membranes that can be applied in areas where existing commercial membranes showed limitations.

In this talk, we will present how a novel synthetic polymeric membrane with better separation performance has been developed by the combination of two completely different materials, i.e. a water repellent and a hygroscopic polymer [1]. In addition, the fundamental results needed in the laboratory for subsequent manufacture will be described in detail.

A summary of current and new developments on membranes at DeltaMem will be also presented. Thus, we would like to draw attention of young scientist to foster collaboration in the membrane field, especially in pervaporation, a low energy intensive separation technique for dehydrating solvents in the pharma and chemical process industry.

[1] Yave et al. (manuscript submitted)

Chemical Crosslinking of Hyaluronic Acid-Based Filler: The Importance of Rheological Parameters

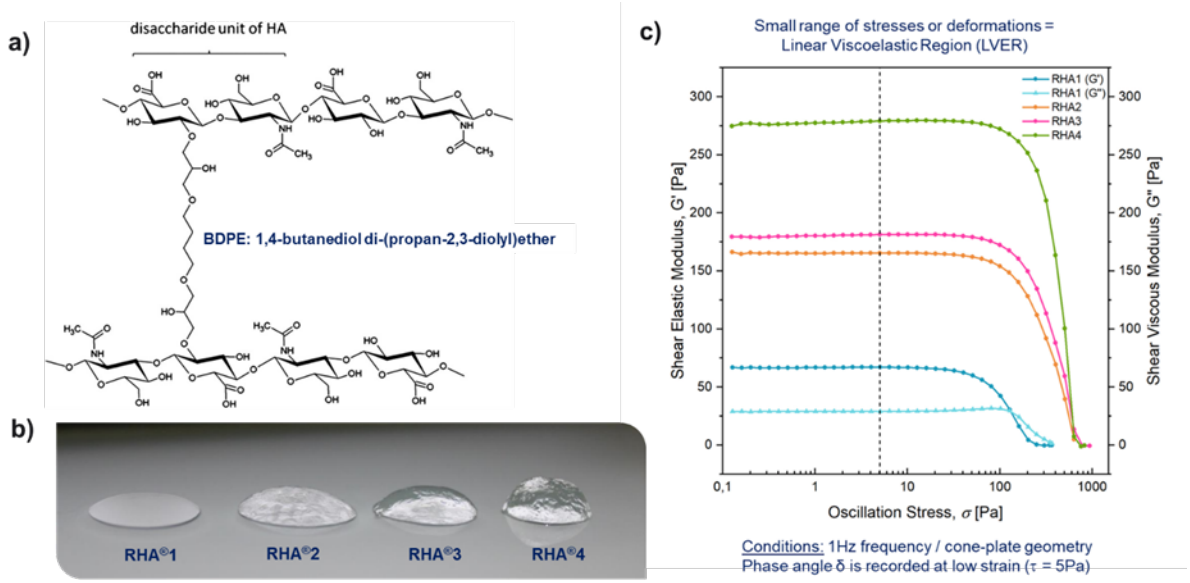
Julien IEHL

Department of Research and Development, Teoxane Laboratories, Geneva, Switzerland

Hyaluronic acid (HA) is a natural and linear polysaccharide that plays important physiological and biological roles in the human body. It consists of alternating units of D-glucuronic acid and N-acetyl-D-glucosamine, connected by β-1,3- and β-1,4-glycosidic bonds.[1] Nowadays, among biopolymers, HA is emerging as an appealing starting material for hydrogels design in the cosmetic field due to its biocompatibility, native biofunctionality, biodegradability, non-immunogenicity, and versatility. Since HA is not able to form durable gels alone, chemical modifications like covalent crosslinking, is needed in order to obtain hydrogels which maintain their mechanical properties overtime [1].

Chemical crosslinking turns out to be a versatile method to obtain hydrogels with excellent chemical, mechanical and thermal stability. Bisepoxide appeared as one of best type of molecules for the crosslinking of HA. In the field of dermal fillers, 1,4-Butanediol Diglycidyl Ether (BDDE) [2] is the most used crosslinker and has proven its reliability for manufacturing finished devices such as RHA® products developped by Teoxane (Figure a). More importantly, by tuning the conditions of the crosslinking reaction with BDDE to get HA-based fillers, the visco-elastic properties of the injected materials could be significantly affected (Figure b).

The rheological study of HA-based fillers is a substantial characterization to predict their mechanical behaviors once implanted in the body [3]. Traditionally, the elastic modulus G' has often been selected as the gold standard used to sort fillers by clinical indications. G' (and other related parameters alike) is a key structural parameter of the gel, but it is measured at very low stresses or deformations which are not representative of most facial movements in vivo. However further rheological parameters need to be considered especially to characterize the gel mechanical resistance and cohesivity. Taking the LVER (Linear Visco-Elastic Region) into consideration when characterizing a filler allows to assess the range of stress or deformation for which the gel is able to maintain its viscoelastic properties and results in a more informative description of the filler (Figure c). New rheological parameters presented by Teoxane may thus help to better predict filler behavior in situ notably when injected in dynamic areas where gels are submitted to high stresses and deformations of the face.



[1] Khunmanee S, et al. Crosslinking method of hyaluronic-based hydrogel for biomedical applications. Journal of tissue engineering, 2017; 8, p. 1-16.

[2] De Boulle K, et al. A Review of the Metabolism of 1,4-Butanediol Diglycidyl Ether–Crosslinked Hyaluronic Acid Dermal Fillers. Dermatol Surg, 2013; p. 1-9.

[3] Gavard Molliard S, et al. Key rheological properties of hyaluronic acid fillers: from tissue integration to product degradation. Plast Aesthet Res, 2018; 5:17.

Talks

Complex-shaped cellulose composites made by wet densification of 3D printed scaffolds

Michael K. Hausmann [1,2], Gilberto Siqueira [1], Rafael Libanori [2], Dimitri Kokkinis [2], Antonia Neels [3], Tanja Zimmermann [1], André R. Studart [2]

[1] Applied Wood Materials Laboratory, EMPA
[2] Complex Materials, Department of Materials, ETH Zürich
[3] Center for X-ray Analytics, EMPA

Cellulose is an attractive material resource for the fabrication of sustainable functional products, but its processing into structures with complex architecture and high cellulose content remains challenging. Such limitation has prevented cellulose-based synthetic materials from reaching the leAvel of structural control and mechanical properties observed in their biological counterparts. To address this issue, we developed a simple approach to manufacture complex-shaped cellulose-based composites in which the shaping capabilities of 3D printing is combined with a wet densification process that increases the concentration of cellulose in the final part. Densification is achieved by solvent exchange, which induces attractive interactions between the cellulose particles. The effect of the solvent mixture on the final cellulose concentration is rationalized using solubility parameters that quantify the attractive interparticle interactions. Using X-ray diffraction analysis and mechanical tests, we show that 3D printed composites obtained through this process exhibit highly aligned microstructures and mechanical properties significantly higher than those obtained by earlier additively-manufactured cellulose-based materials. These features enable the fabrication of cellulose-rich synthetic structures that more closely resemble the exquisite designs found in biological materials grown by plants in Nature.

Developing a fluorescence force probe: peptides interacting with polydiacetylene

J. Nuck, K. Sugihara

Department of physical chemistry, University of Geneva, Geneva Switzerland

Opening mechanosensitive ion channels, cellular virus infection and killing bacteria by antimicrobial peptides, all involve an application of forces to the cell membranes. Characterization techniques such as giant unilamellar vesicle aspiration and force spectroscopy are able to extract information about the surface tension and binding forces respectively. However, until now there is nAo possibility to measure the local molecular forces in lipid bilayer. Therefore, the goal of this project is to develop a calibrated fluorescence probe for mapping forces in cell membranes by the mechanosensitive polymer polydiacetylene (PDA).

PDA is a popular mechanosensitive polymer, used as chromic and fluorescence biosensors for the detection of ions, ligands, bacteria and peptides. The current center of debate is the molecular mechanism of the PDA activation by these ligands, where how these biomolecules alter the PDA structure and thus change its optical properties are left unexplored. In this work, to clarify the mechanism of the PDA activation by peptides, we investigated the interaction between PDA and an antimicrobial peptide from bee venom, melittin, by fluorescence and atomic force microscopy. These microscopy techniques provide spatio-temporal resolution in contrast to the traditional spectroscopy technique used in previous works, which revealed unique interaction kinetics between the peptides and PDA. Our new approach lets us furthermore observe the phase transition of the PDA domains induced by peptides and compare it to classic differential scanning calorimetry technique [1]. Understanding the peptide-PDA interaction mechanism is the first step to engineer this material for the use as a peptide force sensor.

[1] Nuck, J.;Sugihara, K. Manuscript in preparation. (2020).

Phase separation of active Brownian disks in the presence of alignment

E. Sesé-Sansa [1], I. Pagonabarraga [1,2,3], D. Levis [2,3]

[1] CECAM Centre Européen de Calcul Atomique et Moléculaire, EPF Lausanne
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[3] UBICS University of Barcelona Institute of Complex Systems, Universitat de Barcelona, Spain

We study the phase behavior of Active Brownian Particles (ABP) moving in two-spatial dimensions and interacting through volume exclusion and local alignment. The interplay between steric effects and velocity alignment has recently led to a number of studies [1-4]. In the present study we propose a model of active disks subjected to a Vicsek-like velocity alignment [5]. We analyze the Motility-induced phase separation (MIPS) [6,7] of the system in the regime of weak alignment interaction, i.e. below the flocking phase transition. Using particle-based simulations of the microscopic model we show that, as the alignment strength is increased, orientational correlations grow, rendering the diffusive reorientation dynamics slower. As a consequence, the tendency of particles to aggregate into isotropic clusters is enhanced, favoring the complete de-mixing of the system into a low and high-density phase. We also extend the work done by Redner *et. al.* [8] and propose a simple kinetic argument that reinforces what we observe in simulations: the presence of alignment enhances particles' aggregation into macroscopic clusters [9].

Subsequently, we present a theoretical description starting from the N-body Smoluchowski equation of a system of polar active disks. Following the work done by Bialké *et. al.* [10,11], we perform a mean-field approximation to close the hierarchy of evolution equations and obtain the effective hydrodynamic equations, which we use to analyze the stability of the homogeneous and isotropic phase. This formalism sheds light into the underlying mechanisms leading to the phase separation in systems of polar active disks. Moreover, it is extensible to different types of local alignment interactions (i.e. nematic alignment), and therefore constitutes a general theoretical framework for the study of active systems subjected to alignment interactions of different nature.

[1] van Damme R., Rodenburg J., van Roij R. and Dijkstra M., *J. Chem. Phys.*, 150 (2019) 164501

[2] Jayaram A., Fischer A. and Speck T., *arXiv* preprint arXiv:1910.06547 (2019)

[3] Grossmann R., Aranson I. S. and Peruani F., *arXiv* preprint arXiv:1906.00277 (2019)

[4] Bär M., Grossmann R., Heidenreich S., Peruani F., *Ann. Rev. Cond. Matt. Phys.*, Vol. 11 (2020)

[5] Vicsek T., Czirók A., Ben-Jacob E., Cohen I. and Shochet O., *Phys. Rev. Lett.*, 75 (1995) 1226

[6] Cates M. E. and Tailleur J., *EPL*, 101 (2013) 20010

[7] Cates M. E. and Tailleur J., *Annu. Rev. Cond. Matt. Phys.*, 6 (2015) 219

[8] Redner G. S., Hagan M. F. and Baskaran A., *Phys. Rev. Lett.*, 110 (2013) 055701

[9] Sesé-Sansa E., Pagonabarraga I. and Levis D. *EPL*, 124 (2018) 30004

[10] Bialké J., Löwen H. and Speck T., *EPL*, 103 (2013) 30008

[11] Speck. T., Menzel A. M., Bialké J. and Löwen H., *J. Chem. Phys.*, 142 (2015) 224109

Delayed elastic storage in foams

François A. Lavergne, Véronique Trappe

Department of Physics, University of Fribourg

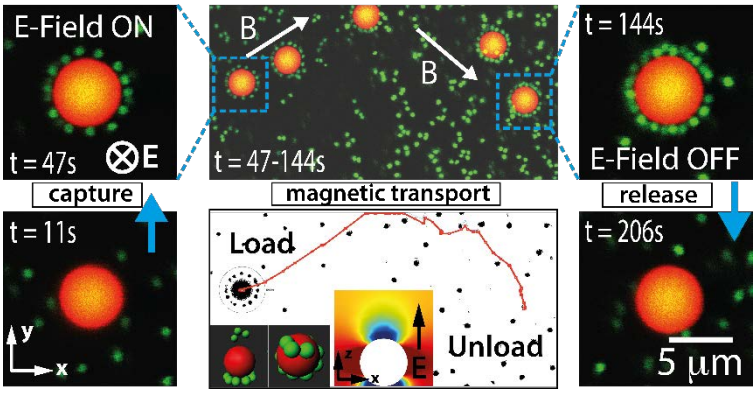
Foams are dense assemblies of bubbles that constantly reconfigure due to coarsening-induced intermittent bubble rearrangements. Hence, while the instantaneous response of foams to an applied stress is elastic, the long-time response is fluid-like. Within this simple picture, releasing the applied stress at some moment in time should simply result in an instantaneous elastic recovery. However, experiments reveal an additional recovery process that occurs slowly over the course of time. This indicates that elastic energy can also be stored in a delayed fashion under stress, beyond the prediction of Hooke's law.

