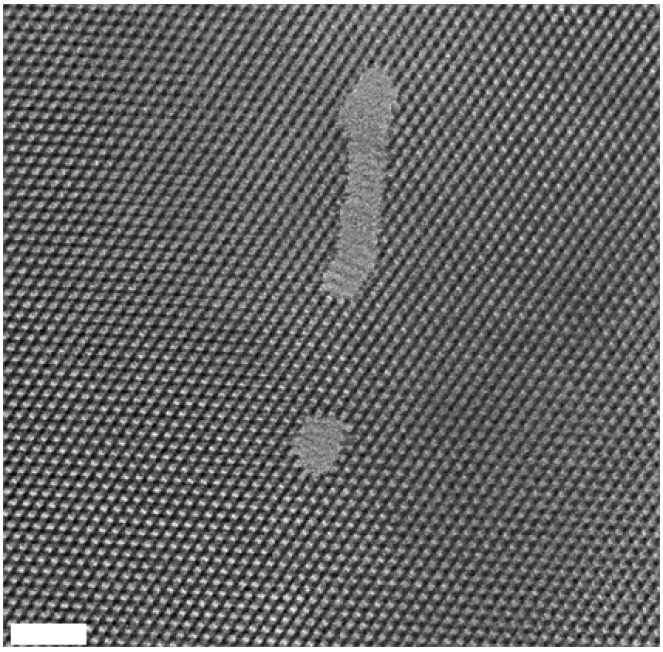
OMM Report 2006-2008

Activities during the first 2 1/2 years of the Linnaeus center of excellence Organizing Molecular Matter, Department of Chemistry, Lund University



LUND UNIVERSITY

Organizing Molecular Matter

OMM website: http://www.omm.lu.se

This report was edited by Lennart Piculell

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1 Organizing Molecular Matter - the First 2 1/2 Years

In 2005, the Swedish Research Council (VR) launched a call for collaborative research efforts from strong Swedish research environments with an obligation for a long-term so-called Linnaeus support. In response to this call, a group of nineteen senior researchers from the divisions of Physical Chemistry, Theoretical Chemistry and Biophysical Chemistry at the Department of Chemistry, Lund University, worked out a proposal called *Organizing Molecular Matter* (OMM). Fortunately, the OMM application was accepted in June 2006, making money available from June 1st.

The OMM research program, as presented in the OMM application, can be found at the OMM website (http://www.omm.lu.se). The program is focused on intermolecular interactions and their manifestations in a liquid environment. Four different types of problems are addressed. The theoretical basis for the description of intermolecular interactions and their consequences are treated, using both quantum chemical calculations and statistical mechanical simulations. On the next level, carefully selected model systems are studied experimentally. The interplay between theory and experiment is an essential feature of the program. An important part of the experimental studies is an ongoing improvement of methods. It is very useful to have well characterized systems, for which one can test the validity and usefulness of the methods. A final part of the program is to apply the understanding obtained in the basic studies for solving applied problems both in the biophysical/molecular biology field and in the industrial area.

By the end of 2008, the OMM Linnaeus center has been running for two and a half years. The support level from VR is 7.5 million SEK/year. In addition Lund University, partly through the Faculty of Science, adds an additional 1 million SEK/year on top of the general university support. The combined support is a substantial addition of resources for the group of currently 20 senior scientists that are members of the OMM center. The grant has clearly given new scientific opportunities. The money is basically spent as described in the proposal and it goes to three main objectives. These are funding of graduate students, funding of postdoctoral students and funding the salary for younger researchers. The funding covers approximately half the cost in all three cases and the rest has to be raised from other sources. In addition, a small proportion of the OMM funds are used to finance guest researchers, seminar speakers and administration.

A main ambition in distributing the grants among the senior researchers has been to strengthen the intellectual coherence of the program. Specific projects thus typically involve active participation of two or more the senior researchers. Also the OMM seminars, normally given every second week, are geared at forming a common base for scientific discussions. On an annual basis we have also had one-day meetings where the whole group, seniors and students, have gathered to discuss two selected scientific topics relevant to the program. There have also been annual half-day meetings focusing on reporting the scientific made within the program.

In this report you find accounts of the progress made and the plans for projects that have been specifically supported by OMM. There are also other related scientific activities, which are supported by other sources and which have themes mentioned in the original proposal. We have considered this circumstance when distributing he OMM resources. Presentations of all OMM-related projects, both those specifically supported by OMM and the related projects, are given on the OMM webpage.

It is our hope that the present report will give a good insight into both the scientific activities supported by the OMM program and also the principles used for distributing the resources.

2 Organization

Since autumn 2008, OMM has a new formal organization, following the decision of a general meeting of the OMM senior scientists. The *board of OMM* has three members, currently *Håkan Wennerström* (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 *Lennart Piculell*, has the operative responsibility for the administration of OMM.

Discussions regarding the long-term strategy of OMM are held at the *annual meeting* of OMM, where all scientists active within OMM participate. In addition, OMM has an advisory board, 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.

3 The People

The tables below list researchers active in OMM during the period 2006-2008. The *senior scientists* 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. A number of additional junior scientists work with OMM-related projects in the OMM research environment, but are funded mainly from other sources. Finally, a number of *guest students* have worked in OMM projects during 2006-2008.

3.1 Senior scientists

Viveka Alfredsson	associate professor	physical chemistry
Jan Forsman	associate professor	theoretical chemistry
Bo Jönsson	professor	theoretical chemistry
Gunnar Karlström	professor	theoretical chemistry
Roland Lindh	professor	theoretical chemistry
Björn Lindman	professor	physical chemistry
Sara Snogerup Linse	professor	biophysical chemistry
Per Linse	professor	physical chemistry
Mikael Lund	associate professor	theoretical chemistry
Per-Åke Malmqvist	associate professor	theoretical chemistry
Tommy Nylander	professor	physical chemistry
Ulf Olsson	professor	physical chemistry
Björn Roos	professor	theoretical chemistry
Lennart Piculell	professor	physical chemistry
Karin Schillén	professor	physical chemistry
Emma Sparr	assistant professor	physical chemistry
Olle Söderman	professor	physical chemistry
Daniel Topgaard	assistant professor	physical chemistry
Håkan Wennerström	professor	physical chemistry
Torbjörn Åkesson	associate professor	theoretical chemistry

3.2 Junior researchers

Mehran Asad Ayobi	PhD student	physical chemistry
Jonas Boström	PhD student	physical chemistry
Richard Campbell	post-doc	physical chemistry
Jonas Carlstedt	PhD student	physical chemistry
Tiago Ferreira	PhD student	physical chemistry
Erik Hellstrand	PhD student	biophysical chemistry
John Janiak	PhD student	physical chemistry

Dan Lundberg	post-doc	physical chemistry
Peter Nilsson	post-doc	physical chemistry
Agnieszka Nowacka	PhD student	physical chemistry
Nikolay Oskolkov	post-doc	physical chemistry
Björn Persson	PhD student	theoretical chemistry
Juanfang Ruan	post-doc	physical chemistry
Joakim Stenhammar	PhD student	physical chemistry

3.3 Guest students working in OMM projects

Marieke Bode (Utrecht University)	physical/theoretical chemistry
Johannes Stigler (Munich)	biophysical chemistry
Marianna Yanez (U. Simón Bolívar, Caracas)	physical chemistry

3.4 Visiting scientists and guests

3.4.1 Alexei Khokhlov and Irina Nasimova

The creation of the OMM center made it possible for the OMM research environment to initiate a long-term strategic collaboration with professor *Alexei R. Khokhlov* (Moscow State University/Russian Academy of Sciences) and his group. Alexei Khokhlov is an internationally outstanding polymer scientist with an exceptionally broad overview of polymer science, from theory to applications. Khokhlov has published around 500 scientific papers, 6 books and 25 article reviews, and he ranks among the 10 most-cited Russian scientists in all fields for the papers published during the last 8 years.

During 2007 and 2008, Khokhlov made several visits, funded by OMM, to Lund University. He proposed a carefully designed joint research program, connecting his research group and OMM, which has led to the initiation of several collaborative post-doc and PhD projects supported by OMM (see below). Moreover, Khokhlov gave a series of five very well attended seminars (see list of seminars below) under the collective heading *New Developments in Smart Polymer Systems*. Finally, in April of 2008, he lectured a one-week PhD course (see Courses below).

As a consequence of the intensified collaboration, a group of OMM scientists made an application to the Swedish Foundation for Strategic Research, SSF, for a so-called strategic international recruitment of Khokhlov as a visiting professor (half-time) during 3 years at Lund University. The application was successful, and Khokhlov is planning to commence his visiting professorship on June 1, 2009.

As an important part of the above collaboration, *Dr. Irina Nasimova* from Khokhlov's group at Moscow State University has spent several months at Physical Chemistry in Lund. During this time, she has worked on two projects together with OMM scientists (see below).

3.4.2 Short Term Guests

Dusan Bratko (Univ California Berkeley, USA)
Christophe Labbez (Univ Bourgogne, France)
Patrick Kekicheff (Inst Charles Sadron, Strasbourg, France)
Johan Bergenholtz (University of Gothenburg)
Claudia Schmidt (University of Paderborn, Germany)
Yuru Deng (Singapore National University)
Stefan Egelhaaf (Heinrich-Heine-Universität, Düsseldorf, Germany)
Luis A. Bagatolli (MEMPHYS - Center for Biomembrane Physics SDU, Denmark)
Björn Åkerman (Chalmers University, Gothenburg)
Lise Arleth (University of Copenhagen, Denmark)
Gerhard Gröbner (Umeå University)

Phil Attard (University of Sydney, Australia)
Ka Yee Lee (University of Chicago, USA)
Lars Nordenskiöld (Nanyang Technological University, Singapore)
Karen Edler (University of Bath, UK)
Petr Stepanek (Institute of Macromolecular Chemistry, Prague, Czech Republic)
Sture Nordholm (University of Gothenburg)
Alexey Kabalnov (Hewlett Packard, San Diego, USA)

4 Young Senior Scientists Receiving OMM support

The age structure of the OMM group is such that a partial renewal of the staff will be necessary during the grant period. One of the objectives of OMM is therefore to specifically support younger senior scientists (associate and assistant professors) presently hired in the group, with the goal of facilitating their scientific careers. At present, Viveka Alfredsson, "lektor" (associate professor), and Mikael Lund, newly recruited "biträdande lektor" (assistant professor) receive such support from OMM. For both of these recruitments, the OMM support was essential. Below, they present their OMM research.

4.1 Viveka Alfredsson: Mesoporous Materials and Liquid Crystals

My research interests are ordered materials, in particular mesoporous materials, which is my principal research topic. I am also interested in other systems that in different ways are related to mesoporous materials, such as lyotropic liquid crystals and zeolites.

Here I describe the part of my research that is funded by OMM via a PhD grant (mesoporous materials) and a Post Doc grant (lyotropic liquid crystals). In addition to these two major topics I am also involved in studies of compaction of DNA with dendrimers via a EU financed project ("Neonuclei"), and in another EU-project ("Biocontrol") where the aim is to use mesoporous silica as a controllable host for biomolecules. Further, as my main technique is transmission electron microscopy, in particular cryogenic, I am also involved in various projects where this technique is employed.

Mesoporous materials (MM) are materials with repeating units in the meso-range, that is, 2-50 nm (figure 1). The "crystallinity" is hence not on an atomic level but analogous to that of lyotropic liquid crystals formed by amphiphilic molecules in a solvent. Such molecules are also the structure promoters for MM. Like zeolites, MM possess a huge internal surface area once the structure directing amphiphile is removed. The area is in the order of 1000 m^2/g. Pore size, pore geometry, structure, morphology and particle dimensions are all (potentially) controllable parameters. As the pores are well defined, MM can be suitable as matrices for incorporation of different types of nanomaterials, for instance CdS-clusters, or for biomolecules such as enzymes.

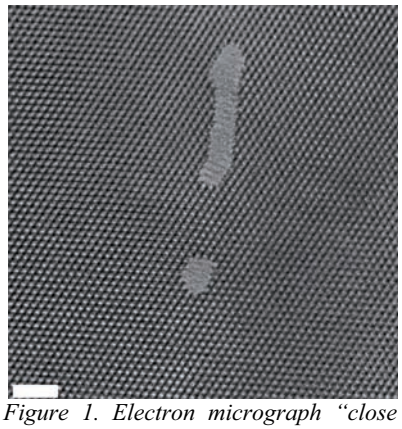


Figure 1. Electron micrograph "close up" of the MM SBA-15 with typical holes that occur in as a result of the peculiar growth mechanism. Scale bar 50 nm.

