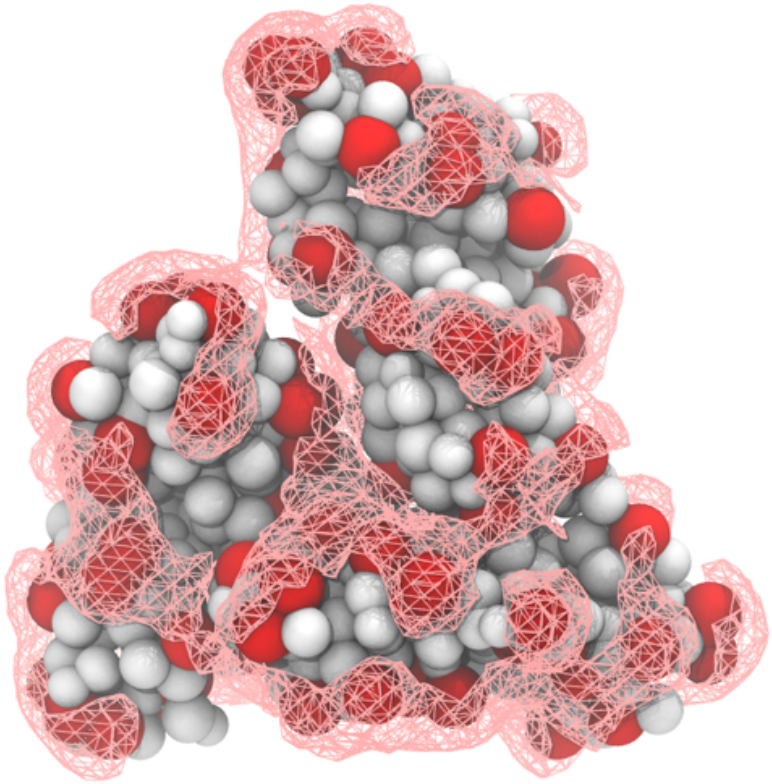
OMM Annual Report 2012

Activities of the Linnaeus center of excellence
"Organizing Molecular Matter"
Department of Chemistry, Lund University



La^{3+} binding to human serum albumin.

LUND UNIVERSITY

Organizing Molecular Matter

1. ORGANIZING MOLECULAR MATTER

The environment *Organizing Molecular Matter* (*OMM,* www.omm.lu.se) was established in 2006, with an unusually long term - 10 years – grant from the Swedish Research Council, of 7.5 MSEK annually. There are only a few Linnaeus environment in Sweden. 20 environments were established in 2006, followed by some more in 2008. In 2006, OMM was the only Linnaeus environment created in chemistry, and the only Linnaeus environment at the Science Faculty of Lund University. Thus, the Linnaeus grant is a very prestigious grant, offering long term economic base for research.

The strategy, from the very beginning in 2006, was to use a significant part this resource to recruit new faculty support young scientists in the beginning of their career. Furthermore, as the environment spans a broad competence, we have worked very actively to stimulate collaborations and combine different relevant competences in the research projects supported within the environment. This means in practice for example that two, and sometimes more, senior scientists with complementary expertise engage themselves in a project and co-supervise a PhD student. These concepts have proven to very fruitful and have allowed us to tackle more complex research problems. To stimulate creativity, exchange of ideas and cross-disciplinary collaborations it is important create meeting places. A joint seminar series, and joint PhD courses within the environment has contributed significantly. However, very important was also the co-localization of the Physical and Theoretical Chemistry Divisions when we moved to the newly renovated area in 2010, including a common coffee/lunch room, just next to the Biochemistry Department. This co-localization has led to many spontaneous informal meetings and discussions that probably otherwise never would have taken place. Within the Physical Chemistry division we today identify ourselves more or less completely with the OMM environment, which has brought tremendous vitality and renewal to our activities.

In 2011, it was time for the mid-term evaluation of the Linnaeus environments, with a site visit by an external panel of experts in February 2012. The site visit, as well as the self-evaluation and report we had to produce in advance, were very useful as they allowed us to very deeply analyze our own work and put it into perspective. The panel was very impressed and pleased with our achievements, the way we work and how we are organized. Shortly before the summer we received the formal decision from the Research Council that they will continue to support us at an unchanged level until the end in 2016.

Discussion have begun concerning the fate of this environment beyond 2016. Given the success of the OMM environment, one should possibly consider ways in which it can continue to prosper. However, continuation can by no mean be automatic. There has to be a critical evaluation and new concrete vision formulated. Creating cross-disciplinary environments, like the OMM, require specific funding. It will be challenge in the years to come to identify the ideas and the support on which a new program or programs can be based.

Ulf Olsson

Chairman of the OMM environment

February 2013.

The midterm review of the 2006 year's Linnaeus environments can be downloaded from here: http://www.vr.se/download/18.9e84b161380f0c1c1c2b2/1340623069626/Midterm+Evaluation+Report+of+the+2006+Linnaeus+Environments+and+Doctoral+Programmes.pdf

2. SCOPE OF THE ANNUAL REPORT

The main part of this annual report contains descriptions of currently active projects that are specifically supported by OMM, with an emphasis on progress made during 2011. Within the OMM environment, there are also other related scientific activities, which are supported by other sources. Presentations of all OMM-related projects, both those specifically supported by OMM listed here and the related projects, are given at the OMM website. The report also lists the scientists active in OMM during 2011 and gives accounts of OMM meetings and seminars.

3. ORGANIZATION

The *board of OMM* has three members, currently *Ulf Olsson* (chairman), *Sara Snogerup Linse* and *Torbjörn Åkesson*. The board has the economical responsibility for OMM, and takes all formal decision on long-time strategies and major expenditures. The *director* of OMM, currently *Emma Sparr,* has the operative responsibility for the administration of OMM. *Lennart Picullel* was the OMM directer until August 2012.

Discussions regarding the long-term strategy of OMM are held at the *general meetings* of OMM, where all scientists active within OMM participate. In addition, OMM has a scientific advisory committee, currently *Bernard Cabane* (ESPCI, Paris), *Jannette Carey* (Princeton University), and *Sture Nordholm* (University of Gothenburg). The main forum for interactions with the advisory board members is the annual meeting of OMM.

4. THE PEOPLE

The tables below list researchers active in OMM during 2012. The *senior scientists*, also referred to as the OMM members, are professors, associate professors and assistant professors who receive funding from OMM. The list of junior researchers is restricted to PhD students or post-doctoral fellows salaried by OMM funds. Six new junior researchers were funded by OMM in 2011 (Alexei Abrikossov, Aleksandra Dabkowska, Sebastian Lages, Manja Behrens, Joao Henriques, Weimin Li). A number of additional junior scientists work with OMM-related projects in the OMM research environment, but are funded mainly from other sources.

Senior scientists (OMM members)

Viveka Alfredsson	professor	physical chemistry
Jan Forsman	associate professor	theoretical chemistry
Bo Jönsson	professor	theoretical chemistry
Gunnar Karlström	professor	theoretical chemistry
Björn Lindman	professor	physical chemistry
Sara Snogerup Linse	professor	biochemistry
Per Linse	professor	physical chemistry
Mikael Lund	assistant professor	theoretical chemistry
Per-Åke Malmqvist	associate professor	theoretical chemistry
Tommy Nylander	professor	physical chemistry
Ulf Olsson	professor	physical chemistry
Lennart Piculell	professor	physical chemistry
Karin Schillén	professor	physical chemistry
Peter Schurtenberger	professor	physical chemistry
Marie Skepö	assistant professor	theoretical chemistry
Emma Sparr	professor	physical chemistry
Anna Stradner	associate professor	physical chemistry
Olle Söderman	professor	physical chemistry
Daniel Topgaard	associate professor	physical chemistry
Håkan Wennerström	professor	physical chemistry
Malin Zackrisson Oskolkova	assistant professor	physical chemistry
Torbjörn Åkesson	associate professor	theoretical chemistry

Junior researchers

Alexei Abrikossov	PhD student	physical chemistry
Jenny Algotsson	PhD student	physical chemistry
Mehran Asad Ayobi	PhD student	physical chemistry
Solmaz Bayati	PhD student	physical chemistry
Manja Behrens	post-doc	physical chemistry
Jonas Boström	PhD student	theoretical chemistry
Lucia Casal	post-doc	physical chemistry
Jonas Carlstedt	PhD student	physical chemistry
Celen Cenker	PhD student	physical chemistry
Aleksandra Dabkowska	post-doc	physical chemistry
Marie Grey	post-doc	physical chemistry
Erik Hellstrand	PhD student	biophysical chemistry
Joao Henriques	PhD student	theoretical chemistry
John Janiak	PhD student	physical chemistry
Sebastian Lages	post-doc	physical chemistry
Weimin Li	PhD student	physical chemistry
Anıl Kurut	PhD student	theoretical chemistry
Adriana Mihut	post-doc	physical chemistry
Emelie Nilsson	PhD student	physical chemistry
Agnieszka Nowacka	PhD student	physical chemistry
Ryan Szparaga	PhD student	theoretical chemistry
Mo Segad	PhD student	theoretical chemistry
Joakim Stenhammar	PhD student	physical chemistry
Marianna Yanez	PhD student	physical chemistry

Visiting scientists and guests

Claudia Schmidt

In July 2009, Professor Claudia Schmidt from Paderborn University was appointed as a part-time visiting professor (10% of full time) for a period of three years, financed by OMM. Claudia's research interests are focused on NMR studies and rheology of soft matter. In particular, she was among the first to develop shear cells to be used in NMR instruments. Within OMM she collaborates in particular with the NMR group of Daniel Topgaard, and in projects dealing with shear induced structural and phase transition in the group of Ulf Olsson.

Albert Philipse

Professor Albert Philipse from Van 't Hoff Laboratory for Physical and Colloid Chemistry, Debye Institute for Nanomaterials Science, Utrecht University, The Netherlands, visited OMM from the middle of May to the end of June 2012. He gave a series of six well-attended seminars on colloids. Within OMM he collaborates in particular with the group of Per Linse on structures in solutions of magnetic particles and within the group of Lennart Piculell on experimentally verifying predicted properties of special colloidal solutions.

Robert K. Thomas

Dr Robert K. Thomas, FRS, from University of Oxford became Honorary Doctor at Lund University 2012, due to his pioneering and outstanding work on using neutron reflection to study interfacial layer structures. He is long-time friend and collaborator of researchers in this field at Lund University. We had the pleasure to host him during October 2012.

Robert Vacha

Dr Robert Vacha, Marsaryk University, visited OMM in December 2012, One week. Robert participates in a OMM collaboration on amyloid aggregation kinetics. The collaboration involve Mikael Lund, Sara Linse and Emma Sparr.

Bernard Cabane

Bernard Cabane from ESPCI in Paris visited OMM during August and September. Bernard Cabane Cabane is long-time friend and collaborator of researchers in the OMM environment. The

collaborations cover a wide range of topics, including emulsions, polymer-surfactant interactions cohesion in cement, protein-tannin interactions and skin hydration. The collaborations involve Ulf Ollson, Lennart Picullel, Bo Jönsson, Marie Skepö and Emma Sparr.

Clifford Woodward

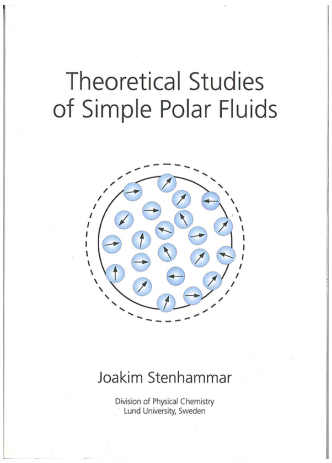
Professor Clifford Woodward, University of New South Wales, Canberra, visited OMM in May 2012. Cliff visits OMM regularly, and participates in a number of collaborative projects involving Bo Jönsson, Mikael Lund, Jan Forsman, Anna Stradner, Peter Schurtenberger, Per-Åke Malmqvist and Torbjörn Åkesson.

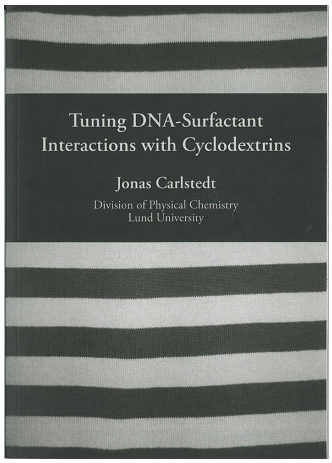
Short Term Guests

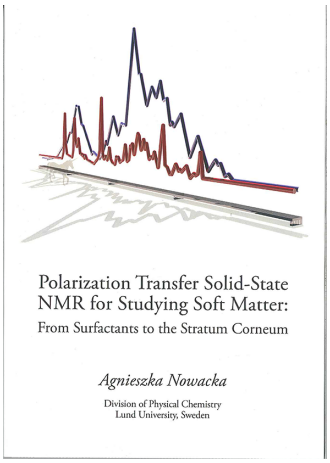
A number of guests have paid short-term visits to OMM during 2011 to give seminars and to discuss with the OMM scientists. Their names are given, together with the titles of their seminars, in section 9 below.

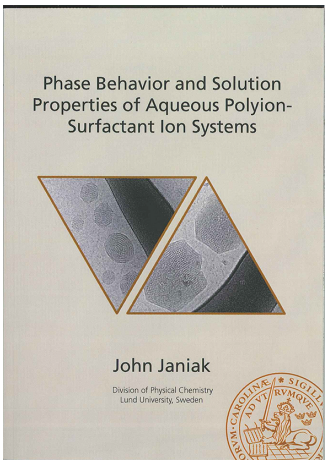
5. OMM PhD THESIS 2012

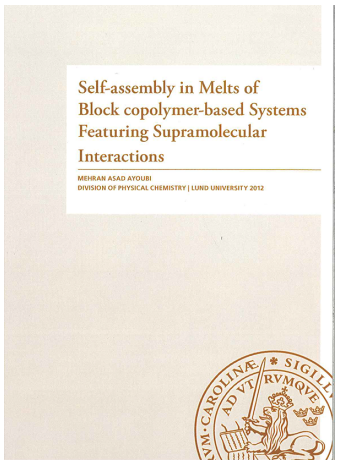
In 2012, six OMM funded PhD projects were completed:

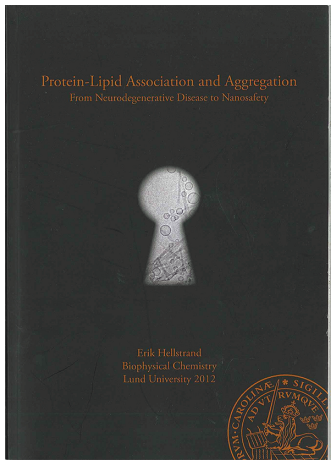












- **Joakim Stenhammar**. *Theoretical Studies of Simple Polar Fluids.* February 3. Faculty opponent: Prof. Martin Neumann, Universität Wien, Austria
- **Jonas Carlstedt**. *Tuning DNA-Surfactant Interactions with Cyclodextrins.* February 24. Faculty opponent: Prof. Julian Eastone, University of Bristol, UK
- **Agnieszka Nowacka.** *Polarization transfer solid-state NMR for studying soft matter: From surfactants to the stratum corneum*. June 1. Faculty opponent: Prof. Dominique Massiot, CEMTHI, Orléans, France
- **John Janiak.** *Phase Behavior and Solution Properties of Aqueous Polyion-Surfactant Ion Systems*. November 16. Faculty opponent: Prof Bo Nyström, University of Olso, Norway

- **Mehran Asad Ayobi.** *Self-assembly in Melts of Block copolymer-based Systems Featuring Supramolecular Interactions.* December 6. Faculty opponent: Prof. Nitash Balsara, University of California, Berkely, USA
- **Erik Hellstrand**: *Protein-Lipid Association and Aggregation - From Neurodegenerative diseases to Nanosafety.* December 14. Faculty opponent: Dr Jenifer Chen Lee, National Institute of Health (NIH), Bethseda, USA

6. YOUNG SENIOR SCIENTISTS RECEIVING OMM SUPPORT

One of the objectives of OMM is to specifically support younger tenure and tenure track OMM members with the goal of facilitating their scientific careers. At present Jan Forsman, Mikael Lund, Daniel Topgaard and Emma Sparr receive such support from OMM. Below, they present their OMM research.

