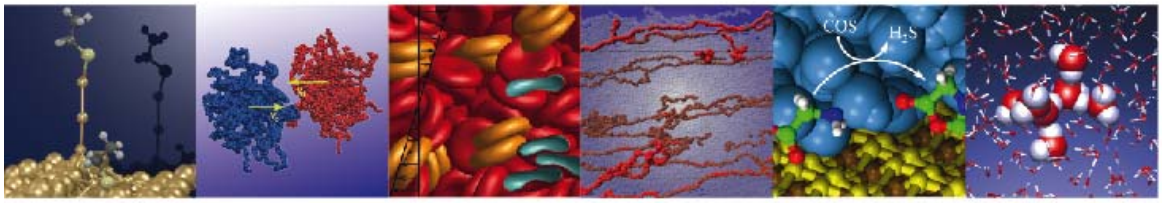
JÜLICH
FORSCHUNGSZENTRUM

Hierarchical Methods for Dynamics in Complex Molecular Systems

IAS Winter School
Forschungszentrum Jülich
5 – 9 March 2012



J. Grotendorst
G. Sutmann
G. Gompper
D. Marx

Poster Presentations

www.fz-juelich.de/wshd

Preface

Generating and analyzing the dynamics of molecular systems is a true challenge to molecular simulation. It includes processes that happen on the femtosecond scale, such as photoinduced nonadiabatic (bio)chemical reactions, and touches the range of seconds, being e.g. relevant in biophysics to cellular processes or in material sciences to crack propagation. Thus, many orders of magnitude in time need to be covered either concurrently or hierarchically. In the latest edition of this series of Winter Schools in 2009 we addressed the topic of *Multiscale Simulation Methods in Molecular Sciences* with a strong focus on methods which cover diversities of length scales. The key issue of the present school is to dwell on hierarchical methods for dynamics having primarily in mind systems described in terms of many atoms or molecules. One extreme end of relevant time scales is found in the sub-femtosecond range but which influence dynamical events which are orders of magnitude slower. Examples for such phenomena might be photo-induced switching of individual molecules, which results in large-amplitude relaxation in liquids or photodriven phase transitions of liquid crystals, phenomena for which nonadiabatic quantum dynamics methods were developed. The other end of relevant time scales is found in a broad range of microseconds, seconds or beyond and which governs e.g. non-equilibrium dynamics in polymer flows or blood cells in complex geometries like microvessels. Special mesoscopic techniques are applied for these time- and length-scales to couple the atomistic nature of particles to the hydrodynamics of flows.

This Winter School has a daily stratification pattern starting with dynamics within the realm of Materials Science with a focus on slow processes which nevertheless require most detailed input at the level of electronic structure and interatomic potentials. In Biomolecular Science one challenge is the concurrent handling of an electronic structure based description of a "hot spot" within an enzyme with a computationally efficient treatment of the protein environment in terms of parameterized interactions. Accelerated sampling is a key issue whenever both slow and fast motion is relevant and applies methods in the fields of metadynamics, force probe molecular dynamics or nonequilibrium dynamics using fluctuation theorems. Finally, getting rid of atoms and molecules but still keeping a particle perspective is achieved by coarse-graining procedures. In Soft Matter and Life Science, the dynamics is often governed by the hydrodynamics of the solvent. A particular challenge is here to bridge the large length- and time-scale gap between the small solvent molecules and the embedded macromolecules or macromolecular assemblies (polymers, colloids, vesicles, cells). Therefore, several mesoscale simulation approaches have been developed recently, including Lattice Boltzmann, Dissipative Particle Dynamics and Multi-Particle Collision Dynamics, which rely on a strong simplification of the microscopic dynamics with a simultaneous implementation of conservation laws on mass, momentum and energy.

Last but not least most efficient implementation on current-day hardware is a strong requirement to overcome computational barriers and to tackle large systems in multiscale environments. Examples will be provided covering basic methods or well-established optimal numerical methods like multigrid. In addition to lectures and poster sessions

this Winter School offers an introductory course to parallel computing techniques with practical sessions.

The target group of the IAS Winter School, organized and supported by the Jülich CECAM Node, are young scientists, especially PhD students and early postdocs. Most of the participants have presented a poster on their scientific work.

This preface also gives the opportunity to thank all the speakers, having prepared their lectures and extended lecture notes. We are greatly indebted to Monika Marx, who has put much effort in the realization of the present book of poster abstracts and lots of plannings. We are also most grateful to Elke Bielitza and Britta Hoßfeld who were indispensable for this School by taking care of logistical details, transports, registration and catering. Furthermore, thanks is expressed to Oliver Bücker for technical and administrational support.

Jülich and Bochum
February 2012

Johannes Grotendorst
Godehard Sutmann
Gerhard Gompper
Dominik Marx

IAS Winter School and CECAM Tutorial 2012
Hierarchical Methods for Dynamics in Complex Molecular Systems