Directed-assembly of Colloidal Shuttles and Micromachines for Programmable Cargo Delivery

Ahmet Faik Demirörs [1], Andre Studart [1], Yunus Alapan [2], Berk Yigit [2], Metin Sitti [2]

[1] Department of Materials, Complex Materials, ETH Zürich
[2] Physical Intelligence, Max Planck Institute for Intelligent systems, Germany

External field gradients are commonly used for separation, contactless manipulation [1] and assembly [2] of nano- and microparticles. Here, we introduce a novel colloidal shuttle by using electric field gradients, so called dielectrophoresis. In a homogenous electric field, a dielectric colloid can act as a field gradient-maker and change the electric field strength around itself. Such field strength alteration around the dielectric colloid was employed as a trap for other particles. Orthogonally using magnetic fields in addition to electric fields and employing magnetic "shuttle-colloid" allowed for loading, transporting and unloading of the trapped cargo. This technique was extended to transport bio-cargo and anisotropic colloids [3]. Furthermore, such interactions can be used to reversibly program and assemble microrobots and mobile micromachines [4].



[1] A. F. Demirörs, D. Courty, R. Libanori, A. R. Studart, Proc. Natl. Acad. Sci. 2016, 113, 4623-4628.

[2] A. F. Demirörs, P. P. Pillai, B. Kowalczyk, B. A. Grzybowski, Nature 2013, 503, 99-103.

[3] A.F. Demirörs, F. Eichenseher, M.J. Loessner, A.R. Studart Nature Communications 2017, 8, 1872.

[4] Y. Alapan, B. Yigit, O. Beker, A. F. Demirörs, M. Sitti Nature Materials, 2019, 18(11):1244

Co-assembly of block copolymer and nanoparticles: nanoparticle anisotropy and (ultra)thin films

Javier Diaz [1], Marco Pinna [2], Andrei Zvelindovsky [2], Ignacio Pagonabarraga [1,3,4]

[1] CECAM, EPF Lausanne
[2] Centre for Computational Physics, University of Lincoln, UK
[3] Departament de Física de la Matèria Condensada, Universitat de Barcelona, Spain
[4] UBICS, University of Barcelona Institute of Complex Systems, Spain

Block copolymers (BCP) are excellent candidates to control the localisation of colloidal nanoparticles (NP) at the nanoscale level. Complex, anisotropic NPs can furthermore achieve orientational ordering within the block copolymer structure. Moreover, the properties of the hosting BCP (morphology, for example) can be modified at high nanoparticle loadings. Cell Dynamic Simulations is a fast, mesoscopic scheme to simulate BCP melts which can be coupled with Brownian Dynamics to simulate hybrid nanocomposite systems (1). A parallel version has been developed to achieve large system sizes.

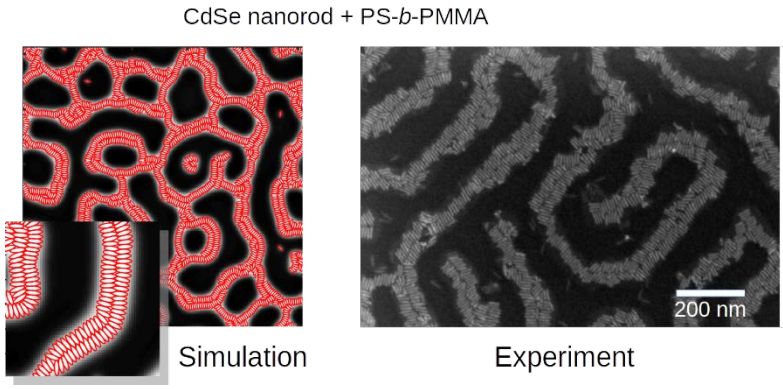


Figure 1: Co-assembly of anisotropic NPs with BCP for (a) ellipsoids -simulations and (b) nanorods-experiments. NR length is 33 nm in moderate filling fraction 0.26.

We report the formation of ordered structures for shape-anisotropic nanoparticles in the case of elongated nanorod-like NPs which can are validated against experiments of nanorods mixed with ultra-thin films of BCP(2), as in Figure 1. Moreover, a general model for anisotropic NPs is presented (3) which can be used to simulate NPs of shapes ranging from rectangles, ellipsoids or rhomboids. Additionally, chemically inhomogeneous NPs with patchy surfaces, Janus NPs are found to strongly anchor at BCP interfaces and, at high concentrations, form ordered side-to-side structures within BCP domains (4).

Three dimensional simulations of BCP/NP systems in the bulk or under confinement highlight the ability of NPs to modify the morphology of the BCP, leading to phase transitions (5). Incompatible NPs can macrophase separate from the hosting BCP leading to new morphologies and control of the contact angle between lamellar domains and NP-rich clusters. Additionally, NPs can induce parallel-to-perpendicular transitions in the orientation of the BCP with respect to the thin film surface.

[1] Diaz J, Pinna M, Zvelindovsky AV, Asta A, Pagonabarraga I. Macromol Theory and Simul. 2017

[2] Ploshnik E, Salant A, Banin U, Shenhar R. Adv Mater. 2010

[3] Diaz J, Pinna M, Zvelindovsky AV, Pagonabarraga I. Macromolecules. 2019

[4] Diaz J, Pinna M, Zvelindovsky A, Pagonabarraga I. Soft matter. 2019

[5] Diaz J, Pinna M, Zvelindovsky AV, Pagonabarraga I. Soft matter 2019

Continuous and on-scale production of polymeric nanoparticles for drug delivery

Giovanni Bovone, Fabian Steiner, Elia A. Guzzi, Mark W. Tibbitt

Macromolecular Engineering Laboratory, Department of Mechanical and Process Engineering, ETH Zürich

Polymeric nanoparticles (NPs) are an important class of soft materials, mainly used as drug delivery vehicles and building blocks in functional biomaterial design. Despite the advances in academic research, one of the current challenges to the clinical translation of NPs is the robust scale-up of laboratory processes, which, at larger scale, are difficult to control [1]. Conventionally, NP production is carried out discontinuously in batch with limited throughput and reproducibility as well as reduced control over NP size (Figure 1a). To address this limitation, we engineered a coaxial jet mixer (CJM) for the continuous, automated, and on-scale production of polymeric NPs with tunable size (Figure 1b) [2–4].

The CJM enabled continuous and reproducible production of NPs in flow from amphiphilic block copolymers such as poly(ethylene glycol)-*block*-polylactide (PEG-*b*-PLA). Control of the flow conditions enabled precise tuning of NP size. To further emphasize the suitability of the CJM for on-scale production, the CJM was automated under computer control with stable operation over 24 h. Batch nanoprecipitation of different formulations such as PEG-*block*-polycaprolactone (PEG-*b*-PCL), PEG-*b*-PLA, and PEG-*block*-poly(lactide-*co*-glycolide) (PEG-*b*-PLGA) produced NPs of 55, 76, and 60 nm (Figure 1a). In the CJM, NPs were produced from each polymer with the same size (49 ± 5 nm; Figure 1b), demonstrating that particle dimension could be controlled independently from the chemistry of NP formulation. Further, the device facilitated both small-scale screening of different NP formulations (~5 mg min^{-1}) as well as on-scale production of particles (~110 mg min^{-1}). Finally, the CJM was effective for the continuous production of functional nanotherapeutics and scaled production of other soft materials, such as injectable polymer–nanoparticle (PNP) hydrogels for local therapeutic delivery [3,5].

The automated CJM permitted the controlled, reproducible, and scalable formation of nanoparticle-based drug delivery systems. This automated approach represents one of the possible opportunities for the on-scale production and clinical translation of this important class of soft materials.

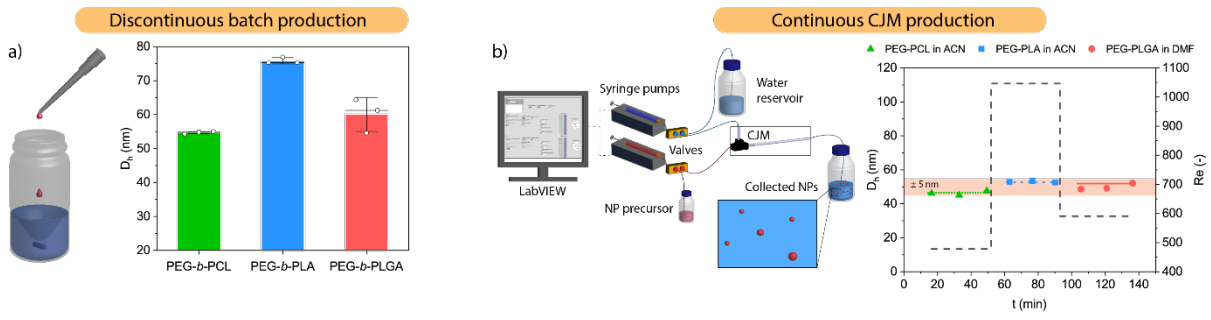


Figure 1: a. Discontinuous batch nanoprecipitation of different formulations of PEG-b-PCL, PEG-b-PLA, and PEG-b-PLGA produced NPs with distinct sizes. **b.** The automated CJM allowed continuous, reproducible, and scaled NP production. The CJM enabled decoupling of the NP chemistry from the resulting particle size, which were within ± 5 nm for all block copolymers tested (D_h ~ 49 nm). In these experiments, NPs were produced with an initial polymer concentration of 10 mg mL^{-1}.

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Immobilizing different types of drops in microfluidic devices

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Many natural materials display unique mechanical properties that are, at least in parts, a result of the locally varying compositions of these materials. [1] Bio-inspired materials usually cannot reach similar sets of mechanical properties than their natural counterparts. A contributing reason for this difference is that they typically possess homogeneous compositions. A possibility to fabricate soft, structured materials with locally varying compositions is the use of reagent-loaded drops as building blocks. [2] In my talk, I will present a microfluidic device that allows immobilization of drops loaded with different reagents at well-defined positions. Thereby, this device offers possibilities to control the local composition of the resulting materials. I will show how we can vary the trapping force of such traps to achieve a selective immobilization of only one type of drops. I will further present a mathematical model that predicts the strength of traps depending on their geometry, which facilitates the design of such devices. To conclude, I will demonstrate an example of how immobilized drops can be transformed into soft materials with locally varying composition. This technology offers new possibilities to design bio-inspired structured hydrogels with improved mechanical properties.

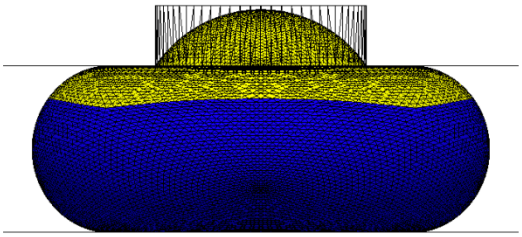

Figure 2: Rendering of a surface evolver simulation showing a drop in a microfluidic trap. [3] The relaxation into the trap is governed by geometric arguments of the confinement, as well as the volume of the drop. [4]

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Incorporation of bone cell mimics within electrospun fiber scaffolds

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Inspired by nature, cell mimicry is an emerging field that aims to provide long-lasting cell-like assemblies to stimulate their biological counterparts with broad envisioned applications in biomedicine [1]. Encapsulation of nanometer-sized functional entities within micro-meter-sized carriers is a common concept to design functional microreactors. However, their long-term stability and influence on biological cells remains little explored, which is crucial when considering administration pathways of artificial cells to patients. To this end, the combination of tissue engineering and cell mimicry has the potential to provide biologically active scaffolds that selectively stimulate resident cells at the site of transplantation with the aim to increase tissue regeneration.

Here, we aim at engineering bioactive 3D-scaffolds by the combination of microreactors and electrospun fibers. The presence of the microparticles within the fiber network not only leads to a substantial increase in scaffold thickness but also to increased pore sizes favoring cell infiltration. Specifically, we entrap 40 µm-sized alginate hydrogel microparticles, which we recently used to generate bone cell mimics from a bottom-up approach [2] by encapsulating extracellular matrix vesicles as the active moiety. There we showed that the cell mimics co-assembled with biological bone-forming osteoblast cells (SaOS-2) and significantly enhanced biomineralization within a 3D cell spheroid model. As fiber material, we selected a biodegradable PLA polymer to electrospin fibers in an alternating sequence with electrospraying the alginate microparticles. In this layer-by-layer approach, the microparticles are entrapped within the fibers, creating a 3D scaffold with its thickness being controlled by the number of layers. We are confident that combining artificial cells with tissue engineering well enable the generation of new bioactive 3D scaffolds with cell-specific properties.

