Project Description – Project Proposal

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Wetting of bio-inspired, stimulus-responsive polymer surfaces by lipid vesicles

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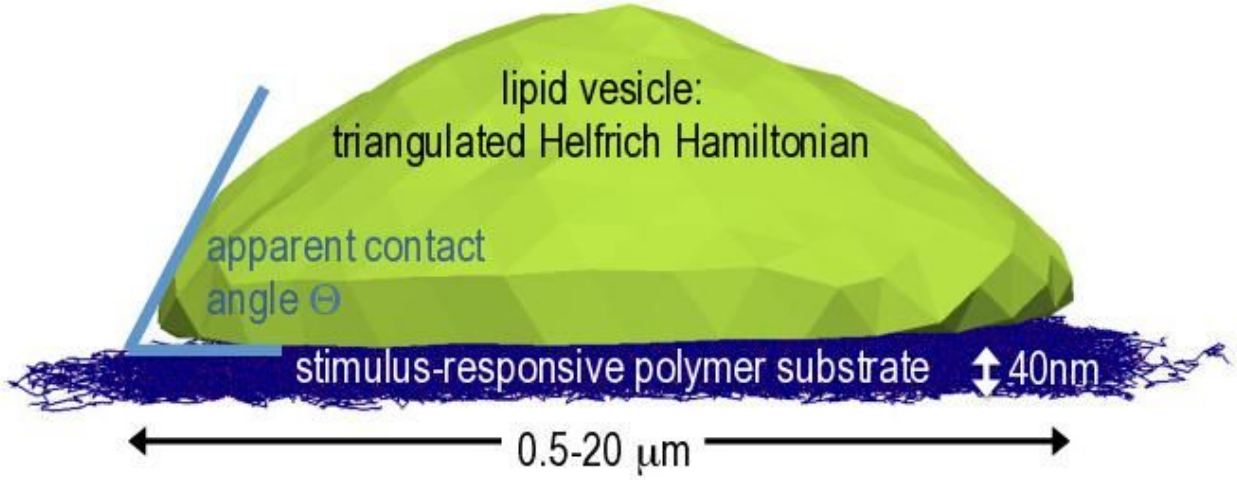


Abstract

The fabrication of switchable interlayers between soft, biological objects and hard solids is one of the major challenges to dynamically regulate the interfacial interactions. In the proposed project, the applicants with strong expertise in theoretical (Müller) and experimental (Tanaka) soft-matter physics will investigate the wetting of bio-inspired, stimulus-responsive polymer substrates by lipid vesicles. In analogy to the wetting by liquid drops, the shape of a vesicle is dictated by the enclosed volume, the membrane-substrate interaction (interface potential), and the properties of the interface (membrane) between the interior and exterior. Unique to wetting by flexible vesicles is the importance of the membrane's bending rigidity in addition to its tension.

The Tanaka group will fabricate and characterize stimulus-responsive substrates based on polymer brushes inspired by naturally occurring proteins in plants. The abrupt change in polymer conformation is followed by dynamic changes in the wetting behavior of lipid vesicles. By the combination of various experimental techniques, the Tanaka group will experimentally monitor the dynamic changes in the global shape of the vesicles (apparent contact angle), vesicle footprint (contact zone), membrane height fluctuations (interfacial potential), and hydrodynamics inside the vesicles. This line of study will be extended to the dynamic wetting on heterogeneous substrates displaying stimulus-responsive and stimulus-inert brushes and the time-periodic switching of the substrate.

The Müller group will complement these experiments by simulations of the dynamic wetting of switchable, deformable polymer substrates by lipid vesicles. To reach the spatio-temporal scales of the experiments, the switchable polymer brush is modelled by a highly coarse-grained particle model whereas the vesicle membrane will be represented by a triangulated sheet within the framework of the Helfrich Hamiltonian. Studying the equilibrium shape of the vesicle, we will determine the interface potential and apparent contact angle, which is required as input into continuum models and will serve to adjust the model parameters to the experiment. Then, we will study the shape change after switching and time-periodic modulation of the wetting properties, which results from a strong coupling between the reversible changes of the substrate wettability, the dynamics of the lipid membrane, and the hydrodynamics of the solvent. Systematically studying the size-dependence of the different dissipation mechanisms we will compare the simulation results of (small) vesicles with the experimental data.

Project Description

1 State of the art and preliminary work

The design of adaptive interlayers between synthetic substrates and soft biological matter is a cross-disciplinary challenge. Controlling and switching of soft biological objects like vesicles and cells is important *inter alia* for sensing and transport. In analogy to wetting of simple liquids on a solid substrate, one can tailor the adhesion of a vesicle by designing the substrate interactions, and the free energy of contact between the substrate and the biological object influences the shape of the vesicle. Similar to the shape of liquid drops on substrates, the shape of a vesicle is dictated by the enclosed volume, the membrane-substrate interactions quantified by the interface potential, and the properties of the interface between the interior and exterior. In the case of a vesicle, that interface is a lipid bilayer characterized by its tension, γ, and additionally by its bending rigidity, κ [1-3].[1] The interface potential, *g(h)*, that quantifies the free energy of placing a unit area of the membrane a distance, *h*, away from the synthetic substrate is characterized by a subtle interplay of short- and long-range forces as well as specific interactions, e.g., due to adhesion proteins or hydrated layers of biopolymers. Thus, the (equilibrium) behavior of vesicles on synthetic surfaces can be conceived as a generalization of wetting phenomena, known from simple liquids on hard, solid substrates.

Towards the control of interactions at biological interfaces, one of the sophisticated approaches consists in employing polymer substrates, whose wetting properties can be modulated by external stimuli. In this context, polymer brushes and gels that can reversibly switch their physical properties (hydrophilicity, molecular conformations and morphology, density of cross-linkers, etc.) have attracted abiding attention [4-6,M1,M2]. These switchable substrates can expose or hide functional moieties or lateral domains (e.g. of microphase-separated polymer components or adhesion ligands) that preferentially interact with the soft biological objects in response to external stimuli (such as temperature, pH, ions or specific ligands) or in response to the contact with vesicles themselves. For example, Okano and his co-workers demonstrated non-invasive harvesting of cell sheets from substrates using thermo-responsive, low critical solution temperature (LCST) polymers, such as poly(N-isopropylacrylamide) [7]. However, the switching of LCST polymer films resulted in the detachment of not only a confluent cell monolayer but also the entire polymer support.

The flexible, deformable vesicle, in turn, will adapt its shape in order to balance the free-energy costs due to the membrane deformation (bending) and the free-energy gain by the polymer-membrane interaction [8-10,M3]. Such a reversible switch of the substrate-vesicle interaction will induce a shape change of the soft biological object that is strongly coupled to the switch of substrate properties [11,12]. Varying the degree of polymerization of the substrate, the size or properties (tension and bending rigidity) of the soft biological object, or the viscosity of the solvent, we can tune the time scale of the wetting dynamics, and we anticipate a rich dynamic interplay between the switching of the substrate properties and the concomitant adaptation of the soft biological object. Moreover, time-periodic switching of the polymer substrate and the concomitant interaction between polymers of the substrate and vesicle can introduce additional non-equilibrium phenomena such as e.g., an increased diffusivity of the adsorbed objects [13].

The goal of our joint, simulation and experimental project consists in studying the shape of vesicles and its dynamic response to switches of the polymer substrate. Our investigation will provide physical insights into the statics and dynamics of wetting of vesicles as a function of their size and mechanical properties and establish a connection to continuum modelling.

The Tanaka lab has utilized a variety of stimulus-responsive polymer brushes and hydrogels and investigated the modulation of polymer chain conformation, viscoelasticity, and wetting/adhesion interactions with lipid membranes and living cells [14]. Previously, in collaboration with S.P. Armes (Chemistry, Univ. Sheffield, UK), they fabricated 5 – 10 nm-thick

[1] A similar description also applies to surfactant-laden liquid-vapor interfaces where the surfactant reduces the interface tension and, in turn, increases its bending rigidity.

films of amphiphilic diblock copolymers containing a poly(diethylaminomethacrylate) block on Si substrates (Fig.1a), and monitored the reversible switching of thickness, density, and Gaussian roughness of polymer brushes under mild pH modulations by using specular neutron reflectivity (Fig. 1b) [15]. In fact, the selective deuteration of the basement layer made out of polymethylmethacrylate (PMMA) and the lipid membrane unraveled that the distance between the lipid membrane and the substrate was switched by a factor of two. By using lipopolymer tethers with tunable thickness (in collaboration with R. Jordan, TU Dresden) [16,17] (Fig. 1c) and cellulose cushions [18] (Fig. 1d), the Tanaka lab quantitatively determined how the interface potential (or, equivalently, disjoining pressure) can be modulated by the fine-adjustment of polymer interlayers. The simulation of deconvoluted disjoining pressures actually demonstrated that the counterbalance of van der Waals attraction and hydration repulsion plays key roles rather than the membrane undulation force described by Helfrich [19].