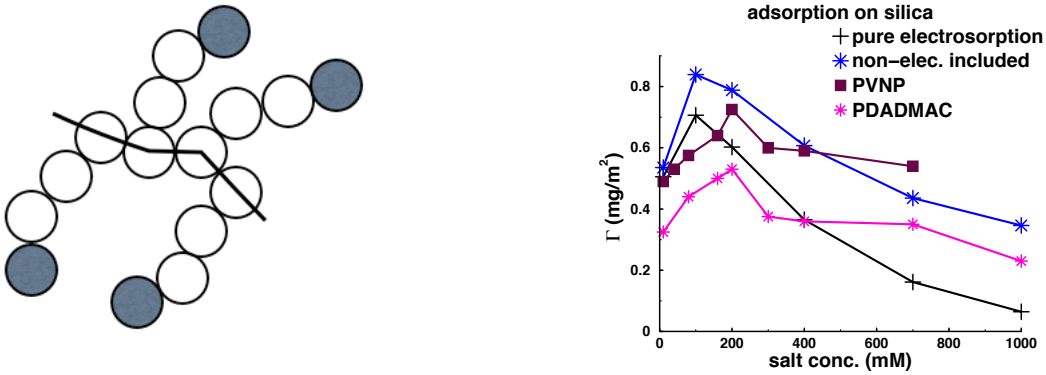
JAN FORSMAN: Polyelectrolyte adsorption and polyelectrolyte-mediated interactions

Project description

The project comprises several minor ones, two of which are described in more detail:

(i) Polyelectrolyte adsorption, and polyelectrolyte-mediated interactions. Using a combination of theory and simulations, we study these phenomena, but also how they are related to surface forces. This sub-project also involves a recent PhD recriutment, Fei Xie, as well as Lennart Picullel (co-supervisor), Torbjörn Åkesson (co-supervisor) and Tommy Nylander. We have also initiated a collaboration with the group of Lars Wågberg, and one of his students (Simon Utsel) has recently visited us. Together with Fei, he perfomed ellipsometry measurements on various cellulose surfaces, the results from which we currently model and interpret.

(ii) Polymer mediated interactions between colloidal particles, including many-body aspects.



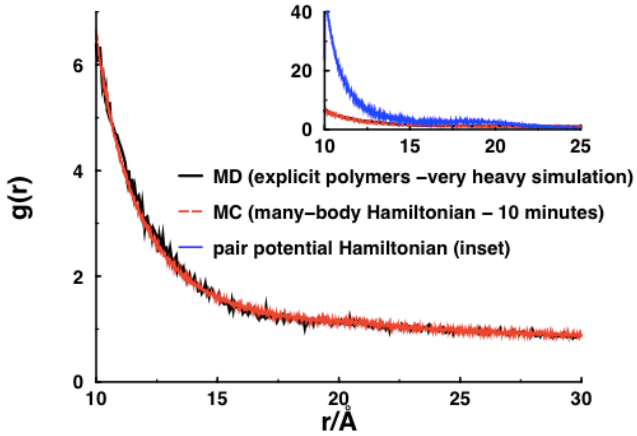
Comparing experimental ellipsometry data with DFT predictions. The polymer model is depicted to the left (we have tested many alternatives, but the predictions are insensitive to model details). The shaded part of the monomers carry a unit charge. The right graph compares calculated (stars) and measured (squares and plus signs) data, for the adsorption of two different types of polymers on a silica surface at pH 9, and for various salt concentrations. The blue curve is calculated with the inclusion of a non-electrostatic component to the adsorption, whereas the magenta curve is the corresponding result for pure electrosorption.
PVNP is expected to be slightly more hydrophobic than PDADMAC.

Progress during 2011

(i) We have developed a polyelectrolyte-density functional theory that accounts for electrostatic correlations. This theory is of vital importance to our current and future studies of polyelectrolytes in the presence of charged particles. Numerous comparisons with simulations have verified that the predictions of our theory are *uniquely* accurate for a broad range of conditions (in fact, no other theory comes even close). We have thus proceeded to make predictions and interpretations of experimentally measured adsorption, as measured by ellipsometry (Lund) and reflectometry (KTH). We focus on silica and cellulose surfaces, which have a high practical relevance. The agreements we have found between theory and experiments are very encouraging. We have also made theoretical estimates of corresponding surface forces, and in a near future we hope to make

comparisons with experiments, utilizing the specific polymers that we have investigated by ellipsometry and reflectometry.

(ii) We have constructed a theory for colloid+polymer dispersion, where an effective many-body Hamiltonian, acting between the colloids, was derived. Explicit comparisons with simulations have revealed that the theory is able to predict structure and phase diagrams in these systems, with a remarkable accuracy (see, for instance, graph below). We are currently working on an extension of the theory, to handle "good solvent" cases (interacting chains).



The black curve shows the particle-particle radial distribution function (g(r)) from an MD simulation of 410 explicit 151-mers, and 10 colloidal particles. An expensive cluster simulation (about 1 CPU-year, on a single processor) was required to produce a particle-particle g(r), in the presence of explicit chains. On the other hand, with the effective many-body Hamiltonian (implicit polymers), the corresponding simulation requires 5-10 minutes on a simple laptop. The inset shows results obtained if the (erroneous) pair potential limit of the Hamiltonian is used. Many-body contributions are clearly of vital importance in this system.

External collaborations

Cliff Woodward, University of New South Wales, Canberra
Rudolf Podgornik, J. Stefan Institute, Ljubljana
Matej Kanduc, University of Munich
Ali Naji, IPM, Teheran
Lars Wågberg and Simon Utsel, KTH
Sture Nordholm, Gothenburg University
Leo Lue, University of Strathclyde, Glasgow
Marius Hatlo, Theoretical Physics, Utrecht University, Utrecht.

Publications during 2012

- J. Forsman, C. E Woodward: A Simple Many-Body Hamiltonian for Polymer-Colloid Mixtures: Simulations and Mean-Field Theory, Soft Matter **8**, 2121 (2012)
- J. Forsman: Polyelectrolyte Adsorption: Electrostatic Mechanisms and Nonmonotonic Responses to Salt Addition, Langmuir **28**, 5138 (2012)
- M. Kanduc, A. Naji, J. Forsman, R. Podgornik: Attraction between Neutral Dielectrics Meidated by Multivalent Ions in an Asymmetric Ionic Fluid, J. Chem. Phys. **137**, 174704 (2012)
- Kurut, B. A. Persson, T. Åkesson, J. Forsman, M. Lund: Ansiotropic Interactions in Protein Mixtures: Self Assembly and Phase Behavior in Aqueous Solution, J. Phys. Chem. Lett. **3**, 731 (2012)
- Woodward, J. Forsman: Many-Body Interactions Between Particles in a Polydisperse Polymer Fluid, J. Chem. Phys. **136**, 084903 (2012)
- M. H. Hatlo, P. Banerjee, J. Forsman, L. Lue: Density functional theory for Yukawa fluids, J. Chem. Phys. **137**, 064115 (2012)
- Woodward and J. Forsman: Many-Body Interactions Between Particles in a Polydisperse Polymer Fluid, J. Chem. Phys. **136**, 084903 (2012)
- J. Algotsson, T. Åkesson, J. Forsman: Monte Carlo simulations of Donnan equilibrium in

cartilage, Magn. Reson. Med. **68**, 1298 (2012)
- J. Forsman and S. Nordholm: Polyelectrolyte Mediated Interactions in Colloidal Dispersions: Hierarchical Screening, Simulations, and a New Classical Density Functional Theory, Langmuir **28**, 4069 (2012)

Conference presentation
- Polyelectrolyte adsorption: classical density functional theory, simulations and experiments. ECIS 2012, Malmö. Oral contribution (J. Forsman)

MIKAEL LUND: Biomolecular Interactions and Organization

Project description
This OMM project involves statistical mechanical investigations of macro-molecular systems of mainly – though not solely – biological interest. This includes protein interactions with other proteins, DNA, membranes and large polyelectrolytes. The focus is on electrostatic intra- and intermolecular interactions and we study how these depend on solution properties such as ionic strength, pH, salt valency and type. Using atomistic as well as mesoscopic computer simulations we estimate key thermodynamic properties such as binding constants, pKa-values, virial coefficients etc. Thus, computer models have direct applications for targetreceptor systems and today, approximate theoretical models are frequently used to systematically screen potential drug molecules. Another useful application is to anticipate favorable crystallization conditions for X-ray diffraction studies.

Depending on solution conditions (pH, salt and solute concentration etc.), proteins may aggregate, crystallize or in other ways organize due to a subtle balance between physical forces acting between the complex molecules. Interestingly, a substantial number of all known protein structures reveal highly uneven charge distributions that suggest that these proteins orient in the electric field generated by proximate charged species. This macromolecular alignment - important for recognition processes - is studied in detail using our public available software for Monte Carlo simulation. The above Figure shows calculated iso-density plots for the protein lysozyme around different antibody fragments and reveals a significant orientational preference.

Specifically we plan to advance in the following areas:
• **Whey and egg protein interactions** and organization. *Food processing*.
• The effect of **multivalent ions** on protein association. *Alzheimer's and related diseases caused by protein aggregation*.
• Draw an **electrostatic atlas** of all known proteins. *Overview of interaction strengths and mechanisms.*
• **Proton fluctuations** in bio-molecules using implicit as well as explicit water models. *pKa calculations and drug design*.
• **Hofmeister-type** or ion-specific effects on protein association and arrangement.

Further, we develop and maintain a complete open source software package for molecular simulation. The freely available package is jointly developed by several people from Theoretical Chemistry as well as from the Academy of Sciences of the Czech Republic. It can be downloaded from http://faunus.sourceforge.net.

Progress during 2012
During 2012 we have developed a new model for intrinsically disordered proteins near surfaces and applied this on the milk protein beta casein. This was done in collaboration with TetraPak in Lund who are interested in creating non-sticking packaging materials. As for Hofmeister effects, we have developed a novel coarse grained model for ion specificity in biomolecular solutions. The basic idea is that not only proteins bind to specific surface groups, but other ions – thiocyante, iodide and other large ions – may bind to exposed hydrophobic pockets. This represents one of the first attempts to include Hofmeister effects in coarse grained protein simulations and we have applied the model on the eye lens protein, gamma crystallin. Interestingly, the model predicts a Hofmesiter reversal when passing the protein iso-electric point and well agrees with recent scattering experiments. This work was presented at the 160th Faraday Discussions meeting in Oxford.

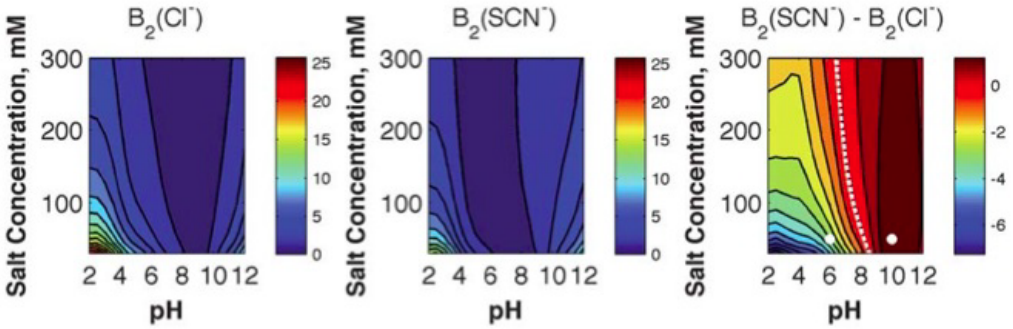


Fig. 3 Left and middle: estimated virial coefficients for γ-crystallin in NaCl and NaSCN, respectively using eqn (5) and eqn (6). Right: difference in second virial coefficient between NaSCN and NaCl. The dashed white line represents zero (Hofmeister reversal), while the two white dots mark the conditions used for the two-body simulations in Fig. 4. Note that the B_2 values are normalized with B_2^{HS}.

OMM junior scientist involved
Anil Kurut (PhD student since March 2010).
Joao Henriques (PhD student since 2012)

External collaborators
Pavel Jungwirth, Academy of Sciences of the Czech Republic, Prague.
Clifford E. Woodward, University of New South Wales, Canberra.
Dereck Chatterton, University of Copenhagen
Robert Vacha, Masaryk University
Said Bouhallab, INRA, Rennes
Kenneth Wärnmark, Lund University

Publications during 2012
- Kurut A., Persson B., Akesson T., Forsman J., Lund M. Anisotropic Interactions in Protein Mixtures: Self Assembly and Phase Behavior. J. Phys. Chem. Lett., 2012. DOI: 10.1021/jz201680m
- Kurut A., Lund, M. Solution Electrostatics Beyond pH: A Coarse Grained Approach to Ion Specific Interact ions Between Macromolecules. Faraday discussions, 2012. DOI: 10.1039/C2FD20073B
- Evers C.H.J., Andersson T., Lund, M., Skepö M. Adsorption of Unstructured Protein beta-Casein to Hydrophobic and Charged Surfaces Langmuir, 2012. DOI: 10.1021/la300892p
- Lund, M. Om svensk rødfarve - historien og jernkemien bag de røde træhuse. Dansk Kemi, 2012, 4

Conference Presentations in 2012
- Faraday Discussion meeting on Ion Specific Hofmeister Effects, Oxford (2012). Invited speaker.
- GRC Biopolymers 2012, Rhode Island (2012). Poster.