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Hydrogel-filled microfluidic valves for isolating, retaining, and studying bacteria

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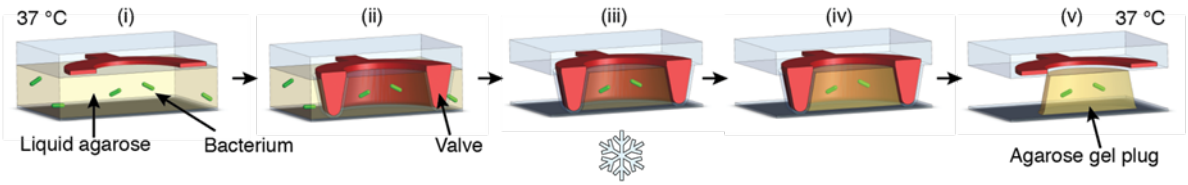
Department of Biosystems Science and Engineering, ETH Zürich

We present a microfluidic platform for isolating small populations of bacteria and selectively exchanging media and introducing transient doses of antibiotics. The platform combines hydrogels, to retain the bacteria, and valves, to control delivery of media and antibiotics to the bacteria.

While steady-state values of drug concentration required to extinguish bacteria are frequently measured (so-called minimal inhibitory concentration, MIC), much less is known about the impact of transient dosing over time. Various microfluidic tools have been developed to expose bacteria to antibiotics and determine MICs, including the use of droplets [1] or wells [2]. However, these devices are typically incapable of transient antibiotic supply because capture and retention of small motile cells under flow remains challenging. A promising solution is the use of hydrogels for cell encapsulation as they allow for the diffusion of nutrients, metabolites, and drugs to and from the encapsulated cells. We combined hydrogels with isolation valves to create a platform for monitoring bacterial growth with transient antibiotic administration.



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Guiding macrophage phagocytic efficiency through particle mechanics

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Immunological clearance of foreign objects and debris is an essential component of tissue homeostasis. These tasks are typically orchestrated by effector cells known as macrophages which are able to engulf a broad spectrum of targets. Cellular capture efficiency is determined by a host of physical and chemical properties and is complicated by the presence of local surface interactions. Both bacteria and viruses have been shown to control their mechanical response to enhance survivability (1,2). Given the importance of local deformability to cell-target interactions, soft and rigid materials might be expected to produce dissimilar internalisation kinetics. To assess the role of target mechanical response to phagocytosis we have synthesised sub-micron polymer particles with tuneable rigidity. Assembly of these particles on functionalised surfaces allows investigation of the complex interactions involved in cellular removal of adsorbed species. We observed that the overall surface presentation impacts the ability of macrophages to effectively clean an area with concomitant impacts on cellular activities such as spreading. Our approach allows for the parameterisation of mechanobiological inputs such as substrate stiffness and local topography to modulate cell behaviour.

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Rheological Tuning of Granular Hydrogels

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Introduction: Traditional polymeric hydrogels are often static in nature and possess nanoscale pores, which can constitute a barrier for cell infiltration, spreading, and extracellular matrix deposition. Granular hydrogels are an attractive class of soft matter on account of their macroporous structure and rheological properties that are independent of the kinetics of an equilibrium. Composed of non-Brownian micron-sized building blocks (microgels), granular hydrogels can undergo a transition from particulate suspension to a jammed hydrogel, which exhibits solid-like properties. [1] The resulting voids between individual microgels form a three-dimensional interconnected network of pores. Despite the wide interest in granular hydrogels for cell culture and regenerative medicine [2], advanced rheological characterization of these systems remains less explored, which is essential to for materials design and translation. In this work, we used microfluidic-based droplet forming for precise synthesis of microgels and provided new insight into the rheological behavior of soft granular systems.

Experimental methods: Uniform spherical droplets in the form of water-in-oil emulsions were produced (Fig 1a). Hydrogel precursor solutions of norbornene functionalized 8-arm polyethylene glycol (PEGNB) and di-thiol crosslinker (DTT) were injected into a flow focusing microfluidic device. Microgels with defined size and elasticity were formed upon 365 nm light exposure in the presence of a radical initiator (LAP). Removal of the oil layer and centrifugal jamming of the microgels yielded the granular gels. Linear viscoelastic region and yield strain were determined via strain sweep measurements. Osmotic compression on the granular hydrogels was achieved via stressing the microgels in a dialysis bag against high molecular weight PEG solutions. The polymer concentration was determined by weighing the packings in the wet and dry states.

Results and discussions: Microgels with different sizes (55 µm and 75 µm) and stiffness were synthesized by adjusting the water and oil flow rates and polymer content (5 wt%, 7 wt% and 10 wt%). Via centrifugation, microgels come into contact via random close packing with no measurable resistance. Under shear, microgels can deform, slip, and rearrange to accommodate the applied stress. At a critical strain value (γ_y), the stress overcomes the packing forces and the resulting behavior is the liquid-like flow of microgels. We observed, at constant microgel size, the yield strain of the granular system was increased from 15% to 30% by decreasing the polymer content of the individual microgels (Fig 1c). This was attributed to the lower elastic modulus of the microgels, allowing the material to accommodate higher amounts of strain via deformations of the microgels before the initiation of flow. In addition, a two-fold increase in storage modulus was achieved by an increase in the particle size without considerably changing the yield point (Fig 1d). Under external osmotic compression, we observed that microgels severely deform and expel water and it is possible to achieve higher packing densities, evidenced by the significant increase in the average polymer concentration in the packings (Fig 1e).

Conclusions: We demonstrated the tunability of the rheological behavior of granular hydrogels. We found that a decrease in polymer content gave rise to a two-fold increase in yield strain and an increase

in size doubled the storage modulus of the jammed granular scaffold. Future studies will investigate the individual microgel stiffness and the effect of jamming extent on the granular hydrogel rheology.

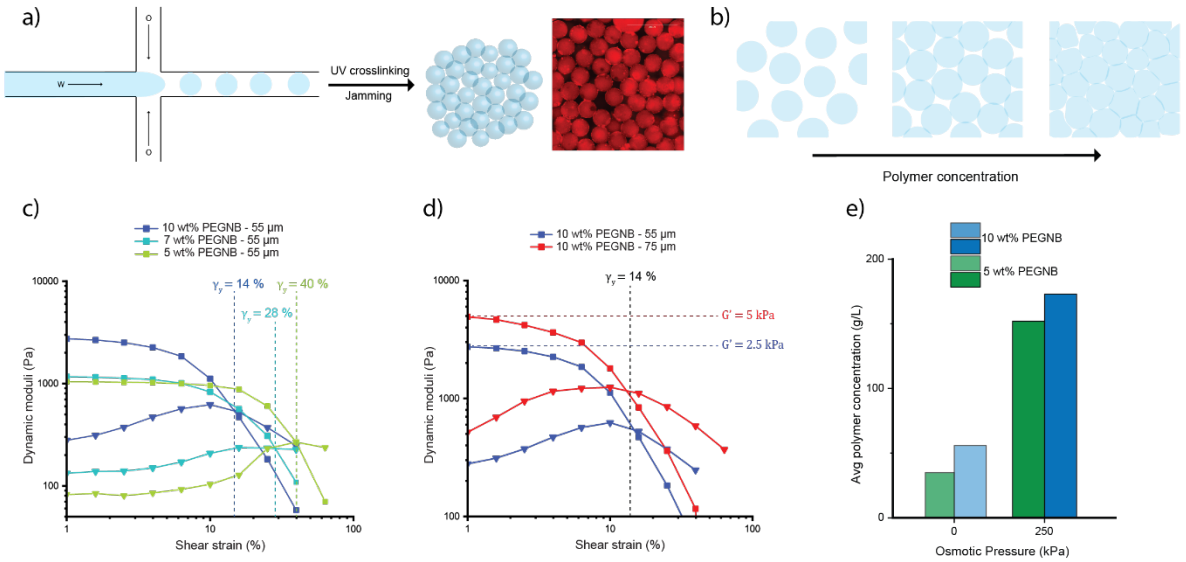

Figure 1: **a.** Microfluidic templating scheme of PEGNB microgels and confocal microscopy imaging of jammed PEGNB microgels fluorescently labeled with Rhodamine (scale bar, 200 µm) **b.** Schematic description of granular hydrogel packing with polymer concentration as a result of increasing osmotic pressure **c.** Yield strain tuning and **d.** Modulus tuning of jammed PEGNB microgels plotted as strain sweep measurements **e.** Average polymer concentration in the uncompressed and compressed granular hydrogel packings.

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Gelation of tuneable bioinspired telechelic hydrogels

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Hydrogels with well controlled and engineered properties are often used in biomedicine, for example for wound healing, or tissue engineering. Hydrogels with a very high toughness, that are well suited as soft dampers, can be fabricated if they are composed of polymer networks containing mixtures of covalent and non-covalent bonds. Moreover, inspired by the marine mussel, hydrogels with tuneable mechanical properties have been developed using telechelic molecules that are crosslinked by coordination chemistry. Most of these systems are composed of 4-armed PEG crosslinked through metal ions. In this talk, I will present an alternative approach to form viscoelastic hydrogels with tuneable mechanical properties that uses linear telechelic PEGs. These linear PEGS are easier to synthesize and hence, enable the fabrication of bulk hydrogel samples. To expand the range of mechanical properties that can be achieved with these hydrogels and inspired by nature, we functionalize these PEGs with pyrogallols. By controlling ions and inorganic precipitates, we are able to tune the mechanical properties of the resulting low-cost biocompatible hydrogels over a wide range.

Polymersome clusters for advanced nanotheranostics

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[2] Department of Biosystems Science Engineering, ETH Zürich, Switzerland

A novel nanotheranostic system based on nanocompartment clusters composed of two different polymersomes linked together by DNA have been developed. The segregation of therapeutic enzyme human Dopa decarboxylase (DDC) and fluorescent probes for the detection unit, in distinct but colocalized nanocompartments, afforded clusters with therapeutic and imaging functions. The diagnostic compartment provides trackability via dye-loading as the imaging component and the ability to attach the cluster construct to the surface of cells. The therapeutic compartment, loaded with active DDC, triggers the cellular expression of a secreted reporter enzyme via production of dopamine and activation of human dopamine receptors D1 (DRD1) implicated in atherosclerosis. This novel two-compartment nanotheranostic platform is expected to provide the basis of a new treatment strategy for atherosclerosis, to expand versatility and diversify the types of utilizable active molecules, and thus by extension expand the breadth of attainable applications.

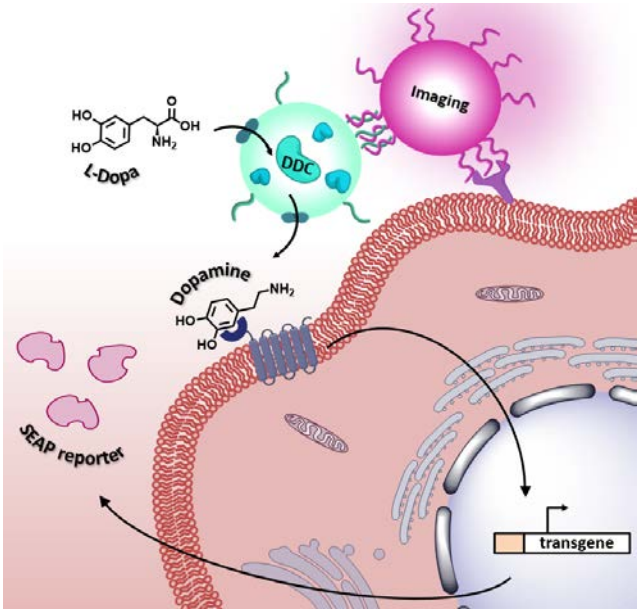

Figure 1: Schematic illustration of cell attachment of DNA-zipped theranostic polymersome clusters composed of two distinct compartments: the therapeutic DDC-Ncomp and the imaging Dye-Ncomp. While Dye-Ncomps contain fluorescent DY-633 dyes, the DDC-Ncomp contain biologically relevant DDC enzymes that convert L-Dopa into Dopamine. This latter bioactive compound is received by cells and triggers gene expression resulting in the production of a detectable SEAP reporter enzyme.