	Monday **5 March** **Materials Sciences**	**Tuesday** **6 March** **Biosystems**	**Wednesday** **7 March** **Advanced Methods**	**Thursday** **8 March** **Flow Simulations**	**Friday** **9 March** **Numerics & Parallel Computing**
9:00-10:00	9:45-10:00 Opening	*Mark E. Tuckerman* Exploration of Multi-Dimensional Free Energy Landscapes in Molecular Dynamics	*Alessandro Curioni* Fast Algorithms for QM on Modern HPC	*Luigi Delle Site* Adaptive Resolution Molecular Dynamics: Extension to Quantum Problems	*Danny Perez* Accelerated Molecular Dynamics Methods
10:00-11:00	*Doros N. Theodorou* Tracking the Dynamics of Systems Evolving through Infrequent Transitions in a Network of Discrete States	*Ivano Tavernelli* Methods on TDDFT-Based Nonadiabatic Dynamics with Applications	*Gerhard Hummer* Non-Equilibrium Molecular Dynamics for Biomolecular Systems Using Fluctuation Theorems	*Burkhard Dünweg* Coupling Molecular Dynamics and Lattice Boltzmann to Simulate Brownian Motion	*Peter Bastian* Simulating Multiphase Flow in Porous Media Using DUNE
11:00-11:30	**Coffee Break**				
11:30-12:30	*Paolo Carloni* Hybrid Car-Parrinello MD / MM Simulations: A Powerful Tool for the Investigation of Biological Systems	*Nikos L. Doltsinis* Simulating Light-Induced Phenomena in Soft Matter	*Teodoro Laino* Multigrid QM/MM Approaches in ab initio Molecular Dynamics	*Roland G. Winkler* Flow Simulations with Multiparticle Collision Dynamics	*Ulrich Rüde* Multigrid on Parallel Computers
12:30-14:30	**Lunch Break**				
14:30-15:30	*Christoph Dellago* Transition Path Sampling for Materials - Hard and Soft	*Frauke Gräter* Simulation Techniques for Studying the Impact of Force on (Bio)Chemical Processes	*Bernd Mohr* Introduction to Parallel Computing	*Pep Español* Dissipative Particle Dynamics	
15:30-16:30	*Jörg Behler* Neural Network Potentials for Efficient Large-Scale Molecular Dynamics	*Christine Peter* Coarse Grained Models for Multiscale Simulations of Biomolecular Systems	Practical Session	*Simone Melchionna* Large-Scale Simulations of Blood Flow with Coarse-Grained Cells	
16:30-17:00	**Coffee Break**				
17:00-18:00	*Alexander Hartmaier* Large-Scale Molecular Dynamics Studies of Dislocation Dynamics, Plasticity and Fracture of Materials	*Volkhard Helms* Particle-Based Dynamics Simulations of Multi-Protein Systems and Cellular Compartments	Practical Session	*Dmitry A. Fedosov* Simulations of Blood Flow on the Cell Scale	
Evening	**Reception and Get-Together**	**Poster-Session I**	**Poster-Session II**	**Conference Dinner**	

Contents

Poster Session A

Poster Session B

Thermal Conductivity Reduction in Potential Thermoelectrics: Carbon Nanotubes and Electrically Conducting Polymers

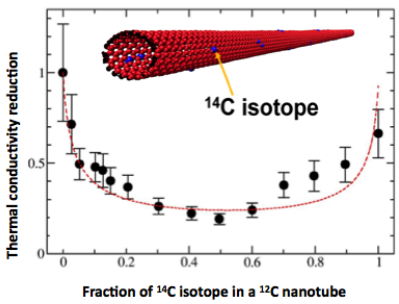
Ganesh Balasubramanian

Eduard-Zintl-Institut für Anorganische und Physikalische Chemie
Technische Universität Darmstadt, 64287 Darmstadt, Germany

E-mail: bganesh@theo.chemie.tu-darmstadt.de

The use of potential thermoelectrics can be facilitated by improving their figure of merit, which depends on their electrical and thermal transport coefficients. Their performance can be enhanced if this figure of merit is improved. One way to achieve this is to reduce thermal transport by lattice vibrations and/or non-electronic interactions in materials.[1]

Carbon nanotube (CNT) is one of the most sought after materials for efficient thermal transport in small scale devices, due to its mechanical strength and excellent transport coefficients. Although CNTs are electrically conducting, still lattice vibrations or phonons provide the major contribution to thermal transport through them. Smoothening the channels for unobstructed motion of phonons could elevate the values of thermal conductivity while defects and impurities can cause impedance to their passage, consequently diminishing the value of the transport coefficient. Thus, a fundamental knowledge of the phonon characteristics allows us to tune a CNT for our specific needs in energy management. From our theoretical-computational investigation of the lowering of thermal conductivity in isotope doped CNTs, we attribute the reduced thermal transport to mode softening (and not scattering) effects, where the peak frequencies at which lattice vibrations occur are shifted to lower values.[2] From our molecular dynamics simulations, thermal conductivity reductions of more than 50% can be realized, thereby permitting the usage of high strength CNT for insulation related applications. A mean-field approximation model based on



Thermal conductivity reduction in isotope substituted carbon nanotubes.

harmonic vibrational behavior of carbon atoms illustrates the interrelationship between atomic masses of the isotopes and CNT thermal conductivity. The model offers a quick and easy quantitative estimation of thermal conductivity for binary dielectric mixtures, potential thermoelectrics and semiconductors, without resorting to any complex theories. While the development of the model is based on atomistic observations, it transcends the barriers of length scales and system dimensions.

Electrically conductive polymers like polyacetylene (PA) and polyaniline (PANI) have potential use as thermoelectrics if their thermal conductivity can be lowered. Thermal transport in these polymers is primarily influenced by bonded interactions and chain orientations relative to the direction of heat transfer. We propose to control phonon thermal transport in these polymers through the application of mechanical strain, and combination of polymers. Molecular dynamics simulations are employed on pure PA and PANI systems as well as their mixtures. Axial thermal conductivity increases when the materials are stretched axially while it reduces when a transverse tensile strain is applied. When these polymers are combined, we observe a significant reduction in the thermal conductivity with the minimum value occurring for PANI containing 60% PA as impurity.[3] The molecular configurations of PA and PANI also contribute in characterizing their thermal transport behavior.