EMMA SPARR: Responding mipid membranes

Project description
One major role of biomembranes is to control transport and separate regions with different properties. As the thermodynamic conditions in the separated regions are different, one can reach the situation where the preferred self-assembled structure is not the same on the both sides of the membrane. As a consequence of this, small changes in the membrane environment may lead to major changes of the membrane structure, which, in turn can alter the membrane barrier properties in rather dramatic ways. Such a scenario are obvious possibilities across the human skin. Interactions between the lipid membrane and other small molecules and large biomolecules can also influence the membrane self-assembled structure, and thereby alter the properties of the

membrane in rather dramatic ways. The coupling between interactions, structure and function form the basis of this research, and it includes a number of different sub-projects:

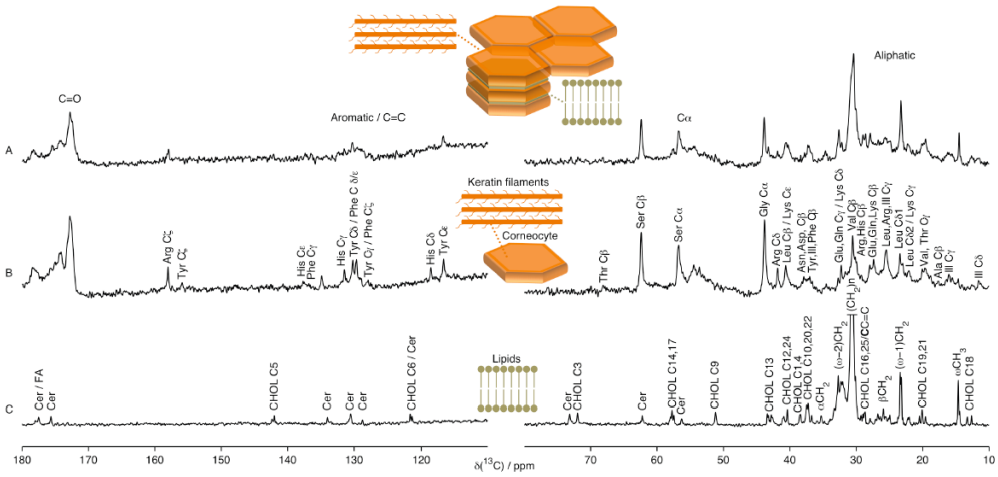
(i) *The skin as a barrier to molecular diffusion:* The human skin is an intriguing example of a responding membrane, as its barrier properties can be altered by changes in its environment. The aim of this sub-project is to reach a molecular understanding of how molecular diffusive transport occurs through the responding skin membrane and to explore how it can be affected.

(ii) *Interfacial lipid/protein films.* This sub-project deals with the "skin" composed of surfactants, polymers or lipids that can form at the interface between an aqueous solution and air. For an open aqueous solution, the water chemical potential corresponding to the ambient RH will, in general, not match the water chemical potential of the solution. There is the possibility that this water gradient across the interface can induce phase transitions in the system, and formation of an interfacial phase. We recently presented a quantitative model for the possibility of forming such a phase, and we now aim to explore the mechanisms for the formation of interfacial films in lipid and lipid/protein systems.

(iii) *Interactions between amyloid proteins and lipid membranes: Amyloid* protein aggregation is associated with over 30 known diseases in humans. In amyloid plaques associated with several amyloidogenic diseases, tightly associated lipids have been identified. For several of the amyloid disorders, protein aggregation has also been associated with membrane disruption in cells and in model lipid systems. In this project, we investigate interactions between aggregating amyloid proteins and lipid membranes, and we explore the basic principles of the amyloid-lipid coaggregation

Progress during 2012

(i) Based on novel PT ssNMR studies of the dynamics in skin lipid and protein molecular components together with our previous work on transport across skin, we were in 2012 able to provide a molecular explanation for occlusion effect in skin, explaining how hydration in influence barrier function. One of the key elements in these studies is methodological approach using natural abundance ^{13}C ssNMR, and one major achievement in 2012 was that we were able to assign the majority of peaks from samples of intact stratum corneum (Fig). We used the same combined approach with diffusion cell experiments together with NMR, SAXS and WAXS to provide an explanation of how small polar molecules ("moisterizers") influence skin, and we initiated studies on the effect of apolar terpenes on skin ("penetration enhancers")



Peak assignment for intact SC: *^{13}C direct polarization MAS NMR spectra of intact SC (A), isolated corneocytes (B), and SC model lipids (C). The schematics illustrate SC with corneocytes filled with keratin filaments, surrounded by a multilamellar lipid matrix. Peaks originating from the keratin and the lipids are assigned in B and C, respectively.*

(ii) In experimental studies we demonstrated that the formation and the properties of interfacial polymer/surfactant films can be controlled by the properties of the surrounding gas phase. We also developed the theoretical model to a general description of interfacial phases in three-phase component systems.

(iii) We studied the molecular determinants for adsorption of the monomeric form of the Parkinson related protein α -synuclein to model lipid using QCM-D and neutron reflectometry. The results imply that α -synuclein adsorbs in the headgroup region of anionic lipid bilayers with extensions into the bulk but does not penetrate deeply into or across the hydrophobic acyl chain region. We also investigated the co-aggregation of α -synuclein with lipids from model membranes. After aggregation, we find spontaneous uptake of phospholipids from an anionic membrane into the amyloid fibrils. Phospholipid quantification, PT ssNMR and cryo-TEM together reveal co-aggregation of phospholipids and a-synuclein in a saturable manner with a strong dependence on lipid composition. The interaction leads to the formation of lipid-protein co-aggregates with distinct structure, dynamics and morphology compared to assemblies formed by either lipid or protein alone.

OMM junior scientists involved
Erik Hellstrand
Marie Grey
Agnieszka Nowacka

External collaborations
Prof Patrik Brundin (van Andel Institute, US & Wallenberg Neuroscience center, Lund univ)
Dr. Christoffer Dunning (Wallenberg Neuroscience center, Lund university)
Prof. Bernard Cabane (ESPCI, Paris)
Prof. Joke Bouwstra (Leiden Univ, the Netherlands)
Prof. Karen Edler (Univ of Bath, UK)
Dr. Johan Engblom (Malmö University)
Prof. Lars Wadsö (Building Materials, LU)
Dr. Marie-Louise Ainalem *(*ESS, Lund)

Publications in 2012
- E. Sparr, D. Millecamp, M. Isoir, V. Burnier, Å. Larsson, B. Cabane. Controlling the microclimate of the skin though the application of occluding films. JRS Interface (2012) 10, 20120788
- A. Michanek, M. Björklund, T. Nylander, E. Sparr. ssRNA base pairing at a bilayer interface can be controlled by acyl chain order. Soft Matter (2012) 8, 10428-10438
- A. Michanek, M. Yanez, H. Wacklin, A. Hughes, T. Nylander, E. Sparr: RNA and DNA association to zwitterionic and charged monolayers at the air-liquid interface. Langmuir (2012) 28, 9621-9633
- C. Åberg, E. Sparr, H. Wennerström. Lipid phase behaviour under steady state conditions. Faraday Discussion (2012). In press
- A. Nowacka, S. Douezan, L. Wadsö D. Topgaard, E. Sparr. Small polar molecules like glycerol and urea can preserve the fluidity of lipid bilayers under dry conditions. Soft Matter (2012) 8, 1482-1491

Conference presentations in 2012
- Discussion on Hydration Forces, Sofia, Bulgaria (Invited lecture)
- Popular science lecture at "Kemimässan", Polhemskolan, Lund (Invited lecture)
- Faraday discussion on Lipids and Membrane Biophysics, London, UK (poster)
- European Colloid and Interface Society (ECIS) conference, Malmö, Sweden (Oral presentation)
- ECIS Advanced school on Calorimetry and Thermodynamics, Malmö, Sweden (Invited lecture)
- Hydration of Biomolecules and Biointerfaces, Malmö, Sweden (Invited lecture)

DANIEL TOPGAARD: Molecular dynamics in organized molecular matter

Project description
Weak intermolecular interactions determine not only the structure of organized molecular matter, but also the dynamic behavior of the molecules. Both the rotational and translational motion is

affected when a molecule takes part as a building block in a larger self-assembled structure. For a complete description of the system, information about the molecular dynamics is required.

The project deals with the study of molecular dynamics in soft matter using a combination of NMR experiments and theoretical approaches. Recent advances in NMR methodology and hardware have made it possible to accurately measure the reorientation of molecular segments and translational diffusion even for multi-component anisotropic materials such as liquid crystals and biomembranes. With proper design of the experimental methods, the estimated parameters have simple geometrical definitions that can be calculated from molecular dynamics simulations, which yield a deeper understanding of the molecular mechanisms being responsible for the experimental observations. The studied systems are chosen to have an optimal complexity with respect to the phenomena under investigation, i.e. they are complex enough for displaying the interesting effects, while still being simple enough for theoretical modeling of the equilibrium structure and the molecular motion.

The same basic laws that govern the behavior of molecules in soft matter are also valid for living systems such as cells and tissues. An important aspect of the project is to apply the new experimental methodologies for the characterization of real biological systems.

The specific goals can be summarized as follows:
1) Developing solid-state and diffusion NMR methods for studying molecular dynamics and supramolecular organization in self-assembled systems being too complex and having too many components for successful studies using currently existing methods.
2) Providing fundamental knowledge about the links between intermolecular interactions, the structure of supramolecular assemblies, and molecular dynamics on the nano- to micrometer scales.
3) Designing new diffusion NMR methods for quantifying structural and dynamic parameters of biological tissues, and implementing the new methods for use in clinical MRI.

Progress during 2012

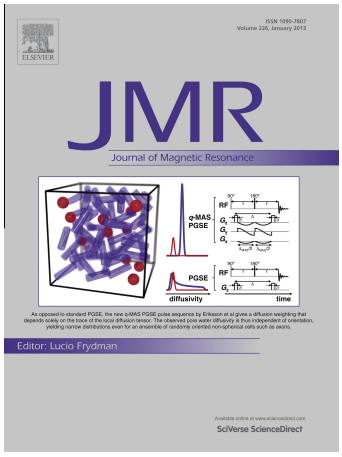
We have developed a new diffusion NMR method for resolving water compartments based on their shape, e.g., spherical or cylindrical. The method is expected to be useful for the characterization of brain grey matter where current state-of-the-art methods fail to give useful information. The work led to two patent applications and was featured on the cover of the Journal of Magnetic Resonance.

OMM junior scientists involved

Agnieszka Nowacka
Jenny Algotsson

External collaborations

Claudia Schmidt, University of Paderborn
Jacob Israelachvili, University of California at Santa Barbara
Freddy Ståhlberg, Medical Radiation Physics, Lund
Magnus Nydén, Chalmers, Göteborg
Winchil Vaz, Coimbra University, Portugal
Michael Grätzel, École Polytechnique Fédérale de Lausanne.



Publications in 2012

- M. Nilsson, J. Lätt, D. van Westen, S. Brockstedt, S. Lasic, F. Ståhlberg, and D. Topgaard, Noninvasive mapping of water diffusional exchange in the human brain using filter-exchange imaging, Magn. Reson. Med. Accepted, (2012).
- T. M. Ferreira, F. Coreta-Gomes, O. H. S. Ollila, M. J. Moreno, W. L. C. Vaz, and D. Topgaard, Cholesterol and POPC segmental order parameters in lipid membranes: Solid state 1H-13C NMR and MD simulation studies, Phys. Chem. Chem. Phys. Accepted, (2012).
- S. Eriksson, S. Lasic, and D. Topgaard, Isotropic diffusion weighting by magic-angle spinning of the q-vector in PGSE NMR, J. Magn. Reson. 226, 13-18 (2013).

- G. W. Greene, B. Zappone, X. Banquy, D. W. Lee, O. Söderman, D. Topgaard, and J. N. Israelachvili, Hyaluronic acid - collagen network interactions during the dynamic compression and recovery of cartilage, Soft Matter 8, 9906-9914 (2012).
- M. Röding, D. Bernin, J. Jonasson, A. Särkkä, D. Topgaard, M. Rudemo, and M. Nydén, The gamma distribution model for pulsed-field gradient NMR studies of molecular-weight distributions of polymers, J. Magn. Reson. 222, 105-111 (2012).
- M. Tang, A. Redler, D. Topgaard, C. Schmidt, and H.-S. Kitzerow, Kinetics of the grating formation in holographic polymer-dispersed liquid crystals: NMR measurement of diffusion coefficients, Colloid Polym. Sci. 290, 751-755 (2012).
- V. K. Thorsmølle, D. Topgaard, J. C. Brauer, S. M. Zakeeruddin, B. Lindman, M. Grätzel, and J.-E. Moser, Conduction through viscoelastic phase in a redox-active ionic liquid at reduced temperatures, Adv. Mater. 24, 781-784 (2012).

Conference presentations in 2012

- Keynote lecture at Magnetic Resonance in Porous Media 11, University of Surrey, UK.
- Invited lectures at the 4th International Conference on Porous Media at Purdue University, USA
- Invited lectures at the Materials for Tomorrow in Göteborg.
- Lecture at the workshop NMR in Heterogeneous Materials in Göteborg.
- Seminars at Applied Physical Chemistry, KTH, Stockholm, and the Center for Language and Literature in Lund.

7. RESEARCH PROJECTS

The ability to control and master intermolecular interactions lies at the heart of modern chemistry and materials science. It enters science at all levels: from the intricate mechanisms that bring together the molecules building up a cell to the processes active in solidifying cement. The research at OMM aims at

- developing the theoretical description of intermolecular interactions and their consequences, including quantum chemical calculations, statistical mechanical theory and computer simulations of multi-molecular systems
- performing experiments on well designed model systems, including the development of new experimental methods and procedures
- implementing the knowledge to a wide number of problems in colloidal biology and in technical/industrial colloidal formulations.

Below, we present ongoing projects, funded mainly by OMM, representing the above three general aims. In addition to the projects below, a number of other related projects funded mainly from other sources are carried out at OMM. A list of all OMM projects can be found at the OMM website http://www.omm.lu.se.

THEORETICAL WORK AND QUANTUM CHEMISTRY AND STATISTICAL MECHANICS

Molecular Interactions in Protein Systems: Leading to Self Assembly and Membrane Affinity

PhD project: *Anıl Kurut, Björn Persson, João Henriques, Marie Skepö, Torbjörn Åkesson, Jan Forsman, Ulf Olsson, Mikael Lund*

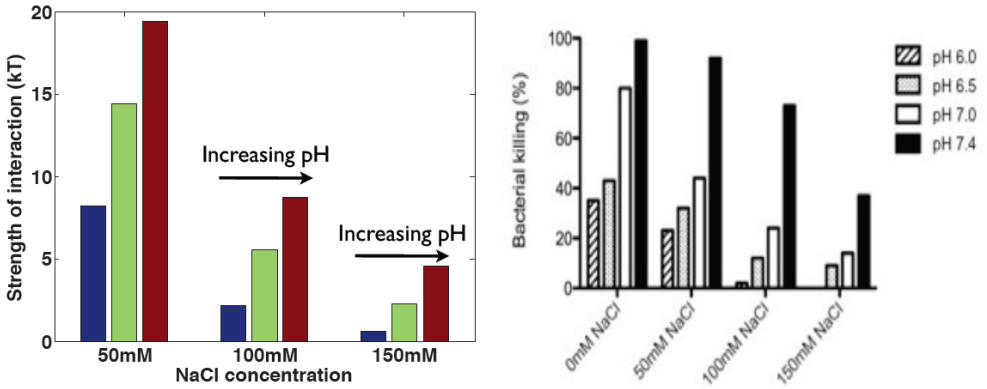
Project description

This project governs statistical modeling of protein systems at a mesoscopic level to illuminate the underlying molecular interactions in their complex behavior. It focuses on the impact of physical conditions such as pH, ionic strength and Hofmeister ions both in biological and food systems. The studied systems, during 2012, are:

• Affinity of midkine to cell membranes in changing physiological conditions and its reflection on the antimicrobial activity (in collaboration with the Dept. of Clinical

Sciences, Lund University).
• Bulk and interface behavior of salivary protein Histatins and the effect of histidine richness.
• Specific ion binding and its effect on protein associations: Reversal of Hofmeister series.
This year, we are planning to proceed in:
• Development of a generic protein model which is applicable to both globular and intrinsically disordered proteins,
• Characterization of interactions that are specific to nanotube forming model peptides,
• Identification of breast milk proteins which bind and activate infant's immune system protein CD14 (in collaboration with the University of Copenhagen),
• Adsorption studies of milk protein beta-casein and salivary protein Histatins on silica surfaces using ellipsometry.

