

## Exploring self-assembly behavior of elastin-like polypeptides

Wafa Hassouneh

Polymeric micelles have gained immense interest in the biomedical field as drug delivery vehicles. Despite reports of the decoration of coronas of micelles with small molecules, peptides and proteins, the majority of these cases do not uniformly present the intact protein and require post-purification conjugation. Herein, we investigate a potential platform for multivalent display of proteins using stimulus-responsive block copolymers, elastin-like polypeptides (ELPs), for which a temperature trigger leads to self-assembly into micelles. This system has the potential to provide two advantages: 1) present multiple copies of the protein uniformly on the corona and 2) eliminate the need for post-purification chemical conjugation in addition to being perfectly monodisperse. ELPs consist of the pentapeptide repeat [Val-Pro-Gly-Xaa-Gly] where Xaa is a guest residue that can be any amino acid except proline. ELPs exhibit lower critical solution temperature (LCST). We have previously found that when two ELP blocks with disparate guest residue compositions (and hence disparate LCSTs) are joined to form a block copolymer (ELP<sub>hydrophilic</sub>-ELP<sub>hydrophobic</sub>), a micellar state is observed for certain block ratios in a temperature range where the hydrophobic block is collapsed and the hydrophilic is still hydrated. A polymeric architecture of protein-ELP<sub>hydrophilic</sub>-ELP<sub>hydrophobic</sub>, which can be easily constructed at the genetic level, would allow for the display of a given fused protein on the corona of the micelle. Our aim is to understand the rules that govern self-assembly behavior for the protein-ELP<sub>hydrophilic</sub>-ELP<sub>hydrophobic</sub>. We hypothesize that the size and hydrophobicity of the fused protein, and the disparity of hydrophilicity between the two ELP blocks are the factors that govern the self-assembly behavior. Four proteins were fused to different ELP diblocks; it was found that two proteins, thioredoxin and fibronectin III domain, did not disrupt self-assembly behavior while two other proteins, blue fluorescent protein and a humanized nanobody, did. The micelles of the former two proteins were characterized by temperature-programmed turbidimetry, dynamic and static light scattering, and cryo-transmission electron microscopy. The findings indicate formation of monodisperse particles with hydrodynamic radii between 24-37 nm that are spherical in shape and are composed of approximately 25-150 monomers/particle; together these results suggest micelle formation. Understanding the effect of the protein on self-assembly have promoted studies in which we first fully understand the ELP diblock behavior with no protein fusion through fitting the model developed by Rubinstein et al. to describe diblock behavior. The model will be fit with experimentally measured parameters for this polypeptide system. This model will allow the prediction of the self-assembly behavior of the ELP diblocks as the lengths and ratios of the blocks are varied, and in particular the change from micellar to cylinder to lamellar structures.

## Polymers confined in lyotropic lamellar mesophases.

Laure Hermann

The effect of hydrosoluble polymers confined in the water lamellae of a lyotropic lamellar mesophase is investigated through structural studies (X-rays diffraction) and through the direct measurement of the interactions between the surfactant membranes using the Surface Force Apparatus technique (SFA).

The stack of lamellae is oriented homeotropically along the two confining surfaces in the SFA. The force-distance profile (see figure) provides several information. First, the compressibility elastic modulus is extracted, allowing us to infer the nature of the interactions between membranes. The results show that in addition to weak repulsive undulation forces, an attractive interaction superimposes due to the presence of the confined polymers. Secondly, the force profile gives insight into the behaviour of the dislocations which appear or annihilate according to the direction of the surfaces movement. For separation shorter than one micrometer small Burger vectors are measured. At larger separations, the measurements show a different behaviour with larger Burger vectors.

In the quaternary phase diagram of the studied system a critical point exists. It is the signature of the coexistence of two lamellar phases with different periodicities. The goal is to approach this critical point, either by varying the membrane fraction, or by changing the concentration of polymer dissolved in the water layers between the membranes.