My research regarding MM essentially follows two major paths, *understanding the processes and molecular mechanisms* that drive the formation, and, *creating materials* with interesting properties. Recently we have identified a peculiar and highly unexpected formation path that leads to the unusual plate-like morphology of the well-known structure SBA-15. Currently we

are seeking ways to make use of this knowledge to produce crystallographically oriented membranes of SBA-15.
Aims of the MM-project are:

- *Obtaining a fundamental understanding for the formation and the molecular mechanisms that control the formation, hence providing tools for rational design (i.e. of structure, morphology, particle/film size, size distribution etc.) of MM. Information on the fundamental level is (or will be) obtained by:*
  - *studying the silica kinetics in relation to our detailed previous knowledge,*
  - *studying why the particles aggregate in different "generations",*
  - *studying why the morphology is dependent on several synthesis parameters.*

- *Creating materials based on MM, destined for different applications.*
  - *Making films by using primary particles as building stones.*
  - *Making membranes by forming MM in macroporous polymer membranes.*
  - *Changing the hydrophilicity/hydrophobicity of the pores by grafting a thermoresponisive polymer inside the pores of silica particles and in membranes/films*
  - *Introducing biomolecules in the mesoporus matrix, controlling activity*

Cryogenic transmission electron microscopy (cryo-TEM) is a powerful technique for investigating liquid samples. Information regarding size and morphology of objects formed by for instance surfactant molecules in an aqueous solution can be obtained. A major advantage of TEM is that local information can be extracted, such as defects in a material or varying morphologies present in a solution. Scattering and diffraction techniques are limited to average information of the samples investigated. A major drawback with cryo-TEM is that the normal plunge vitrification technique is restricted to non-viscous liquids. Lyotropic liquid crystals have structures analogues to MM but are soft matter materials. As transmission electron microscopy has been the principal technique to determine the structures of MM a challenge lies in investigating, by the same methodology, lyotropic liquid crystals. The major obstacle for such investigation is the sample preparation limitations for viscous liquid matter. The normal plunge vitrification technique is not viable and hence other means of preparation need to be evaluated, such as high-pressure freezing and freeze-fracture direct imaging. We are presently investigating such alternative preparation techniques. Once we master the preparation technique, crystallographic information, local defects/intergrowths, domain sizes and related issues will be investigated for a range of lyotropic liquid crystals.

4.2 Mikael Lund: Biomolecular Interactions and Organization

My research within OMM 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 target-receptor 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.

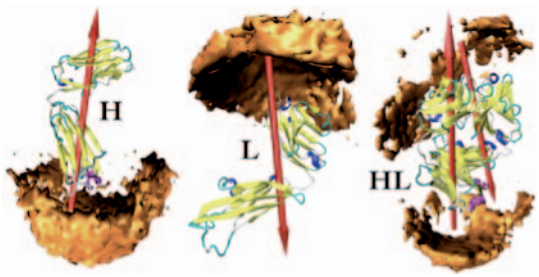


Figure 1. Lysozyme densities (orange iso-surfaces) around various FAB proteins.

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, suggesting that these proteins will orient in an 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.
  pK_a 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.

The research involves external collaboration with Pavel Jungwirth (Academy of Sciences of the Czech Republic, Prague) and Clifford E. Woodward and Grant Collins (University of New South Wales, Canberra).

5 Research Projects

The ability to control and master intermolecular interactions lies at the heart of modern chemistry and material 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 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.

5.1 MOLCAS

Per-Åke Malmqvist, Valera Veryazov, Jonas Boström, Per-Olof Widmark, Fengyi Liu, Björn Roos and Roland Lindh.

Project description

The MOLCAS quantum chemistry program package is a joint effort of the Dept of Theoretical Chemistry (http://www.teokem.lu.se). The project started in 1990 and is based around the CASPT2/CASSCF quantum chemistry model paradigm. From the start, OMM gives direct support to the MOLCAS project. Today, the software is sold under license to research institutes and industry. For more details on the program package, visit the MOLCAS home page (http://www.molcas.org). Literature on research made possible by the software is shown in the MOLCAS showcase room (http://www.teokem.lu.se/~roland/show_case/covers.html).

External collaborations

The MOLCAS program package involves the collaboration between a number of international groups and institutes. The group formed in 2007 the so-called "MOLCAS network". For more information about the members and their activities, visit the MOLCAS network web page.[1]

Results

The MOLCAS project has been directed in the development of

1. a new graphical user interface (MOLGUI, MING and GV),
2. the implementation of and improvement of the RASPT2/RASSCF method,
3. methods to explore several intersection seems around a minimum energy path,
4. new relativistic all electron Gaussian basis sets for the whole periodic table,
5. picture-change free nuclear properties associated to Mössbauer spectroscopy and
6. the use of the Cholesky decomposition in association with 2-electron integral repulsion integrals.

Publications

1. "The restricted active space followed by second-order perturbation theory method: Theory and application to the study of CuO_2 and Cu_2O_2 systems", P.-Å. Malmqvist, K. Pierloot, A. R. M. Shahi, C. J. Cramer, L. Gagliardi, *J. Chem. Phys.*, 128:204109 (2008).
2. "Cholesky decomposition based multiconfigurational second order perturbation theory (CD-CASPT2): Application to the spin state energetics of Co(III)(diiminato)(NPh)", F. Aquilante, P.-Å. Malmqvist, T.B. Pedersen, A. Ghosh, B.O. Roos, *J. Chem. Theor. Comp.,* 4:694-702 (2008).
3. "New Relativistic Atomic Natural Orbital Basis Sets for Lanthanide Atoms with Applications to the Ce Diatom and LuF_3", B. O. Roos, R. Lindh, P.-Å. Malmqvist, V. Veryazov, P.-O. Widmark, A. C. Borin, *J. Phys. Chem.,* 112:11431-11435 (2008).
4. The Douglas-Kroll-Hess Electron Density at an Atomic Nucleus",R. Mastalerz, R. Lindh, M. Reiher, *Chem. Phys. Letters*, 465: 157-164 (2008).
5. "Analytic derivatives for the Cholesky representation of the two-electron integrals", F. Aquilante, R. Lindh, T. B. Pedersen, *J. Chem. Phys.*, 129:034106 (2008).
6. "Accurate ab initio density fitting for multiconfigurational self-consistent field methods", F. Aquilante, T. B. Pedersen, R. Lindh, B. O. Roos, A. Sánchez de Merás, H. Koch, *J. Chem. Phys.*, 129:024113 (2008).
7. "Linear scaling multireference singles and doubles configuration interaction", T. S. Chwee, A. B. Szilva, R. Lindh, E. A. Carter, *J. Chem. Phys.*, 128:224106 (2008).

1.http://maps.google.com/maps/ms?ie=UTF8&hl=en&msa=0&msid=102928773290923073996.00043c8559244a88c9b6f&z=5&om=1

8. "Embedding fragment ab initio model potentials in CASSCF/CASPT2 calculations of doped solids: Implementation and applications", B. Swerts, L. F. Chibotaru, R. Lindh, L. Seijo, Z. Barandiaran, S. Clima, K. Pierloot, F. M. A. Hendrickx, *J. Chem. Theor. Comp.*, 4:586-594 (2008).
9. "Quartic scaling evaluation of canonical scaled opposite spin second-order Moller-Plesset correlation energy using Cholesky decompositions", F. Aquilante, T. B. Pedersen, *Chem. Phys. Letters,* 449:354-357 (2007).
10. "Unbiased auxiliary basis sets for accurate two-electron integral approximations", F. Aquilante, R. Lindh, T. B. Pedersen, *J. Chem. Phys.*, 127:114107 (2007).
11. "Analytic high-order Douglas-Kroll-Hess electric field gradients", R. Mastalerz, G. Barone, R. Lindh, M. Reiher, *J. Chem. Phys.*, 127:074105 (2007).
12. "Low-cost evaluation of the exchange Fock matrix from Cholesky and density fitting representations of the electron repulsion integrals", F. Aquilante, T. B. Pedersen, R. Lindh, *J. Chem. Phys.*, 126:194106 (2007).

5.2 Quantum chemical description of intermolecular interactions in fluids and liquid crystals

Jonas Boström, Gunnar Karlström and Roland Lindh
PhD Project

Project description
Interactions between molecules are the foundation of all structure in condensed systems. The Hartree-Fock method, followed by MP2 calculations, today describes molecular interactions with a very high accuracy at a reasonable computational cost. To further lower the computational cost, something called Cholesky decomposition (CD) of the two-electron integrals can be used. Methods to perform Hartree-Fock and MP2 calculations employing the CD technique are implemented in the program package MOLCAS. To further study the molecular interactions, it would be useful to also be able to calculate analytical gradients for the potential energy with respect to the positions of the nuclei.

Results
We have developed and implemented the equations required to calculate the so-called effective density matrices needed to calculate MP2 gradients with Cholesky decomposition. This means that we already have the machinery to calculate CD-MP2 properties, for example, multipole moments. Furthermore, we have worked on documenting the accuracy of the CD approximation with respect to the decomposition threshold for various wavefunction models and one-particle basis-sets.

External collaboration
Michal Pitonak, Commenius University, Bratislava, Slovakia.

Publication
"Ab inito density fitting: Accuracy assessment of auxiliary basis sets from Cholesky decompositions", J. Boström, F. Aquilante, T. B. Pedersen, R. Lindh, *J. Chem. Theor. Comput.*, submitted.

5.3 Structural properties of polar liquids

Joakim Stenhammar, Gunnar Karlström, and Per Linse
PhD project

Project description

The long-range structural properties of liquids composed of molecular dipoles are a question of longstanding interest within many fields of chemistry and physics. The long range of the dipole-dipole interaction makes the structure of dipolar systems notoriously difficult to probe using computer simulations, although many techniques have been proposed to overcome these problems.

Within the present project, we combine the use of dielectric continuum theory with computer simulations to try to elucidate some fundamental properties of polar liquids. In particular, we have developed an analysis method based on the distance dependent Kirkwood factor $G_k(R)$ to study the formation of so called ferroelectric domains, *i.e.* regions exhibiting a large alignment of the dipoles. These analyses have proven successful in probing the buildup of ferroelectric structuring as the liquids become more strongly coupled. In parallel, we are using dielectric continuum theory to describe the fluctuations of electrical moments in dielectric media.

Results

The long-range order in strongly coupled dipolar systems has been studied using large-scale simulations for systems containing up to 100 000 particles. It is found that the boundary conditions used can strongly influence the result. A periodic system modeled with the Ewald summation technique (Figure 1, left) possesses ferroelectric domains with ordered dipoles that slightly increase in size and ordering with increasing system size. Results obtained using the minimum image approximation displays i) larger and more ordered domains displaying smaller fluctuations in size and ordering and ii) a much larger increase in domain size and ordering at increasing system size (Figure 1, right); both observations clearly show an artificial increase originating from the boundary condition. Analytical expressions together with scaling considerations suggest that dipolar systems are structured on all length scales. However, more extensive studies are needed to fully assess the impact of using different boundary conditions on the long-range structure of polar liquids.

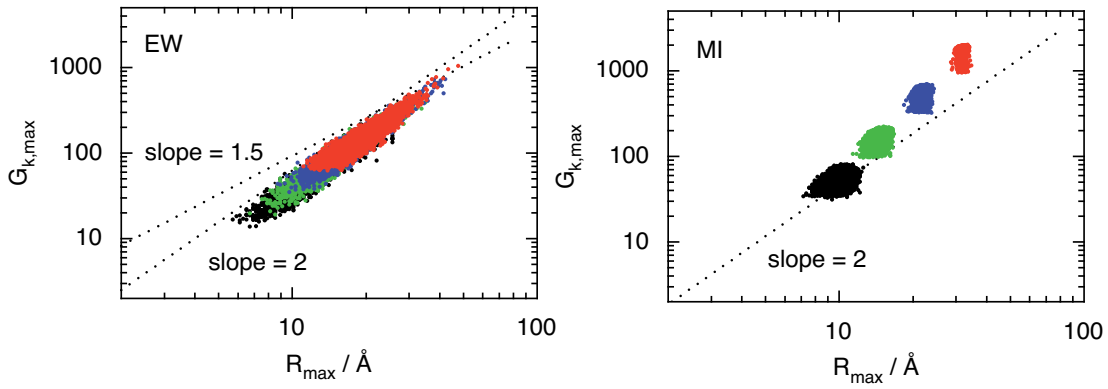


Figure 1. Ferroelectric ordering as a function of the domain size for (left) the Ewald summation technique and (right) the Minimum Image convention using systems containing from 1 000 (black) to 30 000 (red) dipoles.

In the second part, we have derived formulas using dielectric theory, which describes the fluctuations of the electrostatic moments of arbitrary multipoles formed in spherical regions surrounded either by vacuum or coupled to a dielectric continuum. The derived formulas show

excellent agreement with results obtained from computer simulations for weakly coupled polar liquids. Hopefully, the study of how the size of these fluctuations change as the liquids become more strongly coupled can yield valuable information about the different structural properties of the systems and also shed light on how different boundary conditions affect these fluctuations.