Progress during 2012
We have showed that high histidine content of salivary protein Histatin5 leads to uncommon capacitance peak at pH 6 and provides an extraordinary charge regulation ability in oral environments. This ability promotes adsorption on to negatively charged membranes and may facilitate its antimicrobial activity. Histidines also form complexes with divalent zinc ions and generate extra attraction to the membrane due to the additional positive charges. Further, we have predicted a direct correlation between the surface affinity of Midkine and its antimicrobial activity. In the elevated salt concentrations, the affinity to the membrane is decreased dramatically due to screened electrostatics. Midkine has almost constant net charge in the pH range of interest, which implies that the surface charge modification with respect to pH plays role in its microbial activity. In fact, we have showed that modeling of surface charges responsive to pH, predicts experimental observations-see figure below.



Interaction strength of Midkine with negatively charged membrane (left) and Bacterial activity of Midkine as a function of salt concentration and pH.

We have used an approach similar to the implicit proton titration of basic and acidic residues to enable binding of implicit Hofmeister ions to the backbone and the hydrophobic residues of proteins. We have predicted Hofmeister reversal and salting in effect on the protein association.

External collaboration
Dereck Chatterton - Copenhagen University (Denmark)
Arne Egesten – Faculty of Medicine, Lund University

Publications during 2012
- Anıl Kurut, Björn Persson, Torbjörn Åkesson, Jan Forsman, Mikael Lund, Journal of Physical Chemistry Letters, Volume 3, 2012, pg. 731-734
- Anıl Kurut and Mikael Lund, Faraday Discussions, Volume 160, 2013, pg. 271-278

Conference presentations during 2012
- Poster presentation at Conference of the Colloid and Interface Society, ECIS-2012, Malmö, Sweden
- Poster presentation at 9th International Symposium on Polyelectrolytes - ISP 2012, Lausanne, Switzerland

Ionic Liquids

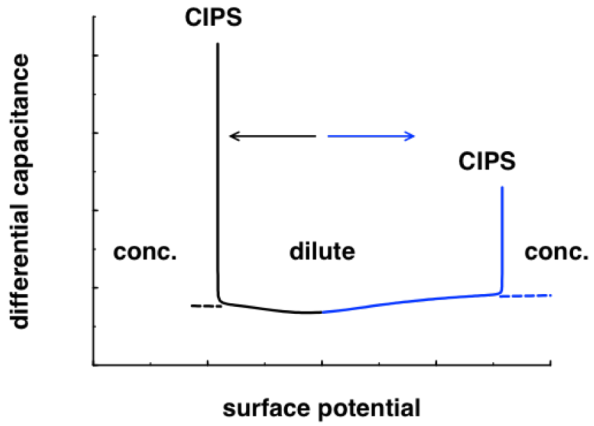
PhD project: *Ryan Szparaga, Jan Forsman*

Project description

This project investigates various fundamental properties and behaviours of Ionic Liquids (ILs). Of particular interest is their high charge concentration, making them interesting candidates for "supercapacitors".

Progress during 2012

We have recently (published 2011) developed a classical density functional theory to treat a simple model of a typical IL. While simple and generic, it was nevertheless the first density functional theory (DFT) constructed for such systems, and it did account for the oligomeric structure of typical ILs. A high accuracy of the theory has been verified via detailed comparisons with simulation data. Subsequently, we have further developed the model, with improved treatments of correlations. Our new model is furthermore polarizable, and can be specifically adapted to reproduce fundamental experimental properties (density-pressure) of *specific* ILs. So far, we have focused on $BmimBF_4$. We will use our model to study the behaviour of ILs in models of electrode nanopores (supercapacitors are made porous, in order to maximize the capacitance). The behaviour of ILs, and the capacaitance they can produce in such environments, is subject to a strong controversy, with conflicting experimental data. We have also devoted efforts to study the tantalizing prospect of capillary-induced phase transitions (CIPS) in nanoporous electrodes, and the p ossibilities these transitions offer for an extremely high fluctuation-enhanced capacitance. Similar effects are conceivable also at a flat electrode surface, provided there is a prewetting transition. In these studies, we have utilized our IL density functional theory, generalized to mixtures, which has been of crucial importance. We anticipate that the pore size polydispersity of typical capacitors will generate broader peaks. These are expected to be of high practical relevance, since one of the strongest drawbacks of supercapacitors is that the voltage *changes* upon discharge, which is problematic for most electrical appliances. A more peaked capacitance is thus highly desirable.



Divergence of the differential capacitance for a nanoporous electrode, immersed in an IL+solvent mixture. The system is close to a first-order capillary-induced phase transition, CIPS. CIPS results upon increasing as well as decreasing the voltage, from its zero reference value.

External collaborations

Cliff Woodward, University of New South Wales (Australia).

Publication during 2012

- R. Szparaga, C. Woodward and J. Forsman, *Theoretical Prediction of the Capacitance of Ionic Liquid Films*, The Journal of Physical Chemistry C **116**, 15946 (2012)

Conference presentations

- *Fluctuation-enhanced differential capacitance in ionic liquid + solvent mixtures.* New Challenges in Electrostatics of Soft Matter, CECAM, Tolouse, France. Invited lecture (J. Forsman).
- *Theoretical Prediction of the Capacitance of Ionic Liquid Films*, Swedish Theoretical Chemistry, Linköping. Oral contribution (R. Szparaga).

Study of noncentrosymmetric dipolar interactions

PhD project: *Alexei Abrikossov, Mikael Lund, Per Linse, Peter Schurtenberger, Gunnar Karlström*

Project description

Modeling of colloidal particles with noncentrosymmetric forces. These could stem from magnetic or electric properties and may be enhanced by external fields. We will also investigate the effect of particle shape and polarisability. The work is done in close collaboration with experimentalists at the division of Physical Chemistry as well as with the van 't Hofft Laboratory in the Netherlands. Besides basic understanding of such systems we will also investigate how noncentrosymmetric forces may inuence phase behavior in concentrated systems with or without the presence of external fields.

Progress during 2012

In our first publication we modeled and simulated using Monte Carlo methods the self-assembly of spherical colloidal particles with off-centered magnetic dipoles. In this publication (submitted to Soft Matter) we managed to reproduce the experimental setup of S. Sacanna. In the immediate future we are working on modeling the experimental setup of professor Peter Schurtenberger where he studies polarizable ionic micro-gels. We hope to be able to reproduce the experimental results using Monte Carlo simulations and help get more insight in that specific case.

External collaborations

Albert P. Philipse, van 't Hofft Laboratory, the Netherlands

STUDIES OF MODEL SYSTEMS

Polymer/surfactant interactions at liquid interfaces

PhD project: *Marianna Yanez, Tommy Nylander, Lennart Piculell*

Project description

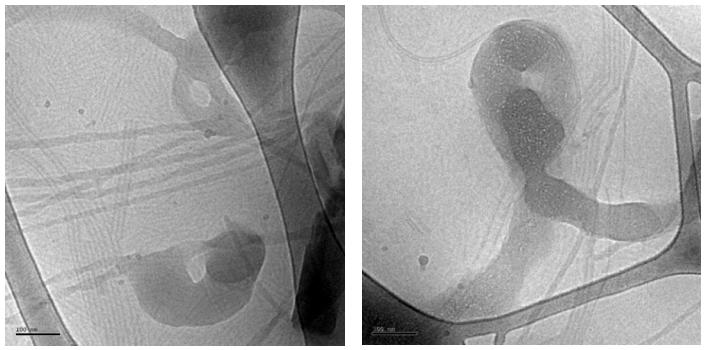
Mixtures of oppositely charged polyelectrolyte/surfactant (P/S) are essential for a range of commercial applications as detergency and pharmaceutics. We have studied the interactions at different interfaces of the cationic polyelectrolytes poly(diallyldimethylammonium chloride) (PDADMAC) and poly(ethylene imine) (PEI) and the anionic surfactant sodium dodecyl sulfate (SDS). These have been investigated on the air/liquid and solid/liquid interface on hydrophobic silica employing neutron reflectometry (NR). The aim of this work was to relate the presence of multilayers at interfaces of an oppositely charged polyelectrolyte/surfactant mixture to the direction of the aggregate transport in the bulk solution. We have also studied the interactions of cationic poly(amidoamine) (PAMAM) dendrimers with different anionic surfactants like SDS and nucleic acid base surfactants/lipids dilauroylphospholiponucleosides (DLPN) derivatives based on adenosine (DLPA) and uridine (DLPU). PAMAM dendrimers are a type of polymer with well-defined and interesting architecture that have been proposed as possible nanocapsules and gene vectors. Their synthesis consists in iterative reactions that produce different dendrimer generations which will increase in size, molecular weight and number of surface groups. PAMAM dendrimers associates strongly with the oppositely charged surfactants and forms complexes of different charge and sizes depending on the P/S ratio. We employ a combination of bulk solution techniques as scattering, cryogenic transmission electron microscopy (Cryo-TEM, see figure 1), electrophoretic mobility and turbidity measurements in combination with surface techniques like NR, quartz crystal microbalance with dissipation monitoring (QCM-D) and ellipsometry to assess the structure and composition of aggregates in the bulk of the solution and at the silica/water and air/water interface. The improved understanding of PAMAM/surfactant interactions outlined in this work broadens the fundamental knowledge towards future dendrimer applications interacting with amphiphiles and allows obtaining more effective gene vectors with capacity for molecular recognition without extensive synthesis.

Progress during 2012

We have demonstrated that multilayers at interfaces of the oppositely charged system PDADMAC/SDS can be the result of the transport under gravity of bulk aggregates with internal molecular structure and the results have been published in J. Phys. Chem. B 2012 (see below). Related work with mixtures of PEI and SDS has shown that for into the adsorption layers at the solid/liquid interface with solid surfaces located both above and below the bulk liquid gravity also plays a major role in the transport and penetration of particles with internal structure.

For the system PAMAM/SDS we have observed that at the air/water interface there is a synergistic enhancement of adsorbed SDS in the presence of PAMAM dendrimers. NR profiles of PAMAM generation 2 with SDS show a Bragg peak depending on the isotopic composition indicating interfacial multilayers, while generation 4 and 8 do not show this behaviour. The NR measurements are being complemented with ellipsometry and small angle neutron scattering measurements to establish the relation between bulk aggregates and the film formation. For the hydrophilic silica/water interface, we have found that PAMAM dendrimers generation 4 and 8 do adsorb on silica and interact with SDS. The layers formed will depend on the SDS concentration and the dendrimer generation as it defines the number of surfactant molecules that binds to the polymer layer. The interactions of solutions of PAMAM/SDS pre-mixed on silica are different from the case with pre-adsorbed polymer and sequential addition of SDS. The adsorption is mainly driven by the polymer-substrate interactions. However, the complexes phase separate around charge neutrality where the adsorption reaches a maximum and forms multilayers. Complexes with excess of SDS will also adsorb but the amount will decrease as the charge ratio becomes more negative. The adsorption process for the mixtures is also dependent of the pathway of adsorption (separated versus sequential injections of mixtures with different SDS concentrations) which indicates that the layers are trapped in metastable states and thus it makes difficult to apply a thermodynamic model. The manuscript of this work is in preparation.

We have been awarded beam time in ILL (Grenoble, France) and ISIS (Didcot. England) to investigate the systems PAMAM/DLPNs with NR. The experiments will be focus on the interfacial composition of DLPNs interacting with pre-adsorbed monolayers of PAMAM-G4 as QCM-D has shown that this system behaves differently to PAMAM/SDS at the silica/water interface. The interactions of single stranded DNA with PAMAM/DLPN layers will also be study to establish if the system has the ability of interact with nucleic acids through base pairing. The interactions at the solid/liquid interface and at the bulk of the solution will be the major focus of the project and we expect to have a manuscript prepared related to this work for the last semester of 2013.



Cryo-TEM images of DLPA/PAMAM aggregates. The scale bar is 100 nm.

External collaborations

Richard Campbell, ILL, Grenoble
Imre Varga, Budapest University of Technology and Economics
Anna Angus-Smyth, Durham University
Debora Berti, University of Florence
Piero Baglioni, University of Florence

Publications in 2012

- Campbell, R. A.; Yanez Arteta, M.; Angus-Smyth, A.; Nylander, T.; Varga; I. *Multilayers at Interfaces of an Oppositely Charged Polyelectrolyte/Surfactant System Resulting from the Transport of Bulk Aggregates under Gravity*. J. Phys. Chem. B., 2012, 116, 7981-7990.

Conference presentations in 2012

- 26th Conference of the European Colloid and Interface Society, Malmö, Sweden.
- Oral presentation: Neutron reflectometry study of the interactions of PAMAM dendrimers with surfactants at interfaces.
- Poster presentation: Interactions of PAMAM dendrimers with designer biosurfactants

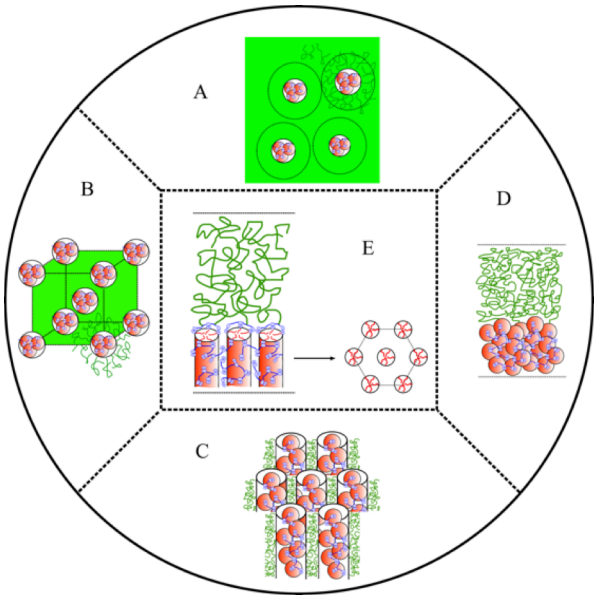
Self-assembly in melts of block-copolymer-based systems featuring supramolecular interactions

PhD project: *Mehran Asad Ayoubi, Lennart Piculell and Ulf Olsson*

Project description

For a diblock copolymer (polyA-*b*-polyB), the thermodynamic incompatibility between polyA and polyB blocks drives a microphase separation in the melt state where alternating A-rich and B-rich microdomains appear in order to minimize the contact between dissimilar polyA and polyB blocks. The block copolymer (BC) microphase separation has previously been studied in detail and it was shown, by both theory and experiment, that the segregated regions of polyA and polyB could form structures that have liquid crystalline ordering.

We study experimentally self-assembly in solvent-free macromolecular systems based on a series of block-copolymers of the composition poly(styrene)-*b*-poly(methacrylic acid) (PS-*b*-PMAA). A comprehensive study is made of a new class of block cobpolymer-based ionic supramolecules, named Linear-b-AmphComb, that feature hirachical self-assembly charateristics. These polymers are produced by a facile and versatile supramolecular synthesis procedure, namely, partial or complete titration of the acidic groups on in the PMAA blocks with the hydroxide form of a cationic surfactant.