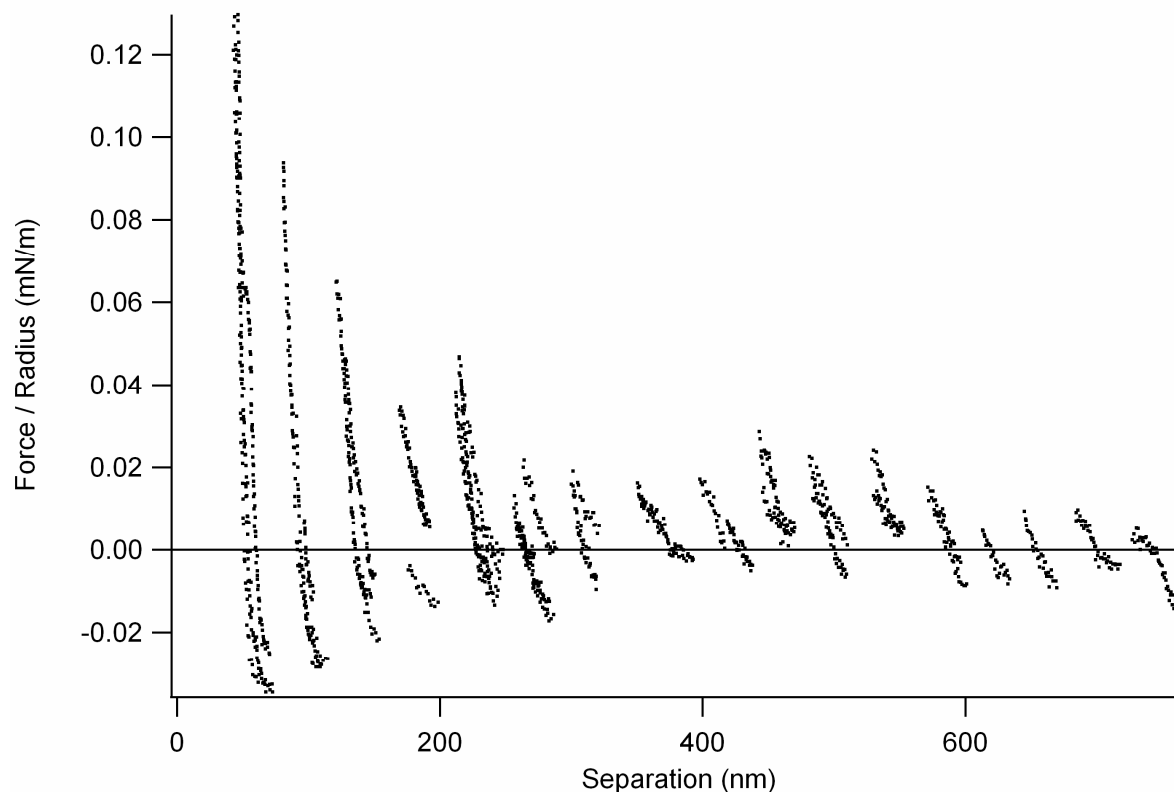


Figure: Typical force-distance profile measured for a lamellar phase with a period  $d = 18.5$  nm (inferred from X-rays). The periodicity of the minima indicates that the Burger vector is  $b = 2$ .

**Title:** *In – situ* small angle x-ray scattering investigations of structural changes in aqueous triblock copolymer/nanoparticle systems

Anne Juggernaut

**Abstract:**

Aqueous solutions of commercial poly(oxyethylene) – poly(oxypropylene) – poly(oxyethylene), triblock co-polymers (PEO<sub>x</sub> – PPO<sub>y</sub> – PEO<sub>x</sub>, Pluronics©) undergo both micellization and structural arrangement as a function of increasing temperature. In the case of Pluronic F127 (PEO<sub>100</sub> – PPO<sub>65</sub> – PEO<sub>100</sub>), this structural arrangement is observed macroscopically as a liquid to gel transition for polymer concentrations > 15 w/v%. This self – assembly and ordering can be controlled through both composition and temperature.