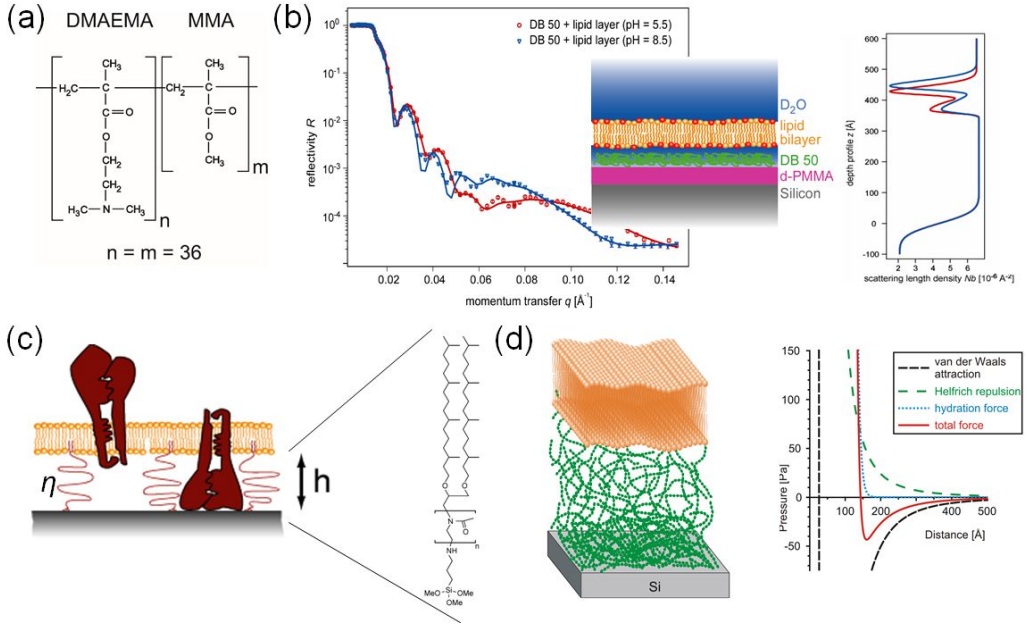


Fig. 1. (a) pH responsive diblock copolymer [T2]. (b) Reversible switching of polymer-membrane contacts detected by specular neutron reflectivity [T2]. (c) "Tethering" of lipid membranes by using poly(oxazoline)-based lipopolymers [16,17]. (d) Interplay of van-der-Waals attraction, Helfrich repulsion [10], and hydration repulsion to determine the equilibrium membrane-substrate distance [T1, 18].

Extending this strategy, the Tanaka lab designed stimulus-responsive hydrogels based on ABA triblock copolymers containing a di(isopropylaminomethacrylate) block, and investigated the interactions with cells [20] (Fig. 2a). Here, to ensure that cells feel the elasticity of hydrogels but not that of the underlying substrate, the film thickness was increased to several μm. We demonstrated that the switching of the degree of ionization of di(isopropylamino) groups resulted in the change in the elastic modulus by a factor of 20 (Fig. 2b), which enables to reversibly switch the cell morphology (Fig. 2c) [20]. Along this line, the Tanaka lab has designed a new class of substrates based on hydrogels in collaboration with M. Nakahata and A. Harada (Chemistry, Osaka Univ., Japan) [21]. These hydrogels are cross-linked by host-guest interactions between β-cyclodextrin and adamantane [22], which can be softened or stiffened by the addition and removal of host- and guest molecules in solution [T5].

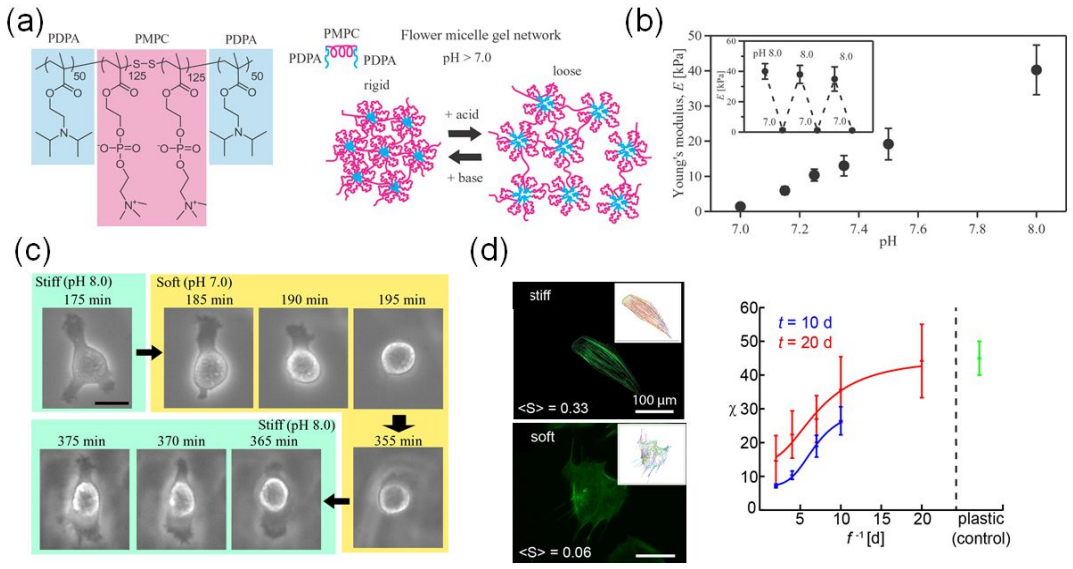
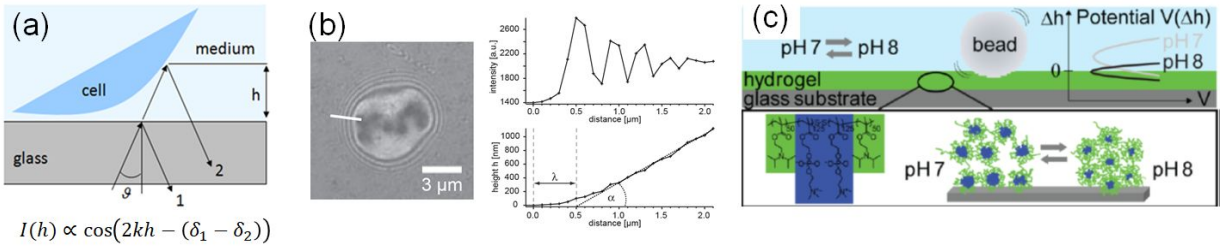


Fig. 2. (a) Physically cross-linked hydrogels based on pH responsive triblock copolymers [20]. (b) Reversible switching of Young's modulus detected by AFM indentation. (c) Reversible switching of cell morphology by changing the substrate elasticity [20]. (d) Frequent changes in the substrate elasticity significantly suppressed the cell division with no loss of multipotency [23].

One of the key biomedical applications of stimulus-responsive hydrogel substrates is to dynamically regulate cell functions. A recent work with A.D. Ho (Hematology, Heidelberg University) has demonstrated that frequent changes in the substrate elasticity mechanically stress human mesenchymal stem cells, suggesting the presence of critical stress frequency, beyond which human stem cells stop proliferation without loss of multipotency (Fig. 2d) [23].



$$I(h) \propto \cos(2kh - (\delta_1 - \delta_2))$$

Fig. 3. (a) Principle of reflection interference microscopy. (b) Reconstructed height profile of a giant vesicle [25]. The length scale, on which the membrane shape is dominated by the elasticity λ, is indicated. (c) Reversible switching of the interface interaction potential V(h) by using pH responsive hydrogels [27].

The Tanaka lab also has a strong expertise in experimentally characterizing interactions of not only cells but also lipid- and lipopolymer vesicles with "soft" substrates, including supported membranes and polymers. One of the key techniques is a label-free microinterferometry, called reflection interference microscopy (RICM, Fig. 3a [24]). The monochromatic light reflected at interfaces with high contrasts in refractive indices causes interference. In case two reflections are dominant, the detected light intensity is given as a function of distance between two interfaces, $I(h) \propto \cos(2kh - (\delta_1 - \delta_2))$, where k is the order of interference and δ the phase shift. This enables one to reconstruct the local 3D profile and hence the apparent contact angle of vesicle and cell membranes [25], yielding the adhesion free energy via a modification of the classical Young's equation that takes the elasticity-dominated deformation of cell membranes into account (Fig. 3b) [26].

Moreover, by monitoring the distribution function, $P(h)$, of the height of a latex particle undergoing a vertical Brownian motion, we have calculated the interface potential within the inverse work functional theorem, $g(h) \sim -kT \ln P(h)$ (Fig. 3c, [T4]). In our previous account [27], we demonstrated that the switching of the degree of ionization of di(isopropylamino) groups resulted in an increase of the curvature of the interface potential g"(h) by almost a factor of three.

The Müller group has developed simulation techniques to compute the interface and surface tensions and the interface potential as well as to accurately locate the wetting transition via (semi)grandcanonical simulations of polymer liquids and binary polymer blends [28,29]. Using computer simulation as well as polymer density functional theory [30,31] we have studied wetting of polymer liquids on polymer brushes of chemically identical species (autophobicity) [32].