Schematics of the structure-in-structure two-scale hierarchical self-assemblies found for various Linear-b-AmphComb ionic supramolecules: (A) S-in-SLL, (B) S-in-SBCC, (C) S-in-C, (D) S-in-L and (E) C-in-L.

Progress during 2012

A series of PS-*b*-PMAA BCs have been provided and characterized by our external collaborators Bo Nyström and Kaizheng Zhu (University of Oslo) and Kristoffer Almdal (Danish Technical University), respectively. SAXS and WAXS were performed at MaxLab synchrotron facility and rheology experiments were carried out at DTU. The melt phase behavior was completely determined. Compared to theoretical predictions, the experimental systems featured a stronger curvature towards the domains of the minority PMAA blocks. This deviation could be explained by the polydisperse nature of PMAA blocks.

A class of ionic BC-based supramolecules was synthesized as described above, made up of one linear non-polar polymeric block and one *strongly* amphiphilic comb-like AmphComb supramolecular block containing a polar ionic backbone to which *single*- and *multi*-tail alkyl side-chains were attached. The following conclusions were reached.

(1) Micro- and nanophase separations can occur simultaneously between the Linear and the AmphComb blocks and within the AmphComb block, respectively, resulting in a variety of hierarchical *structure*-in-*structure* morphologies, including *S*-in-*S*, *S*-in-*C*, *S*-in-*L* and *C*-in-*L*, where *S*, *C* and *L* stand for spherical, cylindrical and lamellar, respectively.

(2) First, an increase in the volume fraction of the AmphComb block $\Phi_{AmphComb}$ was accompanied by various microdomain morphological changes in favor of a *less* curved interface. Second, keeping $\Phi_{AmphComb}$ unchanged, upon an increase in (i) the number of the alkyl tails per side-chain branch point, (ii) the number of carbons per alkyl tail, (iii) the overall molecular weight of the parent block copolymer, or (iv) the composition of the parent block copolymer Φ_{PMAA}, the system either maintained its microdomain morphology or adoptedd a microdomain morphology in favor of a *less* curved interface.

(3) The presence of the alkyl side-chains affects the size characteristics of *S* and *L* microdomain morphologies of the systems in the following manner: For *S* microdomain morphology, an increase in the number of alkyl tails per side-chain branch point is accompanied by an increase in the interfacial area per block junction Σ_S. For *L* microdomain morphology, upon an increase in either the number of alkyl tails per side-chain branch point, or the number of carbons per alkyl tail, the interfacial area per block junction Σ_L increases, the thickness of the microlayer of the Linear block d_{Lin} decreases and the thickness of the microlayer of the AmphComb block $d_{AmphComb}$ (generally) increases.

External collaborations
Kristoffer Almdal (Micro- and Nanotechnology, DTU)
Bo Nyström and Kaizheng Zhu (University of Oslo)
Alexei Khokhlov (Moscow State University/Russian Academy of Sciences).

Publications during 2012
Mehran Asad Ayoubi wrote his thesis titled " Self-assembly in melts of block-copolymer-based systems featuring supramolecular interactions" successfully defended it on December 6, 2013. The faculty opponent was Nitash Balsara, UC Berkeley. One paper from the thesis was accepted for publication during 2013 in Soft Matter.

Soluble Complex Salts of Surfacant Ions and Polymeric Counterions: Composite Macromolecular Self-Assembly

PhD project: *John Janiak, Karin Schillén, Lennart Piculell*

Project description
The aim of this work is to study intermolecular interactions in systems containing a charged polyion (polyacrylate, PA_n^-, n=polymerization degree), cationic surfactant ($C_{16}TA^+$) and nonionic surfactant ($C_{12}E_5$ or $C_{12}E_8$). Two different so-called complex salts, $C_{16}TAPA_{25}$ and $C_{16}TAPA_{6000}$, both consisting of ($C_{16}TA^+$) with polyions PA_{25}^- or PA_{6000}^- as counterions have been prepared (no simple salt is present). They are insoluble in water and by adding nonionic surfactant they can be solubilized. Decreasing polyion length and increasing the PEO chain length of the nonionic surfactant important factors for increasing the solubility of the complex salt. The previous phase studies on systems containing $C_{16}TAPA_y$ complex salts in water mixed with either $C_{12}E_5$ or $C_{12}E_8$ have been carried out by visual inspection of the samples and by using small-angle X-ray scattering (SAXS).

Progress during 2012
Several studies were carried out in parallell. The dilute aqueous solution properties of composite self-assembled aggregates of $C_{16}TAPA_{25}$ or $C_{16}TAPA_{6000}$ ion complex salts and $C_{12}E_8$ (i.e the fully dissolved complex salt) have been investigated at different temperatures by means of dynamic light scattering (DLS), isothermal titration calorimetry, cryo-transmission electron microscopy, SAXS and nuclear magnetic resonance (NMR) diffusometry. Using the basis of the phase study previously performed, nanoparticles with internal order (bicontinuous cubic, Ia3d or hexagonal, H_1) were formed by dispersing poly(acrylic acid)$_{6000}$, $C_{16}TAOH$ and $C_{12}E_5$ in water with mixing ratios coinciding with the two-phase areas of the phase diagram of $C_{16}TAPA_{6000}/C_{12}E_5$/water. The internal ordering was identified by synchrotron-SAXS. The particles, which are stable for more than one month, have a well-defined size and a positive net-charge. In the third project, two novel complex salts were prepared with the cationic surfactant, hexadecyltrimethylammonium, and two different copolyions constituted by a poly(methacrylate) main chain randomly grafted with

oligo(oxyethylene) side chains in order to increase the solubilization. Surface tension experiments revealed that the complex salts form, in the absence of all other ions, soluble aggregates by surfactant self-assembly with a distinct critical micellar concentration. The physcio-chemical nature of the aggregates was investigated by DLS, NMR diffusometry, steady-state fluorescence spectroscopy. Finally, soluble aggregates formed in dilute aqueous mixtures of two different polyacrylates, the cationic surfactant decyl betainate (DB), and $C_{12}E_8$ have also been characterized as potenital devices for controlled release using NMR techniques. The polyion acts as a counter ion to the DB-$C_{12}E_8$ mixed micelles. DB is a cleavable surfactant that degrades under hydrolysis into decanol and betaine at pH=7 or higher. By controlling pH, the polyelectrolyte can be released into the solution while the otherwise insoluble decanol is dissolved into mixed micelles. The kinetic studies were also carried out. It was releaved that the rate of hydrolysis of DB was decreased with the polyion present in the system.

External collaborations
Dan Lunberg (Colloidal Resource, CR Competence, Lund, Sweden)
Matija Tomšič (University of Ljubljana, Slovenia)
Watson Loh and Ana Maria Percebom (University of Campinas, Brazil)
Luciano Galantini and Nicolae Viorel Pavel (University of Rome "La Sapienza", Italy)

Publications in 2012
- M. Percebom, J. Janiak, K. Schillén, L. Piculell and W. Loh, Micellization of Water-Soluble Complex Salts of an Ionic Surfactant with Hairy Polymeric Counterions. Soft Matter (2013) 9, 515-526.
- 4. J. Janiak, S. Bayati, L.Galantini, N. V. Pavel and K. Schillén, Nanoparticles with Bicontinuous Cubic Internal Structure Formed by Cationic and Nonionic Surfactants and an Anionic Polyelectrolyte. Langmuir (2012) 28, 16536-16546.
- 5. J. Janiak, L. Piculell, K. Schillén and D. Lundberg, Responsive Release of Polyanions from the Soluble Aggregates Formed with a Hydrolyzable Cationic Surfactant, and a Nonionic Surfactant. Soft Matter (2013), accepted.
- PhD thesis with the title *Phase Behavior and Solution Properties of Aqueous Polyion-Surfactant Ion Systems*

Conference presentations 2012
- J. Janiak, K. Schillén, S. Bayati, N. V. Pavel and L. Galantini, Internally Structured Nanoparticles of Surfactant Ion-Polyion Complex Salt and Nonionic Surfactant, *XXVI European Colloid and Interface Society Conference*, Malmö-Lund, Sweden, *(poster)*

Amphiphilic Polymers – Their Formation of Supramolecular Structures with Cyclodextrin and Interaction with Other Amphiphilic Molecules in Aqueous Solution and at Solid/Liquid Interfaces

PhD project: *Solmaz Bayati, Karin Schillén, Tommy Nylander*

Project description
The aim of this PhD project is to study amphiphilic block copolymer systems with temperature-sensitive behavior and their interaction with other amphiphilic molecules, e.g. oppositely charged block copolymers, as well as their the formation of supramolecular structures with cyclodextrin (CD). The specific objectives are to investigate (not in order of performance): a) the spontaneous mixed micellar formation in water of oppositely charged diblock copolymers with the same neutral hydrophilic block (e.g. poly(*N*-isopropylacrylamide), PNIPAAM) and the effect of cyclodextrin addition on the mixed micellar structure, b) CD-copolymer inclusion complexes at solid/liquid interfaces: the structure and thermal response behavior of layers of PNIPAAM-containing copolymers adsorbed at different solid/liquid interfaces (flat or curved), with or without the presence of CD.

Progress during 2012
Inclusion complex formation between temperature-responsive PNIPAAM-containing copolymers and cyclodextrin at solid/liquid interfaces. The temperature response of cationic diblock

copolymers of PNIPAAM and poly((3-acrylamidopropyl)trimethyl ammonium chloride [PAMPTMA(+)] adsorbed at silica/liquid surfaces and the effect of γ-CD on the polymer layer structure have been investigated by ellipsometry, neutron reflectivity (NR) and quartz-crystal microbalance with dissipation monitoring (QCM-D). The PNIPAAM block length was varied keeping the PAMPTMA(+) block constant. The NR measurements showed that the copolymers adsorbs to the surface with a layer thickness that depends on the PNIPAAM block length (thicker the longer the PNIPAAM block). The layer thickness responded reversibly with a change in temperature below and above the effective lower critical solution temperature (LCST) of PNIPAAM. It was found from the γ-CD-copolymer inclusion complex adsorption experiments using NR that the adsorbed polymer layer was thinner indicating a different structure compared to the bare polymer case (see Figure 1). This is in accordance with the ellipsometry measurements.

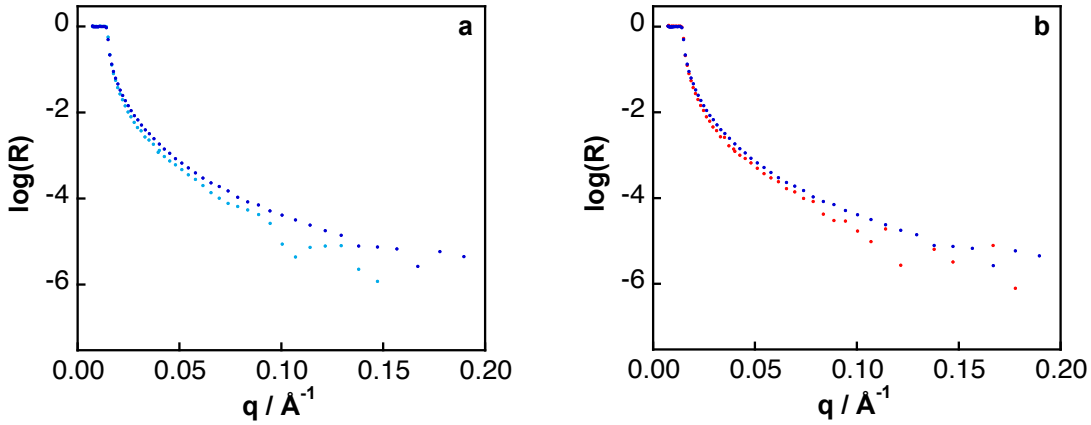


Figure 1. *Neutron reflectivity profiles (log(reflectivity, R) as a function of the magnitude of the scattering vector, q) of a) $PNIPAAM_{65}$-$PAMPTMA_{20}$(+)copolymers adsorbed on a hydrophilic silica surface (light blue symbols) compared to the bare surface (blue symbols) b) γ-CD-$PNIPAAM_{65}$-$PAMPTMA_{20}$(+) inclusion complexes adsorbed on a hydrophilic silica surface (red symbols) compared to the bare surface (blue symbols) in 1 mM D_2O at 20 °C.*

Mixed micelles of oppositely charged PNIPAAM diblock copolymers in aqueous solution. Complex coacervate core micelles formed in water by electrostatic attraction between two oppositely charged diblock copolymers both containing a PNIPAAM block of the same length have been studied using dynamic and static light scattering in combination with turbidimetry and zeta potential measurements (see the Bachelor thesis project of Hanna Bergenholtz).

External collaborations

Bo Nyström (Oslo University, Norway)
Richard A. Campbell (Institut Laue-Langevin (ILL), France)
Giuseppe Lazzara (University of Palermo, Italy)

Conference presentations 2012

- G. Lazzara, N. Reichardt, S. Bayati, R. A. Campbell, K. Zhu, B. Nyström, T. Nylander and K. Schillén, Temperature-Response of γ-Cyclodextrin-PNIPAAM Diblock Copolymer Inclusion Complexes at the Solid/Liquid Interface, *XXVI European Colloid and Interface Society Conference*, Malmö-Lund, Sweden, September 2012 *(poster)*

EXPERIMENTAL METHODOLOGIES

Solid-state NMR studies of molecular dynamics and nanoscale organization in molecular matter

***PhD project**: Agnieszka Nowacka, Daniel Topgaard, Emma Sparr, Sara Linse, Dan Lundberg, Sebastian Björklund, Erik Hellstrand, Azat Bilalov, Nils Bongartz, Jens Norrman*

Project description

Many biological and technically important materials are mixtures of several types of molecules in coexisting crystalline solids, amorphous solids, liquid crystalline domains, and a fluid microphase. One example is the *stratum corneum*, the outer layer of the skin with ceramides, fatty acids, moisturizers such as urea and glycerol, and water. Another example is shampoo, typically consisting of water, fatty acids, detergents, and a plethora of minor components. In order to fully characterize these systems one would like to determine in which kind of aggregates the molecules are organized, the dynamic state of the molecules, and the molecular composition in the various microdomains. Most experimental techniques can detect either solids or liquids, or requires long-range order.

Within this project we combine existing and develop new NMR methods for obtaining molecularly detailed information from complex mixtures of the type described above. In order to validate the methods, suitable model systems having the optimal degree of complexity are used. Cationic surfactant with oligomeric counterions, the aqueous phase behavior of which has been in detail characterized by the group of Piculell, was shown to be a suitable model system with solid crystalline, liquid crystalline, and isotropic liquid phases within a convenient range of temperatures and relative humidities. NMR methods based on ^{13}C detection under magic angle spinning and ^{1}H decoupling yields excellent resolution of various molecules and molecular segments. Optimized polarization transfer methods can be used to "filter" the recorded ^{13}C spectra based on the segment mobility. Rigid segments are selectively detected with the cross polarization technique, while fluid segments yield signal with the INEPT (Insensitive Nuclei Enhanced by Polarization Transfer) method. For solid segments, the values and the distribution of the ^{13}C chemical shifts gives information on if the segments have solidified in a ordered or disordered local environment, i.e. if the microdomain is crystalline or amorphous. The new set of NMR methods was used to investigate the low humidity phase behavior for the binary systems hexadecyltrimethylammonium succinate/water, hexadecyltrimethylammonium poly-acrylate/water and octyl maltoside/water and the ternary systems hexadecyltrimethylammonium succinate/decanol/water, hexadecyltrimethyl-ammonium DNA/decanol/water, 1,2-dimyristoyl-sn-glycero-3-phosphocholine/glycerol/water, and 1,2-dimyristoyl-sn-glycero-3-phosphocholine/urea/water. Furthermore, the method was applied onto more complex systems of amyloid fibrils, skin samples and stratum corneum extracts.