Acknowledgements: F. Leroy and M.C. Böhm at Technische Universität Darmstadt, Germany and S. Pal and I.K. Puri at Virginia Tech, USA

References

1. A.A. Balandin Nat. Mater. **10(8)**, 569, 2011.
2. G. Balasubramanian, I.K. Puri, M.C. Böhm and F. Leroy Nanoscale **3**, 3714, 2011.
3. S. Pal, G. Balasubramanian and I.K. Puri J. Chem. Phys. **136**, 044901, 2012.

Effects of Rational Mutations on the Biological Activity of Acyltransferase Domains: MD and QM/MM Studies

Kenny Bravo-Rodríguez[1], Uschi Sundermann[2], Hansel Gomez Martinez[1], Elsa Sánchez-García[1], and Frank Schulz[2]

[1] Max-Planck-Institut f˙ur Kohlenforschung
Kaiser-Wilhelm-Platz 1, 45470, Mülheim an der Ruhr, Germany

[2] Technische Universität Dortmund, Otto-Hahn-Str. 6, 44221 Dortmund, Germany

E-mail: kenny@mpi-muelheim.mpg.de

Polyketide synthases (PKSs) are a family of multi-domain enzymes responsible for the biological synthesis of secondary metabolites with polyketide structure in bacteria, fungi, plants and some animals. In the industrial synthesis of drugs like rapamycin (immunosuppressant), erythromycin (antibiotic), lovastatin (anticholesterol drug), and epothilone B (anticancer drug) PKSs play an important role.[1] Rational mutations of specific amino acids in the structure of PKSs are of key importance for the synthesis of novel compounds with enhanced biological activities.

6-deoxyerythronolide B synthase (DEBS) is a type-I PKS that synthesizes the macrocyclic core of erythromycin. DEBS is formed by 3 large homodimeric units, each unit possess two modules and each module is formed by, at least, a ketosynthase (KS), an acyltransferase (AT), and an acyl carrier protein (ACP) domain.[2,3] This study focuses on the AT domain of module 6 (AT6) of DEBS and its interaction with (2R)-methylmalonyl-CoA. For this particular module no X-ray structure has been reported. Therefore, a homology model of the wild type of the AT6 domain was built. In a second step, the AT6 domain was systematically studied experimentally through site-directed mutagenesis, giving rise to more than 250 single-site mutants. The effect of point mutations on the properties of AT6 was investigated using MD and QM/MM techniques as well as fermentation assays using the bacterium Saccharopolyspora erythraea as expression host, with a special concern on the impact on substrate selectivity. Excellent agreements were found between theoretical predictions and experimental data on these complex MDa-sized enzymes, suggesting an increasing capability of rational or semi-rational enzyme design. Amino acid residues which have an impact on the substrate binding and turnover were clearly identified and their role theoretically explained. In the near future, it may thus be possible to rationally alter the substrate specificity of PKSs, enabling a biosynthetic access to non-natural polyketide antibiotics.

References

1. Walsh, C. T. Science **303**, 1805 - 1810, 2004.
2. Staunton J. and Weissman K.J. Nat. Prod. Rep. **18**, 380 - 416, 2001.
3. Hertweck, C. Angew. Chem. Int. Ed. **48**, 4688 - 4716, 2009.

Role of Lattice Vibrations in Optical Transitions of Two-Dimensional TiO_2

Letizia Chiodo [1] **and Maurizia Palummo** [2]

[1] Center for Biomolecular Nanotechnologies @UNILE, Istituto Italiano di Tecnologia
Via Barsanti, 73010 Arnesano (LE), Italy
and European Theoretical Spectroscopy Facility (ETSF)
present address: Center for Life@Nanoscience CLNS@Sapienza, Physics Department
P.le Aldo Moro 5, I-00185 Roma, Italy

[2] European Theoretical Spectroscopy Facility (ETSF), CNISM, Dipartimento di Fisica
Università di Roma, "Tor Vergata", via della Ricerca Scientifica 1, 00133 Roma, Italy

E-mail: letizia.chiodo@iit.it

Due to the rapid progress in the synthesis methods, TiO_2-based nanomaterials are nowadays the object of a strong research interest for their promising performances in photocatalysis and photovoltaics applications. In particular large quantities of two-dimensional (2D) nanosheets (NSs) can be produced and used for further assembling of new nanostructured materials with different morphologies and functionalities.[1,2] To investigate the microscopic nature of their opto-electronic properties is a fundamental prerequisite for rationalizing experimental data and improving devices performances. By means of first-principles excited-state simulations we reveal the excitonic nature of radiative transitions in the VIS-UV spectral range of TiO_2-based NSs. Furthermore these calculations on top of finite temperature molecular dynamics simulations could explain the large Stokes-shifts experimentally observed, and confirm if the nature of optical transitions in these two-dimensional oxide materials is due to strongly bound excitons. A simplified but realistic way for evaluate the role of phonons in the optical response is performing *ab-initio* molecular dynamics simulations at finite temperature and for selected snapshots compute the optical response. This approach has been recently used[3] to explain the temperature dependence of the dielectric function of semiconductor bulk compounds. Here we performed first-principles finite temperature molecular dynamics calculations with the software package QUANTUM-ESPRESSO[4]. A limited number of atomic configurations have been randomly selected and for each structure we have performed the BSE calculations.[5,6] The average of the obtained optical spectra for various configurations is used to estimate the lattice vibrations role. Results are discussed in comparison with T=0 K spectra and experimental data of optical absorption.