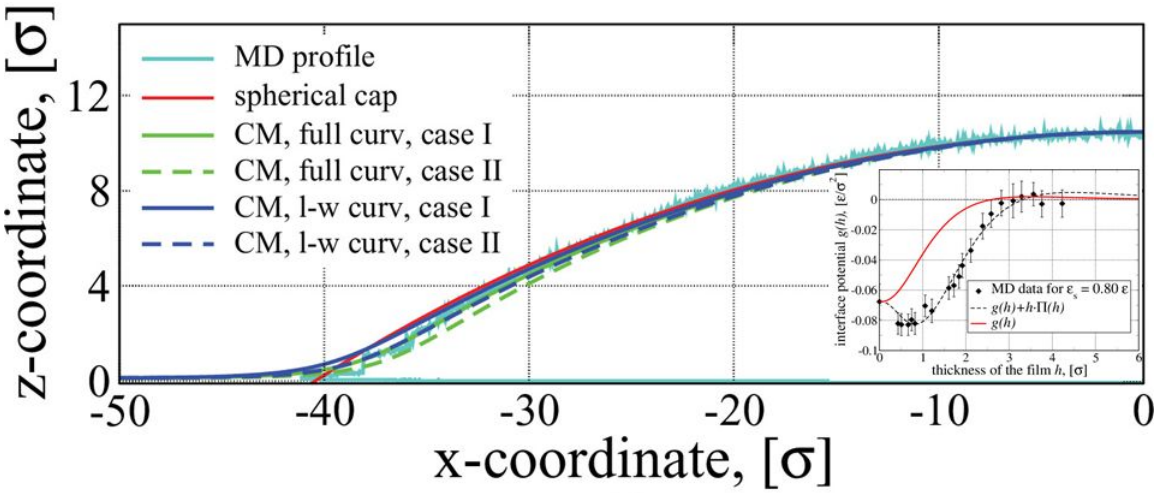


Fig. 4. Droplet profiles of a Lennard-Jones fluid on a substrate. The solid curve (light blue) presents the liquid-vapor interface as obtained by MD simulation, whereas the gray solid curves (red) depicts the corresponding spherical cap fit. Results of the continuum model using the full curvature Hamiltonian and the long-wavelength approximation are indicated by solid and dashed lines, respectively. Case I refers to the interface Hamiltonian that uses the liquid-vapor surface tension γ as prefactor of the interface area, whereas the prefactor is $\gamma+g(h)$ in case II. The inset demonstrates how to compute the interface potential, $g(h)$, from MD simulations by measuring the anisotropy of the pressure. Note that the interface potential adopts its minimum at $h=0$, *i.e.*, there is no precursor film. Adapted from [M4]

More recently we devised techniques to obtain the interface potential from measurements of the pressure anisotropy that is accessible by canonical molecular dynamics simulations. Fig. 4 illustrates the quantitative comparison of droplet shapes between particle-based simulations and continuum models in collaboration with U. Thiele (Münster University) [M4].The wetting of liquids on soft, deformable substrates, e.g., polymer brushes, has also been studied by molecular simulations of Lennard-Jones liquids. Fig. 5 shows the ridge formation of a droplet on a polymer brush [M5].

To bridge between molecular simulations of flow and transport and a continuum description, the Müller group has devised techniques to extract the hydrodynamic boundary condition for flow past surfaces [33], demonstrated the failure of the Navier-slip condition for attractive surfaces [34], and studied the motion of polymer drops and the size-dependence of the concomitant dissipation mechanisms under an external body force (gravity) [35]. Such a finite-size study allows to separate different dissipation mechanisms and permits us to extrapolate the simulation results for the small droplet sizes of the simulation to experimentally relevant sizes. We have extended these studies to polymer droplets on topographically structured [36] and vertically vibrating substrates [37].

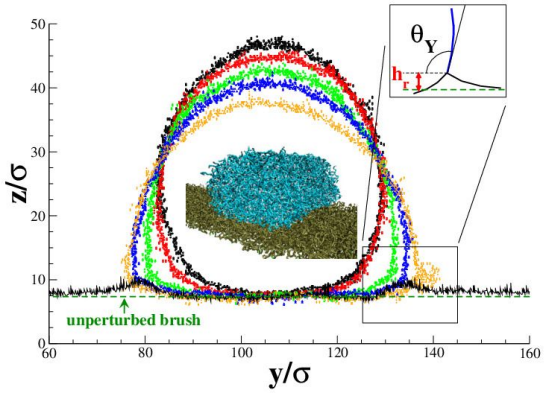


Fig. 5. Droplet profile of a Lennard-Jones polymer liquid, *N=10*, on a brush-coated substrate, *N=40*, as a function of the incompatibility between liquid and brush. The dashed line represents the average free surface position of the unperturbed brush. The lifting-up of the contact line and the formation of a ridge is visible. Right inset: Sketch of the procedure used to extract the equilibrium wetting contact angle and the lifting-up. Center inset: Configuration snapshot of a liquid drop (blue) on a brush-coated substrate (dark green). Adapted from [M5]

Additionally, we have studied the formation of supported monolayers by spreading of vesicles on hydrophilic substrates. Depending on the strength and range of membrane-substrate interaction we observed different spreading mechanism (c.f. Fig. 6) that differed in the orientation of the resulting bilayer (inside-up *versus* outside-up) [M3].

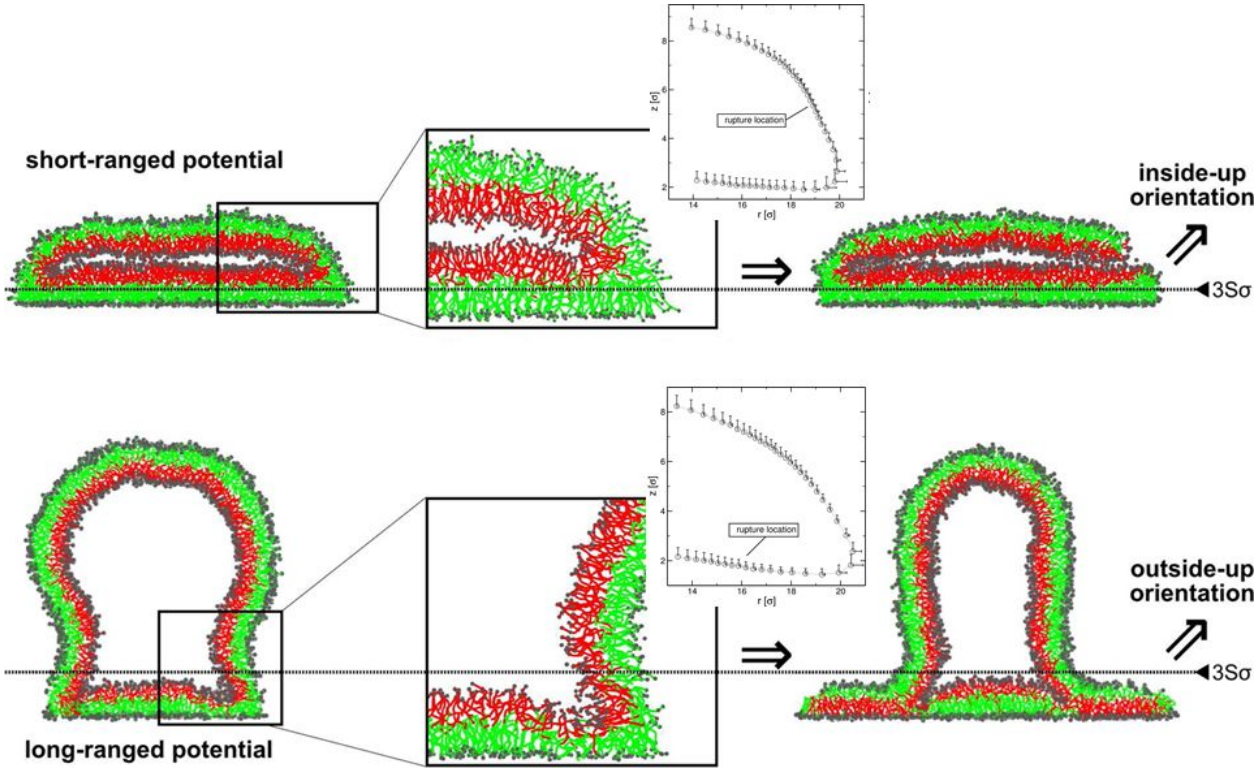


Fig. 6. Spreading of lipid vesicles on hydrophilic substrates. Gray circles represent lipid head groups, and red and green lines represent lipid tails from the inner and outer monolayer, respectively. The snapshots illustrate the decisive role of interaction range for choosing the spreading pathway and the corresponding orientation of the resulting supported lipid bilayer. Shown are rupture at the side of the vesicle's top at short potential range (top, receding-top mechanism) and poration in the vesicles bottom at long potential range (bottom, parachute mechanism). The ranges of the vesicle-substrate potentials are indicated by the horizontal, dashed, black lines. The insets quantify the shape of the outer edge of absorbed vesicles prior to rupture. The points mark the location of the midplane of the bilayer, vertical bars quantify the thickness of the hydrophobic core, and horizontal bars indicate the curvature found at the respective points. Adapted from [M3]

In collaboration with M. Stamm (IPF Dresden), K. Hinrichs (ISAS, Berlin), S. Minko (University of Georgia at Athens, USA), und I. Luzinov (Clemson University, USA), and A. Revzin (UC Davis), the Müller group has studied the stimulus-response of binary homopolymer brushes and copolymer brushes as model systems for controlling the interactions of biopolymers, particles

and cells with substrates. These studies focused on equilibrium properties of the brush substrate [38-42] and only modeled the adsorbate either as a point particle [M1] or a flat, infinitely extended surfaces [M2] as illustrated in Fig. 7. While these past works illustrate our interest and experience, the present proposal goes significantly beyond the previous scope because (i) the vesicle adapts its shape to the switchable polymer substrate and (ii) the focus lays on the dynamics of switching and concomitant shape adaptation.