Continuous production of acoustically aligned cells within hydrogel fibres for musculoskeletal tissue engineering

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In many tissues, cells are organized spatially within an extracellular matrix. In skeletal muscle, for example, myocytes form aligned and multinucleated myotubes within a protein support matrix. However, production of large-scale constructs with reproducible cellular organisation remains a challenge. Acoustofluidics is a contactless method to manipulate particles or cells within a fluidic cavity enabled by the formation of standing pressure waves [1]. The objects move within the fluid to the pressure nodes or antinodes, depending on their density and compressibility. Recently, acoustofluidics has been used for manipulation of cells for engineering neuronal tissues [2] and vascularisation [3]. In this work, we used acoustofluidics to pattern cells in a hydrogel precursor. We preserved the cell pattern by photo-polymerising the liquid precursor into a solid hydrogel. By conducting this process within a low friction fluidic channel, we produced hydrogel fibres continuously with parallel alignment of encapsulated cells. We have demonstrated the versatility of the device by producing hydrogel fibres with tuneable cell spacing and viability of encapsulated cells.

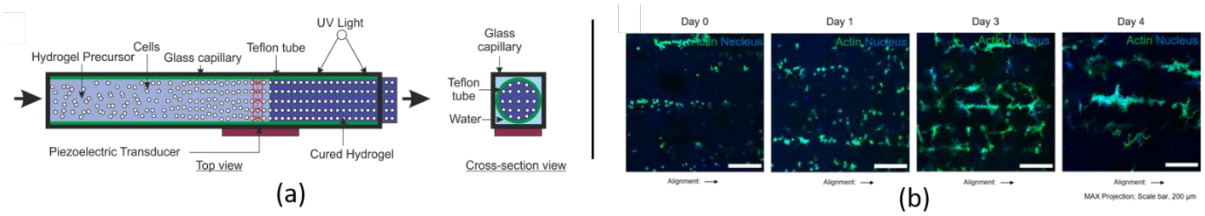

Figure 3 a) Schematic representation of acoustic cell alignment device, b) Aligned encapsulated cells in hydrogel over time

We engineered a Teflon-in-glass capillary device with a piezoelectric transducer to form the acoustic standing wave (Figure 1a). The Teflon tube facilitated continuous flow of the fibres, post-polymerisation. Changing the frequency of operation provided control over cell spacing. 3T3 fibroblasts were included in the gel precursor and patterned acoustically under flow. Ultraviolet light was used to trigger gelation of the hydrogel precursor solution [methacrylated gelatin and poloxamer 407 with lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) as photoinitiator]. The solid hydrogel fibres were transferred to the incubator after fabrication. Cells embedded within the hydrogel fibre were stained with DAPI (nuclei, blue) and phalloidin iFluor 488 (actin, green) at various time points to evaluate the effect of the fabrication process and the hydrogel (Figure 1b). The embedded cells spread within the hydrogel in the direction of alignment.

Current work is exploring how we can use this approach to patterning myocytes and tenocytes to engineer musculoskeletal tissue mimics. Tissue constructs produced with this method could find use as soft actuators or in drug screening as functional tissue mimics.

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Basicle: Giant lipid vesicles as culture vessels for E. coli

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Microbial cells are widely in research and industry. Great interest in single cell studies and parallelization for screening applications drove the development of miniaturized platforms to culture bacteria and other cells. Technological advances in microfluidics, such as microemulsions or microgel beads further improved throughput and reduced culturing volumes for bacterial cultures to nanoliters or lower and are also compatible with high throughput analysis [1,2]. However, in case of droplets and emulsions addition of water-soluble compounds through the oil phase is difficult. On the other hand, gel-microgel beads cannot retain water-soluble molecules produced by encapsulated bacteria. As an alternative to the existing methods, researches explored the possibility to use giant vesicles as culture vessels for microbes [3]. In research, liposomes are mostly used to study lipid membranes or as cell models. The lipid membrane creates a hydrophobic and biocompatible barrier around an aqueous compartment which renders liposomes interesting as vessels, e.g. to encapsulate drugs or cells. Here, we advanced this concept and built bacteria encapsulating vesicles, called *basicles*.

We optimized the protocol to encapsulate bacteria inside giant unilamellar lipid vesicles (GUVs) of about 4 picoliter volumes, formed by the emulsion transfer method [4]. A PDMS-based microfluidic device facilitated monitoring and cultivation of encapsulated *E. coli* on a microscope for up to 15 h. Next, we demonstrated that hydrophilic molecules produced by *E. coli*, here fluorescent riboflavin, are retained and accumulated inside the giant vesicle. Additionally, we show that the microbial production of liposomal encapsulated *E. coli* can be stimulated or inhibited through the lipid membrane by passive diffusion of inducing or antibiotic compounds, respectively, which were added to the extravesicular buffer. Finally, production of giant vesicles and encapsulation of bacteria as well as culturing were realized on the same microfluidic device.

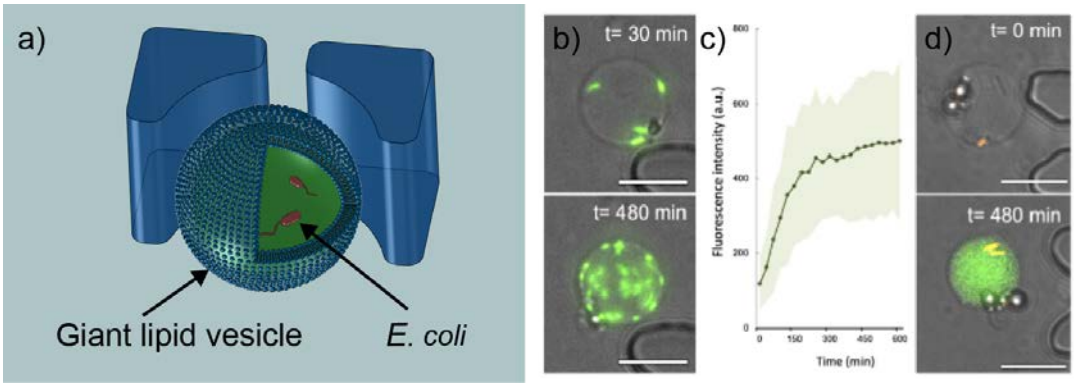

Figure 1 a) Sketch of a bacteria-encapsulating GUV trapped between PDMS posts in a microfluidic device. b) GFP-producing *E. coli* growing inside a GUV. c) Mean GFP-fluorescence measured in basicles (n = 12). d) Production and accumulation of riboflavin (green fluorescent) by E. coli (red) inside a GUV. Scale bars are 20 µm.

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Bioinspired molecular factories with architecture and in vivo functionalities as cell mimics

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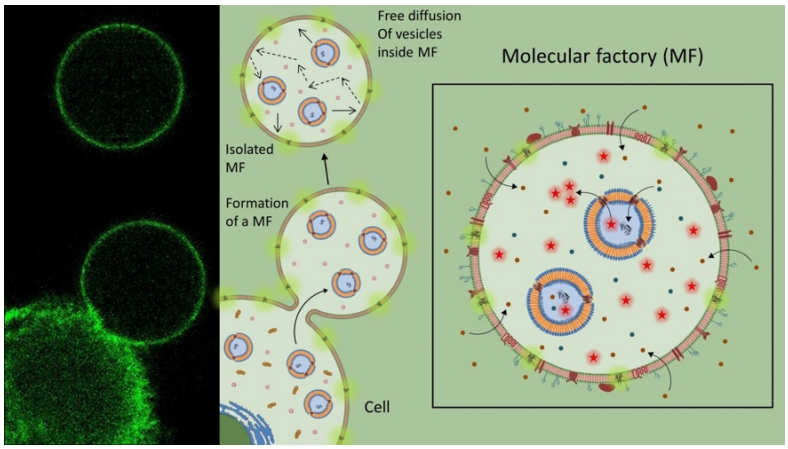
There is a tremendous need to develop new ways for tackling diseases both through early diagnostics and efficient therapeutics. Properly functional cell mimics could be used to address both of these, if made sufficiently life-like, robust and flexible in their customization.

Here we demonstrate a simple, yet general strategy for making tailored cell mimics that have a natural membrane and cytosol interior combined with artificial cargoes, which support functionality. Using a robust, flexible strategy we overcome previous material limitations of artificial cell mimics by designing "molecular factory" giant plasma membrane vesicles generated by donor cells equipped on demand with specified functional elements. The MF-GPMVs inherit the donor cell's natural cytoplasm and membrane, which are combined with with introduced functional elements ranging from small synthetic molecular compounds to biomolecules (e.g., enzymes, proteins) up to nanometer-sized artificial organelles that house reactive components and provide cell-like functionality. Our strategy allows control of the artificial cargos with which these artificial cells are equipped in order to facilitate specific interactions, reinforce their stability and tune their overall efficiency. Our cell-like molecular factories have a remarkable stability and activity, being able to produce desired compounds "on demand" in a cell-like compartmentalized manner. We show for the first time that these cell mimics with unprecedented complexity are functional in vivo and are non-toxic taking another view on bio-inspired artificial cells. We further prove that in a zebrafish vertebrate animal model our MF-GPMVs show no apparent toxicity while retaining their structure and function, successfully reducing hydrogen peroxide as a model reaction.



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Posters

Chemical Networks for Time-Domain Programming of Soft Materials

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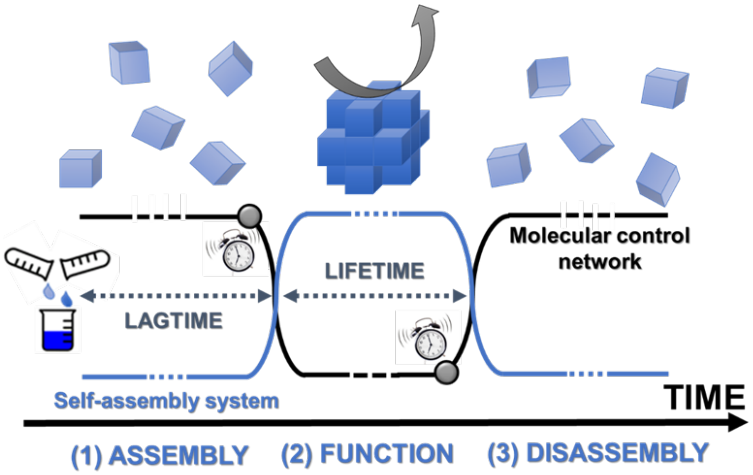
Living systems are able to grow materials with the highest degree of sophistication and an overall efficiency which remains largely unparalleled by artificial fabrication techniques. Such astonishing ability comes from the control and exploitation of complex reactions networks organized with a precise spatio-temporal sequence.

Programming self-assembly in the time domain can be achieved by means of networks of chemical reactions (systems chemistry) [1]. This strategy will enable to tailor the development of advanced materials, towards the design of self-regulating materials with life-like properties.

Here, we will discuss how, by means of "clock reactions", relatively simple chemical reactions exhibiting nonlinear kinetics, we can achieve time-domain control over the assembly of several building blocks, from the molecular to the colloidal scale, but also on supramolecular complex formation, allowing the synthesis of soft materials with a tailorable lifetime. To this end, we will show our latest results in programming the formation of biopolymer particles [2] and of supramolecular aggregates [3], including transient self-assembly [4-6].



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Fungal melanin-based electrospun membranes for heavy metal detoxification of water

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[2] Laboratory for Cellulose and Wood Materials, Empa
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In recent years, heavy metal pollution in water resources has become a severe environmental and public health problem worldwide. Thereby, enhanced treatments are urgently needed with respect to eco-friendliness, filtration efficiencies and low operational costs. This study demonstrates how fungal melanin extracted from Armillaria cepistipes (Empa 655) can be applied as a promising biosorbent for removal of toxic heavy metals from water. For this aim, an electrospinning technique was developed to incorporate fungal melanin particles, a novel source of adsorptive species, into polymeric nanofibrous membranes to obtain stable and highly porous filtration systems. Starting spinning dispersions were investigated with respect to their rheological behaviour and electrical conductivity and related to morphological and surface properties of the resulting composite fibres and membranes. Metal adsorption assays were then performed on both raw melanin and melanised membranes. At the physiotoxic concentrations of Pb^{2+}, Cd^{2+}, Ni^{2+} and Cr^{3+}, fungal melanin was able to remove >90% of heavy metals in single-component solutions. In multi-component solutions incorporating Ca^{2+} and Zn^{2+}, fungal melanin showed a different affinity to different metals in the following order: $Pb^{2+} > Cr^{3+} > Ni^{2+} > Cd^{2+} > Zn^{2+} > Ca^{2+}$ with an extreme preference for Pb^{2+} (80% removal) over the essential metals (0% and 12% removal for Ca^{2+} and Zn^{2+}, respectively). The metal adsorption profiles also showed that melanised membranes were able to maintain the adsorption capacity of the raw melanin. Thus, these novel membranes can be efficiently used as filtration membranes for removal of heavy metals from water.

Characterization of the dispersion of silica nanoparticles in epoxy-based microstructures using FIB-SEM tomography

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Nanoparticle-based composite materials are of interest in various fields due to the possibility of changing and enhancing a large variety of material properties. It has been widely accepted that the final properties of the composite material not only depend on the material, size, and concentration but also depends on the dispersion of the nanoparticles (NPs) within the matrix (1-3). However, a major issue with these composite materials in most applications is the lack of quantitative understanding of the degree of dispersion within the polymer matrix. Various techniques to determine the morphology and the inter-particle distance of the dispersion of these nanofillers within the polymer matrix are available. The obtained information can be useful in understanding the relationship between the dispersion state and the final properties of the composite material.