Publications

Karlström, G.; Stenhammar, J.; Linse, P.
Effects of different boundary conditions on the long-range structure of polar liquids
J. Phys.: Condens. Matter, **2008**, 20, 494204-1—9
Stenhammar, J.; Linse, P.; Malmqvist, P.-Å., and Karlström, G.
Multipole moment fuctuations in polar liquids
Manuscript in preparation

5.4 Protein-protein interactions and organization

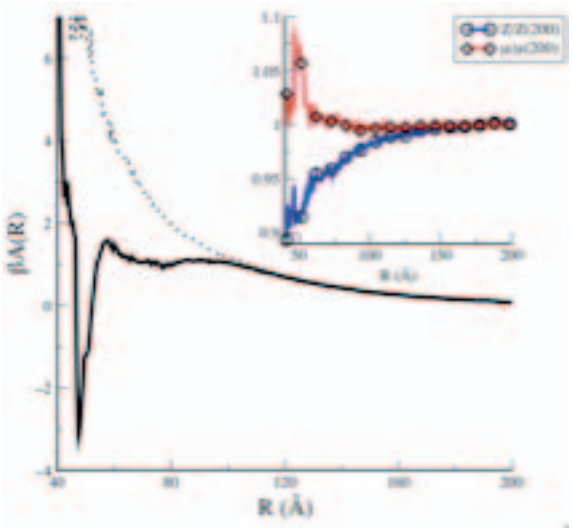
Björn Persson, Jan Forsman, Bo Jönsson, Mikael Lund and Torbjörn Åkesson
PhD project

Project description

Distributions of molecules, such as proteins, DNA and other solutes in biological fluids are determined by their intermolecular interactions. The organization of these molecules in fluids, such as milk, blood or the cytoplasm, is prescribed by the solution conditions (e.g. temperature, pH, salt and solute concentration). Most biological fluids contain a substantial amount of charged solutes, but even under such screened conditions, electrostatic interactions are often found to play an important role in biological systems.

Many proteins and biomolecules have very complex charge distributions. In this context it is especially interesting to investigate the influence of van der Waals forces and the mutual influences of these forces. Such short ranged van der Waals forces can strongly influence the organization of proteins.

Using computer simulations and model descriptions that range from fully atomistic to coarse-grained, we compute thermodynamic properties such as interaction free energies, second virial coefficients, binding constants and titration curves. We are developing software to calculate properties of a wide variety of systems, ranging from the pK_a-shift of small aliphatic carboxyl acids to pair interactions in between entire proteins in solution.



The figure shows the free energy of interaction between two *Lactoferrin* proteins. The full line is obtained including both van der Waals and electrostatic interactions, while the dotted line is for the same system but with only electrostatics included. The inset displays the relative regulation response of the charges and dipoles of the proteins.

Results

We have developed and released a complete open source software package for molecular simulations. Using this software we have studied antibody-antigen interactions and identified a significant orientational ordering due to an intricate coupling between electrostatic and van der Waals interactions. Similarly we have showed that whey and egg proteins aggregate in highly

specific orientations and that this may be governed by the presence of salt as well as protein binding of divalent ions. We have also found that *Lactoferrin* may form dimers in a process that is driven by mutual amplifications of electrostatic and van der Waals interactions. A study of the proton equilibrium of whey proteins has revealed that experimental titration curves are reproduced.

External collaboration
Fernando Luís B. da Silva (Universidade de São Paulo, Brazil), Bengt Jönsson and Eva Thulin (Biophysical Chemistry, Lund University).

Publications
Lund, M., Trulsson, M., Persson, B. Faunus: An Object Oriented Framework for Molecular Simulation. *Source Code Biol. Med.* 2008, 3:1
Persson, B., Jönsson, B., Lund, M. Amplified Steering of Proteins: Synergism of van der Waals and electrostatic interactions. *Manuscript*
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5.5 Polymer-surfactant interactions at liquid interfaces

Richard Campbell, Katrin Tonigold (guest PhD student), Marianna Yanez (MSc student), Tommy Nylander and Lennart Piculell.
Post-doc project

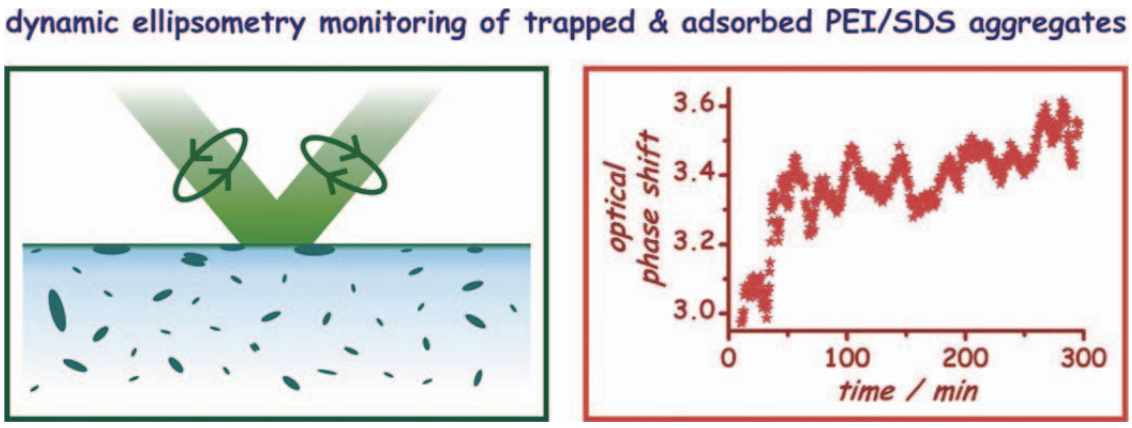
Project description
There is considerable industrial interest in understanding the nature of surface and bulk interactions between polymers and surfactants because such mixtures are used extensively in commercial products such as shampoos and fabric conditioners. Over the last two decades a considerable effort has been spent on gaining an understanding of the nature of the interaction between polyelectrolytes and oppositely charged surfactants in the bulk phase. Most of the work has been carried out on linear polyelectrolyte systems. These investigations showed that usually a one-phase transparent system forms in the presence of a small amount of surfactant. By increasing the bulk surfactant concentration, the solution becomes turbid, and an associative phase separation occurs (i.e., a concentrated phase enriched in both polymer and surfactant separates from a dilute aqueous phase containing mostly small ions). With further increases in the bulk surfactant concentration, the turbidity may decrease, and redissolution of the polyelectrolyte/surfactant complexes can occur. The surfactant binding in the bulk phase is usually interpreted in terms of a two-step equilibrium process.

Poly(ethylene imine) [PEI] has captured a lot of attention from the academic and industrial research communities in recent years. The following factors make PEI an interesting polymer both from a fundamental and a practical perspective.

1. The polymer size as well as molecular architecture can be readily varied from linear to hyperbranched, which affects its morphology in bulk solution and at interfaces.
2. The polyelectrolyte charge can be set by modifying the solution pH: PEI has a high positive charge density at low pH but a diminished charge density at high pH.
3. The physicochemical properties are affected by the ionic strength because the addition of electrolyte increases the surface activity of polymer/surfactant complexes.

A useful optical technique for the characterization of polymer/surfactant adsorption layers at the air/liquid interface is ellipsometry, where the reflection of elliptically polarized light depends on the dielectric (refractive index) profile normal to the interface. The phase change of light upon reflection at the surface of a polymer/surfactant solution, relative to that of a clean interface, is

determined by the structure and amount of adsorbed material. We exploit ellipsometry in the present project by analyzing fluctations in the optical signal, features that would most likely not be detected in the relatively slow and macroscopic measurements made using for instance neutron reflectometry (NR). Furthermore, the comparison of ellipsometry measurements, both with changing bulk composition and evolving time, allows us to track the relative amount of adsorbed material.



Results

We have exploited the spatial and kinetic resolution of ellipsometry to monitor the lateral movement of inhomogeneous patches of material in mixed adsorption layers of poly(ethylene imine) and sodium dodecyl sulfate at the air/liquid interface. We show that the choice of sample preparation methods can have a profound effect on the state of the interface for chemically equivalent samples. The extent of aggregation in the bulk solution on relevant time scales is affected by specific details of the polymer/surfactant mixing process, which produces varying numbers of aggregates that can become trapped in the interfacial layer, resulting in an enhanced and fluctuating ellipsometry signal. It can be beneficial to apply the surface-cleaning method of aspiration prior to physical measurements to remove trapped aggregates through the creation of a fresh interface. At low pH, the ellipsometry signal of samples with surface cleaning is remarkably constant over a factor of >500 in the bulk composition below charge equivalence, which is discussed in terms of possible adsorption mechanisms. At high pH, through observing temporal fluctuations in the ellipsometry signal of samples with surface cleaning, we reveal two important processes: there is the spontaneous adsorption of aggregates >0.2 μm in diameter into the interfacial layer, and with time there is the fusion of smaller aggregates to generate new large surface aggregates. We attribute the favorability of the adsorption and fusion processes at high pH to reduced electrostatic barriers resulting from the low surface charge density of the aggregates. It is inappropriate in this case to consider the interface to comprise a homogeneous adsorption layer that is in dynamic equilibrium with the bulk solution. Our work shows that it can be helpful to consider whether there are macroscopic particles embedded in molecular layers at the air/liquid interface for systems where there is prior knowledge of aggregation in the bulk phase.

External collaboration

Imre Varga and Róbert Mészáros (Eötvös Loránd University, Budapest; Hungary); LSS Group, Institut Laue-Langevin, Grenoble, France (present affiliation of Richard Campbell).

Publication

K. Tonigold, I. Varga, T. Nylander, R. A. Campbell, “Effects of aggregates on mixed adsorption layers of poly(ethyleneimine) and sodium dodecyl sulfate at the air/liquid Interface” Langmuir 2009 (in press).

5.6 Soluble complex salts of surfactant ions and polymeric counterions

John Janiak, Karin Schillén, Lennart Piculell, Gerd Olofsson and Viveka Alfredsson
PhD project

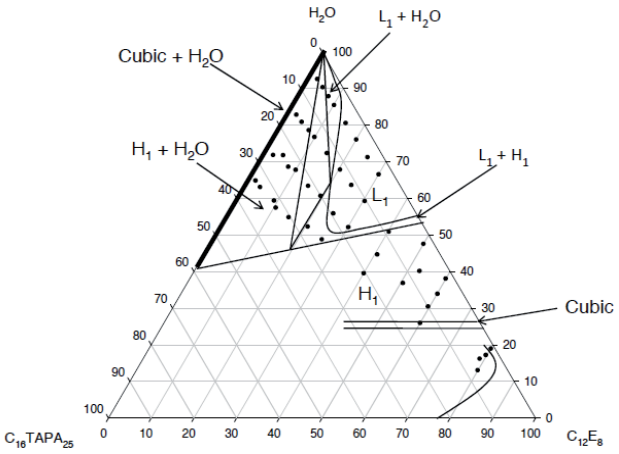
Project description

The aim is to understand the physical chemistry of soluble complex salts in aqueous solution and the intermolecular interactions involved. A complex salt is defined as the neutral salt of surfactant ions (aggregated into highly charged micelles) neutralized by a charged polymer (the polyion). The complex salts studied contain polyacrylate (PA^-_y) and cationic $C_{16}TA^+$ surfactant ions, denoted $C_{16}TAPA_y$, where *y* is degree of polymerization. At high water contents, the investigated complex salts exhibit miscibility gaps that consist of co-existing phases: a concentrated phase (either cubic or hexagonal internal structure) and a less concentrated phase. In order to make the complex salts soluble, in the form of a composite self-assembled macromolecular aggregate, PEO-containing nonionic surfactants of the type C_iE_j are added.

The project has two parts: a) initial phase studies of ternary mixtures of $C_{16}TAPA_y$, C_iE_j surfactants and water, b) investigation of the composite macromolecular self-assembly in dilute solution (main part). The solution properties of these new composite self-assembled structures at different temperatures are investigated by varying the polyion length (y=25 or 6000) and the PEO length of the nonionic surfactant. The phase studies are carried out by visual inspection of the samples and by using small-angle X-ray scattering (SAXS). The size of the aggregates formed is investigated by dynamic light scattering (DLS). Cryo-transmission electron microscopy and SAXS will also be used for structural (internal) characterization of these composite aggregates. For further insight into the intermolecular interactions between $C_{16}TAPA_y$ and C_iE_j, isothermal titration calorimetry (ITC) will be employed. Finally, the solution properties of the complex salt (without C_iE_j) in organic solvents will investigated in order to create a new purification procedure of $C_{16}TAPA_y$.

Results

Ternary phase diagrams of $C_{16}TAPA_{25}/C_{12}E_8$/water, $C_{16}TAPA_{25}/C_{12}E_5$/water, $C_{16}TAPA_{6000}/C_{12}E_8$/water and $C_{16}TAPA_{6000}/C_{12}E_8$/water are currently being determined. The phase diagram of $C_{16}TAPA_{25}/C_{12}E_8$/water is presented below. The one-phase areas demonstrate that $C_{12}E_8$ is able to solubilize $C_{16}TAPA_{25}$. Preliminary DLS results indicate that at high water contents different $C_{16}TAPA_{25}$-$C_{12}E_8$ self-assembled aggregates are formed, the size of which may be influenced by temperature. ITC experiments, where small portions of $C_{12}EO_8$ solution are added to a dilute two-phase $C_{16}TAPA_{25}$/water system, show that the interaction between $C_{16}TAPA_{25}$ and $C_{12}E_8$ consists of two processes. The first process, which is highly endothermic, starts below the critical micelle concentration of $C_{12}E_8$. Simultaneous ITC and DLS measurements are currently being performed to screen the $C_{12}E_8$ concentration regime where aggregates, possibly of specific stoichiometry, are formed.