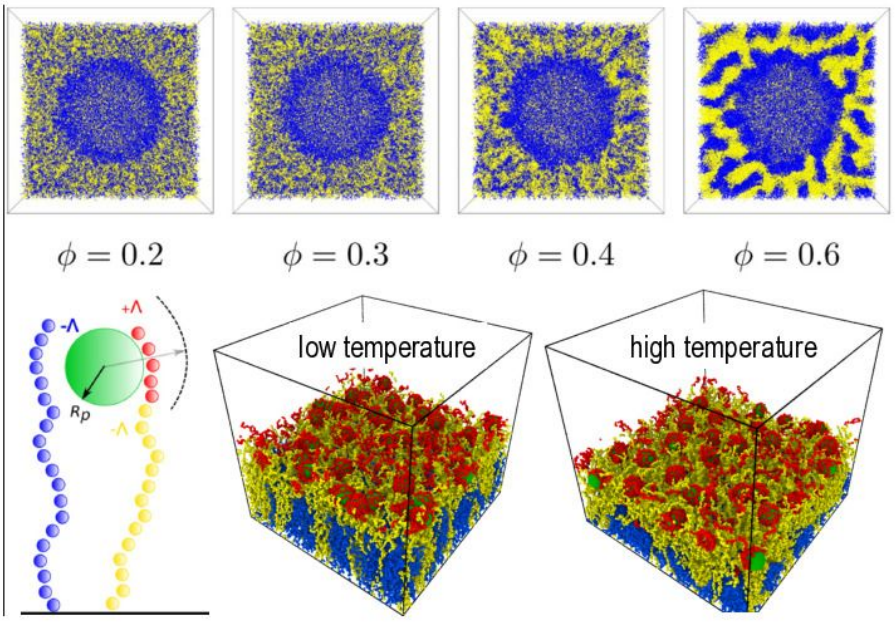


Fig. 7. Top row: Top views of the response to a spot pattern applied to the top of a mixed brush as a function of the fraction of composition. The interactions mimic a polystyrene(PS, blue)-polyarylicacid(PAA, yellow) mixed brush in the cosolvent, dimethylformamide (DMF). The pattern consists of a surface that is neutral decorated with a PS-attractive spot of radius $4R_e$. In contact with the non-preferential top surface, the mixed brush exhibits lateral segregation into PS-rich and PAA-rich domains. Underneath the PS-attractive spot, however, the brush adopts a layered sandwich morphology. Bottom row: left – Sketch of the interaction of a nanoparticle with a mixed PAA (yellow)-poly(N-isopropylacrylamide)(PNIPAm, blue) brush. The PS chains are functionalized at their ends with a block (red) that attracts the nanoparticle. The snapshots display configurations at low and high temperature where the PNIPAm chains (blue) are expanded or collapsed, respectively. Adapted from [M1,M2]

Despite of the accumulated knowledge on both, experimental and theoretical sides, a comprehensive understanding how such switchable/adaptable polymer substrates influence the shape and dynamics of lipid vesicles is still missing. The priority program SPP 2171 *Dynamic wetting of flexible, adaptive, and switchable substrates* offers a scientific environment to systematically explore these biological model systems and compare their shape dynamics on switchable surfaces to related non-equilibrium wetting phenomena of liquids (e.g., motion of droplets on polymer brushes).

1.1 Project-related publications

1.1.1 Articles published by outlets with scientific quality assurance, book publications, and works accepted for publication but not yet published.

[M1] F. Léonforte and **M. Müller**, Functional Poly(N-IsoPropylAcrilaMyde)/Poly(Acrylic Acid) mixed brushes for controlled manipulation of nanoparticles*, Macromolecules* **49**, 5256 (2016)
[M2] F. Léonforte and **M. Müller**, Morphology modulation of multi-component polymer brushes in selective solvent by patterned surfaces**,** *Macromolecules* **48**, 213 (2015)
[M3] M. Fuhrmans and **M. Müller**, Mechanisms of vesicle spreading on surfaces: Coarse-

grained simulations*, Langmuir* **29**, 4335 (2013)
[M4] N. Tretyakov, **M. Müller**, D. Todorova, and U. Thiele**,** Parameter passing between Molecular Dynamics and continuum models for droplets on solid substrates, *J. Chem. Phys.* **138**, 064905 (2013)
[M5] F. Léonforte and **M. Müller**, Statics of polymer droplets on deformable surfaces, *J. Chem. Phys.* **135**, 214703 (2011)
[T1] **M. Tanaka**, E. Sackmann, Polymer Supported Membranes as the Model of Cell Surfaces, *Nature* **437**, 656-663 (2005).
[T2] F. Rehfeldt, R. Steitz, R. von Klitzing, S.P. Armes, A.P. Gast, **M. Tanaka**, Reversible Activation of Diblock Copolymer Monolayers at the Interface by pH Modulation, 2: Membrane Interactions at the Solid/Liquid Interface, *J. Phys. Chem. B* **110**, 9171-9176 (2006).
[T3] E. Schneck, T. Schubert, O. Konovalov, B. Quinn, T. Gutsmann, K. Brandenburg, R.G. Oliveira, D.A. Pink, **M. Tanaka**, Quantitative determination of ion distributions in bacterial lipopolysaccharide membranes by grazing-incidence X-ray fluorescence, *Proc. Natl. Acad. Sci*. **107**, 9147-9151 (2010).
[T4] Y. Higaki, B. Fröhlich, A. Yamamoto, R. Murakami, M. Kaneko, A. Takahara, **M. Tanaka**, Ion-Specific Modulation of Interfacial Interaction Potentials between Solid Substrates and Cell-Sized Particles Mediated via Zwitterionic, Super-Hydrophilic Poly(sulfobetaine) Brushes, *J. Phys. Chem. B.* **121**, 1396-1404 (2017).
[T5] M. Hörning, M. Nakahata, P. Linke, M. Veschgini, S. Kaufmann, Y. Takashima, A. Harada, **M. Tanaka**, Dynamic Mechano-Regulation of Myoblast Cells on Supramolecular Hydrogels Cross-Linked by Reversible Host-Guest Interactions, *Sci. Rep.* **7**, 7660 (2017).

1.1.2 Other publications

1.1.1 Patents

1.1.2.1 Pending

none

1.1.2.2 Issued

[a] M.P. Stoykovich, H. Kang, K.Ch. Daoulas, J.J. de Pablo, **M. Müller**, and P.F. Nealey, *Methods and compositions for forming patterns with isolated or discrete features using block copolymer materials*, US 8133534 B2, US 8501304 B2
[b] P.F. Nealey, M.P. Stoykovich, K.Ch. Daoulas, **M. Müller**, J.J. de Pablo, and S.M. Park, *Fabrication of complex three-dimensional structure based on directed assembly of self-assembling materials on activated two-dimensional templates,* US 8168284 B
[c] R. Shenhar, P.F. Nealey, **M. Müller**, and K.Ch. Daoulas, *Quasi-block copolymer melts, processes for their preparation and uses thereof,* US 9181403 B2

2. Objectives and work programme

2.1 Anticipated total duration of the project

6 years in total

DFG funds will be necessary for the entire duration. The present proposal details our plans for the first funding period of 3 years. Intended project start is October 2019

2.2 Objectives

By uniting the experimental and theoretical expertise of our two groups, we will investigate the static and dynamic wetting of lipid vesicles on bio-inspired, stimulus-responsive polymer substrates. The goal of our project consists in understanding the fundamental aspects of wetting for a prototypical model system -- lipid vesicle -- that is not only characterized by tension but additionally by bending rigidity. First, we will characterize the shape of the vesicle in contact with the switchable and deformable polymer substrate and extract the parameters (i.e., interface potential) for describing it within continuum models. Second, we will study the dynamics of shape changes after sudden switches or time-periodic modulation of the substrate properties.

Systematically varying the size and mechanical properties, γ and κ, of the vesicle, we will distinguish the different dissipation mechanisms and bridge between the small accessible vesicle sizes in the simulation and the μm-sized vesicles in the experiment. Extensions to laterally inhomogeneous substrates (e.g., via lateral phase separation in multi-component polymer brushes or gels) will be also considered. Through our joint, experimental and theoretical collaboration, we will obtain physical insights of the key factors that control the dynamics of vesicles on switchable surfaces as a function of the vesicle properties. These simulation and experimental results enable a comparison to analytic continuum theory (e.g., in order to highlight the similarities and differences to the wetting dynamics of liquids) and may guide the design of switchable substrates for sensing or separating vesicles as a function of their size or bending rigidity.

Within the framework of the priority program SPP2171, we will address the following questions:

a. How are the thickness and perpendicular profiles as well as the lateral structure of the switchable polymer substrate modulated by an external stimulus?
b. How does the contact of the adsorbed vesicle alter the substrate properties of the adaptable polymer substrate? On which time scales do these adsorption-induced changes occur? How deep into the substrate do they reach?
c. How is the shape of the adsorbed vesicle influenced by stimuli-response of the brush substrate?
d. How does the shape and lateral position of the vesicle respond to a sudden switch of the substrate properties?
e. Does the periodic switching of the surface-vesicle interactions induce an active deformation and motion of the vesicles? Can one exploit this effect to sort vesicles according to size or stiffness?
f. Can a gradient of thickness, density, or viscoelasticity of the brush induce directed transport?

2.3 Work programme incl. proposed research methods

The Tanaka group will utilize their expertise in interface physics and will design stimulus-responsive polymer brushes and gels, whose physical properties can be reversibly switched by modulating the degree of ionization, density of ion-bridges and host-guest pairs.
The Müller group will use their expertise in modeling stimuli-response brushes and combine it with a Helfrich-Hamiltonian description of lipid vesicles to study the wetting dynamics (shape deformation, adsorption/desorption, as well as lateral motion) in response to a sudden switch or a time-periodic modulation of the interface potential between the brush-coated substrate and the soft, deformable vesicle. The simulations will provide guidance to the experimental study and make connection to other groups in the priority programme that use effective interface-Hamiltonians to describe the dynamics of soft objects (e.g., droplets or gels) on switchable substrates.
Our joint project exploits the length and time scale separation between lipid membrane, brush substrate, and vesicle shape. The thickness of the lipid membrane, approx 3 nm, sets the smallest length. Since we do not consider changes of the membrane topology (e.g., poration or spreading) we will not describe the details of the lipid self-assembly and conceive the lipid membrane as a thin, elastic sheet that is characterized by its tension and bending rigidity. Such a Helfrich description [1-3] can be augmented by a laterally inhomogeneous composition in case of multi-component membranes or the local, lateral concentration of adhesion proteins.
The next length scale is the thickness of the stimulus-responsive brush substrate, approx. 40 nm. Since wettability us dictated by the immediate contact between the top of the polymer brush and the vesicle, which can be switched by an external stimulus, we will describe the polymer substrate by a highly coarse-grained model that allows us to describe the change of the perpendicular and lateral brush structure, and thereby the wettability changes. If the grafting

points of the polymer brush are immobile, switching involves molecular rearrangements on the scale, R_e, of a polymer and occurs within less than a second.[2]
The lateral extension of the adsorbed vesicle is large, i.e., micrometers, and the concomitant time scale of shape changes is on the order of minutes. These scales are conveniently accessible by optical microscopy, and they are separated from the scales of the switching of the brush substrate. In the simulation the large scale of the vesicles is a challenge, and we will (i) systematically study the size dependence of the vesicle response and extrapolate the finite-size simulation data to the experimentally relevant regime and (ii) replace the brush substrate by an effective interface potential. Eliminating the brush-scale will allow us the access larger time and length scales.