In addition to this thermoresponsive behavior, dispersions containing low concentrations of both F127 and inorganic Laponite nanoparticles have been shown to undergo a liquid to gel transition upon UV exposure when a photoacid generator (PAG) is added as a third component. This transition is attributed to interactions between the Laponite particles within the system. We recently reported on the factors affecting macromolecular gel formation and kinetics using photorheology. However, the UV – induced structural changes causing gelation are not well – understood.

Here, we use *in – situ* small angle x-ray scattering (SAXS) studies to probe the solution organization of these systems. Simultaneous UV – SAXS experiments were conducted to investigate the UV – induced structural changes. The experimental results were correlated to the macroscopic gelation kinetics investigated separately via photorheology to better understand the physical interactions and changes leading to gelation.

**Presentation Preference:** *no preference whether contributed talk or poster*

Milos Knezevic and Mark Warner

### Theory of photoresponsive ferroelectric liquid crystals

Photoferroelectrics are materials in which ferroelectricity can be affected by exposure light. Liquid crystals can acquire photoferroelectric properties by dissolving small quantity of a photochemical isomer in a ferroelectric host phase. In the case of ferroelectric smectic C\* liquid crystals, the rod-like *trans* isomer of the azobenzene fits well into the structure of a smectic C\* phase. On the other hand, the smectic C\* order can be locally disturbed by the presence of photochemically-induced, bend-shaped *cis* isomers. In particular, the spontaneous polarization can be changed by interaction with light. We use a model of nonlinear optical absorption to describe *trans* – *cis* state transitions along with their spatial dependence, and the process of thermal relaxation back to the *trans* state. Our predictions for polarization both in static and dynamic regime are in good qualitative agreement with experimental results.

# Computational models of stiff fiber networks: linear and nonlinear elasticity

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(Dated: May 1, 2012)

The response of living cells to mechanical stress is governed by the viscoelasticity of complex networks of stiff filamentous proteins that make up the cytoskeleton. At a larger scale, cells interact mechanically with extracellular matrices that also consist of stiff fiber networks. Recent theoretical research on such systems has aimed to explain the microscopic origins of viscoelasticity. These models have highlighted the importance of effects such as the semiflexible nature of the constituent filaments, network geometry, and connectivity. We develop lattice-based simulation methods to study the mechanics of random fiber networks, in which we are able to independently control these various aspects. We report results for both linear and nonlinear elastic properties of fiber networks. We also examine the validity of continuum elasticity for these networks.

# Polymer networks with mobile force-applying crosslinks

Student: Jacob Mohau Mateyisi  
Supervisor: Kristian Müller-Nedebock  
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May 2012

## Abstract

We construct and study a simple model for an active gel of extensible polymer filaments crosslinked by a molecular motor cluster that perform reversible work while translating along the filaments. The filament end points are crosslinked to an elastic background. In this sense we employ a simplified model for motor clusters that act as slipping links that exert force while moving along the strands. Using the framework of replica theory, quenched averages are taken over the disorder which originates from permanent random crosslinking of network end points to the background. We investigate how a small motor force contributes to the elastic properties of the network. We learn that in addition to the normal elastic response for the network there is an extra contribution to the network elasticity from the motor activity. This depends on the ratio of the entropic spring constant for the linked bio-polymer chain to the spring constant of the tether of the motor.