External collaboration

P. Stepanek (Institute of Macromolecular Chemistry, Czech Republic); W. Loh (Campinas University, Brazil).

5.7 Water-soluble polymers containing amphiphilic repeating units and their interactions with ionic surfactant micelles

Irina Nasimova and Lennart Piculell
Post-doc project

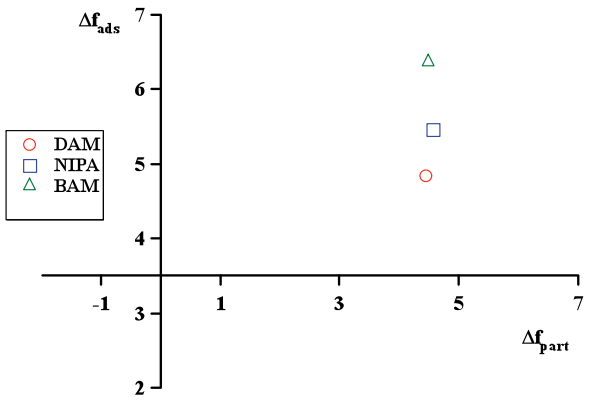
Project description

The description of water-soluble polymers is one of the main research tasks of polymer chemistry and physics. The monomer units of such polymers are usually divided into two classes: hydrophobic (H) versus polar (P) or hydrophilic (P) units (HP classification). However, from the chemical structures of typical monomer units it is evident that in most cases these are neither purely hydrophilic nor purely hydrophobic, but rather amphiphilic, since they contain functionalities of both types. Based on these considerations, a new dumbbell model (HA-model) for amphiphilic (co)polymers was introduced in the group of Khokhlov. It was shown that conformational properties of polymers containing amphiphilic units are significantly different from those predicted by the HP model. The main reason is that for amphiphilic dumbbells a location at an interface is most probable, i.e. these units possess a significant surface activity. Both the interfacial activity and the partitioning between water and hydrocarbon solvents could be key parameters for the classification of monomers and, based on these considerations, a two-dimensional classification diagram has been proposed by I.M. Okhapkin et al. The positions of monomer units of various synthetic water-soluble polymers in such a diagram was determined based on interfacial tension and partition coefficient measurements.

In this project we are using the two-dimensional description to classify certain alkylacrylamide monomers with the aim to rationalize the varying tendencies of the corresponding polymers to bind to surfactant aggregates in water. Usually, the tendency of a nonionic polymer to bind ionic surfactant micelles is explained in terms of the polymer hydrophobicity. However, since a large fraction of the micellar surface contains hydrocarbon in direct contact with water, the interfacial activity of the monomer units should also be taken into account.

Results

The interfacial tensions and partition coefficients of the alkylacrylamide monomers (N,N'-dimethylacrylamide (DAM), N-isopropylacrylamide (NIPA) and N-tert-butylacrylamide (BAM)) were measured, and the results are presented in the figure below.



In this diagram Δf_{part} is a normalized standard free energy of partition between water and hexane, and Δf_{ads} is a standard free energy of adsorption at water/hexane interface. These parameters are defined in such a way that the affinity to the water phase (hydrophilicity) increases from left to right and the interfacial activity increases from bottom to top.

The figure shows that the interfacial activity of the alkylacrylamide monomers increases from DAM to BAM. Note that the monomers exhibit much more pronounced differences in their interfacial activity than they do in their partition between water and oil.

The obtained values of Δf_{ads} were compared with the critical association concentrations (CAC) for the binding of cationic and anionic surfactants to the corresponding alkylacrylamide polymers. Clearly, a stronger surface activity of the polymer corresponds to a stronger tendency of the polymer to bind surfactant micelles.

Table. Surfactant CAC values (in mM) for various ionic surfactant/alkylacrylamide polymer pairs compared with the interfacial activity of corresponding alkylacrylamide monomers.

	CAC (C16TAB)	CAC (C16TAAc)	CAC (SD-(EO)2-S)	CAC (SDS)	Δf_{ads}
DAM	-	-	-	≈6	4.84
NIPA	0.7	0.9	0.4	1	5.46
BAM	≈0.7	0.8	0.35	≈0.8	6.37

External collaboration
Alexei Khokhlov (Moscow State University/Russian Academy of Science)

5.8 Catalysis of surface-active substrates at interfaces in dispersed media: oil in water emulsions

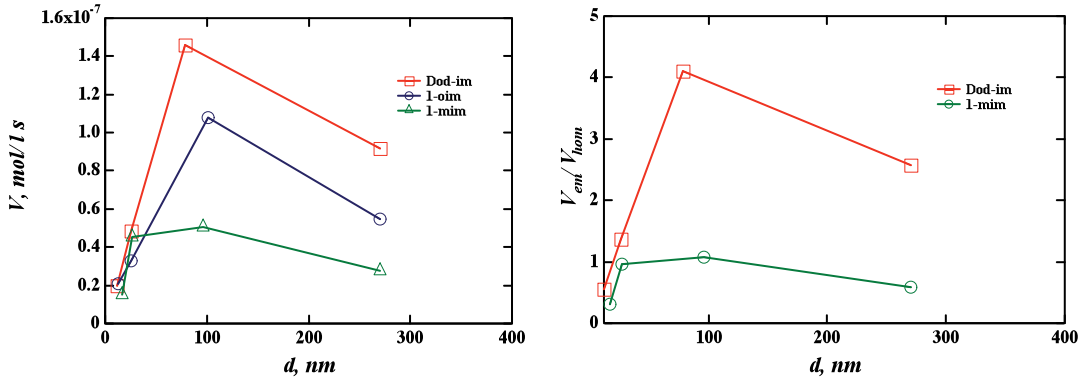
Irina Nasimova and Ulf Olsson
Post-doc project

It is known that one efficient way to increase the rate of a catalytic reaction is to accumulate the reagents in a set of micro-reactors, distributed uniformly in the system. We propose another route to concentrate reagents in limited volume, namely, to use the interfacial adsorption of surface-active amphiphilic molecules at the boundaries of immiscible phases in, for example, oil-in-water emulsions. If the adsorbing molecules can react with each other, the interfacial layer becomes a reactor of nano-scale thickness (a "surface nano-reactor"). Computer modeling and theoretical considerations from Khokhlov's group have pointed to a possibility to control the rate of catalytic reactions carried out in emulsions. At a certain size of the emulsion droplets (several hundreds of nanometers) the reaction rate was predicted to exhibit a maximum. This could be simply explained as follows. For small droplet radii, the available surface area is too large and the concentrating effect at the interface is low. On the other hand, for large radii the surface area is too low, thus reducing the probability that the catalyst and the substrate will meet at the interface. The experimental investigation of this possibility is of special interest. Therefore, this project focuses on experiments on catalysis of surface-active substrates in oil-in-water emulsions.

Results
The hydrolysis of p-nitrophenylbutyrate (an amphiphilic surface active substrate) by two types of amphiphilic surface active catalysts, 1-octylimidazole (1-oim, oil soluble) and N-(2-(imidazolidin-4-yl)ethyl)dodecanamide (Dod-im, water soluble), in hydrocarbon/water emulsions stabilized by the nonionic surfactant dodecyl pentaethylene glycol ether ($C_{12}E_5$) was studied. The results were compared with experiments with a significantly less surface-active catalyst (1-methylimidazole (1-mim)). Micro- and macro-emulsions with oil droplet diameters varying from 15 to 300 nm were obtained by variation of the surfactant/oil ratio and the hydrocarbon length and by using different methods of emulsion preparation (extrusion and passing through the phase inversion temperature).

For the surface-active catalysts, the reaction rate exhibited a pronounced maximum at droplet diameters around 100 nm for both oil-soluble and water-soluble catalysts. By contrast, for 1-methylimidazole this maximum was almost absent (figure 2 (a)). For surface-active Dod-im the

reaction rate in an emulsion with droplet size around 100 nm was 4 times higher than in homogeneous solution, while for 1-mim it was almost the same.



(a) (b)

Variation of the (a) reaction rate and (b) ratio between reaction rate in emulsion and in homogeneous solution of catalyst (only data for water-soluble catalyst presented) with a droplet size in hydrocarbon/water emulsions.

External collaboration
Alexei Khokhlov (Moscow State University/Russian Academy of Science)

5.9 Structures formed by block copolymers containing amphiphilic repeating units

Mehran Asad Ayobi, Lennart Piculell and Ulf Olsson
PhD project

Project description
Block copolymers are composed of two or more chemically distinct and typically immiscible polymer blocks. For a diblock copolymer (poly-A + poly-B) the immiscibility between A and B blocks drives a microphase separation in the melt, with alternating A-rich and B-rich microdomains. The melt phase behavior of linear diblock copolymers with random coil blocks is determined by the overall degree of polymerization N, the volume fraction of the A component f_A, and the A-B segment-segment interaction χ. With increasing f_A from 0 to 0.5, at a fixed high value of χN, one experimentally and theoretically obtains i) A-spheres arranged in a body-centered cubic lattice, ii) A-cylinders arranged in a hexagonal lattice, iii) a region of gyroid phase and iv) alternating A and B lamellae.

Very recently Khokhlov *et al.* reported computer simulation results for diblock copolymers where one of the blocks contains *amphiphilic* repeating units: One part of each amphiphilic unit interacts athermally (zero χ) with the other block, whereas the other part has a strongly repulsive interaction (strongly positive χ). The amphiphilic block is predicted to give a new morphological variation in the block copolymer phase separation, featuring thin channels and slits of amphiphilic units penetrating through the matrix of a major nonpolar components (See figure 1).

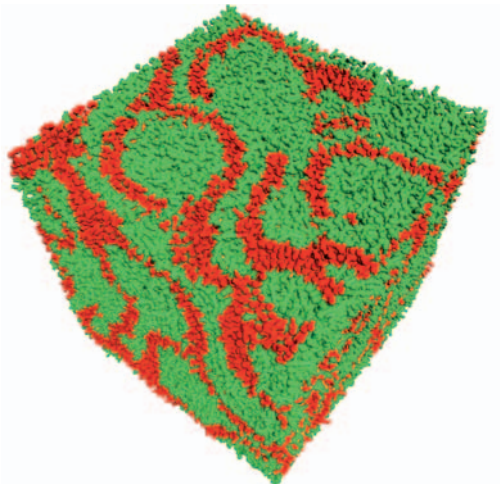


Figure 1. Snapshots from a simulation at $f = 0.5$ ($f_A = 1/3$) and $\chi_{AB} = 38.25$. Amphiphilic segments are shown in red/dark.

The project seeks first to test these new predictions by experimental structural studies of block copolymers containing one hydrophobic and one strongly amphiphilic block. In order to vary the volumes of the hydrophobic and amphiphilic microdomains, a hydrocarbon solvent and/or water will be added to the system. Experimental methods include SAXS and NMR.

Results

Two diblock copolymer samples containing a hydrophobic polystyrene block and an amphiphilic poly(methacrylic acid) block have been chosen for the initial studies. Samples titrated to obtain the cesium salt form of the methacrylic acid have also been prepared, in order to vary the amphiphilicity of the methacrylic acid units. Preliminary SAXS data have been obtained both for the dry polymers and for their mixtures with two selective solvents, water and cyclohexane. More detailed SAXS measurements will now be conducted at the MAX laboratory in Lund, and methods are being developed for preparing shear-aligned polymer samples.

External collaboration

Alexei Khokhlov (Moscow State University/Russian Academy of Sciences); Bo Nyström and Kaizheng Zhu (University of Oslo).

5.10 Diffusive transport in responding lipid membranes

Peter Nilsson, Emma Sparr, Christoffer Åberg, Håkan Wennerström and Daniel Topgaard
Post-doc project

Project description

In a simplified description of membrane transport, one considers a concentration gradient across a static barrier. In a more dynamic approach, the barrier is allowed to respond by changes in lipid phase behaviour along the concentration gradient. It is typical for the rich phase behaviour of lipids that small changes in the external conditions can trigger large structural changes with distinctly different diffusion characteristics. This response in membrane structure can thus act as a kind of switch for diffusive transport, and thereby introduce non-linear elements to the transport process. Beside the basic scientific interest in the mechanisms for steady-state transport in responding membranes, several applications in biology and technology can be seen in, for example, the barrier properties of stratum corneum (the upper layer of the skin) and the formation of plastic polymer-surfactant films.