WP T1: Fabrication and Characterization of Stimulus Responsive Polymer Brushes
For polymer brush systems, we plan to focus on polymer brushes inspired by natural proteins existing in plants, called phytochelatin, which captures divalent heavy metal ions via an extremely high affinity, $K_D \sim 10^{-17}$ M. The extremely high sensitivity is realized by the multivalent binding to thiol and carboxyl side chains. Our collaborating partner, M. Nakahata (Chemistry, Osaka Univ., Japan), has synthesized polymers possessing both carboxyl and thiol side chains (Fig. 8a).

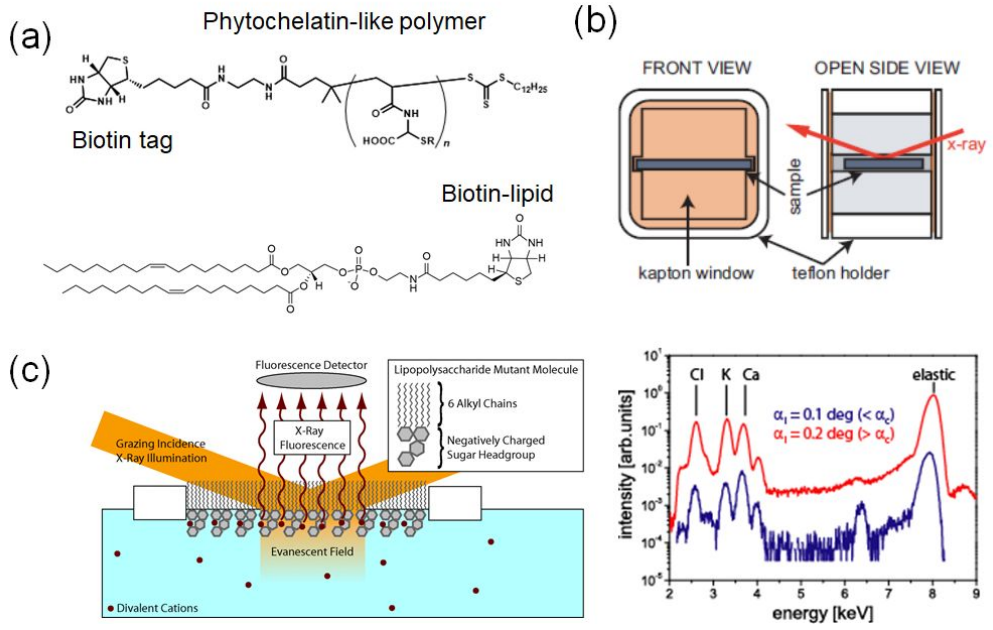


Fig. 8. (a) Stimulus-responsive polymer brushes used in the proposed project. The materials are available in Tanaka Lab. (b) Sample environment for high energy specular X-ray reflectivity measurements. Use of Mo Kα (17 keV) allows the measurements under water. (c) Grazing incidence X-ray fluorescence at the air/water interface. Coupling to anchor lipids enables the precise localization of specific ions in the vicinity of interface (Δz = ± 3 Å).

We will graft polymer chains onto the supported membranes displaying well defined surface density of high-affinity anchors. As indicated in Fig. 8a, the polymer terminated with biotin (biotin tag) will be anchored to the biotin head group of the anchor lipid via a neutravidin cross-linker. This enables us to precisely control the surface density of pre-synthesized brushes precisely by adjusting the doping ratio and self-assembly of anchor lipids [38,39]. After membrane formation, the sample temperature will be decreased to room temperature that is well below the chain melting temperature of the matrix lipid (e.g. dipalmitoylphosphatidylcholine (DPPC) with T_m = 41 °C). Since the lateral diffusion of lipids in the gel phase below T_m is more than 2 orders of

[2] For mobile grafting points, lateral phase separation inside of the brush may occur on macroscopic length scales, which involves significantly longer time and larger length scales.

magnitude smaller than that in fluid phase, one can assume that the grafting point is “immobile”. This helps us stay consistent with the time window of theoretical models.[2]
In the first step of characterization, the homogeneous grafting of stimulus-responsive brushes will be verified by atomic force microscopy and spectroscopic ellipsometry. Changes in polymer conformation (thickness and density profile) will be monitored by specular neutron reflectivity and high energy X-ray reflectivity. Neutron reflectivity, performed at D17 and FIGARO beamlines (ILL, Grenoble) allows us to highlight subtle changes in degree of hydration and thickness/roughness variation by using D_2O as solvent. On the other hand, as we have demonstrated in our previous work [18], high energy X-ray reflectivity, performed at ID10 and ID33 beamlines (ESRF, Grenoble) or using an in-house instrument with Mo Kα source, is a powerful tool to probe the interface buried under bulk water owing to a high transmittance of the high-energy X-ray beam (Fig. 8b).
For the polymer brushes mimicking phytochelatin, we will measure the density profile and binding stoichiometry of divalent metal ions captured by the brush by grazing-incidence X-ray fluorescence measurements at ID10 beamline (ESRF, Grenoble, Fig. 8c [T3]). Following our previous studies [40], we will take Co-Kα (6.93 keV) or Ni-Kα (7.48 keV) as the target core levels by considering the sensitive energy range of the fluorescence detector available at ESRF.

WP M1: Modeling of conformational changes of stimulus-responsive polymer brushes
In this work package, the Müller group will use a soft, highly coarse-grained polymer model, where the nonbonded interactions are described by a free energy as a functional of the local densities. This model has previously been utilized to study one-component polymer brushes, copolymer brushes, and mixed brushed comprised of two homopolymer species [41-45, M1,M2]. In contrast to these previous studies, we will use an explicit solvent that will be represented by soft DPD particles. The non-bonded interactions along the polymer are harmonic bonds. These define the polymer architecture, and we will consider linear brushes as well as crosslinked gels. We will adjust the model parameters, the effective virial coefficients of the free-energy functional, and the grafting density to mimic the behavior of the specific, experimental system. In particular we will focus on describing the changes of the density profile as a function of the distance from the grafting surfaces as well as the molecular conformations under good and poor solvent conditions, and delineate parameter regimes, where the brush collapses homogeneously or form dimples. Moreover we will consider two-component brushes that will exhibit lateral structure formation. In this WP we will also study the mixtures of stimulus-responsive and inert brushes describe in WP T3. In addition to these equilibrium properties of the brush-coated substrates or gels, we will study the kinetics of switching between different substrate states. This initial work package also serves to establish a fruitful and efficient collaboration between the experimental and simulation groups.

WP T2: Dynamic wetting of Homogeneously Grafted Stimulus-Responsive Polymer Brushes with Lipid Vesicles
The wetting of stimulus-responsive, phytochelatin-mimicking polymer brushes with lipid vesicles will be studied by RICM as a function of Co and Ni ion concentrations. The change in brush conformation with (collapsed) and without ions (swollen) will be utilized to parameterize the non-bonded interactions in the simulation model. Here, we first investigate the dynamic wetting of polymer brushes during the vesicle-substrate contact in the collapsed or swollen state of the switchable substrate. If one considers the brush height (typically 5 - 50 nm), we expect that the switching of polymer chain conformation is complete within 1 - 10 s. Thus, in the next step, we will monitor how the dynamic wetting by lipid vesicles follows. As the typical time window for the vesicle shape change is 1 - 10 min, the time scale for the switching of substrates is by 1 - 2 orders of magnitude faster.