Progress during 2012

Three manuscripts were completed and submitted during 2012. The first one describes a refinement of our theoretical model for predicting the efficiency of polarization transfer as a function of the rate and anisotropy of CH bond reorientation. The model was tested using molecular dynamics simulations and experiments on the model system octyl maltoside/water. The second deals with the changes of molecular dynamics of lipids and proteins in intact *stratum corneum* as a function of water content and temperature. The third is a study of the coaggregation of lipids and proteins during the formation of amyloid fibrils.

External collaboration

Rachel W Martin (University of California, Irvine)
Joke Bouwstra (Leiden University, Netherlands)

Publications in 2012

- A. Nowacka, S. Douezan, L. Wadso, D. Topgaard, E. Sparr, Small polar molecules like glycerol and urea can preserve the fluidity of lipid bilayers under dry conditions, Soft Matter, 2012, 8, 1482-1491

COLLOIDAL BIOLOGY

Diffusive transport of multivalent ions in cartilage

PhD project: *Jenny Algotsson, Olle Söderman, Daniel Topgaard, Jan Forsman*

Project description

In this project, which was initiated in November 2010, articular cartilage is investigated. Damaged cartilage is depleted from negatively charged proteoglycans that reside on the structure-building collagen network. $Gd(DTPA)^{2-}$ can be used as a MRI contrast agent to monitor the proteoglycan concentration in cartilage. In healthy and damaged cartilage, the concentration of $Gd(DTPA)^{2-}$ will be low and high, respectively. However, many questions remain unanswered. What is the dynamics of the Gd-complex in cartilage? Can we quantify the proteoglycan concentration in terms of T_1 contrast? Within this PhD project we are focusing on these questions and try to answer them by a combination of computer simulations and NMR.

Progress during 2012

During 2012 we have performed NMR measurements on a model system of cartilage that show the diffusion and distribution of $Gd(DTPA)^{2-}$ with spatial and temporal resolution. The system is based on a polyelectrolyte solution where the charge density can be varied in a systematic fashion. The model system has been designed to capture the essential features of cartilage as well as being amenable to computer simulations we have done previously.

External collaborations

Leif Dahlberg, Joint and soft tissue unit, Faculty of medicine, Lund University.
Eveliina Lammentausta, Department of Diagnostic Radiology, Oulu University Hospital

Publication in 2012

- J. Algotsson, T. Åkesson, J. Forsman, *Monte Carlo simulations of Donnan equilibrium in cartilage*, Magn. Reson. Med., 68, 1298-1302 (2012)

Conference presentations in 2012

- *European Colloid and Interface Society (ECIS),* Malmö, Sweden (Poster)
- *International Bologna Conference on Magnetic Resonance in Porous Media (MRPM),* Guildford, UK (Poster)
- *Nordic Meeting on Quantitative Imaging of Cartilage*, Malmö, Sweden (Oral presentation)

Dynamics of proteins in a crowded environment

Post-doc project: *Lucia Casal-Dujat, Saskia Bucciarelli, Daniel Topgaard, Sara Linse, Mikael Lund, Peter Schurtenberger, Anna Stradner*

Project description

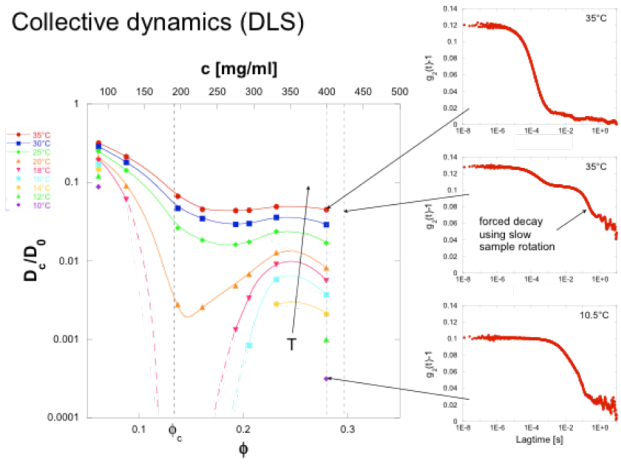
Diffusion of proteins in cells is essential, as it strongly influences numerous processes such as signal transmission or reactions between proteins. It is thus vital to measure, understand and predict the diffusion of proteins in the cell cytoplasm. In the current project we mainly rely on a combination of different scattering techniques in order to study the diffusion of proteins in a concentrated protein background mimicking the cell environment. Dynamic light scattering (DLS) gives us information on the collective diffusion, while neutron spin echo (NSE) experiments provide us with short time dynamics, over length scales directly comparable to those over which we will have structural information from small-angle X-ray and/or neutron scattering (SAXS and SANS). In addition, PGSE-NMR (pulsed-gradient spin-echo NMR) will provide the long time self-diffusive motion of the individual proteins over much larger distances.

Progress during 2012

During the first months of this project we focused on the interplay between critical phenomena and dynamical arrest in concentrated solutions of the lens protein γ_B-crystallin. This globular protein closely resembles the phase behaviour of colloidal particles interacting via a T-dependent short-range attractive potential and exhibits a metastable liquid-liquid phase separation. We used a combination of 3D SLS and DLS, SAXS and NSE measurements to study the structural properties as well as the collective and self diffusion of the protein at the relevant length and time scales as a function of temperature at concentrations close to and above the critical concentration. With DLS we indeed find very different divergence of the characteristic decay time of the intermediate scattering function along the critical isochore and along isochores at higher concentrations, with a clear signature of critical slowing down along the former, and dynamical arrest caused by the presence of an attractive glass transition along the latter. This scenario is supported by NSE measurements, which probe the local self diffusive motion of the individual proteins. These results allow us to gain a better understanding of the role that γ_B-crystallin plays in lens diseases that are ultimately linked to the attractive interactions of this protein.

T- and c-dependence of the normalized collective diffusion coefficient D_c/D_0 in γ_B-crystallin solutions: Around the critical concentration (ϕ_c), collective diffusion is completely dominated by the critical slowing down and D_c/D_0 goes to zero at the critical point. At concentrations above the critical point, the collective dynamics is influenced both by critical fluctuations upon approaching the spinodal as well as dynamical arrest because of the nearby arrest line.

T- and c-dependence of the normalized collective diffusion coefficient D_c/D_0 in γ_B-crystallin solutions: Around the critical concentration (ϕ_c), collective diffusion is completely dominated by the critical slowing down and D_c/D_0 goes to zero at the critical point. At concentrations above the critical point, the collective dynamics is influenced both by critical fluctuations upon approaching the spinodal as well as dynamical arrest because of the nearby arrest line.



T- and c-dependence of the normalized collective diffusion coefficient D_c/D_0 in γ_B-crystallin solutions: Around the critical concentration (ϕ_c), collective diffusion is completely dominated by the critical slowing down and D_c/D_0 goes to zero at the critical point. At concentrations above the critical point, the collective dynamics is influenced both by critical fluctuations upon approaching the spinodal as well as dynamical arrest because of the nearby arrest line.

External collaboration

Bela Farago, Institute Laue Langevin, Grenoble, France
George Thurston, Rochester Institute of Technology, Rochester, NY, USA

Conference presentations in 2012

- *SoftComp Annual Meeting 2012*, Heraklion, Crete, Greece (oral presentation)
- *European Colloid and Interface Society (ECIS) conference 2012*, Malmö, Sweden (oral presentation)
- *International Conference on Molecular Crowding 2012: Chemistry and Physics meet Biology*, Monte Verità, Switzerland (Invited Lecture)

Self-Association and Interactions in Patchy Protein Solutions

PhD project: *Weimin Li, Björn Persson, Mikael Lund, Malin Zackrisson Oskolkova*

Project description

This project, initiated in October 2012, involves studies of protein-protein interactions and possible self-association behavior. We are interested in the link between anisotropic protein interactions, often assumed to have a "patchy" character, and the corresponding structures formed along with the overall phase behavior. We have chosen to start by investigating the globular protein Lactoferrin, a relatively large, globular, water-soluble protein consisting of about 700 amino acids and a molecular weight of 80 kDa. This generic protein is found in milk, saliva, tear fluid and nasal secretions and it plays a major role in the immune system as an antibacterial agent. Lactoferrin is believed to to self-associate under certain solution conditions (e.g.temperature, pH, salt and solute concentration). The project is done in collaboration with M. Lund and co-workers who found, using computer simulations a dimer formation when the pH was increased, approaching isoelectric conditions (pI = 9.4). The dimerization is believed to be driven by a coupling between electrostatic and van der Waals interactions and found to be stereo-specific i.e. a charged patch at the surface of a protein gives rise to, under certain conditions, a highly complementary physical bond between two proteins. In the first part we will set out to experimentally verify the formation of dimers, measure and quantitative compare the strength of the interactions via measurements of the second virial coefficient. Lactoferrin can then be used as a model for a one-patch attractive protein where we want to explore the analogy with one-patch attractive colloids and Lactoferrin proteins.

Results during 2012

We have started to investigate the solution behavior of Bovine Lactoferrin using Static Light Scattering (SLS) along with Dynamic Light Scattering and Small-Angle X-ray Scattering (SAXS). A purification and concentration protocol has been worked out producing well-behaving, monomeric Lactoferrin with a well-defined background in terms of control of pH and ionic concentration. The first results show that under dilute-ideal conditions at low pH, no self-association occurs, as expected. We see from static light scattering (SLS) only monomeric Lactoferrin with a molecular weight in good agreement with the literature value. This was further supplemented by measurements of the form factor using SAXS. In the analysis the scattered intensity is found to compare nicely to that calculated using the crystal structure of Lactoferrin. However, upon increasing pH, we are expecting to see dimers form. Still under dilute-ideal concentrations, from Dynamic Light Scattering (DLS), we indeed observe a decrease in the dilute-limiting diffusion coefficient, corresponding to an increase in the apparent hydrodynamic radius. In addition, from SLS the apparent molecular weight was obtained which is also increasing, as the pH is increased. Thus, from LDS and SLS we have good indications of the onset of dimerization.

External collaborators

Paula Sofia daSilva, Department of Biochemistry, University of Coimbra

Atomistic modelling of exible proteins

PhD project: *Joao Henriques, Anil Kurut, Sara Snogerup Linse, Mikael Lund, Marie Skepö*

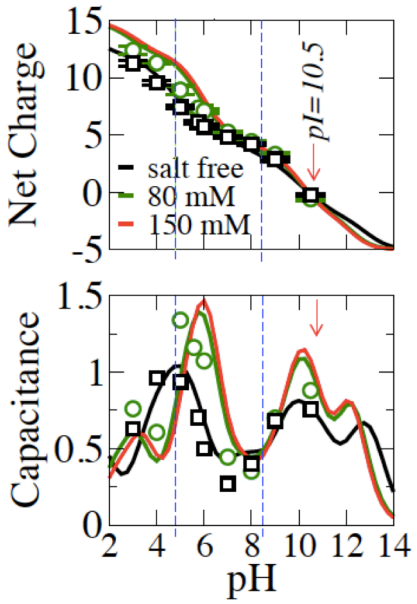
Project description

Histatin 5 is a small flexible protein (24 aa) found in saliva with particularly interesting clinical (highest candidacidal activity of all histatins) and modeling properties (contains 7 histidine residues which give rise to charge regulation effects at physiologically relevant pH values). Despite its importance in the nonimmune oral host defense system, there are only a few reports on the secondaty structure and structure-function analyses.

The main goal of this project is to study intrinsically disordered proteins (flexible proteins) and relate their structure and function in solution with the adsorbed state. For this we propose a combined theoretical and experimental approach using histatin 5 as a model for the histatin protein family and as a starting point towards the understanding of other flexible proteins of higher structural complexity. Constant-pH atomistic molecular dynamics (CpH-MD) and experimental techniques such as circular dichroism (CD), size exclusion chromatography and small-angle X-ray scattering (SAXS) will be used in order aid the development of a coarse-grained model of flexible proteins which can be used for the modeling complex systems such as protein-protein and protein-surface interactions,and ultimately saliva.

Progress during 2012

Theoretical studies involving CpH-MD and coarse-grained Monte Carlo (MC) simulations of histatin 5 in aqueous solution at different pH values, salt concentrations and valencies, and temperatures, produced similar electrostatic properties (net charge and capacitance as a function of pH, see figure). This is an important finding due to the lack of experimental data so far and because, to some extent, it validates the electrostatics used in the current coarse-grained MC model, which is less computationally expensive and allows the simulation of more complex systems as mentioned above. The understanding of systems of higher complexity is of great interest to the project but also prohibitively demanding at an atomistic level of detail.



Net charge and capacitance of histatin 5 as a function of pH and 1:1 salt concentration calculated using coarse-grained MC (lines) and atomistic constant-pH MD (circles) simulations. The area in between the dashed lines shows salivary conditions.

Conference presentation in 2012

- *9th International Symposium: Polyelectrolytes,* Lausanne, Switzerland (Poster presentation)
- *1st Annual Retreat for COMPUTE*, Åhus, Sweden (Poster presentation)
- *26th Conference of the European Colloid and Interface Society*, Malmö, Sweden (Poster presentation)

Interactions between lipid membranes and amyloid proteins in Parkinson disease

Post-doc project: *Marie Grey, Erik Hellstrand, Emma Sparr, Sara Snogerup Linse*

Project description

This post-doc project is a joint collaborative effort between Emma Sparr, Sara Snogerup Linse and Patrik Brundin (Wallenberg Neurosciencecenter, Lund university). The postdoc project it is financed 50% by OMM and 50% by the Linnaeus center BAGADILICO (a basal ganglia disorder research consortium).

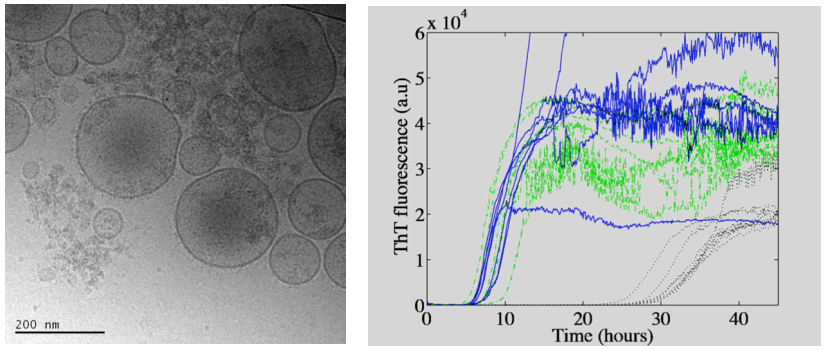
In Parkinson's disease (PD), α-synuclein (αS) aggregates, together with lipids and mitochondria, into Lewy bodies and Lewy neurites, which are the neuropathological hallmarks of the disease. The mechanism whereby α-synuclein mediates neurotoxicity is not clear and it is debated whether the αS aggregates *per se* are toxic or represent a way by which cells' disarm more toxic intermediate αS species. Observations of αS aggregates in neurons grafted into brains of PD patients have suggested cell-to-cell transfer of αS and a prion-like mechanism. Recently, exosomes (secreted membrane vesicles 100nm in size) were suggested to play a role in

intercellular transfer of αS [5,6]. Therefore we investigate the exosome interaction with aggregating αS.