In this study, we investigated the dispersion of silica nanoparticles (SiNPs) in epoxy microstructures using FIB-SEM slice & view tomography. Image processing followed by segmentation were performed on the stack of images to create a 3D model of the nanofillers dispersion within the composite system. 60 nm SiNPs with two different concentrations (1 and 2% by weight of the monomer) were evaluated. Additionally, the effect of the variation of the solvent:monomer ratio was investigated. By comparing the 3D reconstructed dispersion of the nanoparticles, we found that at lower solvent concentration, 60 nm SiNPs are more dispersed within the bulk of the material compared to the same SiNPs loading with higher solvent concentration.

FIB-SEM tomography has proven to be a reliable method for providing quantitative information about the dispersion of silica nanoparticles within a composite volume. In this work, we show that the concentration and solvent:monomer ratio significantly influences the dispersion of the nanofillers in an epoxy-based microstructured system. This work allows for a better understanding of the distribution of nanoparticle within the host polymer and to rule out the common misconception that only the surface chemistry of NPs plays a role in NPs dispersion within the polymer matrix. Collectively, this study is potentially useful in the optimization of the composition, processing conditions and determination of the right concentration, and the size of nanoparticles to obtain better performing composite systems.

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Capillary-Assisted Deposition of Bacteria as a Tool for Studying Population Heterogeneity

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A large number of studies have established that cultures of bacteria display heterogeneity in behaviour [1]. Examples include stochastic variation in cell size and gene expression, 'division of labour' in biofilm growth [2,3] and the existence of slow growing cells, known as 'persisters', that can survive toxic levels of antibiotics despite lacking any genetic immunity to the drug [4,5]. Understanding how cell populations differentiate and interact at the community level is increasingly seen to be critical to our understanding of infection mechanisms and the development of novel treatments.

To study these systems, we need tools that allow us to image populations of bacteria with single-cell resolution. These tools need to combine 3 key factors: control, resolution and scalability. Here we present a method, based on Capillary-Assisted Particle Assembly (CAPA) [6], for immobilising populations of bacteria onto PDMS substrates. A droplet of cells is dragged across a PDMS surface containing holes, engineered to trap individual cells. We demonstrate this can be achieved with the spherical bacterium Staphylococcus aureus: the cells are deposited, imaged and growth re-established on the substrate. The range of potential applications for this technique will be discussed, including population-wide response to antibiotic treatment, communication mechanisms between members of a community, and fabrication of micro-robots and active matter systems.

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Engineered nano-carrier ink platform for additive manufacturing of precision biomaterials

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A critical need for the additive manufacturing (AM) of precision biomaterials is the design of functional inks for printing. The engineered inks must satisfy specific constraints based on the selected AM technology and intended application (1,2). For extrusion-based AM, the biomaterial inks should flow upon the application of pressure (shear-thin) and reform their molecular network to ensure post-fabrication stability (self-heal). Currently, ink formulation and property tuning is a time-intensive procedure, requiring significant material design and optimization [1,2]. General ink platforms that provide suitable rheology for extrusion-based AM (i.e., shear-thinning and self-healing) and are compatible with a broad range of common biomaterials, could accelerate the development and design of customized inks for biofabrication. To develop such a general ink platform, we engineered a universal nano-carrier ink (UNI) platform for direct ink writing (DIW) based on reversible cross-links between polymers and PEG-b-PLA nanoparticles (NPs) (Figure 1a) [3]. The rheology of the UNI platform was assessed with fractional Maxwell and Kelvin-Voigt models and used to characterise the effect of NP size and concentration on the nanocomposite biomaterial. Thus, the material properties of the transient physical network were tuned by the content and ratio of polymer and PEG-b-PLA NPs, and formulated with suitable viscosity, shear-thinning and self-healing characteristics for DIW. Uniquely, several secondary polymers (such as collagen, hyaluronic acid methacrylate, PEG diacrylate (PEGDA), alginate, gelatin methacrylate, fibrinogen, chitosan, and agarose) were formulated with the UNI platform for facile production of a range of functional inks. In each case, the UNI provided the rheology for DIW without the need for further engineering of the multicomponent ink, while the secondary polymers ensured post-fabrication stability and customized biofunctionality for tissue engineering and drug delivery.

To demonstrate the utility of the UNI platform for biofabrication, human mesenchymal stem cells (hMSCs) were encapsulated in UNI-collagen ink to produce cell-laden scaffolds with high cell viability (>80%) and functional spreading over 48h (Figure 1b). In addition to bioprinting, the hierarchical structure of the UNI platform enabled direct encapsulation of hydrophobic (encapsulated in the NPs) and hydrophilic (in the aqueous phase of the gel) molecules. Drug-loaded UNI-PEGDA ink was used to print controlled release devices with spatial definition. According to the Ritger-Peppas equation ($M_t/M_\infty = k \cdot t^n$), the release of model hydrophilic molecules and model hydrophobic small molecules was governed by Fickian diffusion ($n \sim 0.5$) and erosion-based release in the printed scaffolds ($n \sim 1$ for UNI and $n \sim 0$ for UNI-PEGDA), respectively (Figure 1c).

Overall, the robustness of the UNI platform enabled the rapid and facile formulation of versatile biomaterial inks for DIW in tissue engineering and drug delivery applications. Thus, the engineered self-assembly properties of the UNI platform is a transformative approach with significant potential for AM of precision biomaterials.

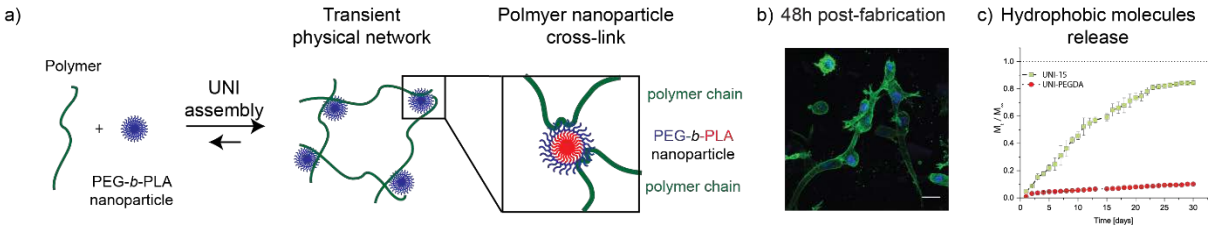

Figure 4: a) Schematic representation of the engineered universal nano-carrier ink (UNI) platform based on reversible cross-links between polymers and PEG-b-PLA nanoparticles (NPs). b) Cells remain viable and spread within bioprinted UNI-Col scaffolds. Scale bar, 25 □m. c) Release of hydrophobic molecules from UNI-15 and UNI-PEGDA scaffolds.

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Adaptive multifunctional composites of inorganic nanoparticles and bio-inspired intrinsically disordered proteins

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The assembly of protein and inorganic nanoparticles represents an attractive approach to generate composite materials with multiple functions. In contrast with inorganic materials, biomolecules are adapted to respond to their surroundings. Here, we report on a strategy to transfer the adaptability of biological systems to inorganic materials by functionalizing nanoparticles with intrinsically disordered domains of proteins associated with the formation of membrane-less compartments in cells. This recently emerging class of protein sequences, defined as low complexity domains (LCDs), are enriched in specific aminoacids and encode intermolecular interactions that drive controlled, dynamic self-assembly in response to environmental changes. We demonstrate that the properties of the LCDs can be transferred to inorganic nanoparticles, inducing controlled phase separation that exhibits dynamicity and stimulus-responsiveness to ionic strength and pH. We illustrate this concept with magnetic nanoparticles, generating dynamic protein-composite magnetosomes of controlled morphology and microreactors that can localize enzymatic reactions and sense the presence of molecules in the surrounding environment.

Lipid droplet biogenesis is driven by liquid-liquid phase separation

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Cells store energy in the form of neutral lipids packaged into micrometer-sized organelles named lipid droplets (LD). These structures emerge from the endoplasmic reticulum (ER), but their biogenesis remains poorly understood. Using molecular simulations, we found that fat accumulation and LD formation are described by a liquid-liquid phase separation (LLPS) process. Within this framework, we could identify how ER membrane properties modulate LD formation, and we could directly test our computational predictions by combining yeast genetics with fluorescence microscopy. Our data suggest that the specific lipid composition of the ER together with its peculiar physical properties, such as low membrane tension and membrane curvature, promote the packaging of neutral lipids into LD, preventing their accumulation in the ER membrane. Our results provide a new conceptual understanding of LD biogenesis in the context of ER homeostasis and function.

Acceleration of an Enzymatic Reaction in Liquid Phase Separated Compartments Based on Intrinsically Disordered Protein Domains

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Spontaneous liquid demixing of biomolecules is emerging as an efficient strategy developed by cells to organize reactions in space and time. This process allows accelerating reaction rates by locally changing the concentration, the composition and the environment of specific components. A class of intrinsically disordered sequences known as low complexity domains plays a key role in driving the interactions underlying liquid demixing. Here, we exploit biologically inspired low complexity domains to develop synthetic microreactors with controlled chemical and physical properties, including concentration and composition of proteins and substrates, polarity, and rheological properties. We show that these changes in the local environment modulate the activity of proteins and can lead to acceleration of biomolecular reactions. We demonstrate this concept by creating micro-reactors that locally increase the concentration of a model kinase up to 140-fold and accelerate the corresponding enzymatic rate up to 5-fold.

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A numerical investigation of active nematic liquid crystals in a channel with hybrid alignment at the walls

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In nematic liquid crystals the coupling between the orientational order of the molecules and the flow is controlled by several material and flow parameters, moreover, the nematic configuration is highly sensitive to geometrical constraints. This complex dynamics is of great promise for microfluidic applications since it provides a means to control and finely tune the flow overcoming the intrinsic difficulties of directing and pumping isotropic fluids at the microscale [1,2].

With this study we focus our attention on *active* nematic liquid crystals in a channel-flow geometry. It was shown theoretically that vanishingly small levels of activity are capable of driving flows between two parallel plates given mixed (homeotropic and planar) anchoring at the walls [3,4]. These flows are referred to as thresholdless active flows [3].

We perform numerical calculations in a quasi-one-dimensional channel geometry by integrating the nemato-hydrodynamic equations with a hybrid finite-difference Lattice-Boltzmann method. We show how the velocity and nematic profiles evolve as the activity parameter increases in magnitude and changes sign and, more generally, as we move away from the limit region in parameter space where analytical solutions [3] were derived. We finally discuss aspects related to the more general nature of models formulated in terms of a tensor order parameter, Q_{ij}, versus models expressed in terms of the nematic director field n_i.

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Engineered bioactive single cell niches to study cell function in 3D

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Introduction: Cell function is influenced by biophysical and biochemical cues in the extracellular matrix (ECM) environment. [1] The individual and synergetic effects of these cues on cell function are still not fully understood. The controlled study of cell-ECM interactions is constrained by the limitations of current cell culture strategies [2] that often employ bulk polymeric materials, which offer limited control over the properties of 3D cellular microenvironments. Individual cells within encapsulated population are exposed to heterogeneous mechanical and geometrical cues and, therefore, respond heterogeneously. The heterogeneity of the external signals and inherent variability in the cell populations limit an accurate investigation of the experimental conditions and study of cell-niche interplay. To address these issues, we developed a cell culture platform that offers robust and simultaneous control over niche properties allowing for decoupling of the different cues that act on the cell. Importantly, the platform offers additional control over the geometry, including morphology and volume, of the individual cell niche. [3] Instead of encapsulating cells in bulk, our platform allows for encapsulation of the individual cells within biochemically, mechanically, and geometrically defined microniches (Figure 1A). The precisely defined position of the cells and spacing between the niches eases imaging and real-time cell tracking and enables automated analysis of the imaging data. Here, we have applied this platform to investigate how niche volume and stiffness couple to influence cell proliferation and apoptosis.

Methods: The platform was designed as a hydrogel matrix adhered to a standard glass slide patterned with structured arrays of microniches that can host single cells. The niches with controlled geometry, volume, and stiffness were fabricated using peptide-functionalized, PEG-based hydrogels. A negative of the micropattern was cast in Teflon using soft lithography and transferred on the hydrogels. The hydrogels were formed via thiol-ene photopolymerization between norbornene-functionalized star PEG and thiolated linear precursors (Figure 1B). The network was functionalized with the RGD cell adhesion motif to mimic the adhesiveness of native ECM. The hMSCs were sedimented into the niches, which were then sealed with a second hydrogel layer creating confined 3D cell niche. The surfaces of the two hydrogel layers were adhered by coupling substrate peptides, used in the formulation of the hydrogels, via an enzymatic ligation with Sortase A (Figure 1C).