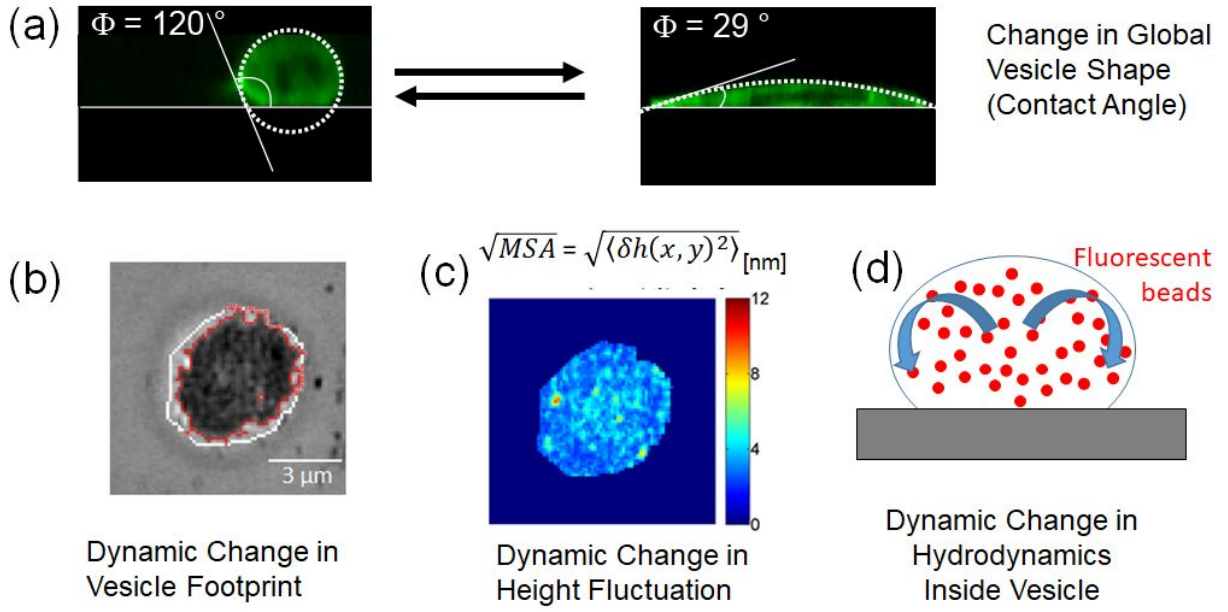


Fig. 9. Multiscale observation of dynamic wetting of switchable polymer substrates by lipid vesicles. (a) Dynamic change in the global shape and hence the contact angle can be monitored by confocal microscopy. (b) RICM intensity thresholding enables to follow the dynamic change in the vesicle footprint (contact zone). (c) Mean square amplitude (MSA) analysis enables to observe the transition between strong and weak coupling. From the probability function of the height, P(h), one can calculate the effective interfacial potential. (d) Dynamic changes in hydrodynamics inside vesicles will be followed by encapsulating fluorescent nanoparticles inside the vesicles.

Thus, in the next step, we will experimentally monitor how the dynamic wetting by lipid vesicles follows the abrupt switching of the polymer substrate. To comprehensively shed light on the finite-size effect together with the simulation by the Müller group, we will examine the influence of vesicle size on the wetting of vesicles. As pointed out in Sec. 2.2 Objectives, one of the uniqueness of our project is to study the wetting by lipid vesicles, whose deformation is not only dominated by tension but also by bending elasticity. Thus, in this study, we will fine-tune the bending rigidity of lipid vesicles by changing the lipid compositions, such as the mixing ratio of cholesterol, and measuring the bending rigidity from the thermal fluctuation of the shape, by so-called flicker spectroscopy.

The dynamic wetting of our switchable substrates with lipid vesicles will be assessed by the combination of various microscopy techniques, and directly compared to the simulations as described in WP M2. First, the dynamic change in the global shape of vesicles and hence the contact angle will be captured by confocal microscopy (Fig. 9a). Second, the dynamic change in the area of vesicle-polymer contact ("footprint" of vesicles) will be determined by RICM (Fig. 9b). From the reconstructed height profile of vesicle membranes in the close proximity of the surface, we can calculate the free energy of adhesion/wetting by taking the elastic deformation of lipid membranes into account (Fig. 3). The mean square amplitude (MSA) analysis (Fig. 9c) allows for the observation of transitions between weak and strong coupling. Moreover, from the probability function of height $P(h)$, we will calculate the dynamic change in interfacial potential within the framework of inverse work function theorem, $g(h) \sim - k_B T \ln P(h)$ [T4]. Last but not least, we will monitor the dynamic change in hydrodynamics inside the vesicles by incorporating latex nanoparticles labeled with fluorescence dyes (Fig. 9d). Since the characteristic timescale of the substrate switching is 1 - 2 orders of magnitude shorter than the dynamic adaptation of the shape of vesicles, we will investigate the dynamic change in the wetting of vesicles in response to the time-periodic switching of homogeneous polymer substrates, which is modeled in WP M3.

We would like to point out that these experimental readouts are fully complementary to the coarse-grained simulations of the Müller group.

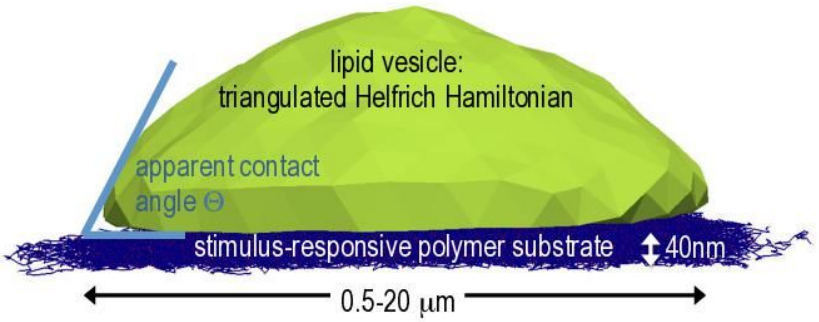


Fig. 10. Sketch of the modelling of a lipid vesicle on a stimulus-responsive polymer brush. The vesicle is represented by an interface Hamiltonian of Helfrich whereas the switchable polymer substrate is described by a particle model with soft interactions. Solvent particles are not shown. The apparent contact angle of the vesicle is indicated.

WP M2: Modeling of lipid vesicles on switchable, stimulus-responsive polymer brushes

Since the brush is significantly thicker than a lipid membrane and we need to access large spatial and long temporal scales we decided to model the lipid membrane of the adsorbed vesicle in the framework of a Helfrich Hamiltonian [1-3,46]. This level of description is appropriate because (i) we will not consider vesicle formation via the self-assembly of individual amphiphilic molecules (ii) nor do we investigate changes of the membrane topology such as fusion, fission, or pore formation. To this end, we will represent the vesicle membrane by a triangulated sheet. The energy of the vesicle configuration is comprised of the bonded interactions of the Helfrich Hamiltonian that characterize the membrane by its membrane tension and bending rigidity. Additionally, the model includes adhesive interactions of the nodes of the triangulated sheet with the components of the polymer brush. These nonbonded interactions can represent the interaction of the constituent lipids with the polymer substrate or localized, specific interactions due to adhesion proteins. To this end, the nodes of the triangulated membrane are characterized by an additional scalar variable that indicates the local lipid composition of the membrane (in case of two-component lipid mixtures) or the local density of proteins. A preliminary snapshot of a vesicle in contact with an attractive substrate is presented in Fig. 10. In our project, the vesicle will be “filled” with a DPD-like solvent. The interactions of this solvent will be soft enough to exploit the separation between the soft interactions among solvent particles and the stiffer interactions associated with the impenetrability of the membrane via a multiple time step integrator in our molecular dynamics simulation and hard enough to restrain changes of the volume enclosed by the vesicle.

After implementing and validating the vesicle model, we will study the shape of a vesicle in contact with the polymer substrate investigated in WP M1 and quantitatively compare our finding to the experimental measurements in WP T2. Particularly, we fill focus on two aspects: (i) the shape of the highly bent rim of the vesicle that corresponds to the three-phase contact line in wetting of a simple liquid and the concomitant deformation of the soft, deformable polymer substrate [47,48], and (ii) the role of spatial inhomogeneity of the interaction of the brush-coated substrate and the vesicle in the case that the brush exhibits lateral structure formation (i.e., dimples for a one-component brush in a poor solvent or microphase-separated domains in two-component brushes or gels). In the latter case, we expect that the soft polymer substrate will adapt to the contact with the vesicle and change its morphology [M2] and/or that the vesicle will slightly move to optimize its interaction with the laterally inhomogeneous adhesion pattern as observed for particles by Santer [13].

The goal of this WP consists in systematically studying the static wetting of vesicles on polymer substrates and optimize the properties of the brush (adhesion and lateral structure) and the vesicle (bending rigidity, strength and range of interactions *versus* local, mobile adsorption sites) to tailor the response of the vesicle shape over a broad range. The simulations will use model parameters that closely mimic the experimental system and contribute to tailor the experimentally accessible characteristics of the polymer substrate (grafting density, molecular weight, composition of two-component brushes or location of specific adhesion sites along the

molecular contour). Additionally, we will extract from the simulations the effective interaction between the vesicle and the substrate that is the analog of the interface potential in the wetting of simple liquids. Using this interface potential in conjunction with the Helfrich description (without brush) we will be able to describe the highly curved rim of the vesicle, whose shape is experimentally studied in WP T2 as well as the apparent macroscopic contact angle [9] that characterizes the shape on large scales. This quantity will allow us to make direct contact to continuum models that predict the shape of the vesicle by an interface Hamiltonian. Such an effective approach has proven extremely useful for the wetting of simple liquids [49,50], and in our project we will generalize it to membranes (i) whose tension depends on the shape of the vesicle because the membrane area will increase upon adsorption but the number of lipid molecules is conserved and (ii) whose free energy is not only dictated by the area of the membrane but also by its curvature. Using this description we expect to make contact to other groups in the SPP (e.g., Uwe Thiele) employing related interface-Hamiltonian approaches for equilibrium properties or thin-film equations for the wetting dynamics.

WP T3: Wetting of Dynamically Phase-Separated Polymer Brushes with Lipid Vesicles

In the next step, we will further extend the strategy to understand how the microphase separation of polymer brushes influences the dynamic wetting by lipid vesicles. The phase separation of polymer brushes can be achieved by mixing stimulus responsive brushes and brushes that are “inert” to stimuli. In the proposed project, we plan to use lipids coupled to poly(ethylenglycol) (PEG) chains with defined molecular weights, such as PEG2000 and PEG5000. These lipopolymers are commercially available. We prepare the membrane displaying the mixture of PEG-lipids and biotinylated lipid anchors (Fig. 8a) by the horizontal dipping of hydrophobic substrates into the water subphase (Langmuir Schaeffer transfer). Afterwards, stimulus responsive, phytochelatin-like brushes (Fig. 8a) will be harnessed via neutravidin cross-linkers. This enables us to precisely control the grafting densities of both stimulus-responsive and stimulus-inert brushes on the substrates.