Progress during 2012

We study α-synuclein in the presence of biological membranes in exosomes from N2a cells (a semi-adherent, fast growing, mouse Neuroblastoma cell line), without or with induced overexpression of α-synuclein. We have characterised the exosomes in terms of size, morphology, zeta potential by means of cryo-TEM, dynamic light scattering (DLS) electrophoretic mobility. In on-going mass spectrometry studies, we also aim at a characterisation of the lipid composition in the exosome membranes. We have shown that the exosomes are remarkably unilamellar and the surface char ge differs between the system with overexpressed α-synuclein compared to the reference system. The overexpressed protein was also detected in the cryo-TEM images (Figure, left panel).

We studied aggregation kinetics for α-synuclein in the presence of exosomes, and compared to aggregation in the presence of lipid vesicles with different composition and different charge (anionic, cationic and zwitterionic lipids). It is remarkable that the presence of exosomes has the effect to accelerate the aggregation process (Figure, right panel), while for all model unilamellar vesicle systems investigated, only retardation has been observed. A manuscript describing these results is under preparation (Grey, Dunning, Brundin, Sparr, Linse).



Aggregation of Parkinson disease related protein α-synuclein in the presence of isolated exosomes. left: Cryo-TEM image of exosomes with associated protein. right: A-syn aggregation kinetics in the presence (blue and green) and absence (black) of exosomes. Exosomes accelerate α-syn aggregation.

External collaborations

Christopher Dunning (Neuronal Survival Unit, LU)
Patrik Brundin (LU and Van Andel Institue, USA).

Conference presentation in 2012

- 100 Years of Lewy Bodies - Where are we now? Munich,Germany (poster presentation)
- 3rd Scandinavian Amyloid meeting, ADAM-2012, Sigtuna, Sweden (oral presentation)

Amyloid aggregation and amyloid-lipid interactions

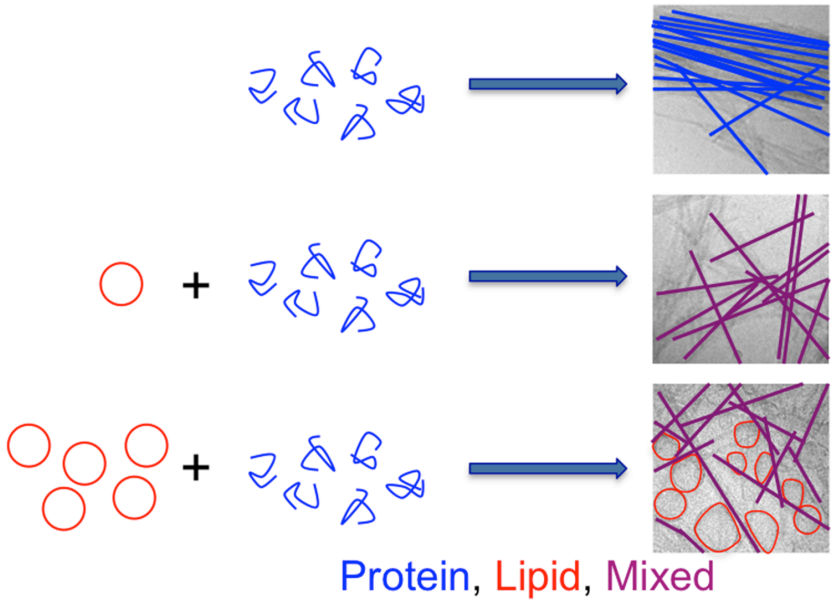
PhD project: *Erik Hellstrand, Sara Snogerup Linse, Emma Sparr, Agnieszka Nowacka, Daniel Topgaard, Tommy Nylander*

Project description

Disease-causing amyloid fibril formation can be modulated by many factors including interactions with biological lipid membranes. An increasing amount of evidence suggests that the process of fibril formation *in vivo* and the mechanism of toxicity involve membrane interactions. The amyloid fibril formation proceeds via transient oligomers that eventually go on to more stable fibrils. There is consensus in the field that it is not necessarily the mature large fibrils that cause damage to cells, although the molecular mechanisms are not understood. Our research in this field focuses on the questions of how membrane interaction varies at different aggregation stages, and if the presence of lipid membrane affects the properties of the final aggregate.

The proteins Aβ and α-synuclein are found in the protein aggregates characteristic for Alzheimer and Parkinson disease, respectively. In this project, we study interactions between the amyloid proteins Aβ (M1-40), Aβ (M1-42) or α-synuclein and model lipid membranes. For both proteins,

we have identified conditions leading to reproducible kinetic experiments, and this is taken advantage of when following membrane interactions for aggregates at different stages along the fibrillation process.



***Amyloid-lipid co-aggregation**. Main acyl chain region of the PT ssNMR spectra (a-d) and cryo-TEM images (e-h), scale bars 200 nm) of α-synuclein fibrils co-aggregated with different amounts of DOPC:DOPS 7:3 vesicles. Inserted boxed peaks are INEPT and CP signals for the unresolved peaks from C_{4-7} and C_{12-15} baseline adjusted for background protein CP signal. Spectra are scaled to give equal protein CP intensity at 20 ppm. Filled dark spots in the cryo-TEM images are frost defects and are not part of the experimental system.*

Progress during 2012

We investigate amyloid-lipid co-aggregation in systems of α-synuclein and model membranes with different composition. The questions asked in this sub-project are whether co-aggregation occurs, if the co-aggregation process is specific to any lipid class, and how co-aggregation affect the amyloid aggregates. We have been able confirm lipid-protein co-aggregation of α-synuclein with anionic phospholipids by means of phosphorous analysis and ssNMR. cryo-TEM studies show that the aggregate morphology is affected by the presence of co-aggregates lipids (Figure). From PT ssNMR of the same aggregates we could also confirm that mobility in some parts of the lipid molecules are affected by the co-aggregation.

In QCM-D and neutron reflectometry (NR) studies we have monitored the association of α-synuclein in different aggregation state to model membranes with varying composition. The highest amount of membrane-associated α-synuclein is found for cardiolipin containing membranes at lower pH (5.5). The NR studies show that α-synuclein associate in the interfacial region of the membrane, while there is no penetration into or through the membrane.

Our studies of the aggregation process starting from homogeneous monomeric Aβ42 peptide in pure buffer with no co-solvents have lead to important mechanistic insights. In collaboration with Tuomas Knowles and colleagues in Cambridge, we have found that our data are incompatible with a model including only primary nucleation, elongation/dissociation and fibril breakage. Instead, secondary nucleation of monomers on already formed aggregates is the dominant nucleation route, except at the very beginning of the reaction when there is only monomer around. This finding is backed up with kinetic experiments with small amounts of pre-formed seed andradio-labelled peptide The study is currently under review in PNAS (third submission after very minor revision). In a follow up study we have investigated the aggregation mechanism Aβ40 peptide, which in spite of lacking only two residues at the C-terminus, is much less aggregation-prone than Aβ42 and also much less toxicity. Our findings suggest that also in this case is secondary nucleation important.

Finally, we studied Aβ42 together with model lipid membranes with different composition. We studied the aggregation kinetics in the presence of lipid vesicles as well as adsorption and membrane disruption of protein to the lipid model membranes. The monomeric Aβ does not adsorb in any detectable amounts to any uncharged or anionic bilayers, and adsorption was only detected to cationic bilayers. Cationic bilayers were also found to significantly increase the rate of aggregation of Aβ42.

External collaborations:
Marie-Louise Ainalem (ESS AB)
Trevor Forsyth (ILL, France)
Tuomas P. J. Knowles (Cambridge University, UK)
Michele Vendruscolo (Cambridge University, UK)
Patrik Brundin (LU and van Andel Institute, USA)

Publications in 2012

- Samuel . A. Cohen, Sara Linse, Leila Luheshi, Erik Hellstrand, Duncan A. White, Luke Rajah, Daniel E. Otzen, Michele Vendruscolo, Christopher M. Dobson, Tuomas P. J. Knowles: *Proliferation of toxic Ab 42 oligomers occurs through secondary nucleation*. PNAS, Under revision after minor revision.
- PhD thesis: Protein-Lipid Association and Aggregation – From Neurodegenerative Disease to Nanosafety

Conference presentation in 2012

- 3rd Scandinavian Amyloid meeting, ADAM-2012, Sigtuna, Sweden (oral presentation)

Peptide self-assembly

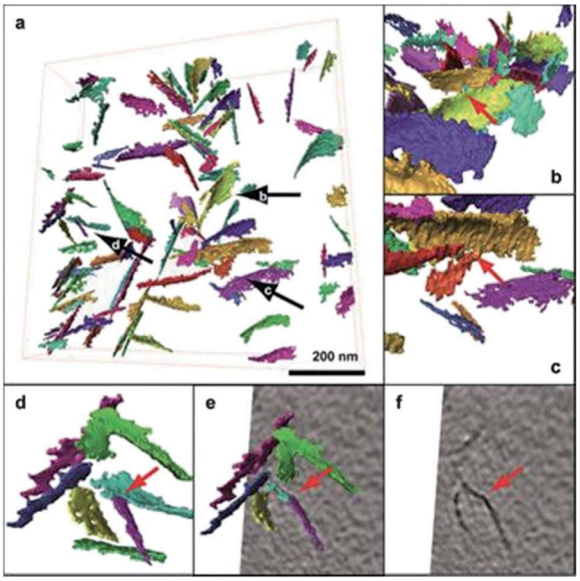
PhD Project: *Celen Cenker, Ulf Olsson*

Project description

The development of modern peptide chemistry has opened for the possibility of custom peptide synthesis that allows for systematically investigating peptide interactions and aggregation. Much work is focussed on the synthetic small peptides A_nK (A=alanine, K=lysine), where n is the number of alanine residues. These peptides allows for a systematic investigation of e.g. the hydrophobicity and peptide length on the self-assembly behavior.

Progress during 2012

A_6K forms hollow nanotubes in water in the concentration range ϕ=0.10–0.15 (volume fraction). During 2012 we focussed on the formation and dissolution processes of these spectacular structures. Time resolved cryo-TEM and cryo-electron tomography experiments were performed in collaboration with the group of Nico Sommerdijk, Einhoven University of Technology. The peptides are crystalline ordered in the nanotube walls. They form in supersaturated solutions by a classical nucleation and growth mechanism, where the growth phase involves both molecular and oriented fragment attachments.



Computer assisted visualization of the cryo-electron tomogram recorded for an A_6K solution (ϕ=0.115) prepared using temperature assisted dissolution after 30 min. (a) An overview showing different colors for individual fragments. (b–d) Enlargements of the areas indicated by the arrows (b–d) in (a) and viewed along the direction of the respective arrows. Red arrows indicate the fusion edge of two touching sheets. (e) Overlay of the computer assisted visualization and a slice through the original tomogram, (f) a slice through the tomogram shown in (e).

A computer reconstruction from a cryo-electron tomography experiment is presented in Fig. 1, showing the initial fragments formed in a supersaturated solution shortly after a temperature quench.

External collaborations
Seyda Bucak (Yeditepe University, Istanbul)
Paul H. H. Bomans, Heiner Friedrich, and Nico A. J. M. Sommerdijk (Eindhoven Technical University)
Burcu Dedeoglu and Viktorya Aviyente (Bogaziçi University, Istanbul)

Publications in 2012
- Ç. Ç. Cenker, P. H. H. Bomans, H. Friedrich, B. Dedeoglu, V. Aviyente, U. Olsson, N. A. J. M. Sommerdijk, S. Bucak, Soft Matter 8, 7463 (2012)

Organizing molecular matter for specific functions

Nanoparticle-protein interactions: towards understanding cellular response to nanoparticles

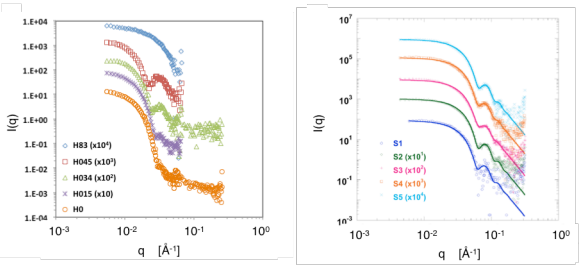
Post-doc project: *Lucia Casals, Marc Obiols-Rabasa, Sara Linse, Mikael Lund, Peter Schurtenberger*

Project description
Presently, our ability to predict the colloidal stability of nanoparticles (NPs) in a particular cell medium, with or without different concentrations of serum components, is quite limited. Medium-dependent alteration of nanoparticle properties may directly affect their cellular fate, uptake, metabolism, and clearance, thereby determining nanotoxicity in biological systems. This project aims at monitoring and understanding the interaction of well-defined nanoparticles currently developed for biomedical applications with serum proteins and cellular media.

We study the interactions of these particles with a set of model proteins covering a representative array of protein sizes and charges. If there is for example adsorption of the protein on the particle surface, this will also change the interactions between the NPs accordingly.

Experimentally, we combine several scattering techniques (Static and dynamic light scattering, SAXS, SANS, confocal and electron microscopy), various labeling schemes that allow for the detection of complex formation, and combine these investigations with computer simulations.

Progress during 2012
We use Au NPs with different surface functionalization as an ideal model system to study the behavior of NPs in the presence of proteins. Here we profit from their unique optical properties that make them extremely sensitive probes to use depolarized light scattering to study protein adsorption. However, these experiments do only provide us with overall hydrodynamic parameters and are thus not unambiguous with respect to the structure of the adsorbed layer. We thus performed additional SANS experiments in order to directly access the structure of the adsorbed layer on the relevant length scales under different conditions (protein concentration, ionic strength) using a neutron contrast variation study. Here we profit from the fact that the match points for the Au NPs (approx. 75% D_2O) and the protein (albumin, approx. 40% D_2O) are sufficiently different to allow for a detailed contrast variation series. We also varied the salt concentration to highlight the role of electrostatics on the protein adsorption. These SANS experiments were complemented by SAXS experiments, where we used the much



Examples of SANS (left) and SAXS (right) data. SANS data AuNPs with negative coating at different contrasts (H_2O/D_2O mixtures), SAXS data shows all particle types (from top to bottom: bare (dilute), bare (concentrated), negative, neutral and positive coated AuNPs.

higher resolution of the in-house SAXS instrument to independently determine the Au core and use this as an additional input for the analysis of the SANS data.