References

1. Z. Liu, M. Misra, ACS Nano **4**, 2196, 2010.
2. V. Bavykin, F. C. Walsh, Eur. J. Inorg. Chem. **8**, 977, 2009.
3. Z. A. Ibrahim, A. I. Shkrebtii, M. J. G. Lee, K. Vynck, T. Teatro, W.Richter, T. Trepk, T. Zettler, Phys. Rev. B **77**, 125218, 2008.
4. P. Giannozzi, et al., J. Phys.: Condens. Matter **21**, 395502, 2009.
5. G. Onida, L. Reining, A. Rubio, Rev. Mod. Phys. **74**, 601, 2002.
6. A. Marini, C. Hogan, M. Grüning, D. Varsano, Comput. Phys. Commun. **180**, 1392, 2009.

Transport of Self-Propelling Bacteria in Micro-Channel Flow

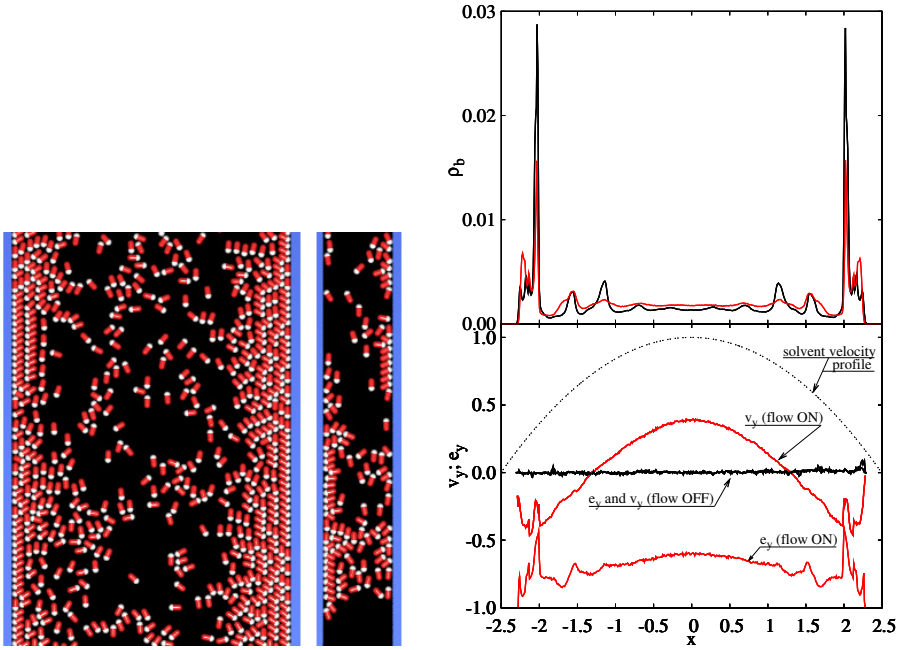
Andrea Costanzo[1], **Roberto Di Leonardo**[1,2], **Giancarlo Ruocco**[2], **and Luca Angelani**[1,2]

[1] CNR-IPCF, UOS Roma, Piazzale A. Moro 2, I-00185, Roma, Italy

[2] Dipartimento di Fisica, Università di Roma "Sapienza", I-00185, Roma, Italy

E-mail: a.costanzo@fz-juelich.de

Understanding the collective motion of self-propelling organisms in confined geometries, such as that of narrow channels, is of great theoretical and practical importance. Although not yet fully understood and quantitatively scrutinized, transport properties of active particles through thin channels have a great potential for developing microfluidic devices



Left: Snapshot of simulations (cutout of the full simulation box). Wide channel ($L_x = 20$) with external fluid flow, and small channel ($L_x = 5$) without external flow. Walls at $x = \pm L_x/2$ and periodic boundary conditions along y. Right: Density profile ρ_b (top panel), vertical velocity profile v_y and vertical orientation profile e_y (bottom panel) with (red lines) and without (black lines) shear flow (fluid speed at the center $V_0 = 1$). Channel with walls at $x = \pm L_x/2 = \pm 2.5$ and periodic boundary conditions along y ($L_y = 62.5$). In the case of shear flow the tumbling is deactivated ($N = 234$ particles and $\rho = 0.75$).

that are able to control and sort motile cells. Moreover, it provides new and intriguing examples of the very unusual behavior of active matter (e.g. migration phenomena, spontaneous ratchet effect).

Using numerical simulations the authors studied the motion of model bacteria in 2D channels with Poiseuille flow. The two main findings are: (i) bacteria tend to accumulate on the channel walls where they start swimming upstream; (ii) the net bacterial flux changes sign, from upstream to downstream, depending on the presence or absence of random tumble events, by which each cell changes its own swimming direction.

Detailed analysis of bacterial velocity and orientation fields allows to quantify the phenomenon by varying cell density, channel width and fluid velocity. Based on this knowledge, a time dependent flow protocol is developed that can enhance the flux of bacterial cells through the channel. By performing periodic inversions in the direction of the solvent's flow, one can observe a particle flux which is three times greater than that corresponding to steady solvent flow. These findings suggest possible promising strategies to enhance the flow of active tracers in microfluidic channels. Moreover, the reported results could suggest novel strategies to design lab-on-chip devices that are capable of sorting living and non-living organisms as well as tumbling and non-tumbling bacteria.

Transport techniques of passive matter could also be developed using active-matter-mediated transport mechanisms.

References

1. A. Costanzo, R. Di Leonardo, G. Ruocco and L. Angelani,
Transport of self-propelling bacteria in micro-channel flow,
J. Phys.: Condens. Matter **24**, 065101 (2012).