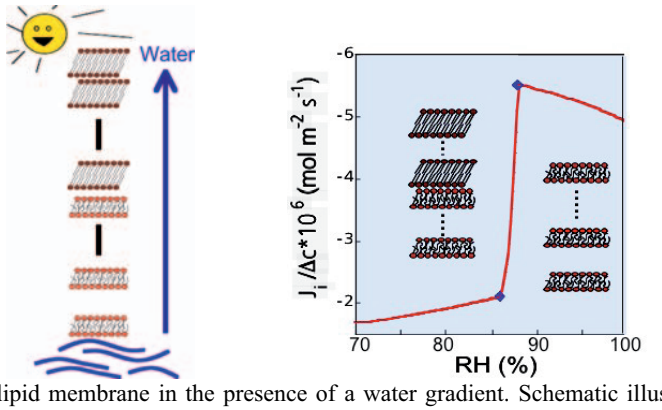


Figure 1. Responding lipid membrane in the presence of a water gradient. Schematic illustration of how the water gradient induce phase transformations in the lipid membrane(left) and calculated flux of a small solute across the membrane at different water gradients (right). It is shown that the external osmotic gradient can regulate the barrier properties of the membrane.

In this project we use a combined experimental and theoretical approach to explore the mechanisms for diffusive transport in responding membranes, and how external gradients that

induce phase transformations and domain formation can regulate the membrane barrier (Figure 1). The experimental work involves transport studies in model lipid membranes using recently devolved system of so-called double-porous membranes, where lipid lyotropic phases are confined inside the pores of a synthetic polymer membrane.

Results

We have developed a novel model membrane system that we call "double-porous" membranes that is used in the studies of transport mechanisms across responding membrane. The basic principle of the double-porous membrane is the use of a porous, micron size, polymer membrane as a scaffold for the lipid lyotropic structure. Primarily this provides mechanical stability, but by appropriately choosing the polymer material one can also obtain a surface induced orientation of anisotropic liquid crystalline phases. The location and the phase behavior of the confined structure was investigated, and the transport studies confirm the theoretical prediction that the osmotic gradient induced phase change dramatically affects the diffusive transport of small solutes through the membrane (1). Recently, the double-porous membrane system was taken one step further in the use of well-defined track-etch membrane with perfectly cylindrical pores arranged perpendicular to the membrane surface as the scaffolding support (5), which clearly facilitates the quantitative analysis. Figure 2 shows the track-etch membrane with lipids inside the cylindrical pores.

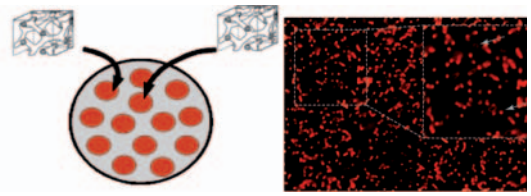


Figure 2: Double-porous lipid membranes: the pores of a synthetic membrane is filled with lyotropic lipid membranes (left). Confocal microscopy image showing lipids located inside the pores (right).

The responding lipid membrane was used in diffusion cell studies to study diffusional transport in responding lipid membranes. It was shown that an external osmotic gradient can be used to regulate transport, and the experimental data could also be predicted by a theoretical model developed by us for transport in responding membranes (Figure 3) (1,4). The same experimental set-up for studying diffusion in the presence of an external osmotic gradient was also used in studies of drug permeation through intact skin (6). The in vitro data from this study indicate that the osmotic gradient can be used to regulate the drug flux over (responding) porcine ear skin membranes but not over (non-responding) silicone sheeting.

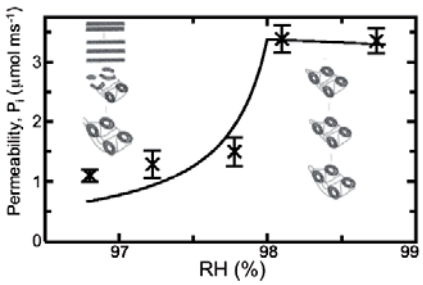


Figure 3: Experimental data (x) and calculated data from theoretical model (line) for diffusive transport of a hydrophilic dye, eosin, across a responding monoolein double-porous membrane at varying osmotic gradient. The gradient can induce phase transitions in the membrane and thus alter the barrier (1)

The experimental studies of diffusive transport across responding membranes are combined with theoretical modelling of the same systems, as illustrated in Figure 3 (1). We also explored

some related problems of coupled transport processes in responding membranes. One study concern the origin of the so-called "acidic mantle" of the skin surface, and we investigated how different transport processes can influence the local proton concentration inside a responding membrane that consist of oriented lipid bilayers (2). The membrane is exposed to an osmotic gradient and a gradient in CO2, and we studied how these gradients influence the lipid structure and the local electrostatics. It was shown that diffusive transport across an oriented bilayer stack of titrating lipids in the presence of an osmotic gradient and/or a gradient in CO2 can give rise to a substantial gradient in pH.

External collaborations
Fátima Costa-Balogh (Coimbra university, Portugal); Karen Edler (University of Bath, UK).

Publications
1. C. Åberg, C. Pairin, F. Costa-Balogh, E. Sparr; *Double-Porous Lipid Membranes: Lyotropic Phases in a Polymer Scaffold.* Biochim. Biophys. Acta – Biomembranes (2007) 1778, 549-558
2. C. Åberg, H. Wennerström, E. Sparr; *The Effect of Transport Processes on the pH Gradient across Stratum Corneum.* Langmuir (2008) 24, 8061-8070
3. C Åberg, E. Sparr, K. Edler, H. Wennerström; *A Gradient in Water Chemical Potential Can Induce the Formation of a Separate Phase close to the Air/Water Interface.* Manuscript in preparation
4. E. Sparr, C. Åberg, P. Nilsson, H. Wennerström; *Diffusing transport in responding lipid membranes*, Submitted to Soft Matter
5. P. Nilsson, A. Clemens, E. Sparr; *Transport of across well-defined lipid membranes – effects of membrane structure and hydrophobicity of the diffusing compounds.* Manuscript in preparation
6. S. Björklund, E. Sparr, K. Thuresson, J. Engblom; *Skin permeability can be regulated by an external osmotic gradient.* Manuscript in preparation.

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

Agnieszka Nowacka, Daniel Topgaard, Emma Sparr, Dan Lundberg, Azat Bilalov, Nils Bongartz and Jens Norrman
PhD project

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 require 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.

Results
Cationic surfactant with oligomeric counterions, the aqueous phase behavior of which has been characterized in detail 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 segment 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 an 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 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.

External collaboration
Rachel W Martin (University of California, Irvine)

5.12 Molecular dynamics in concentrated surfactant systems: Influence of intermolecular forces

Tiago Ferreira, Daniel Topgaard, Gunnar Karlström and Ulf Olsson
PhD project

Project description
Weak intermolecular interactions determine not only the structure, but also the molecular dynamics in self-assembled systems. New solid-state NMR equipment and techniques allow for the determination of segment order parameters (S_{CH}) and translational self-diffusion coefficients (D) even in concentrated anisotropic self-assembled systems without the use of isotopically labelled molecules. The experimentally measured parameters can also be estimated from molecular dynamics simulations (S_{CH} and D) and Monte Carlo simulations or statistical mechanics calculations (S_{CH} only).

The aim of the project is to provide fundamental knowledge about the links between intermolecular interactions, the structure of the supramolecular assemblies, and molecular dynamics on the nano- to micrometer scales. For this purpose, NMR studies on a number of surfactant systems are combined with theoretical approaches. Topics to be studied include the influence of oligo(ethylene oxide) conformation on the molecular orientation in liquid crystals composed of non-ionic surfactants, and the influence of counterion valency and size on the molecular dynamics in liquid crystals formed by cationic surfactants. In the course of the project we expect to further develop the NMR methods to provide data with higher accuracy for systems with more components.

Results
Separated local field NMR experiments (Figure 1)were applied and optimized for ethylene oxide surfactant systems, yielding temperature dependent order parameter profiles with unprecedented resolution. The results indicate an extension of the ethylene oxide segments and a contraction of the alkyl chain upon increasing temperature. Such detailed data are valuable for comparison with results from the theoretical approaches of Karlström.

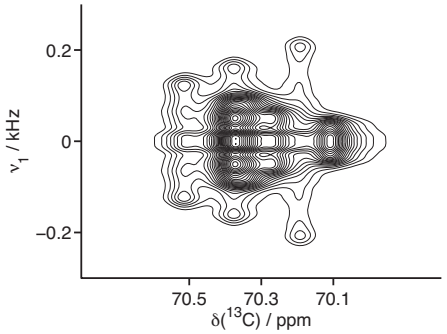


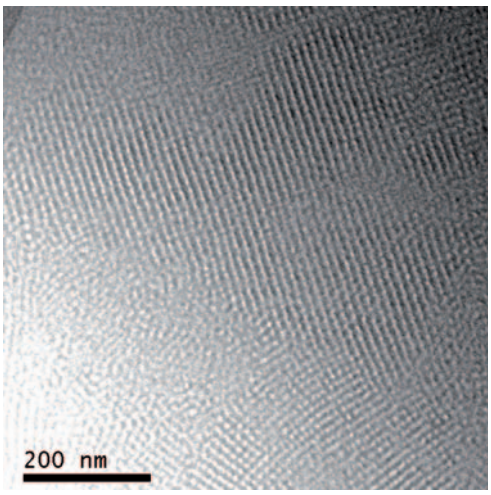
Figure 1. Detail of a 2D separated local field NMR experiment in which information about segment order parameters, being proportional to the ^{1}H-^{13}C dipolar frequency n_1, are correlated with ^{13}C chemical shift d. Each 2D peak corresponds to one CH_2 segment in the ethylene oxide chain.

External collaboration
Rachel W Martin (University of California, Irvine), Bruno Medronho (Coimbra University)

Publication
T.M. Ferreira, B. Medronho, R.W. Martin, and D. Topgaard (2008) Segmental order parameters in a nonionic surfactant lamellar phase studied with ^{1}H-^{13}C solid-state NMR. Phys. Chem. Chem. Phys. 10, 6033-6038

5.13 Cryogenic transmission electron microscopy - imaging lyotropic liquid crystals

Juanfang Ruan, Anna Carnerup and Viveka Alfredsson
Post-doc project



Cryogenic transmission electron microscopy is a powerful tool for investigating structures/particles in liquid samples. One major drawback is the sample preparation where specimens of viscous liquids are difficult or, in some cases, even impossible to prepare with the normal cryogenic plunge methodology. In this project the aim is to develop methodologies to prepare specimens of viscous samples, in particular of lyotropic liquid crystals. Lyotropic liquid crystals have structures (see inserted micrograph) equivalent to those formed by mesostructured silica materials (*c. f.* the OMM project Mesoporous silica – formation and functional materials). Electron micrographs offer unique information regarding the structure of materials as direct information is obtained (Both amplitude and phase are obtained as compared to diffraction which do not provide the phase information). The structures of mesoporous materials have been solved with electron microscopy using a methodology developed by Professor Osamu Terasaki and coworkers at Stockholm University (SU). In collaboration with the group at SU we will use this methodology for the study of structures formed by lyotropic liquid crystals. Other interesting aspects of liquid crystals that can be investigated are for instance domain sizes, intergrowths and defects.

Results
Preliminary results (cryo-TEM) from cubic lyotropic systems have been obtained (figure above)

External collaboration
Yasuhiro Sakamoto and Osamu Terasaki (Stockholm University); Matthias Mörgelin (Lund University)

5.14 Amyloid-protein aggregation

Erik Hellstrand, Sara Snogerup Linse, Emma Sparr and Anna Assarsson
PhD project

Project description
Protein aggregation can result in a major disturbance of cellular processes, and is associated with over 20 known diseases. Important questions concern the molecular properties of the protein and/or the environment that either prevent or promote protein aggregation and amyloid

fibril formation. In this project we are mainly focusing on the effects of membrane lipids on fibrillation kinetics, but also the effects of fibrillating peptides on membrane integrity and structure. We work with the Alzhemier's disease-associated amyloid β peptide (of two lengths, Aβ40 and Aβ42). We are studying the aggregation process of Aβ40 and Aβ42 (wt and mutants) as a function of peptide concentration and as a function of liposome composition and concentration. To make this possible we have eliminated every possible source of error in the experiment and achieved a very high level of reproducibility. This puts us in a unique position to acquire highly reproducible data to approach the mechanism of association of Aβ into aggregates of different sizes, including the small neurotoxic oligomers. The importance of this fact should not be underestimated. The low level of reproducibility reported by most labs have lead to a general picture that the nucleation is more or less random, and poor data quality has hindered any molecular understanding of the phenomenon. The precision that we acquire can lead to a molecular understanding of the nucleation event and the onset of Alzheimer's Disease.

Results

We have cloned the peptides into production plasmid, obtained high-level expression in *E. coli* and developed an efficient purification protocol [1]. This is a major achievement and the implications go far beyond the benefits for our own studies. Systematic studies of Aβ fibrillation have been hampered by the very high costs of synthetic peptide. Earlier cloning and purification protocols rely on affinity tags also leading to expensive isolation of the Aβ peptide. Our protocol leads to high level expression and purification can be achieved using simple and inexpensive tools. It has allowed us for the first time to achieve systematic studies with a large number of replicates. Below are shown preliminary data from our study of the concentrations dependence of Ab42 fibrillation. A manuscript is in preparation [2].