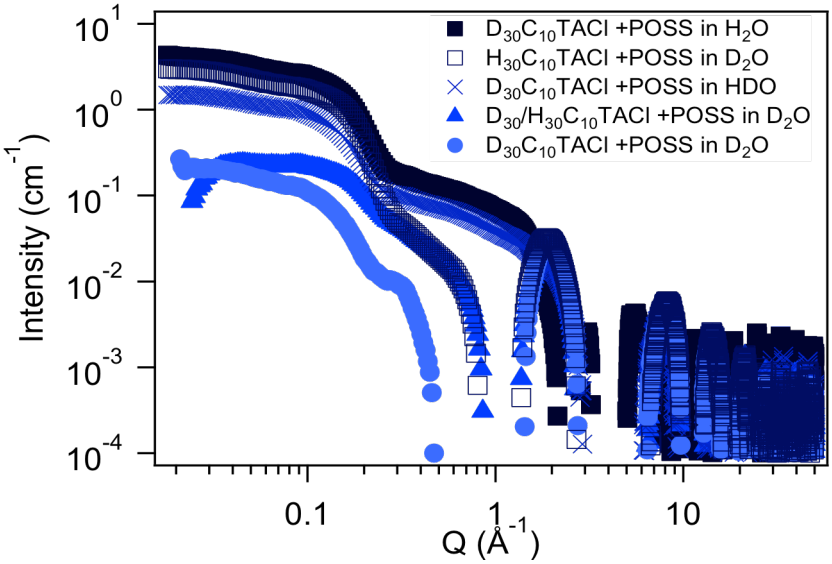
External collaboration
Prof. Alke Fink, Adolphe Merkle Institute, University of Fribourg, Switzerland

Mesostructured systems: "equilibrium" and molecular interactions – structural control

PhD project: *Emelie Nilsson, Viveka Alfredsson, Olle Söderman*

Project description
The seminal ordered mesostructured silica material (MCM-41) was based on a synthesis protocol using CTACl as structure director in basic aqueous solution (i.e. negatively charged silica species). The interactions have been described as relying on electrostatics between the negatively charged silica and the cationic surfactant. Typically the surfactant packing parameter is used as rational for the structures formed. Recently a novel structure, a tricontinous hexagonal phase (defined by a minimal surface), was discovered using a surfactant with a geometrically large head-group. It has been claimed that this structure also can be found in the traditional CTACl-based synthesis silica-system by addition of butanol. The tricontinous structure has a curvature falling in between that of the 2 D hexagonal and the bicontinous Ia3d structure, *i. e.* in the part of the phase diagram (of the pure surfactant – water system) where intermediate phases previously have been identified in the related DOTACl-systemOne fundamental difference between the liquid crystal system and the analogues mesostructured silica systems lies in the possibility to reach thermodynamic equilibrium. The silica system may or may not, depending on the silica kinetics, reach the analogue's mesophases. Although the silica kinetics may be a complication in the synthesis it could also be used as a factor of control, providing means to arrest the mesostructure in metastable phases (normally not reachable with the pure surfactant-water system).

Progress in 2012



Neutron diffraction data showing five contrasts of an aqueous solution of cationic surfactants in the presence of a silica model.

A wide q-range neutron scattering study was done at ISIS, in the UK, to investigate the interaction between cationic micelles and a range of anionic counterions. A silica molecule, (a polysilsesquioxane) was used as a model for silica. Fitting of the data has been initiated.

Conference presentation in 2012
- Poster presentation by Emelie Nilsson at "Materials for Tomorrow" Göteborg 23-25 October.

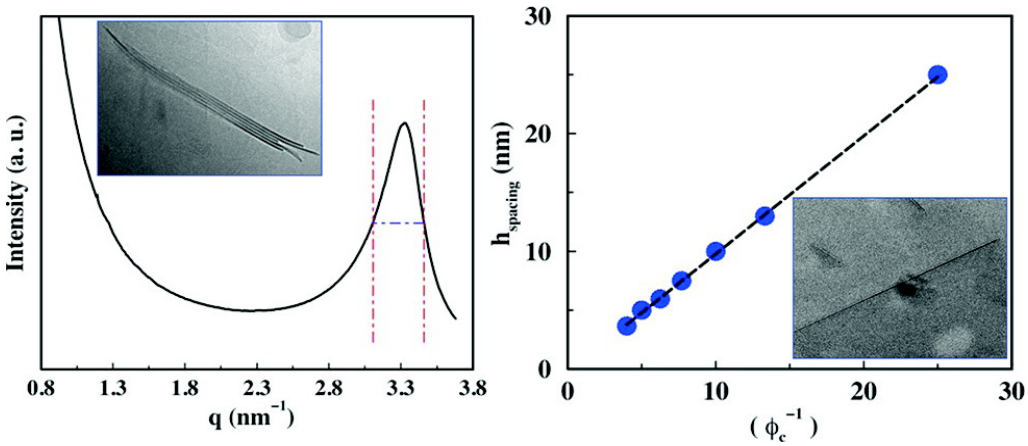
External collborations
Karen Edler (University of Bath, UK and in 2012 guest professor at LU), Sven Lidin (CAS, KILU, LU).

Experimental and theoretical studies of structure, forces and stability of clays

PhD project: *Mo Segad, Bo Jönsson, Ulf Olsson and Torbjörn Åkesson*

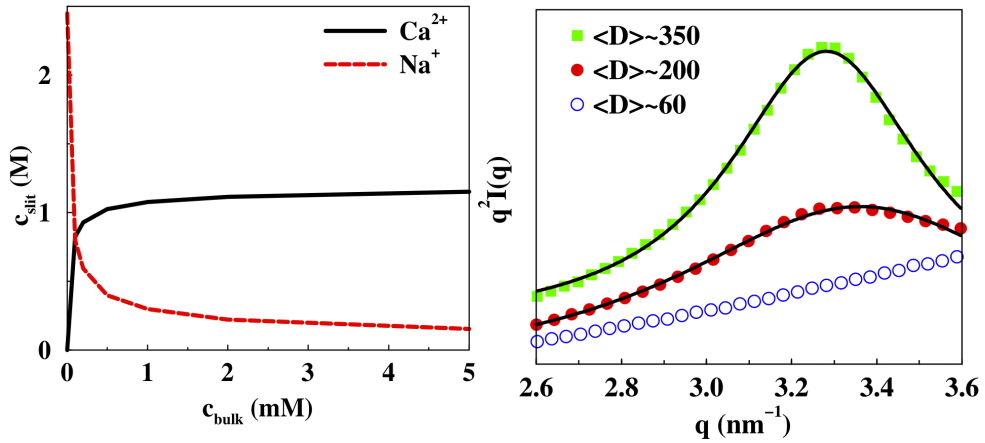
Project description

One of the most interesting behaviour in clay science is the swelling property in presence of divalent/monovalent counterions. Therefore, it is important to gain a good understanding of different swelling mechanisms for clay-water systems. Many European countries plan to deposit the nuclear waste in geological repositories. Wyoming bentonite (MX-80) is supposed to be used as a sealing material for nuclear waste. Thus, it is of utmost importance to have as good picture of the structure as possible. The structure will determine its quality as sealing material. Besides, there is also a general interest in clay structure for use in various industrial applications such as drilling, paint and cosmetic. The purpose of the project is to characterize the structure of a natural bentonite and purified montmorillonite suspensions from the nm up to μm length scale, under different conditions. This can be done theoretically with the help of statistical-mechanical simulations (Monte Carlo) and experimentally by small/wide angle x-ray scattering techniques, TEM, Cryo-TEM microscopy and osmosis studies.



Left: Typical tactoid along the edge view exhibiting the intra-lamellar structure in Ca montmorillonite. This finding is in agreement with SAXS results. Right: Repeat distance of the Na montmorillonite platelets obtained from SAXS as a function of inverse clay volume fraction. Note that the inset image showing a single clay platelet.

Progress during 2012



Left: Simulated concentrations of mono- and divalent counterions in the slit between the two charged surfaces. The slit is in equilibrium with a bulk solution. The bulk concentration of NaCl is kept fixed at 20 mM, while the bulk concentration of $CaCl_2$ is varied. Right: SAXS spectra of dispersions of Na montmorillonite showing a clear effect of different average platelet sizes on tactoid size.

The investigations during 2012 have focused on the characterization of the microstructure of pure montmorillonite and the tactoid (small clusters of clay platelets) formation in montmorillonite. We have provided, for the first time, a new evidence for the evolution of tactoids, <N>, using small-angle X-ray scattering (SAXS), cryo-TEM and swelling experiments combined with Monte Carlo

simulations. In 2012, we have studied based on SAXS measurements, different type of bentonite that comes from various origins. This is to characterize the similarity in the microstructure or the swelling behavior for clay-water systems. We also performed additional optical observations and hyperspectral characterization of a dispersion of montmorillonite and Laponite, by means of CytoViva hyperspectral microscope system at Auburn in the US.

Publications in 2012

- M. Segad; S. Hanski; U. Olsson; J. Ruokolainen; T. Åkesson; Bo Jönsson; *J. Phys. Chem. C* 2012, 116, 7596-7601.
- M. Segad; Bo Jönsson; B. Cabane; *J. Phys. Chem. C* 2012, 116, 25425-25433.

Conference presentations in 2012

- The 15th International Small-Angle Scattering Conference, November 2012, Sydney, Australia. **Awarded a prize for the best poster at the International SAS2012 Conference**

8. OMM DIPLOMA PROJECTS

Mixed Micelles of Oppositely Charged Diblock Copolymers in Aqueous Solution. A Dynamic and Static Light Scattering Study

Bachelor thesis project: *Hanna Bergenholtz, Solmaz Bayati and Karin Schillén*

Project description

The aim of this project was to study complex coacervate core micelles formed in water by electrostatic attraction between two oppositely charged diblock copolymers both containing an uncharged block (poly(*N*-isopropylacrylamide), PNIPAAM) of the same length. The diblock copolymers are either cationic or anionic depending on the polyelectrolyte block used: poly((3-acrylamidopropyl)trimethyl ammonium chloride [PAMPTMA(+)] or poly(2-acrylamido-2-methyl-1-propanesulfonic sodium) [PAMPS(-)]. The solution behavior of the mixed copolymer system at a 1:1 ratio of charged groups was investigated using dynamic and static light scattering in combination with turbidimetry and zeta potential measurements. The micelles consist of a PAMPTMA(+)/PAMPS(-) mixed core surrounded by a thermoresponsive PNIPAAM corona. They carry no net charge. Below the LCST of PNIPAAM (about 32 °C) the micelles are sterically stabilized by their PNIPAAM corona. As the temperature (or total copolymer concentration) increases, larger aggregates are formed. The results indicate that the formation of the structures is reversible.

External collaborations

Bo Nyström (Oslo University, Norway)

9. OMM MEETINGS AND SEMINARS

OMM general assemblies 2012

OMM organizes two general meetings per year, one in spring and one in late summer/early autumn. In 2012, the spring meeting was devoted to discussions of th evaluation of the center. The fall meeting was dedicated to scientific presentations and discussions on the themes Intermolecular interactions (Sture Norholm, Gunnar Karlström, Per Linse), consequences of intermolecular interactions (Janette Carey, Mikael Lund) and interactions at the colloidal length scale (Bernard Cabane, Peter Schurtenberger). Members of the board for the next 2-year period were elected.

OMM Seminars during 2012

2012-02-06: Richard Campbell, Institute, Laue Langevin, Grenoble, France. *Impact of bulk non equilibrium effects on an oppositely charged polyelectrolyte/surfactant mixture at the air/water interface.*

2012-02-21: Marianne Impéror-Clerc, Laboratoire de Physique des Solides, Université Paris-Sud, Orsay, France. *Structure and Formation of Periodic Silica-based Templated Materials: Investigation using Small Angle X-Ray Scattering.*

2012-02-27: Pavlik Lettinga, Research Centre Jülich Institute of Solid State Research (IFF), Soft Matter Division, Jülich, Germany. *Dynamics and colloidal rods at rest and in external fields.*

2012-04-12: Drew Parsons, Canberra, Australia. *Hydration and Ions.*

2012-05-21: Karen Edler, Department of Chemistry, University of Bath, United Kingdom. *Surfactant Templated Inorganic Films at the AirSolution Interface.*

2012-05-28: Agnieszka Nowacka, Physical Chemistry, Lund University. *Polarization Transfer Solid-State NMR for Studying Soft Matter: From Surfactants to the Stratum Corneum..*

2012-05-31 Dominique Massiot (CEMHTI-CNRS, Orléans) *Order and disorder in materials: from atomic to nanometer scale*

2012-08-23 Luc Jaeger, Chemistry and Biochemistry Dept, University of California, Santa Barbara. *RNA self-assembly*

2012-10-08: Jan K.G. Dhont, Forschungszentrum Juelich. *Charged Colloids in Electric Fields and Thermal Gradients.*

2012-10-22: Robert K. Thomas, University of Oxford. *How Not to Determine Surface Excess: A Century of Wasted Measurements?*

2012-11-05: Andrew Jackson (European Spallation Source (ESS)) *Explosives and Milk - Nanoscale to Microscale Structure*

2012-12-03: Erik Hellstrand, Biophysical Chemistry, Lund University. *Protein-Lipid Association and Aggregation in Neurodegenerative Disease.*

2012-12-06: Nitash P Balsara, Department of Chemical and Biomolecular Engineering Environmental Energy Technologies and Materials Sciences Divisions Lawrence Berkeley National Laboratory, University of California, Berkerley. *All-Solid Lithium Batteries and the Clean Energy Landscape*.

2012-12-07: Luca Monticelli, Inserm, Paris. *Simulating nanoparticles into membranes.*

2012-12-10: Philip Kuchel, University of Sydney. *^{13}C DNP NMR in kinetics of cellular systems.*

2012-12-17: Johan Bergenholtz, Physical Chemistry, Göteborg University. *Dissociation Dynamics of Colloidal Clusters.*

OMM seminar series 2012

Albert Philipse

Albert Philipse (van't Hofft Laboratory, the Netherlands) was visiting OMM during his sabbatical leave in May and June. He gave a series of 6 lectures on recent advances regarding rigid colloidal particles and discussed with several OMM scientists on problems of common interest.

I. Magnetic colloids

a) Dipolar structure formation in iron-oxide dispersions
b) Osmotic pressures from a table-top centrifuge

II. Anisometric Colloids

a) Shape-sensitive crystallization in superball fluids
b) Random packings and the ideal glass law

III. Charged Colloids

a) The Donnan equilibrium: new life from old roots
b) The unscreened pendant of the DLVO-repulsion

OMM minisymposia 2012

Biomolecules at Interfaces

- George Attard, University of Southampton: *Bioprocesses in structured and reduced-dimensionality environments*
- Rita Dias (University of Coimbra) *Monte Carlo studies on polyelectrolyte adsorption at surfaces*
- Erik Reimhult (University of Natural Resources & Life Sciences Vienna*) Functional nanoparticle design and application at membrane interfaces*

- Michael Rabe (Chalmers) *Understanding surface-induced protein aggregation processes*
- Erik Hellstrand (Lund University) *Interaction between aggregating amyloid proteins and model lipid membranes*
- Marité Cardenas (Nano science center, University of Copenhagen) *Antibacterial dendrimers at model cell membranes*

Date: 2012-01-12
Organizer: Emma Sparr & Tommy Nylander

Lipids and protein aggregation

- Jennifer Chen Lee (NIH): *Protein-lipid interactions*
- Christopher Dunning (LU) *Prion-like spread of alpha-synuclein in Parkinson's disease*
- Robert Vacha (Brno): *Cellular uptake and intracellular release of nanoparticles*
- Anna Stradner (LU): *Reexamining the colloid analogy for casein proteins*
- Tommy Nylander (LU): *The lipid-aqueous interface beyond bilayers*

Date: 2012-12.13
Organizer: Emma Sparr & Sara Linse