## Low-force single-molecule elasticity of ssDNA: sequence dependence and ion counting

Dustin McIntosh

The structure of macromolecular complexes, whether entangled in a gel, densely grafted to a surface (e.g., polymer brushes), or coiled up and crowded in the cell (e.g., proteins, RNA), depends on the microscope mechanical properties of the constituent polymers. These properties include the local chain rigidity as well as the long-range monomer-monomer interaction strength. Here, we present a method for directly measuring these properties: single polymers are stretched with a known force whilst their extension is monitored. As force and extension are thermodynamic conjugate quantities, these data are easily compared to theoretical models. In applying this method to heterogeneous-sequence ssDNA molecules, we are able to reconcile our data with scaling theory for polymers in good solvent. Data on homogeneous ssDNA, particularly poly(dA), show signatures of cooperative base-stacking with sections of polymer fluctuating between flexible random coils and rigid stacked helices. By varying the sequence of the ssDNA we demonstrate an ability to control the effective rigidity of the polymer. In an application of this data, we use a thermodynamic identity to relate single molecule elasticity data to the number of ions associated with the DNA. This analysis reveals that ions are released from the DNA to the bulk as the polymer is elongated and that the quantity of released ions depends nontrivially on the polymer's rigidity, being generally larger for more flexible polymers. Based on these findings, we argue that the entropy of release of polymer-associated ions to the bulk should contribute substantially to the free energy differences between competing states of charged, flexible polymers such as RNA and proteins.

## Microstructure of bidisperse ferrofluids in a monolayer

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Ferrofluids are colloidal suspensions of magnetic nanoparticles (typical size 10-20 nm), usually stabilized by steric coatings (in non electrolyte carrier liquids) or by electrical double layers (in aqueous solutions). These magnetic particles can form various cluster structures in monolayers in the absence of an external magnetic field. The clusters in constrained geometry are different from the ones in 3D. Recent quasi-2D experiments performed by cryogenic transmission electron microscopy (cryo-TEM) [1] have demonstrated the formation of chains and rings. However, the microstructure of ferrofluids in 2D is not yet completely understood.

In the present investigation we describe the microstructure of bidisperse ferrofluids in quasi-2D geometry where the centres of all particles are trapped in one plane and their magnetic moments can rotate in 3D. This system is the model case of a real liquid which is polydisperse. However, the influence of the polydispersity is observed even in the bidisperse system [2].

The approach of this research work is based on a combination of DFT and molecular dynamics simulations to quantitatively describe various chain and ring structures and their equilibrium area fractions. The simulations were realized using simulation package ESPResSo [3]. We also show that to reach a good agreement between simulation data and theoretical predictions in q2D geometry in theory one needs to allow for more possible chain configurations than in the bulk system. We provide explanations why the microstructure of bulk bidisperse ferrofluids differs noticeably from the one in q2D layer.

[1] M. Klokkenburg et al., *Phys. Rev. Lett.*, **99** (2006) 037203.

[2] A. Ivanov, S. Kantorovich, *Phys. Rev. E.*, **70** (2004) 02401-01-10.

[3] <http://espressomd.org/>



Poster contribution: E. Novikova, C. Storm. Catch bond clusters: strength in numbers.

Abstract: At focal adhesions, clusters of integrins provide a mechanical link between the intracellular cytoskeleton and the extracellular matrix. They serve as transmitters not only for biochemical regulatory signals but also for purely mechanical signals: forces and deformations. Some integrins, most notably  $\alpha_5\beta_1$  (the primary receptor for fibronectin) have been shown to display so-called catch bond behavior: a bond lifetime that increases with applied force. In this poster, we present results on the collective behavior of such catch bonds. Modeling both the shared loads, the collective binding/unbinding dynamics when loaded and the forces that molecular motors may apply to the cytoskeletal actin, we demonstrate that the catch bond cluster strengthens under tension and as such may serve as a basic mechanosensory unit, whose bound integrin content reports on the applied force.

Title: Modelling of actin-based protrusions: growth dynamics and steady-state shape

Gilad Orly

Abstract:

A common phenomena in cell morphology is cellular protrusions containing a core of parallel, inter-connected actin filaments. While diverse in physical properties and functionality, the underlying mechanism that controls their growth is the same, and is the unidirectional polymerization of actin filaments at the bundle's tip. This process is regulated by many protein types. The diversity of regulating proteins and their transportation mechanism is responsible for the differences in protrusion shapes. We propose a general theoretical model for the dynamical growth and steady-state shape of such protrusions. Our model describes the forces acting on the actin bundle, and the dynamics of the bundle tip's radius. These process are effected by the activity of the regulating protein. We believe that such a general model will greatly enhance our understanding of this important biological phenomenon, and will be of value for future physical and biological research.