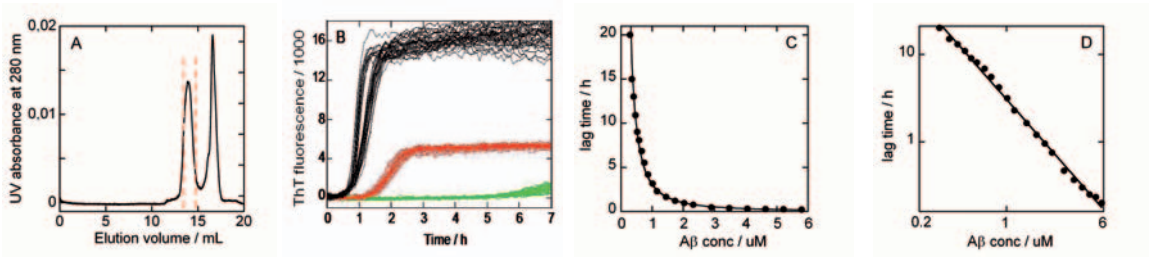


Figure 1. Concentration dependence of Aβ42 fibrillation. A) isolation of monomeric Aβ42 by gel filtration. The fraction collected between the dashed red lines is cleared from small amounts of dimer, buffer and salt. This step is instrumental to obtaining reproducible data. B) 32 replicates at 2.4 □M (black), 32 at 1.2 □M (red) and 32 at 0.6 □M (green) Aβ42. Clearly, the lag time is highly reproducible at each concentration. C and D) Lagtime versus Aβ42 concentration is with linear (C) and logarithmic (D) axes. The fitted line in panels C and D is a power function and the exponent obtained is -1.62, indicating steep concentration dependence and a high molecularity of the nucleus.

We have studied the influence of solution conditions like NaCl concentration, buffer composition and concentrations, additives like DMSO, etc on fibrillation kinetics. A clear dependence on ionic strength is found with shorter lag phase for Aβ fibrillation the higher the ionic strength. Aβ peptide has a net charge of -3 at pH 7, so probably the effect of salt is to screen electrostatic repulsion between peptides, which would favour their association. Many kinds of biomolecules and surfaces also seem to extend the lag phase of Aβ fibrillation. Our studies using DOPC liposomes as model membranes show a clear extension of the lag phase for fibrillation. These studies have been performed as a function of salt concentration, and retardation is seen at all salt concentrations examined. Preliminary data for the fibrillation of Aβ in the absence and presence of DOPC liposomes at 100 mM NaCl are shown below. Our data also show distinct effects depending on the lipid composition of the liposomes. Liposomes of sphingomyelin or sphingomyelin:cholesterol mixtures have much smaller or no effects, while for liposomes with

lipid rafts (sphingomyelin:cholesterol:DOPC) we see very interesting fibrillation traces that are often biphasic. We are starting to write a manuscript [3].

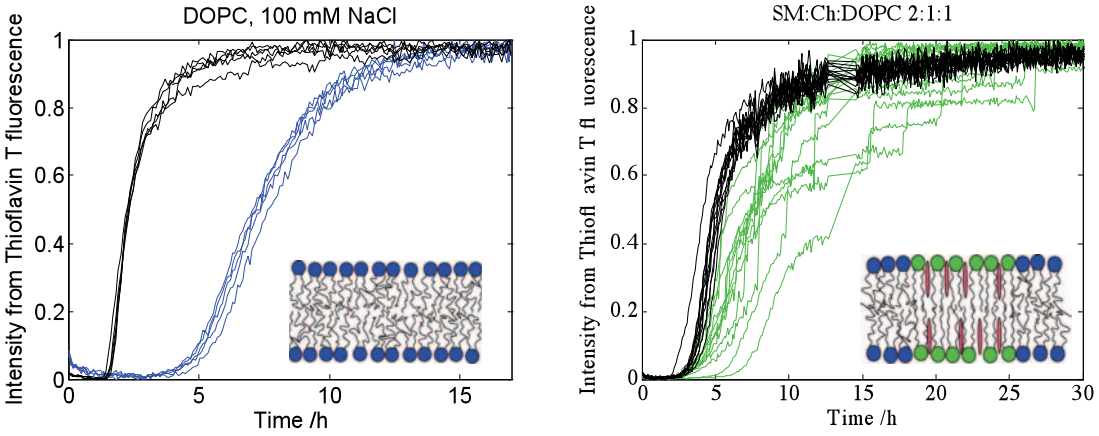


Figure 2. Fibrillation of Ab40 alone (black) or in the preswence of DOPC liposomes (blue) or liposomes fromed from a 2:1:1 mixture of sphingomyelin:cholesterol:DOPC, i.e with lipid rafts (green).

We have also in the form of a Master thesis project investigated the influence of proteins on Aβ fibrilation kinetics. To look for general effects we chose two irrelevant proteins that Aβ normally does not see: the intestinal protein calbindin D_{9k} (with net charge -7) and the plant protein monellin (wt with net charge +2 and two mutants with net charges +8 and -2).

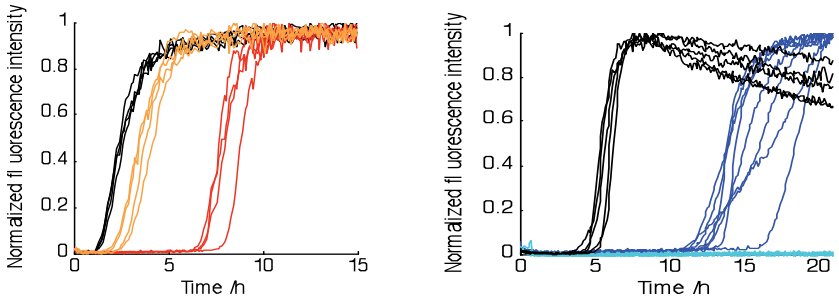


Figure 3. Fibrillation of Ab40 alone (black) or in the presence of a negative protein calbindin D_{9k} (orange and red-7, tenfold higher concentration for the red traces), and positive proteins (blue +2, cyan +8).

External collaborations

Dominic Walsh (University College Dublin); Patrik Brundin (BMC Neurocentrum, Lund University).

Publications

1. A facile method for expression and purification of the Alzheimer disease-associated amyloid β-peptide. Walsh DM, Thulin E, Minuogue A, Gustafsson T, Pang E, Teplow DB, Linse S. *FEBS J. In press* (2009).
2. On the fibrillation of Alzheimer disease-associated amyloid β-peptide. *Manuscript in preparation*.
3. Role of lipid membrane composition on the fibrillation of Alzheimer disease-associated amyloid β-peptide. *Manuscript in preparation*.

5.15 Cyclodextrins in DNA compaction

Jonas Carlstedt, Björn Lindman, Alfredo González-Pérez
PhD project

Project description

Important cellular processes involving DNA, such as transcription and replication, can be strongly affected by the extent of condensation of the chromatin fiber. The degree of condensation affects the access of regulatory factors. In synthetic gene delivery systems, the use of cationic lipids can protect and compact the large and highly biodegradable DNA molecule. Once the DNA:compacting agent complex reaches the target inside the cell, the DNA should be decompacted to be accessible to the cell machinery responsible for translating the enclosed information. Obviously, it is desirable to achieve a reversible DNA condensation process in order to be able to control the transfection efficiency. Many chemical agents have been successfully used *in vitro* to compact DNA, thus mimicking the natural process occurring in the cell. In the last years, the fundamental understanding of the compaction process using different chemical agents has improved. Various strategies have also been used in order to decompact the condensed DNA, such as the introduction of non-ionic and anionic surfactants.

It was recently reported that β-cyclodextrin (β-CD) can be used to decompact DNA:CTA complexes. Cyclodextrins are cyclic oligomers of glucose shaped like truncated cones that are resistant to degradation of human enzymes and not producing an immune response in mammals. They are therefore of interest in therapeutical applications. In general, cyclodextrins are used to encapsulate and solubilize various hydrophobic molecules (or parts of thereof) in aqueous solution by forming host-guest complexes by association of the hydrophobic parts into the hydrophobic cavity of the cyclodextrin. The inclusion complexes formed by β-CD and the cationic surfactant cetyltrimethylammonium bromide (CTAB) were investigated by Cabaleiro-Lago and coworkers, and a strong association constant was found. Both 1:1 and 2:1 β-CD:CTAB complexes were found.

In the present study, the efficiencies of α-CD and β-CD (differing in size by one glucose unit) as well as 2-hydroxypropyl-β-CD (the 2-HP substitution increases the water solubility substantially) of varying degrees of substitution in the DNA decompaction process of DNA previously compacted by CTAB is investigated. The decompaction process is studied by fluorescence microscopy and fluorescence spectroscopy as well as by density and sound velocity measurements. Furthermore, the possibility for direct interactions between DNA and CD is studied by thermal melting and circular dichroism. Additionally, macroscopic phase separation studies are also being performed.

This novel approach in DNA decompaction makes it possible to control the conformation of DNA without introducing new surfactant structures into the solution and we believe it could be of interest from a gene therapy perspective.

Results

DNA compacted by CTAB has successfully been decompacted by addition of all investigated types of cyclodextrins. The decompaction is a non-first-order transition since no coexistence region between coils and globules was observed for intermediate CD concentrations. Evidence of direct interactions between DNA and CD has been found in the thermal melting experiments, however, no conformational disturbance of the DNA helix has been observed from the circular dichroism experiments. The nature of the DNA:CD interaction and its role in the decompaction process are both unclear at present.

External collaboration
Dr. Rita Dias, University of Coimbra, Portugal

Publications
1. Alfredo González-Pérez, Jonas Carlstedt, Rita S. Dias, Björn Lindman. Cyclodextrins in DNA decompaction. *Manuscript*
2. Jonas Carlstedt, Alfredo González-Pérez, Manuel Alatorre-Meda, Rita S. Dias, Björn Lindman. Release of DNA from DNA-surfactant complexes induced by 2-hydroxypropyl-β-cyclodextrin. *Manuscript*

5.16 Physico-chemical behavior of aqueous systems containing DNA, proteins and amphiphiles

Dan Lundberg, Anna Carnerup, John Janiak, Karin Schillén, Viveka Alfredsson, Daniel Topgaard, Björn Lindman
Post-doc project

Project description
The behavior of systems where DNA coexists with both proteins and amphiphiles is of great biological importance. Most notably, there are indications that interactions between the lipid portions of the cell nucleus with chromatin, which is a DNA-protein complex, are involved in organization of the chromatin and regulation of gene expression. Another example is the finding that the inclusion of proteins in DNA-lipid complexes for gene therapy can greatly enhance the transfection efficiency. Despite the biological relevance, investigations performed to study well-defined aqueous systems of DNA, protein and amphipihiles are few. The aim of this project is to gain an improved understanding of the physicochemical behavior of such systems. Of particular interest is the structure and composition of aggregates and complexes formed by the components and a multitude of techniques are applied for characterization of these. The work is focused on three classes of systems: 1) model systems of well-characterized proteins, DNA and different types of amphiphiles, 2) systems containing nucleosome core particles (NCPs), i.e. the basic unit of chromatin, which consist of DNA wrapped around a core of eight histone proteins, and different types of amphiphiles, and 3) complexes comprising plasmid DNA, amphiphiles and certain proteins that have been evaluated with regards to their efficiency in transfection experiments.

Results
In the initial studies the well-characterized small cationic enzyme lysozyme has been used as a model protein and before amphiphiles were introduced some effort have been put into understanding the interactions between this substance and DNA. A multi-technique investigation of aqueous system of lysozyme and DNA from salmon sperm show that a separate phase is formed at very low concentrations of either or both of the macromolecular components and suggest that direct interactions between the protein units are involved both in driving the phase separation and in controlling the morphology of the formed assemblies. The DNA-lysozyme assemblies formed at the phase border consistently show a worm-like shape and probably have a molecular organization that is fundamentally different from that found in the toroidal constructs commonly formed on complexation between DNA and multivalent cations. A related study on lysozyme and monodisperse T7 DNA show similar results but provide additional details on the mechanisms of co-assembly. When the single-tailed cationic surfactant dodecyltrimethylammonium chloride is added to a complex of lysozyme and DNA, the surfactant gradually replaces the protein.

External collaboration
Maria da Graça Miguel, Henrique Faneca and Maria C. Pedroso de Lima at University of Coimbra, Coimbra, Portugal; Lars Nordenskiöld and Nikolay Korolev, Nanyang Technological University, Singapore.

Publications
One manuscript is submitted and three are in preparation.

5.17 Structure and self-assembly of viruses

Nikolay Oskolkov and Per Linse
Post-doc project

Project description
The project comprises studies of the packaging of double stranded DNA (genome) inside viral capsids using a density functional theory and constitutes an extension of previous computer simulations of polymers in confined geometries at the Division of Physical Chemistry. Of special interest is to investigate the nematic transition in the spherical capsid and elucidate possible conformation transitions of the genome in confined geometry.