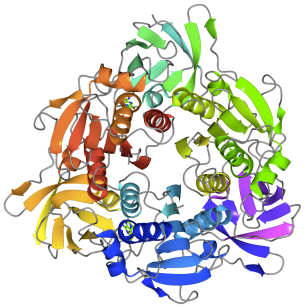
QM/MM Studies of a DUF-62 Water Activating Enzyme

Luke Crawford and Michael Bühl

School of Chemistry
University of St. Andrews
St. Andrews, Scotland

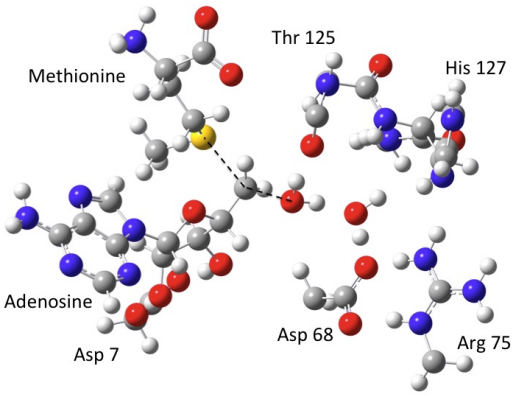
E-mail: {lc437,buehl}@st-andrews.ac.uk

S-Adenosylmethionine (SAM) is ubiquitous within biological systems, being pertinent to a wide range of cellular functionalities, key reactions and synthetic pathways[1]. While this substrate is most commonly recognized for its role in methylation, the sulfonium moiety allows for a diverse range of reactivity. Previously, it has been shown that SAM can partake in nucleophilic attack at the C5' position with a suitable halogen-nucleophile, a reaction that is labilized by enzymes with the residues necessary to stabilise a bare anion[2]. Genetic sequencing of the bacteria which produce such halogenase enzymes, *Streptomyces cattleya*, revealed a similarity to the DUF-62 (domain of unknown function) genes though over-expression studies and subsequent analysis showed that the DUF-62 protein performed a reaction that yielded L-methionine and adenosine, thus incorporating hydroxide as a nucleophile[3].



Trimeric structure of the hydroxide adenosyltransferase enzyme.

Using QM/MM methodologies[4] we have explored alternative routes through which the hydroxide adenosyltransferase can facilitate the activation of water for nucleophilic attack. The enzyme acting through a proximate method wherein water attacks the electrophilic carbon and the resulting protonated adenosine product is then deprotonated by means of the nearby aspartate residue has been investigated. Alternatively, the surrounding aspartate, arginine and histidine residues acting to produce a stabilised hydroxide which then partakes in the suspected S_N2 reaction has also been subjected to scrutiny.



Transition State for the attack of water upon SAM within the active site of the protein. The nucleophilic water is assisted by a partner molecule undergoing proton transfer with Asp 68.

By conducting initial investigations at the PM3/CHARMM level whereby the QM region is described by semi-empirical methods, we have been able to afford the luxury of modelling the three residues considered to be key to the enzymatic activity in addition to portions of the amide backbone which may serve a prominent hydrogen bonding role. These low level calculations have been supported by a M06-2X/6-311+G**/CHARMM//B97-D/6-31+G**/CHARMM protocol. Our results have thus far shown relatively high barriers and explorations are continuing to assess how the system may respond to an alteration in protonation state at the active site and to characterize the intermediate proton transfer steps.

References

1. G. Markham, *Encyclopedia of Life Sciences*, 1-8 , (2010).
2. H. Senn, D. O'Hagan and W. Thiel, *JACS*, **127**, 13643, (2005).
3. H. Deng, S. A. McMahon, A. S. Eustáquio, B. S. Moore, J. H. Naismith and D. O'Hagan, *Chembiochem*, **10**, 2455, (2009).
4. H. Senn, and W. Thiel, *Current Opinion in Chemical Biology* **11**, 182, (2007).

Discretization of a Non-Linear Diffusion Equation

Jaime Arturo de la Torre[1], **Daniel Duque**[2], **and Pep Español**[1]

[1] Departamento de Física Fundamental
Universidad Nacional de Educación a Distancia
Senda del Rey 9, 28080 Madrid, Spain

[2]Departamento de Enseñanzas Básicas de la Ing. Naval
ETS Ingenieros Navales, Universidad Politécnica de Madrid
Avda. Arco de la Victoria, 28040 Madrid, Spain

E-mail: jatorre@bec.uned.es

We formalize the process of discretization and continuation of a concentration field for the diffusion equation. By defining a *discretization operator* D_x and a *continuation operator* C which satisfies a Petrov-Galerkin finite element scheme, we are able to generalize the discretization process, ensuring the conservation of the number of particles for the non-linear diffusion equation and a H-theorem.

We perform simulations for the non-linear diffusion process starting from the following equation

$$\partial_t c(\mathbf{r},t) = \nabla\mu(c(\mathbf{r},t))\nabla\frac{\delta\mathcal{F}}{\delta c(\mathbf{r})}[c]\,, \tag{1}$$

where $\mu(c)$ is a mobility coefficient and $\mathcal{F}[c]$ is the free energy functional. This equation can be explicitly written for the discrete field using a Delaunay tesselation.[1] We choose, as examples, two separated models:

- A gaussian model with a quadratic free energy and a concentration independent mobility, $\mu(c) = \mu_0$, whose results was previously studied.[2]
- An ideal gas model.

Both models has the advantage that, in the continuum limit, they produce exactly the same diffusion equation.

In a 1D situation, we study the behaviour of the evolution for the discrete concentration field $c_\mu(t)$ for both models. It is showed some relevant properties which match the continuum exact equation with an error that scales with the lattice spacing.

References

1. P. Español, I. Zúniga, J. Chem. Phys. **131**, 164106, 2009.
2. J. A. de la Torre, P. Español, J. Chem. Phys. **135**, 114103, 2011.