Results: The niches of different size and stiffness were fabricated. We investigated three niche volumes: small (35'000 μm^3) intermediate (61'250 μm^3) and large (125'000 μm^3); and three stiffnesses: low, medium and high (E = 5, 16, and 30 kPa, respectively). The cells were seeded in different concentrations to achieve an optimal individual encapsulation incidence, which was 10.000-15.000 cells cm^{-2}. Time-lapse imaging indicated cell spreading within several hours (Figure 1D). The cells were cultured in the niches for 1 and 3 days and the viability and proliferation rates were studied. The cells in small niches expressed high apoptosis rates that increased with an increasing modulus. The medium and large niches showed highest viability at medium stiffness (Figure 1E). The preliminary results indicated that proliferation rate increased in larger niches and at higher stiffness. Additionally, YAP/TAZ nuclear localization was investigated and correlated with apoptosis and proliferation rates.

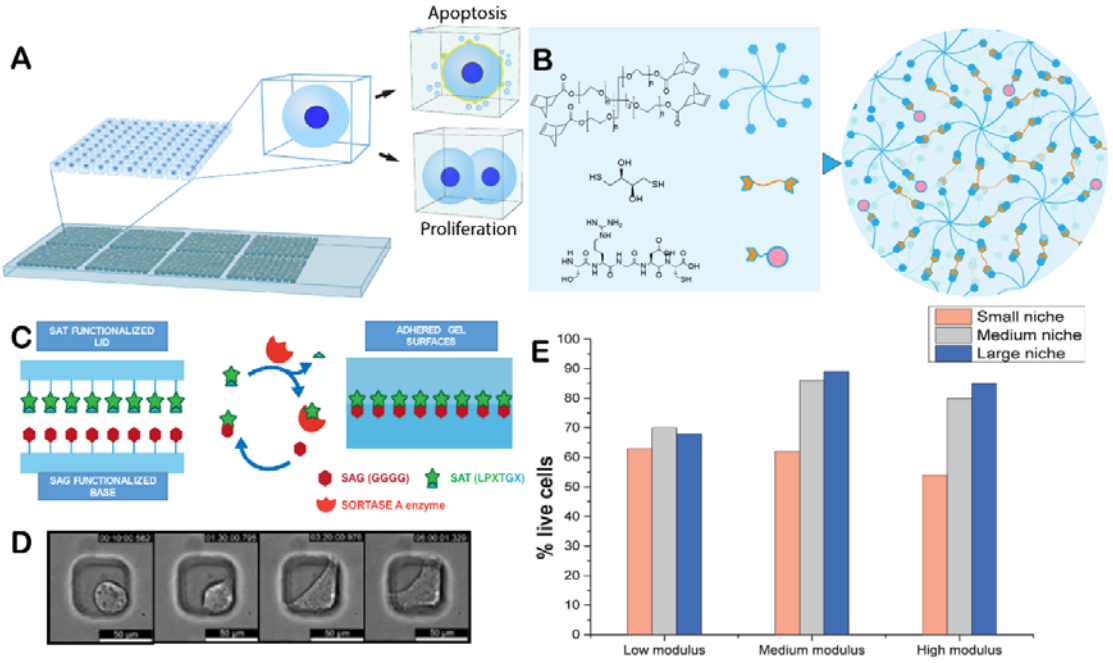

Figure 1: A. The single cell hydrogel platform on a standard glass slide patterned with structured arrays of micron-scale niches that can host single cells was used to study the effects of niche stiffness and size on proliferation and apoptosis rates. B. The hydrogels are formed via thiol-ene photopolymerization between norbornene-functionalized star PEG and thiolated linear monomers. The hydrogels were functionalized with RGD motif for cell adhesion. C. The niches are sealed with a second hydrogel layer using enzymatic Sortase A ligation creating confined 3D cell niche. D. The time-lapse imaging after cell encapsulation indicated cell spreading within several hours. E. The medium and large niches showed maximum viability at medium stiffness, the apoptosis rates were highest in small niches and increased with an increasing modulus.

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Organic deposits in methanation catalyst Ru/C

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Introduction: Catalytic hydrothermal gasification of organic matter over ruthenium (Ru) nanoparticles supported on high-surface-area carbon is the best catalytic system for selective production of methane. The deactivation mechanisms of such catalysts have been partially explored focusing on sulfur poisoning and deactivation by sintering of the Ru nanoparticles. We have used small-angle neutron scattering (SANS), transmission electron microscopy (TEM), Brunauer-Emmett-Teller (BET) together with ultrahigh-pressure liquid chromatography coupled with hyphenated high-resolution mass spectrometry (UHPLC-HRMS) as an analytical strategy for investigation of catalyst's deactivation by fouling, i.e. organic deposits on the catalyst surface. The obtained results shade light on the morphological and chemical characteristics of catalyst deactivation by organic fouling in supercritical water. Further, the washing of the partially deactivated catalyst using a mixture of organic solvents results in full activity reconstruction of the catalyst. SANS indicates that the deposition of a thin film of organic molecules contributes to the deactivation of the catalyst.

Methods: Using SANS, transmission electron microscopy (TEM), Brunauer-Emmett-Teller (BET), and high-resolution mass spectrometry (HRMS), we have studied the composition of organic deposits and the resulting structural changes in used and active as well as used and inactive Ru/C catalysts [1].

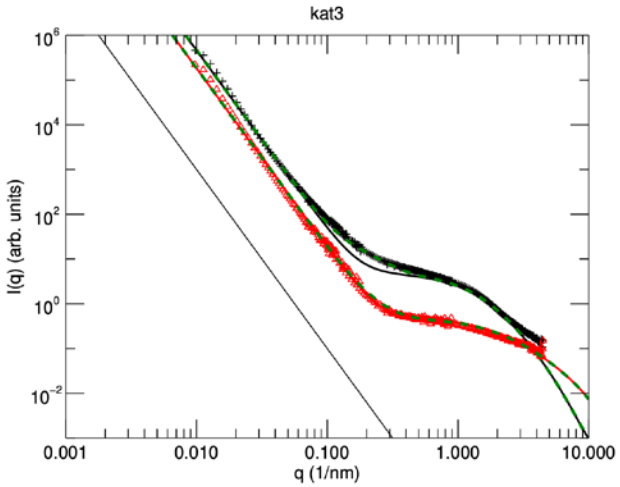

Fig. 1: SANS curves of spent Ru/C catalyst in air (black +) and D_2O (red △). The solid curves show fits with the pore model of Refs. [2,3] including a thin layer of organic deposits. The dashed curves also include the contribution of Ru nanoparticles on the catalyst surface.

Soluble deposits on the catalyst (150-300 g/mol) were removed with a mixture of organic solvents and were analyzed with BET and HRMS, the average composition was found to be CnH1.1nO0.21n.

Results and Discussion: Using SANS, we find that the active carbon matrix is well described by the pore model of Refs. [2,3]. A Porod regime due to meso pores is observed at the lowest q's accessible with SANS, while a shoulder due to micro pores and the start of a second Porod regime due to the micro pores are observed at higher q's, see Fig. 1. The use of the catalyst under super-critical water conditions and the presence of organic deposits are found to leave the pore structure of the active carbon matrix intact. However, a shift in the onset of the Porod regime due to micro pores is observed in used catalysts, which we explain by a thin layer of organic deposits in the micro pores. The thickness of the deposits is found to be in the range of 1 to 3 Angstroms.

Conclusions: The SANS results indicate that a thin film of organic deposits in the micropores contributes to the deactivation of the catalyst, but the pores are not blocked by the deposits and remain open. This result agrees with the finding that the spent catalyst can be reactivated by washing with organic solvents [1]. These findings may allow to optimize the use and the life time of Ru/C catalysts.

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A microfluidic platform for characterizing the structure and rheology of biofilm streamers

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In many environmental or medical settings, biofilm formation is the most successful strategy for bacterial colonization [1, 2]. In the biofilm lifestyle, bacteria embed themselves in a self-secreted matrix of extracellular polymeric substances (EPS), acting as a shield against mechanical and chemical insults [3]. The biofilm matrix has viscoelastic properties: it can adapt under loads, undergoing large deformations before breaking or detaching from its substrate. Due to its gel-like properties, when ambient flow is present, the EPS scaffold can take a streamlined shape, forming biofilm threads suspended in flow, called streamers [4]. In many situations, the streamers architecture can enhance the harmful effects of biofilms, bridging the spaces between obstacles in the flow path [5]. Despite their importance for biofilm survival, little is known about the material properties of the matrix; examples of open questions are how the rheological behaviour is related to the chemical composition of the EPS or how this is determined by the physico-chemical features of the microenvironment. Investigating these relations would allow a better understanding of the mechanisms underlying biofilm resistance to mechanical stresses and would possibly lead to new removal strategies.

In this work we present a microfluidic platform that allows the reproducible growth of biofilm streamers, in controlled chemical and flow conditions [6]. We perform stress tests on streamers by inducing controlled variations of the flow rate. We developed a theoretical framework to estimate the material properties of biofilm streamers from the flow-induced deformation measured in our experiment. Thanks to this platform, we are able to investigate the role of the different EPS components [7] and physico-chemical microenvironment in determining biofilm structure and rheology.

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Capillary deposition of microorganisms for the study of cells in spatially controlled environments

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Controlled and precise deposition of microorganisms into defined spatial arrangements offers unique and innovative possibilities for the study of microbial physiology and interactions. Full control over the geometrical arrangement is highly desirable due to the crucial importance of distances in microbe-microbe interactions, arising from their dependence on the propagation of chemical signals. Coupling accurate spatial patterning and full control over environmental conditions would provide a powerful and versatile platform for single-cell studies in microbial ecology. To this end, I have developed a microfluidic platform to extend a capillary deposition technique originally designed for colloidal particles, called sCAPA [1-3] (sequential capillarity-assisted particle assembly), to bacterial systems. This technology exploits the capillary forces resulting from the controlled motion of an evaporating droplet inside a microfluidic channel to capture individual particles or microorganisms in an array of traps microfabricated onto the substrate. Sequential depositions allow the generation of the desired spatial layout of single or multiple microorganisms. I successfully calibrated this new technique on colloidal particles and tested it on bacteria. I expect that the coupling of single-cell deposition and microfluidic technology allows both geometric patterning and precise control of environmental conditions, and thus opens up a window into the physiology of single microbes and the ecology of microbe-microbe interactions as shown by preliminary experiments.

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Model-free Determination of Interaction Potentials from Small-angle Scattering Data

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Small-angle scattering (SAS) techniques are widely used nowadays because of their potential to structurally characterize nanoscale systems. They allow, in principle, to get information both about the internal structure (size, shape, and size distribution) of diverse entities, such as colloidal particles, polymers, biological macromolecules, or nanoparticles, and also about their mutual interparticle interactions and aggregation capability. However, extracting this valuable information from the scattering intensities typically recorded in this kind of experiments is not an easy task as it requires to analyze and interpret noisy data collected in a very limited region of the reciprocal space.

Indirect Fourier Transformation (IFT) methodologies [1, 2] are the most commonly used tools to reveal self-scattering structural details from data obtained using very diluted samples as they enable to reconstruct, under very few assumptions, the corresponding pair distance distribution function (PDDF), which contains all the information regarding the morphology of the particles in the real-space. On the other hand, the current approaches to study interparticle interference effects rely on estimating the so-called structure factor, which encloses all the interparticle contributions to the scattering curve, by using interaction model potentials and liquid-state theories [3]. As a consequence, these strategies are therefore dependent on parameters fitting and very strong and not always valid assumptions.

For those reasons, the usage of a specific model potential in the analysis of SAS intensities can induce to erroneous reasoning about the spatial particle distribution or the origin of interparticle interference effects, for instance, and therefore the conclusions obtained from this kind of analyses must be taken with care. To circumvent the limitations associated with the aforementioned strategies, in this contribution, I will describe a model-free protocol that allows the inference of interaction potentials from small-angle scattering data without requiring strong predefined assumptions.

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Bacterial Biofilms as Soft Materials

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Bacterial biofilms are formed by communities of microorganisms that are encased by a matrix consisting of self-produced, hydrated extracellular polymeric substances [1]. Biofilm formation is observed in a large variety of microorganisms and provides a protected mode of growth. Recent advances show that biofilms are structurally complex, dynamic systems that exhibit different morphologies depending on the environmental conditions the bacteria find themselves in [2]. In certain growth conditions, large three-dimensional structures, which can be defined as channels, are found within biofilms. These channels show low resistance to liquid flow and therefore enable transport by advection [3] Enhanced molecular transport within the biofilm might confer a biological advantage to the microbial community, but the exact mechanism of channel formation and which benefit bacteria get from them is still unclear.