A density functional theory of packaging of the genome inside a viral capsid is developed. The main idea of the work is to apply the mathematical apparatus elaborated in the theories on nematic ordering to describe the arrangement principles of a long persistent polymeric chain under the conditions of confined geometry. In this case the local self-assembly of different segments of the chain can be regarded as a nematic phase with non-constant (distorted) director. To take into account the energy of nematic distortion, the elastic continuum theory has been used. The director of the ordered nematic phase was specified for the particular case of bend distortion, which models the well-known spool-like conformation of the genome inside a spherical viral capsid. The elastic constant of the bend distortion was calculated in accordance with Grosberg's method.

The developed density functional theory accounts for excluded volume interactions in Onsager's second virial approximation. The inhomogeneous free-energy functional was minimized with respect to polymer density and order parameter of the segments of the genome. As a result, the polymer density and orientational order distribution profiles throughout the volume of capsid were obtained.

At present the predictions of the theory are being explored and comparison with experimental data is in progress.

Results
The free energy functional of the genome inside spherical capsid was numerically minimized with respect to polymer density and order parameter for the two dimensional case, when only radial distance ρ and equatorial angle φ were taken into account, while the azimuthal angle θ was temporary fixed ($\theta = \pi/2$). In other words, the packing of the genome in the equatorial plane of the capsid was considered as a first step. The resulting polymer density distribution and order parameter profiles as functions of the radial distance ρ from the center of capsid at different genome stiffness are shown in Figure 1.

The genome density distribution profiles $\Phi(\rho)$ (Figure 1, left) show that i) the genome is predominantly concentrated both in the center and near the capsid surface at $R = 20$, while a density minimum is observed in between, and ii) the more rigid the genome becomes the more it tends to leave the center and move closer to the surface of capsid. The latter effect is connected

with the smaller bend energy penalty due to relaxation of the chain while moving closer to the capsid surface.

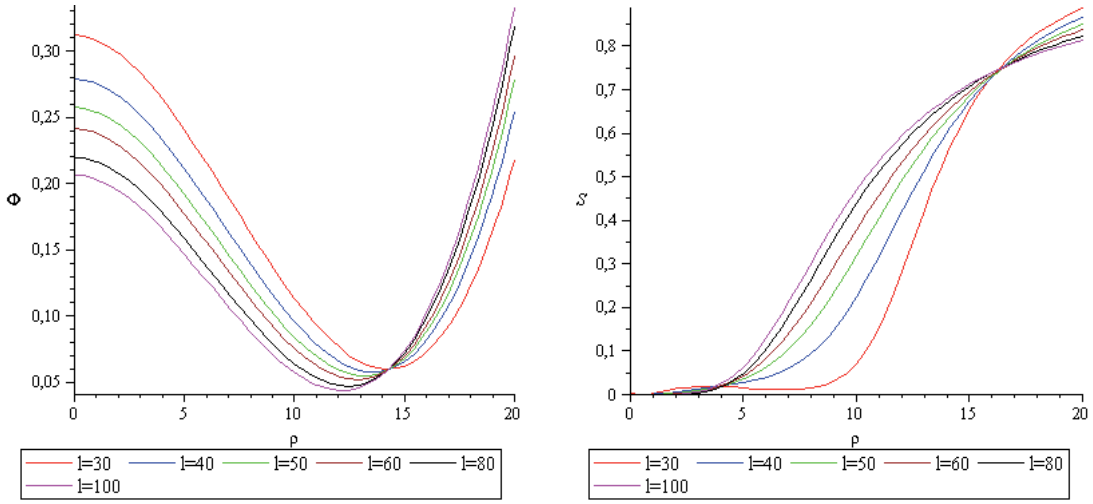


Figure 1. (left) Genome density $\Phi(\rho)$ and (right) genome order parameter $S(\rho)$ as a function of radial distance ρ from the capsid center for genome length L = 200 and capsid radius R = 20 at indicated genome persistent lengths l. All lengths are given in units of the genome diameter.

The order parameter profile $S(\rho)$ (Figure 1, right) is monotonically rising from zero in the center to nearly unity at the capsid surface. This implies a i) disordered domain in the capsid center and ii) demonstrates an orienting effect of the surface in the process of nematic ordering: it is natural to expect that due to the spatial constraints of the surface the genome becomes more and more ordered as it approaches the capsid surface. Furthermore, two opposite behaviours of the order parameter with respect to the persistent length can be observed. In the most of the capsid space, the genome becomes more ordered at increasing persistent length, which is an expected phenomenon for the explored system. However, a reversed behaviour is found at the surface, where a more rigid genome becomes less oriented. This anomalous behaviour can be explained by increasing of the amount of sharp bends of the more rigid genome by interacting with the curved capsid surface.

In summary, the structure of the genome inside a spherical capsid restricted to the equatorial plane displays two characteristic regions: a disorganized core and a highly oriented area at the surface, whereas there is a region of low polymer concentration in between.

External collaboration
Alexei Khokhlov (Moscow State University/Russian Academy of Sciences)

5.18 Guest student projects

5.18.1 Marieke Bode

Supervisors Martin Trulsson and Lennart Piculell

The so-called "over-charging" of colloidal particles, through the accumulation of an excess of multivalent counterions near the particle surface, is a phenomenon that attracts much current interest, both expertimentally and theoretically. In this diploma project, the interaction between negatively charged colloidal particles in the presence of multivalent ions has been studied by Monte Carlo simulations as well as experimentally. The colloids used in the experiments were silica particles or latex particles and the multivalent ions were La^{3+}, spermidine (3+) and spermine (4+). In all cases overcharging by the multivalent ions was observed above a certain

concentration of ions. From the computer simulations it could be concluded that there is a very small repulsive interaction between overcharged particles (between 0 and 1kT, depending on the surface charge of the particles).

In the experiments an increase in stability ratio above a certain ion concentration could be observed, although this did not always correspond to the concentration at which overcharging takes place. For the silica particles a second stabilization mechanism was observed. Possibly this is a steric stabilization by a hairy layer of oligomeric silica on the surface of the particles.

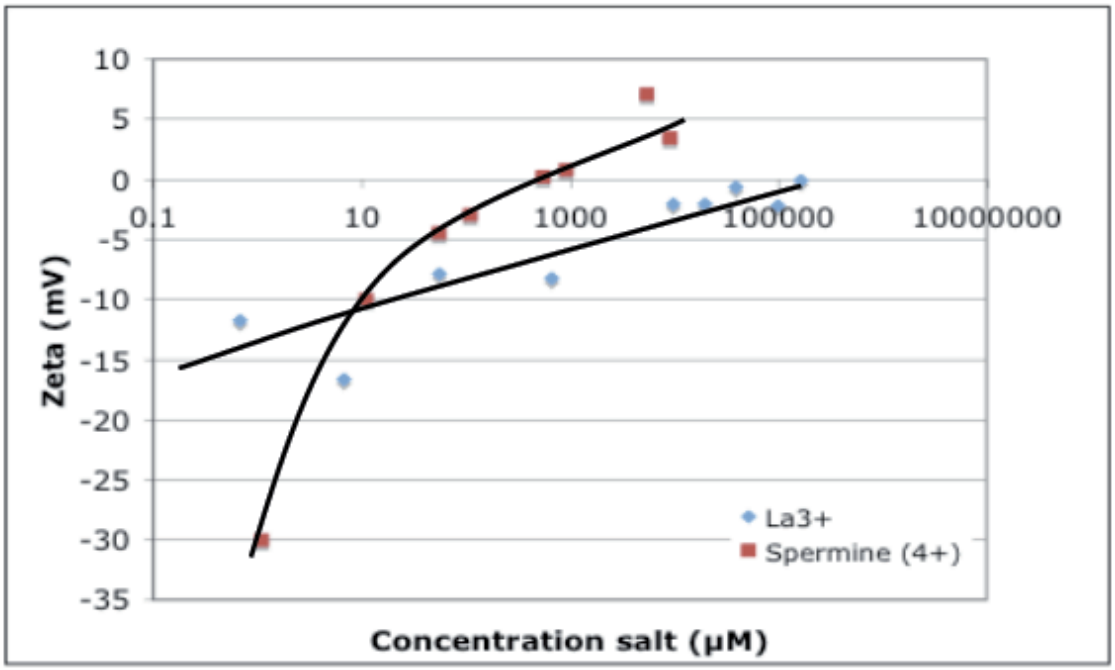


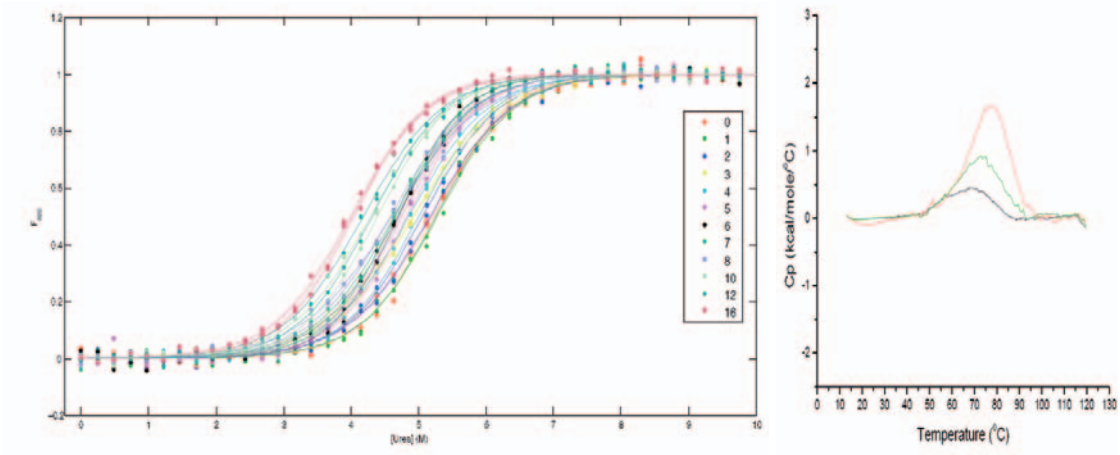
Figure 1. Zeta potential of 6000x diluted latex in $LaCl_3$ and spermine solutions from mobility measurements.

5.18.2 Johannes Stigler

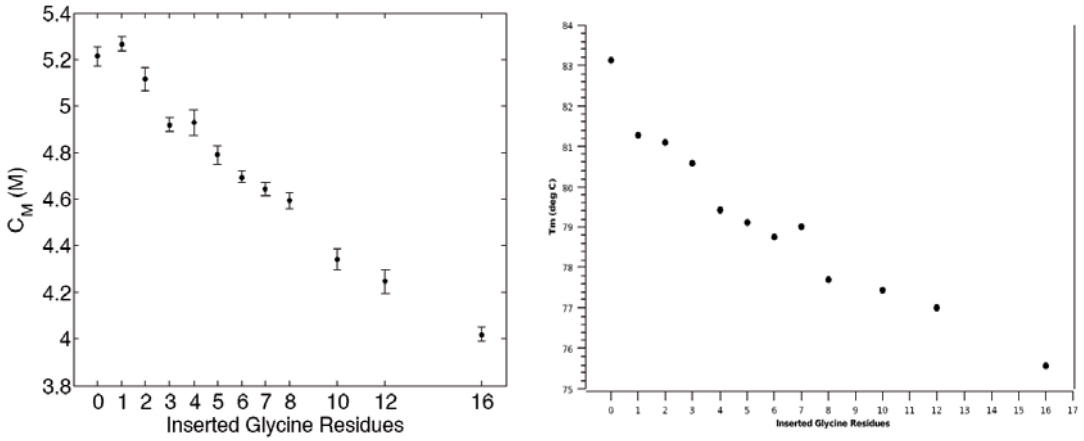
Supervisor Sara Snogerup Linse

This work investigates the effect of protein stability of increased flexibility in joining of subdomains in a protein. We have used a series of mutants of calbindin-D9k, a calcium binding protein with two EF-hand subdomains. We have made a series of variants of this protein where we have extended the linker between the two EF-hands by inserting up to 16 glycines between residues 43 and 44. Parameters studied are the stability of the proteins towards denaturation and the calcium binding properties of the folded proteins.

Results: The stability towards urea denaturation was studied using circular dichroism spectroscopy, and towards thermal denaturation using differential scanning calorimetry. Data for wild-type (0 inserted glycines) and variants with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12 or 16 inserted glycines are shown below. The data have been normalized by base-line subtraction.



The urea concentration (C_M) and temperature (T_m) at the denaturation mid point were obtained by fitting to the un-normalized data and is shown below as a function of the number of linker glycines.



Evidently there is a marked reduction in protein stability by lengthening the linker between the subdomains (with one inserted glycine the only exception) that seems to follow the number of glycines in approximately a linear fashion. We believe this trend arises because the entropic cost of association of the two subdomains into a folded domain is higher the longer the linker. On the contrary, we saw no effect on calcium affinity for the folded proteins, except a small increase for the one-glycine variant.