During the first funding period, we will focus on microphase separation of “immobile” brushes by freezing the lateral diffusivity of anchor lipids. As stated in WP T1 and Footnote 2, macrophase separation induced by adhesion takes place on a much larger length scales and time windows compared to simulations. Instead, we will investigate the influence of chain length of inert PEG chains as well as the mixing ratio of stimulus-responsive and stimulus-inert polymer brushes on the dynamic wetting by lipid vesicles. As described in WP T2, the multiscale readouts in response to the abrupt switching of the substrates that we can extract are: (i) dynamic changes in the global shape and apparent contact angle of vesicles (Fig. 9a), (ii) dynamic changes in the vesicle footprint and adhesion free energy (Fig. 9b and Fig. 3), (iii) dynamic transition between strong and weak coupling and interfacial potentials (Fig. 9c), and (iv) hydrodynamic flow inside vesicles in response to switching (Fig. 9d). As described in WP T2, we will also investigate the dynamics of wetting in response to a time-periodic variation of heterogeneous polymer substrates, which will be modeled in WP M3.

These experimental results will be compared to the complementary simulation data of the Müller group from WP M3. This enables us not only to fine-tune the experimental systems from the feedback from the simulation but also to fine-adjust the simulations based on the experimental results. Such a seamless in-team collaboration is one of the strengths of our project.

WP M3: Modeling of dynamics of wetting in response of the vesicle shape to a sudden switch or a time-periodic variation of the adhesion properties of the stimulus-responsive brush substrate.

Having characterized the stimulus-responsive polymer substrate and the equilibrium wetting properties of the vesicle, we will study the dynamics of wetting. First, we will investigate how the shape of the vesicle changes after an external stimulus switched the adhesive interaction of the polymer substrate. Both, the spreading (wetting) of the vesicle in response to an increase of the adhesive strength, as well as the desorption (dewetting) of the vesicle after a decrease of

attraction will be studied. Here we will systematically study the system-size dependence of the dynamics because the different dissipation mechanism vary distinctly with the system size [35,37], and an understanding of this size-dependence is necessary to quantitatively compare the simulation data to the experimental results.
We expect an interesting interplay between the switching dynamics of the polymer substrate and the kinetics of shape changes of the vesicle – by increasing the molecular weight of the polymer and the decreasing size of the vesicle we can tailor the time scale of the two processes, respectively. Systematically varying the model parameters we aim at identifying conditions that allow for a selective desorption (dewetting) of vesicles as a function of their size or stiffness.
Second, we will study the response of the vesicle shape and position to multiple, time-periodic switches of the substrate adhesion. On the one hand, such a periodic variation allows us to study the frequency-response in this non-equilibrium steady state, i.e., instead of averaging over many stochastic realizations of the response to a sudden switch (as in the first part of this WP), we can average here along the time trajectory. This will facilitate the data analysis and allows us to study the interplay between the response-time scales of system, associated with the stimulus-responsive brush substrate, the vesicle shape and position, and the period of the external stimulus. If the brush is laterally inhomogeneous, the studies of Santer [13] on nanoparticles on stimulus-responsive brush substrates suggest that the particles optimize their position to locally maximize their adhesion. If the domain memory is sufficiently small, this enhances the diffusivity of the vesicles on the substrate. This enhancement will depend on the stiffness of the vesicles as well as the ratio between the vesicle size and the scale of lateral inhomogeneity of the brush.
The goals of this third WP are to (i) explore the wetting dynamics of vesicles on stimulus-responsive brush substrates and qualitatively correlate the different phenomena (wetting/dewetting, enhancement of diffusivity) with the molecular parameters of the polymer brush and the vesicle, (ii) to compare our findings to the experimental studies by systematically study the size-dependence of the vesicle shape and dissipation mechanisms and focus the experiments to parameter regions of particular interest (e.g., selective desorption of vesicles of a pre-determined size), and (iii) to make contact to effective continuum models that related phenomena for droplets (instead of vesicles) by providing input parameters such as the interface potential between the brush substrate and the vesicle as well as materials parameter such as the viscosity of the solvent and the hydrodynamic boundary condition.

Outlook: The wetting dynamics of vesicles on stimulus-responsive is very rich and potentially relevant for applications in sensing and analytics. In the first three years of the project we will focus on the basic physical phenomena using simple model systems. Depending on the progress within the first three years, various future research avenues can be envisioned. Here we briefly outline three that appear most exciting at present: (i) Combining the time-periodic switching with a gradient of the substrate properties we hypothesize that the cyclic switching can induce directed motion. The transport velocity will depend on the size of the vesicle, its bending rigidity as well as the properties of its interior. (ii) Adhesion between vesicles and substrates is often mediated via specific adhesion proteins that are mobile on the vesicle. Thus, not only the substrate can adapt to the presence of the vesicle but also the adhesion properties of the vesicle may adapt in response to the contact with the substrate. (iii) Instead of loading the vesicle with a viscous fluid, we could consider different fluids in the interior of the vesicle and the outside, or a viscoelastic or elastic medium. The latter mimics more closely the properties of a cell.

2.4 Data handling

Numerical data from computer simulation and experiments will be stored on the long-term archives of the Gesellschaft für wissenschaftliche Datenverarbeitung Göttingen (GWDG) or the Jülich Supercomputing Center (JSC). These computing centers offer the information technology

for safe, sustainable and accessible data storage according to the rules of the DFG and good practice.

2.5 Other information

None

2.6 Descriptions of proposed investigations involving experiments on humans, human materials or animals as well as dual use research of concern

None

2.7 Information on scientific and financial involvement of international cooperation partners

M. Nakahata (Osaka, Japan), Steven P. Armes (Sheffield, UK), A. Takahara (Kyushu, Japan), and S. Minko (Athens, Georgia, USA) have their own funding sources. Their projects focus more on the synthesis of substrate-coating materials and their application as sensors. As they are strongly interested in the physical interactions of soft, biological objects such as vesicles and cells in aqueous environments, we have agreed to collaborate by exchanging materials and provide guidance to their experiments. To facilitate collaboration, we apply for funds to host one of the collaborating partners for approximately 10 days every year.

2.8 Information on scientific cooperation within SPP 2171

The SPP 2171 offers a stimulating collaborative environment for our joint, experimental and simulation study of the dynamic wetting behavior of vesicles on stimulus-responsive polymer substrates because (i) the soft deformable and switchable polymer substrate, (ii) the comparison of the wetting dynamics of liquid objects with and without bending rigidity, and (iii) the multiscale experimental and simulation techniques to observe the wetting dynamics, connecting our microscopic model systems to an analytic continuum description, are central themes of the priority programme.

Specifically, we plan to continue our collaboration with the project of **Thiele** on parameter passing by extracting the interface potential between the switchable polymer substrate and the vesicle and explore within the full-curvature model the role of bending rigidity on the statics and dynamics of vesicles. The comparison with continuum modeling will be particularly instrumental to distinguish different dissipation mechanisms by systematically studying different vesicle sizes. With the project of **Schmid/Vollmer**, studying the wetting of droplets on polymer brushes and gels, we will exchange simulation and modeling techniques and compare the shape of droplets and vesicles on soft deformable substrates (e.g., ridge formation). The methods and technical challenges in both projects are similar and, therefore, we have agreed on a close collaboration including the exchange of students. With the project of **Speck/Virnau,** studying polymer-colloid mixtures, we plan to exchange results about the response to a sudden change or time-periodic modulation of the wetting properties as well as simulation techniques. Additionally, we share common interests in advanced multiscale simulation strategies and modeling of stimuli-responsive polymer brushes with the project of **Holm/Jain.**

Moreover, within SPP 2171, there are several groups that could offer us interesting polymer substrates, on which we want to investigate the dynamic wetting by lipid vesicles. In particular, the project of **Jordan**, dealing with polymer “carpet” system, can offer us highly dense brushes with and without lateral density gradient. This seems to be very interesting to study the dynamic movement of lipid vesicles and hydrodynamics inside the vesicles. The Tanaka group has a very fruitful collaboration with this group on the use of polymer brushes to harness lipid membranes on solid substrates, which resulted in 10 joint publications. Also, the project of **von Klitzing** deals with multiple stimulus-responsive microgels based on thermo-responsive PNIPAM, on which we plan to investigate the dynamic change in vesicle shape and the influence of micro-phase separation under different stimuli by experiment and simulation.

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4. Requested modules/funds

4.1 Basic Module

4.1.1 Funding for Staff 2 x PhD students (E13 3/4)

Müller: The PhD student in theoretical part of the project will develop and validate the simulation techniques to study the vesicle in a DPD-solvent and combine it with the modeling of the stimulus-responsive substrate. She/he will study the properties of the switchable substrate and the wetting dynamics of vesicles on the brush-coated substrate in response to a sudden external stimulus or a time-periodic variation. The students will discuss and the compare the results with the Tanaka group and additionally make connects to other groups in the priority programme working on wetting dynamics on switchable substrates.

Tanaka: The PhD student in experimental part of the project will fabricate homogeneous and heterogeneous substrates coated with polymer brushes, which are explicitly introduced in the research plan. She/he will characterize the changes in layer structures (thickness, density, roughness) using specular X-ray/neutron reflectivity, and determine the spatial distributions of specific ions using grazing-incidence X-ray fluorescence (WP T1). The dynamic wetting of stimulus responsive polymer substrates with vesicles consisting of lipids will be monitored by the combination of different techniques introduced in WP T2 and T3.

Total (Staff): 290,250 €

4.1.2 Direct Project Costs

4.1.2.1 Equipment up to Euro 10,000, Software and Consumables 54,941 €

Contact Angle Meter (Lauda Surface Analyzer LSA 60)

Characterization of the wetting property of polymer substrates is a prerequisite for the successful operation of this project. This information is extremely crucial in dealing with not only uniformly grafted polymer brushes (WP T2) but also mixtures of two different brushes (WP T3).