We study the influence of mechanical properties of the biofilm matrix on the formation of channels inside *Pseudomonas aeruginosa* PA01 biofilms. Biofilms are grown in microfluidic devices in controlled flow conditions and channel formation throughout the whole biofilm is observed. Preliminary results show, that biomass production controls a mechanical buckling instability, which triggers the formation of folds and wrinkles. These three-dimensional structures can be identified as hollow channels in which bacterial movement is greatly facilitated compared to regions or biofilms where no channels have formed. Microfluidic techniques allow us to characterize the influence of physical parameters like flow conditions, lateral confinement and substrate wettability on channel formation inside the biofilm. Our work represents a step towards understanding the process of channel formation within a microbial biofilm.

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The role of solvent effects on the aggregation of mixed-monolayer protected gold nanoparticles

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Nanoparticles (NPs) have emerged as a powerful class of materials due to the plethora of their potential applications. Nowadays, NPs have different technological applications and can be used in the biomedical field for biosensing, imaging, targeting, and theranostic purposes. Among NPs, monolayer-protected gold nanoparticles (Au-NPs) have been thoroughly studied for their simple synthesis, tunable size, and prominent optical features such as surface plasmon resonance [1-2]. To investigate physicochemical properties of NPs and their interaction with biological structures such as cellular membranes or proteins, we have used fully explicit all-atom (AA) Molecular Dynamics (MD) simulations [3]. Here, we focused on NP aggregation and we investigated the role of ligand shell chemistry, solvent nature and ion concentration as all these parameters have been shown to affect the propensity for NPs to aggregate, and some of those (e.g. apolar solvents) can mimic NP behavior inside a cellular membrane[4-5]. Using umbrella sampling calculations, we found that the free energy of aggregation is strongly dependent on the surface charge, ion concentration, and solvent nature, and that it can adopt dramatically different profiles upon variations of the overall balance between hydrophobic and hydrophilic interactions between the NP and the solvent. A thorough understanding of these interaction energies is fundamental to understand how nanomaterial interact with cells and to develop advanced materials able to interact with biological membranes in a rational and controlled way.

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Efficient Asymmetric Synthesis of Carbohydrates By Aldolase Nano-Confined In Lipidic Cubic Mesophases

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Class-I aldolases are known for efficiently catalysing stereo-selective aldol-addition reactions in bulk aqueous media and considerable efforts are currently being devoted to engineer the enzyme in order to optimize its activity and stability, primarily by modulating the hydrophobicity of the catalytic active site. Here, we opt for a different strategy based on choosing a nano-confined environment favorable to the enzyme. We report the observation of enhanced activity and stability of a class-I aldolase, D-fructose-6-phosphate aldolase from *E. coli* (FSA) when incorporated into lipidic cubic mesophases (LCMs), a class of biomimetic amphiphilic complex fluids employed in several nanotechnology applications. We infer that this improved in-meso performance is achieved by optimal location of the FSA in the LCMs, as a result of the known interaction between the residues of FSA and the glycerol molecules, which serve as the lipid head groups, and thus locate along the amphiphilic interface encompassing the whole LCM. This continuous interface ensures increased accessibility of the catalytic reaction centre to substrates and high activity in LCM.

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Metal Reinforced Carboxymethyl Cellulose Methacrylate/Poly(Acrylic Acid) Hydrogels

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Hydrogels are polymeric materials capable of absorbing large amounts of water [1]. Thanks to their high biocompatibility, hydrogels were among the first biomaterials expressly designed for their use in biomedicine. Due to their versatility, hydrogels made their way to the market as superabsorbent materials (e.g. diapers), wound dressings, and drug delivery systems. However, state-of-the-art applications of hydrogels are severely limited because they are typically either too soft or too brittle such that they cannot be used for load-bearing applications. To overcome this shortcoming, dually crosslinked hydrogels encompassing covalent and reversible crosslinks have been developed [2]. Here, we propose a metal-coordination ionic crosslink as a mean to reinforce hydrogels. I will present the influence of Fe^{3+} and citric acid concentrations on the mechanical properties of dually crosslinked hydrogels.

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Alignment and differentiation of myoblasts in hydrogel fibers

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A human skeletal muscle contains bundles of long myofibers, which are cells with multiple nuclei termed myocytes. Between the fibers and the basal lamina, the muscular tissue hosts mononucleated stem cells, which activate and differentiate upon tissue damage to regenerate the fibers. An undifferentiated myogenic cell state that shares some properties of these stem cells can be reached by inducing fibroblasts with MyoD and treatment with small molecules. These muscle progenitor cells are then able to differentiate into functional myofibers that contract [1].

Undifferentiated myoblasts were first encapsulated in small hydrogel disks, with GelMA or GelMA+Matrigel as polymeric backbones. After a first period of incubation to allow cell spreading in the polymer matrix, differentiation lead to the formation of tubes that were able to contract spontaneously in the gel and deform the disk.

Using a microfluidic device, the myoblasts were aligned in a hydrogel fiber via acoustophoresis [2]. The cells were suspended in the precursor solution, resisted to the UV exposure necessary for the radical initiated polymerization, and finally the gel was extruded from the device in a continuous manner. Differentiation into fused myocytes and contraction of the myocytes was successful also in the fibers.

After optimization of the cell density and medium diffusion in the fiber, long bundles of aligned myofibers could be fabricated. A better understanding of the triggers that induce myofiber contraction would enable control over this mechanism toward the design of soft robotic actuators.

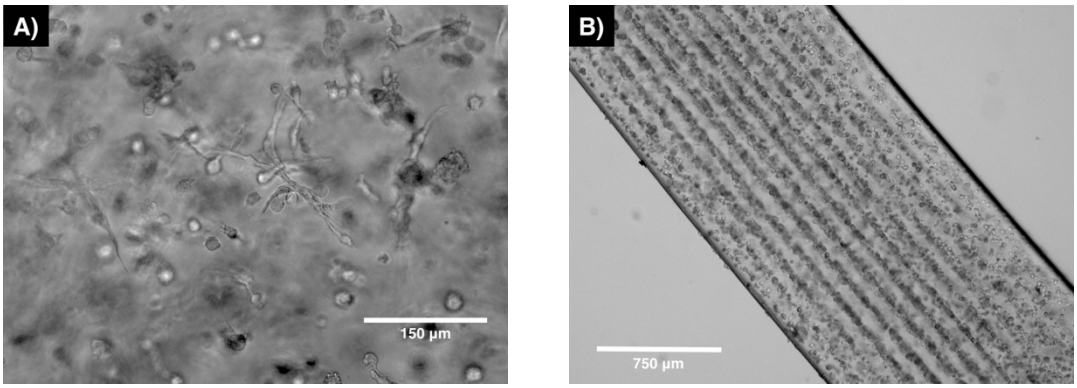

Figure 1: A) Differentiated contracting myocytes encapsulated in a GelMA+Matrigel hydrogel disk (2.5mm diameter, 1mm thickness). B) Aligned myoblasts in a GelMA+Matrigel hydrogel fiber (1.8mm radius, 3 cm length).

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Surface Stress of Soft Solids under Strain

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Surface tension is a phenomenon typically associated with liquids, rather than with solids. However, interest in interfaces of soft solids has revealed the importance of surface tension, for instance in controlling small-scale adhesion behavior. Here, we aim to develop a new technique to investigate the surface tension of soft gels through the analysis of droplets on a stretched substrate. In particular, we find that small droplets on a stretched surface elongate along the stretch direction, forming a saddle-like contour at the contact line. This appears to be consistent with the presence of strongly strain-dependent surface stresses. We will show how the shape of the droplet in brightfield measurements can be used to predict the height of the resulting contact line. Thus a simple 2D measurement can be used to determine 3D information about the system.

Quantitative mechanochromism of polydiacetylenes on the nanoscale

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University of Geneva, Department of Physical Chemistry, Geneva

Polydiacetylenes are mechanochromic polymers, that show a colour change (e.g. blue to red) upon external stimuli such as heat, stress or changes in chemical environment [1]. However, how these stimuli change their structure and how that relates to their optical properties are still not clear to this day. To address these questions, we deposited 10,12-tricosadiynoic acid onto plasma-activated glass substrates, exposed to UV for polymerisation, and applied forces to the polymerised film by an atomic force microscope, while simultaneously measuring the emitted fluorescence. The fluorescence is characteristic of the transformed red phase of polydiacetylenes, thus enabling us to follow the phase transition, while the atomic force microscope registers the forces exerted to the polydiacetylene chains. Combining the two techniques could open a path to the fluorescence - force calibration of the colour change, contributing to a deeper understanding of polydiacetylenes.

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Development of a high throughput assay for screening peptide cooperative effects based on polydiacetylene

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Polydiacetylenes (PDAs), a well-known mechanochromic polymer, possess unique optical properties that the color will change from blue to red in response to environmental changes such as pH changing, temperature variation, and molecular binding. The chromatic properties of polydiacetylenes have been widely investigated as signal transducers for their use in biosensing applications but just detecting the peptide concentrations. In the current crisis of resistance, cooperative effects between different types of antimicrobial peptides (AMPs) play major roles in numerous physiological processes, but so far the existing methods to investigate the cooperativity are too slow and expensive. Here, we describe a novel high throughput colorimetric technique based on supramolecular assemblies of lipid–polydiacetylene vesicles for screening of peptide cooperative effects. The phospholipid/PDA vesicle solutions undergo visible color changes and quantifiable blue to red transition upon binding with individual peptide and their mixture. The sigmoidal dose-effect curve indicates that the colorimetric transitions from blue to red are importantly correlated with the cooperativity between two types of peptides, which can be also quantified by combination index (CI). The results suggest that the new high throughput colorimetric assay could be utilized for studying the cooperative effect between AMPs more effectively.

Double emulsion templated polymer GUVs for studying compartmentalized enzymatic cascade reactions

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Department of Chemistry, University of Basel

Compartmentalization, the spatiotemporal division of biochemical reactions and containment of cellular components, is one of the main features of a living matter. Currently, nanotechnology attempts to replicate this behaviour by separating tiny environments from the exterior into nano- and micro-sized self-assembled synthetic compartments. Tailormade block-copolymers have been used to form such compartments, since they have shown to spontaneously organize themselves into vesicle architectures [1]. Typically, giant unilamellar vesicles (GUVS) are produced through bulk techniques as film rehydration or electroformation [2]. However, vesicles produced via these methods consist of a mixture of characteristic sizes between 1 and 40 μm. Double emulsion microfluidics, on the contrary, offers the alternative of producing monodisperse GUVs at high throughput. Thus, in the present work, we generate W/O/W double emulsions by breaking up droplets of immiscible fluids in a single step six-ways junction in a Silicon-glass microfluidic platform; the hydrophobic fluid is a volatile mixture of organic solvent that contains dissolved PDMS-PMOXA copolymers. We collect the double emulsions and slowly evaporate the organic solvent, which ultimately directs the self-assembly GUVs. Control over fluid flow rates enables precision assembly of polymer GUVs and provides highly efficient encapsulation and co-encapsulation of biomolecules, such as enzymes, within their aqueous core. Since the polymer GUVs generated with PDMS-PMOXA copolymer are impermeable, we insert the outer membrane porin F (OmpF) into the synthetic membrane, for allowing communication among GUVs, which is a prerequisite for conducting enzymatic reactions inter-compartments. Lastly, as a proof of concept, we encapsulate the enzyme β-galactosidase (β-gal) and measure its activity through the conversion of the substrate, resorufin galacto pyranoside (RGP), into the fluorescent product, resorufin. Further cascade reactions are still to be investigated, however, this approach already paves the way for enforcing the richness and versatility of micro-sized assembled compartments for studying their protective role on the overall efficiency of enzymatic reactions.

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Porphyrin containing polymersomes: ROS generation and biological evaluation in mammalian cells

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Stimulus-sensitive systems at the nanoscale represent ideal candidates for improving therapeutic and diagnostic approaches by producing rapid responses to the presence of specific molecules or conditions either by changing properties or by acting "on demand" [1]. Here we introduce an optimized light-sensitive nanocompartment based on encapsulation a water soluble porphyrin (TPyCP) of a photosensitizer inside poly(2-methyloxazoline)-*block*-poly(dimethylsiloxane)-*block*-poly(2-methyloxazoline) polymer vesicles to serve as an efficient source of reactive oxygen species (ROS) "on demand"(fig 1). Polymer-porhyrin nanocompartments were optimized in terms of (i) size, (ii) stability, and (iii) encapsulation efficiency based on a combination of light scattering, TEM, and Fluorescence spectroscopy[**2**]. By irradiation under red LED light, encapsulated TpyCP conjugates generated in situ ROS, which diffused through the polymer membrane to the environment of the vesicles, as proved by electron spin resonance spectroscopy (ESR). Three different cell types (HeLa, HepG2 and HEK 293T) have been tasted allowing us to evaluate *in vitro* the photoactivation of TpyCP both free in solution and most importantly light-sensitive nanocompartments for medical applications which require ROS to be generated with precise time and space control.