Study of Interactions between Block-Copolymer and Biological Interfaces

Antonio De Nicola[1,2], Giuseppe Milano[1,2], Danilo Roccatano[3], Samira Hezaveh[3], and Toshihiro Kawakatsu[4]

[1] IMAST Scalar-Technological District in Polymer and Composite Engineering
P.le Fermi 1, 80055 Portici (NA), Italy

[2] Dipartimento di Chimica e Biologia, Université di Salerno
I-84085 via Ponte don Melillo, Fisciano (SA), Italy

[3] Jacobs University Bremen, Campus Ring 1, D-28759 Bremen, Germany

[4] Department of Physics, Tohoku University, Aoba, Aramaki, Aoba-ku, Sendai 980-8578, Japan

E-mail: adenicola@unisa.it

Phospsholipids are an important class of compounds having both important biological function (cell membrane) and techonological applications (liposome and micelle). The phospholipids can undergo different phase transition in aqueous enviroments characterized by different morphologies (mesomorphism and polymorphism). They form lipid bilayer structure that are fundamental building blocks of cellular membranes. For this reason, lipid bilayer have been attracting the interest of computational biophysics community, where people perform atomistic and coarse-grained molecular dynamics simulations of these systems for long time[1].

Although atomistic simulations can provide very detailded and chemically consitent models of biological phospholipids, they are very expensive way of studing the assembling process[2,3].

Recently, a hybrid simulation technique where self-consistent field theory and molecular dynamics simulation are combined (MD-SCF) has been developed by Milano and Kawakatsu[4,5]. The main idea behind this simulation technique is to obtain a strategy, as far will be possible, having the main advantages and avoiding the main disadvantages of both SCF and atomistic approaches. The computational efficiency of this method is due to the fact that the calculation of intermolecular forces (the most demanding part of a simulation) that in classical MD is calculated by double loop over particle pairs is completely skipped. These interactions are calculated at mean field level considering the interactions, at mean-field level, between single particles in a density field.

Very recently we developed specific coarse-grained models for phospholipids and water. We optimized the model parameters, which are necessary in evaluating the interactions between the particles and the density fields, so that the coarse-grained model can reproduce the structural properties of the reference particleparticle simulations[6].

One interesting application of these methods is the understanding of interactions of biocompatible block polymers with biological interfaces. The use of synthetic polymers

for biotecnological and biomedical applications has rapidly grown in the last years.[7] Synthetic polymers are particularly well suited for implementing physical, chemical, and biological functions at the same time and they permit the length scales to be greatly varied, the superstructure to be controlled, and specific functions to be performed. There is a wide variety of polymers able to adopt functions such as drug encapsulation, protein stabilizer, cell adhesion, and cell recognition. These features are influenced predominantly by the polymer surface. Polymers with hydrophilic surfaces are often well suited and so are those with an inert surface. Hydrophilic, noninteracting materials cannot be recognized by living systems (stealth systems) and therefore have low cytotoxicity. Among the polymers that have a broad use in this sector, polyethyleneoxide (PEO) (or polyethylene glycol, PEG) as homopolymer, grafted or as block-copolymer (with polypropilenoxyde, PPO), are the most popular[8]. In fact, PEO is highly hydrophilic and shows a very low toxicity with respect to similar polymers. Amphiphilic polymers and their association structures are of increasing interest as carriers of active ingredients[9]. Block copolymer micelles are being investigated in many research groups as nanocarriers of hydrophobic active agents and genes. Their core/shell structure resembles that of lipoproteins and viruses[10]. The micelle shell causes the interaction with proteins and cells. These interactions determine the biodistribution of the active component. Despite these applications, molecular details on interaction mechanism of these polymers with the biological system are not yet completely understood.

The present work presents the investigation, using hybrid particle-field molecular dynamics simulations technique, of the interactions between block polymers and biological interfaces.

Acknowledgment: The activities were performed in the frame of the FIRB project ITALNANONET (RBPR05JH2P) granted to IMAST S.c.a.r.l. and funded by the M.I.U.R.

References

1. A. P. Lyubartsev and A. L. Rabinovich, Soft Matter **7**, 25, 2011.
2. M. Venturoli, M. M. Sperotto, M. Kranenburg and B. Smit, CPhysics Reports-Review Section of Physics Letters **437**, 1, 2006.
3. S. Izvekov, G. Voth, Journal of Chemical Theory and Comptation **2**, 637, 2006. Diplomarbeit, Universität zu Köln (2000).
4. G. Milano and T. Kawakatsu, Journal of Chemical Physics **130**, 214106, 2009.
5. G. Milano and T. Kawakatsu, Journal of Chemical Physics **133**, 214102, 2010.
6. A. De Nicola, Y. Zhao, T. Kawakatsu, D. Roccatano, G. Milano, Journal of Chemical Theory and Computation **7**, 2947, 2011.
7. E. Chiellini, C. Migliaresi, J. Sunamoto, Biomedical Polymers and Polymer Therapeutics. Kluwer Academic Publishers: 2001.
8. Y. Kodera, A. Matsushima, A. Hiroto, M. Nishimura, H. Ishii, A. Ueno, T. Inada, Progress in Polymer Science **23**, 7, 1233,1998.
9. M. J. Lawrence, Chemical Society Reviews **23**, 6, 417,1994.
10. A. B. S. Graff, C. Verbert, W. Meier, C. Miemeyer and C. Mirkin, Polymer Nanocontainers. In Nanobiotechnology. Concepts, Applications and Perspectives. Wiley-VCH Verlag: Weinheim, 2004.