Total (Equipment for Tanaka Lab): 9,940.80 €

Consumables (Tanaka Lab):

Chemicals (solvents, commercial polymers, crosskinkers)	4,000 € per year
Biochemicals (lipids, lipopolzmers, fluorescenct lipids)	5,500 € per year
Si blocks, Si wafers (including polishing)	3,500 € per year
Glasswares, electrical parts, filters	2,0000 € per year
Total	**15,000 € per year**

Total (Consumables for Tanaka Lab): 15,000 € per year = 45,000 €

4.1.2.2 Travel Expenses 9,000 € per year = 27,000 €

The total cost will be equally split between Müller's and Tanaka's groups.

Mutual visits to project partners (Göttingen ↔ Heidelberg)	1,000 € per year
Participation in activities of the priority programme	1,500 € per year
Visit to international partners (US, Japan, UK)	5,000 € per year
Participation in conferences (DPG, APS, ACS, CECAM)	1,500 € per year
Total (travel)	9,000 € per year

4.1.2.3 Visiting Researchers (excluding Mercator Fellows) **2,500 € per year = 7,500 €**

To strengthen the collaboration with prominent researchers, we would like to invite the following international collaborating partners.

- Masaki Nakahata (Osaka University, Japan)
- Sergiy Minko (University of Georgia, US)
- Steven P. Armes (University of Sheffield, UK)
- Atsushi Takahara (Kyushu University, Japan)

We have longstanding and productive collaborations with these researchers on topics that are directly related to our project, and we anticipate that they will additionally interact with other groups of the priority programme. We request the funding to host one visitor for 10 days each year.

4.1.2.4 Expenses for Laboratory Animals None

4.1.2.5 Other Costs None

4.1.2.6 Project-related publication expenses **2,000 €**

These costs will allow us to use color figures in selected manuscripts or contribute to publishing in open access journals.

4.1.3 Instrumentation

4.1.3.1 Equipment exceeding Euro 10,000 None

4.1.3.2 Major Instrumentation exceeding Euro 50,000 None

4.2 Module Temporary Position for Principal Investigator Not necessary

4.3 Module Replacement Funding None

4.4 Module Temporary Clinician Substitute None

4.5 Module Mercator Fellows None

4.6 Module Workshop Funding None

4.7 Module Public Relations Funding None

5 Project requirements

5.1 Employment status information

Both, Prof. Dr. Marcus Müller and Prof. Dr. Motomu Tanaka, hold permanent positions.

5.2 First-time proposal data Not applicable

5.3 Composition of the project group

Tanaka's group: Stefan Kaufmann, Dr., permanent staff, state government
Julian Czajior, M.Sc., PhD student, EU Interreg
Benjamin Fröhlich, PhD student, SFB1129

Müller's group: Yuliya Smirnova, Dr., postdoctoral associate, SFB 803
Gaoyang Wang, M.Sc., PhD student, Inst.Theoretical Physics, Göttingen
Jürgen Holm, Dr., staff, IT support

5.4 Cooperation with other researchers

5.4.1 Researchers with whom you have agreed to cooperate on this project (see 2.7)

Sergiy Minko (Univ. Georgia, Athens, USA), Masaki Nakahata (Osaka Univ., Japan), Atsushi Takahara (Kyushu Univ., Japan), Steven P. Armes (Univ. Sheffield, UK)

5.4.2 Researchers with whom you have collaborated scientifically within the past three years

Müller – Galo Soler-Illia and Omar Azzaroni (UNSAM/UNLP, Argentina), Dmitry Bedrov (Salt Lake City, USA), Kostas Ch. Daoulas (MPI Polymerforschung, Mainz), Jochen Hub and Martin Müser (Saarland Univ.), Martin Kröger (ETH Zürich), Weihua Li (Fudan Univ., China) Sergij Minko (U Georgia-Athens, USA), David C. Morse (Minnesota, USA), Juan J. de Pablo, Paul F. Nealey, Jay Schieber (Chicago, USA), Claudio Pastorino (Buenos Aires, Argentina), Francesc Perez-Murano (Barcelona), Boaz Pokroy (Technion, Israel), Roy Shenhar (Jerusalem, Israel), Doros Theodorou (NTU Athens, Greece), Manfred Wilhelm (KIT, Karlsruhe), and J. Enderlein, A. Gholami, C. Ropers, Tim Salditt, Philipp Vana, and Annette Zippelius (Göttingen).
Tanaka – A.D. Ho, T.W. Holstein, W. Stremmel, M. Lanzer (Heidelberg University, Germany), T. Ohta (Univ. Tokyo), M.-P. Krafft (Univ. Strasbourg, France), M. Engstler, Univ. Würzburg, Germany), V. Rousseau (KIT, Germany), S. Kimura, K. Yoshikawa (Kyoto Univ., Japan). S.P. Armes (Univ. Sheffield, UK), B. Gamain (Inst. Pasteur, France), D. Schluter (ETH Zürich, Switzerland), A. Takahara (Kyushu Univ., Japan), M. Nakahata, A. Harada (Osaka Univ., Japan), O. Konovalov, Y. Chushkin (ESRF, France), B. Demé, G. Fragneto (ILL, France), H. Yoshikawa (Saitama Univ., Japan), R.G. Oliveira (Univ. Cordoba, Argentina), A. Makky (Univ. Paris Süd, France), A. Pasc (Univ. Lorraine, France), M. Eickhoff (Univ. Bremen, Germany), E. Monroy (CEA Grenoble, France).

5.5 Scientific equipment

The Tanaka group of Institute of Physical Chemistry in Heidelberg is equipped with an atomic force microscopy mounted on an optical microscopy, a high-energy specular X-ray reflectometer, monochromatic and spectroscopic ellipsometers, and an inverted microscope customized for microinterferometry (RICM). We also have a regular access to the confocal microscopes in Nikon Imaging Center (NIC), as Tanaka is one of the members of NIC.
The Institute for Theoretical Physics in Göttingen runs two clusters of high performance PCs. The institute also provides personnel (Dr. Jürgen Holm) for computer administration. Our compute cluster is part of the GOEGrid. Additional computer resources are available at the GWDG Göttingen, the HLRN Berlin/Göttingen, and the NIC in Jülich. Hence, the computational resources are adequate for a successful accomplishment of the project and no additional computation power is required for this project.

5.6 Project-relevant cooperation with commercial enterprises

Not planned

5.7 Project-relevant participation in commercial enterprises

Not planned

Kurzfassung:
Die Herstellung von schaltbaren Verbindungen zwischen weichen, biologischen Objekten und harten Substraten ist eine große Herausforderung, um Wechselwirkungen an Grenzflächen dynamisch zu regulieren. Die Antragsteller kombinieren ihre komplementäre Expertise in experimenteller (Tanaka) und theoretischer (Müller) Physik der weichen Materie, um die Benetzung von schaltbaren Polymersubstraten durch Lipidvesikel zu untersuchen. In Analogie zur Benetzung durch Flüssigkeitstropfen wird die Form eines Vesikels durch das eingeschlossene Volumen, die Membrane-Substrat-Wechselwirkung (Grenzflächenpotential) und die Eigenschaften der Grenzfläche (Membran) zwischen dem Inneren und Äußeren des Vesikels bestimmt. Neben der Membranspannung ist jedoch auch deren Biegesteifigkeit von Bedeutung.

Die Tanaka-Gruppe wird schaltbare Polymerbürsten, welche durch natürlich vorkommende Pflanzenproteine inspiriert sind, herstellen und charakterisieren. Das Schalten der Polymerkonfigurationen hat eine Änderung der Benetzungseigenschaften zur Folge. Durch Kombination verschiedener experimenteller Methoden wird die Tanaka-Gruppe die Dynamik der globalen Vesikelform - spezifiziert durch den Kontaktwinkel und die Größe der Kontaktzone mit dem Substrat -, die Abstandsfluktuationen zwischen Lipidmembran und Substrat, welche Informationen über das Grenzflächenpotential liefern, sowie die hydrodynamische Strömung im Inneren des Vesikels untersuchen. Diese Untersuchung wird auf das dynamische Benetzen von heterogenen Substraten aus schaltbaren und inerten Bürsten und auf das zeitlich periodische Schalten der Benetzungseigenschaften erweitert.

Die Müller-Gruppe wird diese Experimente durch Simulationen der dynamischen Benetzung von Lipidvesikel auf schaltbaren und deformierbaren Polymersubstraten komplementieren. Um die experimentellen Skalen zu erreichen, wird die schaltbare Bürste im Rahmen eines hoch-vergröberten Teilchenmodells modelliert während das Vesikel als eine triangulierte Fläche im Rahmen des Helfrich-Hamiltonians dargestellt wird. Aus der Gleichgewichtsform des Vesikels werden das Grenzflächenpotential und der effektive Kontaktwinkel bestimmt, die für eine Beschreibung im Rahmen von Kontinuumsmodellen notwendig sind, außerdem werden durch den Vergleich mit den experimentellen Daten die Modellwechselwirkungen angepasst. Danach wird die Formänderung nach dem Schalten und der zeitlich periodischen Modulation der Benetzungseigenschaften studiert, welche sich durch eine starke Kopplung zwischen der reversiblen Änderung der Benetzbarkeit des Polymersubstrats, der Dynamik der Lipidmembran und der Hydrodynamik des Lösungsmittels ergibt. Mittels einer systematischen Untersuchung der Größenabhängigkeit der Dissipationsmechanismen werden die Simulationsergebnisse von (kleinen) Vesikeln mit den experimentellen Daten verglichen.