## Solvent Exfoliation of Graphene in Complex Solvents

Andrew J Oyer

Theoretical and experimental results on the exfoliation of graphite in a complex solvent system of Benzene and Hexafluorobenzene are shown. Molecular dynamics simulations are used to study pure and mixed solvent systems with graphite. Results show that an equimolar mixture of the two solvents form a columnar structure from the graphene sheet due to quadrupolar forces. Experimentally these results were verified with surface interaction measurements as well as spectroscopy and microscopy.

## Title: Modifying Fragility and Length Scales of Polymer Glass Formation with Nanoparticles

Beatriz Pazmino

### Abstract:

We investigate the effects of nanoparticles on glass formation in a model polymer melt by molecular dynamics simulations. The addition of nanoparticles allows us to change the glass transition temperature  $T_g$ , the fragility of glass formation, and both static and dynamical length scales in a controlled fashion. Using the Adam-Gibbs approach, we show how the changes of fragility can be interpreted as a measure of the scale of cooperative string-like motion. We contrast the behavior along isobaric and isochoric paths to  $T_g$ , and find that changes along an isobaric path (most relevant experimentally) are much smaller than those along an isochoric path. We also contrast the length scales of static density changes with the length scale over which nanoparticles perturb the dynamics, as well as the length scale of cooperative string-like motion; we find that, for small NP concentration, the length scale of dynamical perturbation and string size are proportional, suggesting a possible experimental way to directly probe the scale of cooperative motion.

Title: Understanding the Effect of the Substrate on Collective Cell Motion

Adrian Pegoraro

Abstract:

Large groups of cells can demonstrate collective dynamics in a wide range of settings, including wound healing, embryo development, tissue growth, and barrier function. Understanding how cell-cell and cell-substrate mechanical coupling influences both individual cells and their collective mechanical properties is important to understanding these processes. This is complicated since substrate properties can alter cell-cell contacts by changing individual cell stiffness as well as allowing for long range spatial and temporal coupling through the substrate itself. To better understand these long range couplings and what significance they play, we study groups of cells on different types of substrates as the cells become confluent and collective effects become increasingly important. By manipulating the substrate stiffness and geometry, we can influence individual cell stiffness as well as allowing or preventing long range coupling through the substrate. To effectively characterize these systems, we adopt different measures commonly used to study colloidal systems. Initial evidence indicates that collective motion of cells has parallels with jammed colloidal systems.

Nikolay Perunov

“The quantitative theory of hydrophobic effect as a driving force of protein structure”

## **Abstract poster Summer School Boulder**

### **Swelling behaviour of thermal protein gels as influenced by pH\***

Jorien Peters

The extent of swelling of WPI hydrogels is determined by the ability to dissolve in the solution, the elastic properties of the gel and the ions that are present in the environment as well as the structure of the gel. To see the influence of pH on the swelling behaviour of WPI hydrogels, gels were made at various pHs. Some of those gels were dried and others stayed hydrated. Both gels were placed in solutions of a variety of pHs to be able to swell. It was found that when the pH during gelation was around the pI of the native WPI, the swelling ratio of the hydrogel was the highest. Furthermore, when the pH during swelling was around the pI of the hydrogel, the lowest swelling ratio was observed as well as the lowest mesh size of the gel. Finally, it was determined that the pI of the hydrogel became lower than the pI of native WPI when gelation took place above the pI of the native protein. This all showed that the pH has an influence during gelation on swelling by influencing the charge density and microstructure of the formed hydrogel, as well as during swelling.

\* Betz, M., Hörmansperger, J., Fuchs, T., Kulozik, U., Swelling behavior, charge and mesh size of thermal protein hydrogels as influenced by pH during gelation, *Soft Matter* 8, 2477-2485, 2012