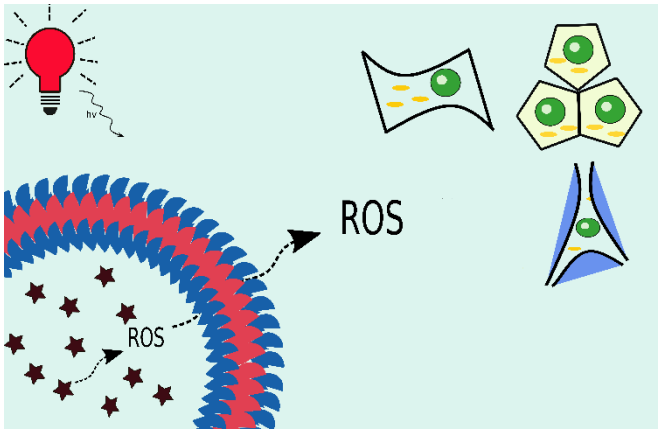

Fig 1: Concept of porphyrin containing polymersomes for ROS generation within mammalian cells

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Synthesis and Complex Self-Assembly of the Amphiphilic PEO-b-PEHOx polymers into Multicompartment Micelles, Pseudo-Vesicles and Yolk/Shell Nanoparticles

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Preparing well-defined amphiphilic block copolymers has become a focus of modern research thanks to their ability to self-organize into various complex structures [1-2]. However, little attention was given to AB diblock copolymers with a long and branched side chain in the hydrophobic block, potentially leading to novel interactions during the self-assembly. The aim of this work is to design such an AB diblock copolymer and study its self-assembly.

By using a new nosylated poly(ethylene oxide) (PEO) macroinitiator, we synthetized a whole library of poly(ethylene oxide)-*b*-poly(2-(3-ethylheptyl)-2-oxazoline (PEO-*b*-PEHOx) amphiphilic AB diblock-copolymers via a microwave-assisted polymerization (Fig 1) [3].

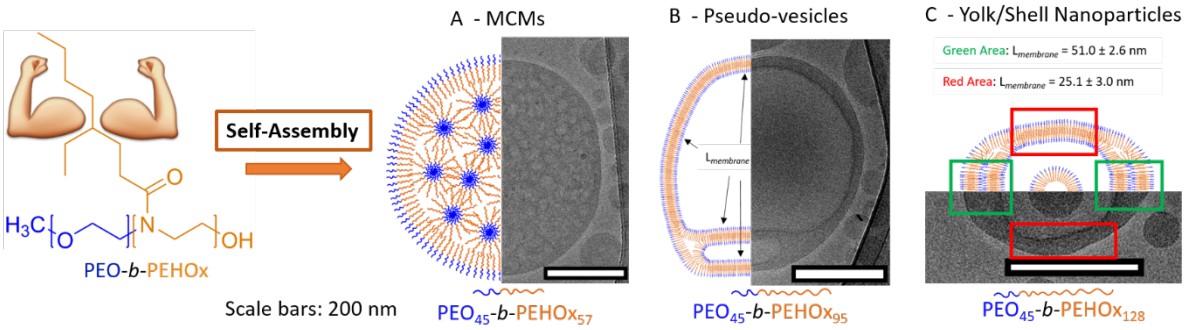

Fig. 5: Amphiphilic diblock copolymer PEO-b-PEHOx and representative cartoons with the corresponding model Cryo-TEM image of the various self-assemblies. Scale bars: 200nm. A - Multi-compartment micelles (MCMs).$R_{micelles}$=13.1 ± 1.3 nm. B - Pseudo-vesicles. $L_{membrane}$=17.9 ± 1.5 nm C - Yolk/Shell Nanoparticles.

Self-assembly of PEO-*b*-PEHOx was performed using film rehydration and solvent switch. Apart from micelles and worms, we were able to prove the formation of multiple complex structures by light scattering, TEM and Cryo-TEM: multi-compartment micelles (MCMs), Pseudo-Vesicles and Yolk-Shell nanoparticles. To the best of our knowledge, this is the first time such complex materials are formed from a single AB diblock copolymer. The side chain of PEHOx with its ethyl branch and long length generated additional hydrophobic-hydrophobic interactions while preventing a compact order or strong entangling of the AB diblock copolymers in a membrane. This shows the unique properties of PEO-*b*-PEHOx and the potential of hydrophobic block with a long and branched side chain to obtain complex nanoparticles. Altogether, our results show that PEO-*b*-PEHOx is a meaningful addition to the canon of self-assembling block copolymers. Combined with its backbone structure close to a peptide make PEHOx a compelling hydrophobic block to lead to new complex self-assembly structures and insights into self-assembled nanoparticles.

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Novel Cancer-Targeted Nanoparticles

S.-L. Abram[1], I. Craciun[1], A. Jarzębińska[2], D. Colecchia[2], M. Zigler[2], Y. Benenson[3], C. G. Palivan[1]

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Significant advances have been made in the field of cancer therapy in the past few years. However, cancer remains a major contributor to morbidity and mortality worldwide. Numerous treatment modalities have been developed and approved for the treatment of solid tumors including small molecules, antibodies and cell-based therapies. However, due to tumor heterogeneity as well as suppression of and escape from anti-tumor immune responses, resistance to treatments continuously emerges. More recently, immune-modulatory antibodies have shown significant efficacy in several indications. Nonetheless, only a subset of patients respond and the majority of patients remain without an effective treatment. To address these challenges, a novel targeted therapy platform technology is being developed. This technology targets the delivery of a payload to cancer cells, mimicking viral infection. This induce cell death while simultaneous release of cytokines activates an immune response acting against neighboring, untransfected cancer cells.[1,2]

To effectively deliver the payload to cancer cells, a carrier system must protect the payload from extracellular enzymatic degradation and facilitate cellular uptake as well as endosomal release. Polymeric vectors containing a targeting moiety are being developed and are utilized to complex with the payload to form nanoparticles. These allow protection from degradation and simultaneously enable selective delivery of the payload to cancer cells overexpressing the corresponding receptor.[4]

As for any other nanoparticulate drug, a thorough characterization of its physico-chemical properties in correlation with its biological activity is necessary for safe drug development.[5] Herein, we systematically study the influence of different formulations on the nanoparticles' characteristics and their reproducible formation. Particle size, size distribution and shape are analysed by electron transmission microscopy. Dynamic light scattering is used to study the hydrodynamic radius and to address stability at different temperatures while nanoparticle tracking analysis gives access to the particle concentration. This approach facilitates the selection of suitable formulations, which are further characterized in more detail, e.g. with respect to morphology by static light scattering or to surface charge. Furthermore, fluorescent labelling of the different components will allow us to elucidate the uptake mechanism as well as the nanoparticles' mode of action in order to correlate structure and biological activity.

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PBO-b-PG Self-Assemblies:
Towards the Effect of Tacticity in Amphiphilic Diblock Copolymers

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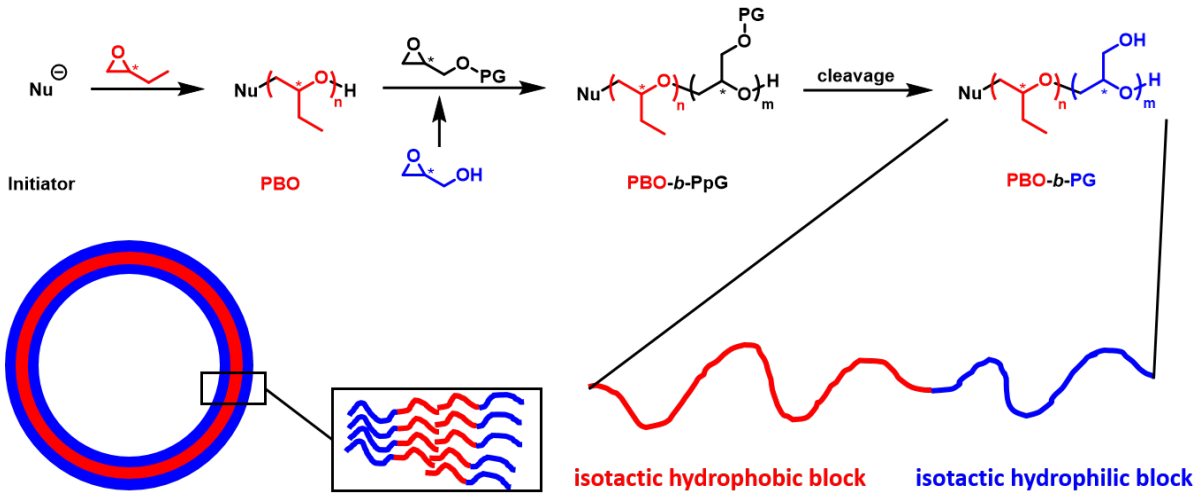
Chirality is a key factor in biological processes as many specific functions strongly depend on chiral recognition [1]. However, the effect of tacticity in block copolymers used for self-assembly applications has been neglected so far [2]. Consequently, interactions of nanoparticles from chiral polymers with enantiopure compounds hold an enormous potential to considerably widen the applications of aqueous self-assemblies.



The diblock copolymer poly(butylene oxide)-block-poly(glycidol) (PBO-b-PG) was synthesized in a microwave-based reaction. Starting from enantiopure monomers, the tacticity of each block could be adjusted accordingly. Self-assembly in water or PBS buffer via film rehydration or solvent exchange led to the formation of chiral micelles, worms or vesicles, establishing this new class of chiral nanostructures. Analysing their chiral interaction with enantiopure compounds will be relevant in many biological or biomedical processes.

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Self-Assembled Peptide Nanoparticles for Safe and Efficient Gene Delivery

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The delivery of therapeutic nucleic acids has a great potential in the treatment of a variety of diseases [1]. Safety concerns related to viral delivery systems in clinical applications led to the emergence of non-viral vectors. However, non-viral methods generally suffer from a low delivery efficiency [2]. To sidestep these limitations, we developed a purely peptidic delivery system that is able to entrap single- and double-stranded DNA of up to 100 nucleotides in length. Our delivery system is based on the amphiphilic peptide (HR)3gT that comprises a hydrophilic domain prone to undergo electrostatic interactions with DNA cargo, and a hydrophobic domain at a ratio that promotes the self-assembly into multi-compartment micellar nanoparticles (MCM-NPs). The (HR)3gT nanoparticles are between 100 to 180 nm in diameter, supporting a rapid and efficient cellular uptake. They have no adverse effects on HeLa cell viability and are structurally stable over months at 4°C. Furthermore, the multi-micellar organization of the (HR)3gT disassembles at 37°C, adding to the release of the DNA. The direct comparison of (HR)3gT to the much shorter peptide H3gT, which was reported to co-entrap a 22-nucleotide single-stranded DNA and drug in nanoparticles, indicates that the additional arginine residues in (HR)3gT not only enable the incorporation of longer DNA fragments, but also convey improved DNA entrapment and increased cellular uptake [3]. Encouraged by this accomplishment, we plan to further modify the peptide to improve the physical and chemical properties of our non-viral nanoparticles such that they entrap and deliver entire genes into cells and organisms.

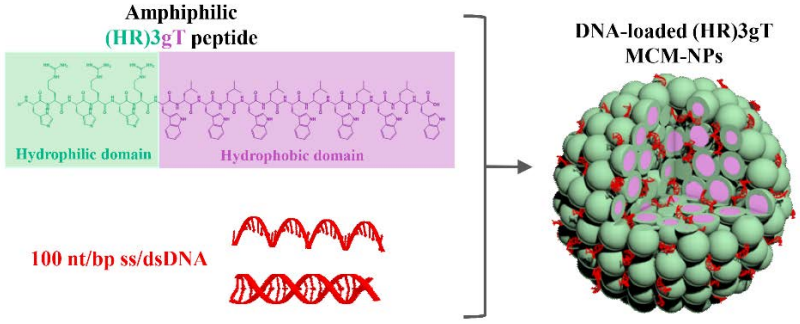

Fig. 1: Schematic representation of the amphiphilic peptide (HR)3g and its self-assembly into multicompartment micelles while condensing DNA through electrostatic interactions.

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Bioactive catalytic nanocompartments integrated into cell physiology and their amplification of cGMP signaling cascade

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Cascade reactions can take place also when the enzymes are compartmentalized in nanometre-sized polymersomes (catalytic nanocompartments, CNC) and can add novel functions to cells. However, to this day, nonanometre-sized object has been used to activate cell-specific pathways. Inducible nitric oxide synthase (iNOS) uses argine to produce nitric oxide, which in turn activates soluble guanylyl cyclase (sGC) to produce cyclic GMP, a second messenger molecule that activates a plethora of cellular responses. By encapsulating the enzymes in PMOXA-b-PDMS-b-PMOXA polymersomes, we produced iNOS-CNC and sGC-CNC, operating in a cascade. We monitored their enzymatic activity both in bulk and with cells, showing how such messenger can be produced and modify the flow of Ca^{2+} into HeLa and C2C12 cells, a fundamental player in cell physiology.

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