6 Scientific instruments

6.1 Plate Reader Fluostar Omega

Support from OMM was used to purchase a plate reader Fluostar Omega. It can read continuously absorbance or fluorescence for 96- and 384-well plates. It is thermostated and the plates can be shaken up to 700 rpm. We use the instrument to study protein fibrillation by means of thioflavin T fluorescence. Important questions concern molecular properties of the protein and/or environment that prevent or promote protein aggregation and amyloid fibril formation, a phenomenon associated with over 20 known diseases. Using this plate reader we study the effect of peptide concentration and the effects of membrane lipids on fibrillation kinetics, but also the effects of fibrillating peptides on membrane integrity and structure. We work with the Alzhemier's disease-associated amyloid β peptide (of two lengths, Aβ40 and Aβ42). We study the aggregation process of Aβ40 and Aβ42 (wt and mutants) as a function of peptide concentration and as a function of liposome composition and concentration.

Main users
Sara Snogerup Linse, Emma Sparr, Erik Hellstrand and Anna Assarsson.
Results
Below are shown typical data acquired with the plate reader.

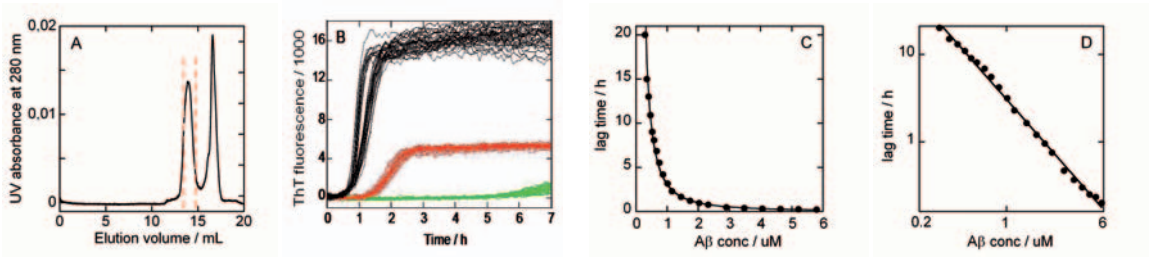


Figure 1. Concentration dependence of Aβ42 fibrillation. A) isolation of monomeric Aβ42 by gel filtration. The fraction collected between the dashed red lines is cleared from small amounts of dimer, buffer and salt. This step is instrumental to obtaining reproducible data. B) 32 replicates at 2.4 μM (black), 32 at 1.2 μM (red) and 32 at 0.6 μM (green) Aβ42. Clearly, the lag time is highly reproducible at each concentration. C and D) Lag time versus Aβ42 concentration is with linear (C) and logarithmic (D) axes. The fitted line in panels C and D is a power function and the exponent obtained is -1.62, indicating steep concentration dependence and a high molecularity of the nucleus.

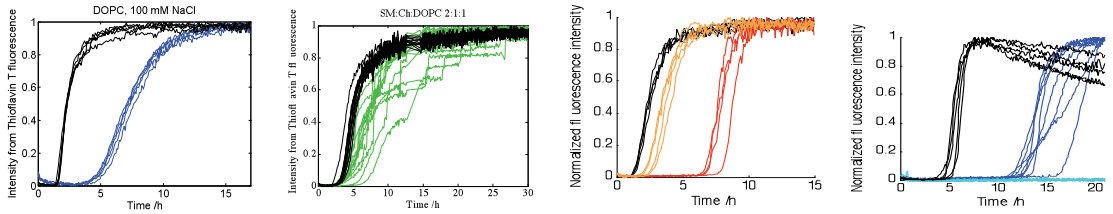


Figure 2. Fibrillation of Ab40 alone (black) or in the presence of DOPC liposomes (blue, left), liposomes with 2:1:1 sphingomyelin:cholesterol:DOPC (green), a negative protein calbindin D_{9k} (orange and red-7, tenfold higher concentration for the red traces), and positive proteins (blue +2, cyan +8).

Publications
1. A facile method for expression and purification of the Alzheimer disease-associated amyloid β-peptide. Walsh DM, Thulin E, Minuogue A, Gustafsson T, Pang E, Teplow DB, Linse S. *FEBS J. In press* (2009).
2. On the fibrillation of Alzheimer disease-associated amyloid β-peptide. *Manuscript in preparation*.
3. Role of lipid membrane composition on the fibrillation of Alzheimer disease-associated amyloid β-peptide. *Manuscript in preparation*.

7 OMM Activities

7.1 Annual meetings

Beginning in January 2007, OMM has arranged two member meetings per year, one in spring and one in late August. Typically, the spring meeting lasts half a day with ensuing dinner, and is dedicated to reviews of OMM research activitites. In the first January meeting, all OMM senior scientists gave their views on what they wished to contribute to, and their expectations from, the OMM collaboration.

The meeting in August is a full-day meeting where each time two themes are reviewed, one in the morning and one in the afternoon. Here, we may also invite talks from external speakers. Themes that have been penetrated so far are *intermolecular interactions*, *interactions in colloidal systems*, *scattering methods* and *themes in colloidal biology*.

7.2 Seminars

OMM seminars and workshops have been arranged with an increasing frequency since the start. Here is a list of OMM seminars during 2006-2008.

2006

2006-10-16 **Håkan Wennerström** (Physical Chemistry 1)
Charged Colloids in Chemistry and Biology
2006-10-30 **Gunnar Karlström** (Theoretical Chemistry)
Ferroelectric Domains in Droplets of Dipolar Molecules
2006-11-27 **Anders Öhrn** (Theoretical Chemistry)
The Ground and Excited State of Quinone in Water - Equilibrium and Non-equilibrium Solvation from Computer Simulations
2006-12-12 **Dusan Bratko** (Univ California Berkeley, USA)
Modeling surface interactions: From proteins to electrowetting

2007

2007-01-29 **Sara Linse** (Biophysical Chemistry)
Protein aggregation and fibrillation - Molecular determinants and possible nucleation events
2007-02-12 **Björn Roos** (Theoretical Chemistry)
MOLCAS - the Quantun Chemistry Software
2007-02-26 **Martin Trulsson** (Theoretical Chemistry)
Repulsion between oppositely charged macromolecules
2007-03-12 **Mikael Akke** (Biophysical Chemistry)
Protein folding/unfolding studied by nuclear spin relaxation
2007-03-26 **Daniel Topgaard** (Physical Chemistry 1)
NMR studies of structure and dynamics in colloidal systems
2007-04-10 **Rita Dias** (Physical Chemistry 1)
Controlling the compaction of DNA
2007-04-23 **Viveka Alfredsson** (Physical Chemistry 1)
Forming mesoporous materials from micellar solutions
2007-05-07 **Per Linse** (Physical Chemistry 1)
Advances in the Simulation of Charged Colloids in Solution
2007-05-21 **Martin Turesson** (Theoretical Chemistry)
Surface forces in the presence of polyelectrolyte
2007-06-04 **Jens Norrman** (Physical Chemistry 1)
Contolling structure and water miscibility of polyion-surfactant ion complex salts
2007-09-21 **Alexei Khokhlov** (Moscow State University/Russian Academy of Sciences)
Towards new functional synthetic copolymers via rational design of their sequences
2007-10-01 **Bo Jönsson** (Theoretical Chemistry)
The Collapse of the House of Cards
2007-10-15 **Christophe Labbez** (Univ Bourgogne, France)
Titrating Mineral Surfaces - The Effect of Ion-Ion Correlations
2007-10-18 **Alexei Khokhlov** (Moscow State University/Russian Academy of Sciences)
Design of Copolymer Sequences. Self-Assembly in Solutions of Amphiphilic Copolymers
2007-10-19 **Patrick Kekicheff** (Inst Charles Sadron, Strasbourg, France)
Intermolecular forces between surfactant aggregates and in multilayers of polyelectrolytes
2007-10-24 **Johan Bergenholtz** (University of Gothenburg)
Aggregation and gelation of colloidal silica dispersions
2007-11-20 **Alexei Khokhlov** (Moscow State University/Russian Academy of Sciences)
Polymer Electrolyte Membranes for Fuel Cells: Computer Modeling and New Experimental Developments
2007-11-21 **Alexei Khokhlov** (Moscow State University/Russian Academy of Sciences)

Bioinspired Oligothiophene-Oligopeptide Hybrid Nanostructures: An Atomistic Simulation
2007-11-26 **Stina Lindman** (Biophysical Chemistry)
Electrostatic Contributions to Protein Stability through the Determination of Residue Specific pK_a Values
2007-12-18 **Olle Söderman** (Physical Chemistry 1)
NMR diffusometry studies of cartilage

2008
2008-02-05 **Alexei Khokhlov** (Moscow State University/Russian Academy of Sciences)
Smart polymer systems in oil recovery
2008-02-11 **Claudia Schmidt** (University of Paderborn, Germany)
NMR investigations of nematic liquid crystals in shear flow
2008-02-25 **Yuru Deng** (Singapore National University)
A long and twisted journey of cubic membranes: from structure to function.
2008-03-05 **Peter Nilsson** (Dept. Pharmacy, Uppsala)
Interaction between Crosslinked Polyelectrolyte Gels and Oppositely Charged Surfactants
2008-03-13 **Stefan Egelhaaf** (Heinrich-Heine-Universität Düsseldorf)
Pathways and Kinetics of Surfactant Phase Transitions
2008-03-31 **Luis A. Bagatolli** (MEMPHYS-Center for Biomembrane Physics SDU, Denmark)
The lateral structure of biological membranes and some lessons from model systems
2008-04-09 **Björn Åkerman** (Chalmers University, Gothenburg)
Transport of DNA and latex-particles in liposome-nanotube networks.
2008-04-17 **Lise Arleth** (University of Copenhagen, Faculty of Life Sciences)
Small-angle scattering on bionanosystems
2008-04-28 **Gerhard Gröbner** (Biophysical Chemistry, Umeå University)
Membrane-Protein Assemblies Involved in Diseases: A Biophysical Approach.
2008-05-12 **Roland Lindh** (Theoretical Chemistry)
Luciferin chemistry: principles of chemiluminescence.
2008-05-26 **Ulf Olsson** (Physical Chemistry 1)
Amorphous and crystalline drug nanoparticles
2008-06-16 **Phil Attard** (University of Sydney)
Nanobubbles: From Little Things Big Things Grow
2008-09-18 **Ka Yee Lee** (Institute for Biophysical dynamics, University of Chicago)
Collapse Mechanism of Lung Surfactant
2008-10-13 **Lars Nordenskiöld** (Nanyang Technological University, Singapore)
Electrostatic interactions in chromatin
2008-10-16 **Karen Edler** (University of Bath, UK)
Formation of Mesostructured Polymer-Surfactant Films at the Air-Solution Interface
2008-10-20 **Petr Stepanek** (Institute of Macromolecular Chemistry, Prague, Czech Republic)
Self-association of polymers and surfactants in mixed solvents
2008-10-27 **Nikolay Oskolkov** (Physical Chemistry 1)
The liquid-crystalline ordering approach to the packaging of DNA inside viral capsids
2008-11-10 **Ruan Juanfang** (Physical Chemistry 1, Division of Structural Chemistry, Stockholm University)
Microscopy study of porous materials
2008-11-17 **Sture Nordholm** (University of Gothenburg)
Thomas-Fermi One-Electron Analysis with Kohn-Sham Correction - New Insight into Atoms, Molecules and Reactivity of Metal Clusters
2008-11-27 **Alexey Kabalnov** (Hewlett Packard, San Diego, USA)
Gravitational Settling of Small Particles in Complex Geometries

7.3 Student conference

OMM supported the Student Conference, organized jointly by ECIS and Lund University, that took place on the island of Ven 30 June - 2 July 2007. The conference was a success attracting 90 PhD students from all our Europe with participants from Austria, the UK, France, The Netherlands, Germany, Italy, Hungary and, of course, Sweden. Scientifically, the conference hosted roughly 60 oral presentations and roughly 20 poster contributions over a two-day period. Two plenary lectures from leading Swedish scientists were also given and were well attended.

7.4 PhD Courses

Two PhD courses were organized in the framework of OMM during 2008. In the spring, Bo Jönsson and Gunnar Karlström gave a 10 ECTS credits course on "Intermolecular Interactions" with ca. 15 students attending. (60 ECTS credits = one year of full time study.) During the week April 14-18, Alexei Khokhlov and Mikhail Tamm from Moscow State University gave an intensive 3 ECTS credits course on "Polymers in Solution" at Klitterbyn Conference Hotel. 30 PhD students, from seven universities in Sweden and Denmark, attended the course.

7.5 Master Program

As a direct consequence of the creation of the OMM center, the Department of Chemistry at Lund University now offers a dedicated two-year (120 ECTS credits) Master program on "Organizing Molecular Matter". The purpose of the program, with courses largely taught by OMM members, is to provide a broad and fundamental knowledge in the field of physical chemistry, with an emphasis on surface and colloid chemistry, nanochemistry, and soft condensed matter. The knowledge comprises advanced laboratory skills, profound theoretical comprehension of fundamental mechanisms as well as a good understanding of practical applications.