Molecular Docking in the Hermite Basis: Application to Rigid-Body Fitting of Atomistic Structures Into cryoEM Density Maps

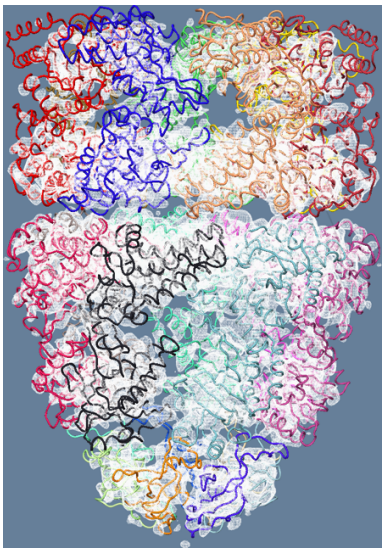
George Derevyanko[1] **and Sergei Grudinin**[2,3]

[1] Institute for Complex Systems (ICS-5)
Forschungszentrum Jülich (FZJ), D-52425 Jülich, Germany
E-mail: {g.derevyanko}@fz-juelich.de

[2] NANO-D, INRIA Grenoble-Rhone-Alpes
655 avenue de l'Europe-Montbonnot, 38334 Saint Ismier Cedex - France

[3] Laboratoire Jean Kuntzmann, CNRS
B.P. 53, 38041 Grenoble Cedex 9, France
E-mail: {sergei.grudinin}@inria.fr

Over two thirds of human proteins and many bacterial proteins are composed of multiple modular interacting domains[1] and contain a significant portion of intrinsically disordered regions[2]. Obviously, these proteins are unsuitable for experimental structure determination in the full-length form. Thus, in most of the cases, only individual domain structure at high resolution for these proteins is known[3]. Cryo-electron microscopy (cryoEM) is a popular experimental method, which yields electron densities of large multi-domain proteins at low-to-mid resolution. This method allows to capture macromolecular complexes in different conformational or structural states, which are physiologically more relevant compared to structures obtained by X-ray crystallography. Various computational methods exist for post-processing of electron densities[4]. They either model the 3D structure of the whole complex starting, if resolution allows, from the amino acid sequence, or more often fit known structures of smaller templates into the electron density of the whole complex. All fitting algorithms start with a first guess assembly obtained by a 6D exhaustive search rigid-body fitting.



Rigid body fitting into a GroES/GroEL complex cryoEM map of 7Å resolution.

Exhaustive 6D search in cryoEM applications, similar to rigid-body protein docking[5], can also be accelerated by means of FFT in the translational space[6] or in the rotational space[7]. The latter is possible thanks to the spherical harmonics decomposition of the

electron density. The local minimization method developed by Navaza[8] also makes use of spherical harmonics in order to efficiently treat symmetrical constraints. Cartesian basis functions, to the best of our knowledge, have never been exploited in this domain.

Here, we demonstrate a framework for fast rigid body fitting of atomistic structures into cryoEM density maps using Cartesian Hermite basis functions. These basis functions have been already successfully exploited in 2D image analysis. In the presented work we generalize 2D algorithms to the case of functions defined in 3D space. Precisely, we derive a fast exact decomposition of a superposition of Gaussian functions into the Hermite basis. Then, we use this decomposition to represent the electronic density of a protein. Then, we derive an exact decomposition of a superposition of stepwise 3D functions. This decomposition is used to represent electronic cryoEM density maps and to regularize voxel representation of 3D models. Finally, we derive a windowed convolution of two Hermite representations and propose a new 6D exhaustive search algorithm using Hermite basis functions. We demonstrate the accuracy and efficiency of the new method on a number of examples.

References

1. S.A. Teichmann, C. Chothia, and M. Gerstein, Curr Opin Struct Biol **9**, 390–99, 1999.
2. A.K. Dunker, I. Silman, V.N. Uversky, and J.L. Sussman, Curr Opin Struct Biol **18**, 756–64, 2008.
3. G. Apic, W. Huber, and S.A. Teichmann. J Struct Funct Genomics **4**, 67–78, 2003.
4. F. Fabiola, and M.S. Chapman, Structure **13**, 389–400, 2005.
5. D.W. Rithie, Curr Protein Pept Sci **9**, 1–15, 2008.
6. P. Chacon, and W. Wriggers, J Mol Biol **317**, 375–84, 2002.
7. J.A. Kovacs, and W. Wriggers. Acta Crystallogr D **58**, 1282–86, 2002.
8. J. Navaza, J. Lepault, F.A. Rey, C. Alvarez-Rua, and J. Borge. Acta Crystallogr D **58**, 1820–25, 2002.

Analysis and Visual Summarization of Molecular Dynamics Simulation

Fredrick Robin Devadoss V.
Michael Berthold, Oliver Deussen, and Thomas E. Exner

Konstanz Research School Chemical Biology, University of Konstanz, Germany
E-mail: fredrick.devadoss@uni-konstanz.de

Conformational transitions of biological macromolecule, especially proteins, with atomistic precision are very difficult to characterize by the experimental techniques like X-ray crystallography and NMR spectroscopy. Molecular dynamics (MD) simulations are well-established methods for modelling the intermediate transitions. These transitions are collected as trajectories - a series of 'snap shots' - over the simulation time. They are huge in size (Tera bytes in the case of long simulations) and the analysis may take longer time than the data generation. Analyzing these trajectories with standard parameter like root mean square deviation (RMSD) - calculated after an optimal rotation and translation of one structure to another - does not reveal the most interesting properties of the simulation. Moreover, RMSD only provides information on the absolute deviation of the coordinates and does not provide any directionality of the structural changes.

To analyze MD generated trajectories by grouping them into different clusters of similar conformations is one of the main objective of this project. Managing the large amount of data and presenting them in a comprehensive manner are the major challenges. To over-come these challenges, C-alpha torsion angle[1] - pseudo dihedral angle defined by four successive C-alpha atoms - used as a parameter and the differences in C-alpha torsion angles between each steps help to identify the conformational changes over the simulation time. Clustering of relatively similar conformations is done by binning the differences of C-alpha torsion angles with respect to the previous snap shot or with respect to the first snap-shot of the MD simulation.

DNA polymerase I from Thermus aquaticus (Klentaq1)[2] - a highly conserved structure resembling a hand-like arrangement, including a thumb, a palm and a finger domain - was identified with two distinct conformational states of the finger domain, namely open and closed forms. The catalytic cycle leading to nucleotide insertion comprises of several steps including a large structural rearrangement leading to a movement of the finger domain towards the thumb domain. To see this major structural changes, a 10ns targeted MD (TMD)[3] simulation were carried out using AMBER[4] - a package of molecular simulation programs - by keeping the closed form as the starting structure and the open form as the target structure. The analysis using C-alpha torsion angle method helps to identify the structural changes locally and gives an overview of the whole MD simulation.

References

1. Maria M. Flocco and Sherry L. Mowbray, Protein Science **4**, 2118-2122, 1995.
2. Li Y., Korolev S., and Waksman G, EMBO J. **17**, 7514-7525, 1998.
3. Schlitter J., Engels M., and Krüger P, J. Mol. Graph. **12**, 84-89, 1994.
4. AMBER: Assisted Model Building with Energy Refinement, http://ambermd.org/

Seamless Integration between Atomistic and Coarse Grained Models

Nicodemo Di Pasquale[1], Daniele Marchisio[1], and Paola Carbone[2]

[1] Department of Applied Science and Technology
Institute of Chemical Engineering
Politecnico di Torino
Corso Duca degli Abruzzi 24, 10129 Torino, Italy

[2] School of Chemical Engineering and Analytical Science
University of Manchester
Oxford Road, M13 9PL, UK

E-mail: nicodemo.dipasquale@polito.it

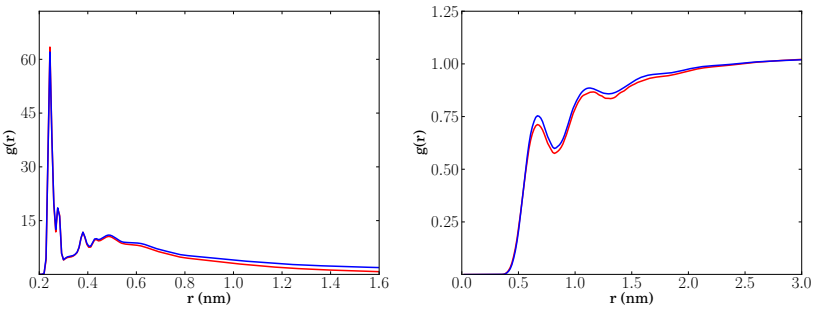
The ability to combine a detailed description of the chemistry of a molecular model with an efficient exploration of the conformation space is a key point in simulating realistic systems. All-atom (AA) simulations, which naturally describe the chemical detail, are a well established tools for the description of soft materials phenomena. However they are often constrained in time scale up to 100 ns and limited in the number of atoms. In order to overcome this problem coarse-grained (CG) methods have been developed[1,2] to expand at the same time the size and the time scale of the simulations. These reduce the degrees of freedom (DOF) of the model collecting several atoms in one superatom. However, in some cases the lack of atomistic details is such a limitation that the AA simulations are preferred, even though their use reduces the dimension of the system and the type of phenomena that can be investigated.

We present a hybrid coarse-grained-atomistic model for soft materials that enables a seamless coupling of the atomistic and coarse-grained approach allowing to keep the advantages of the two model and overcome the limitations. The model employs the coarse-grained force fields developed using the Iterative Boltzmann Inversion and classical atomistic force fields. The model is used on melt of atactic polystyrene showing that the soft coarse-grained potential merges extremely well with the atomistic force field. The method has been implemented in our simulation code IBIsCO[3] and can be readily used to simulate any kind of material interface allowing a proper multiscale approach to material science.

Our hybrid model consists of beads and atoms embedded into the same macromolecular chain. There are three types of interaction to consider: Atom-Atom (AA), Bead-Bead (BB) and Atom-Bead (cross interaction). AA and BB interactions are treated by using an atomistic[4] and CG[5] potential respectively. Bonded cross interaction are described using an harmonic potential whilst the non-bonded cross interaction are mediated by the center of mass of the group of atoms of the atomistic part of each chain which represents a bead

mapped in the CG descriptions (Virtual Bead). Hence non-bonded cross interaction acts between CG beads in the low resolved region and the center of mass in the atomistic one and is set equal to the non-bonded IBI potential acting among pairs of beads. The resulting forces acting on the center of mass is then distributed among the atoms belonging to the Virtual Bead weighing on their masses.

In order to test the robustness of the hybrid model, structural properties, are compared with the corresponding ones calculated on the mono-resolved, both fully atomistic and CG, models showing (see Figure 1) a good agreement of the hybrid model with mono-resolved ones.



On the left: Intra chain RDF between carbon atom in the high resolution part of the hybrid model and the fully atomistic simulation. On the right: inter chain RDF between pseudo-CG chains in the hybrid model and the fully CG simulation

References

1. W. Tschop, K. Kremer, J. Batoulis, T. Burger, O. Hahn Acta Polymerica **49** 61 (1998).
2. D. Reith, M. Putz, F. Müller-Plathe J. Comp. Chem. **24**, 1624 (2003).
3. H. A. Karimi-Varzaneh, H. J. Qian, X. Y. Chen, F. Müller-Plathe J. Comp. Chem. **32**, 1475 (2011).
4. V. A. Harmandaris, N. P. Adhikari, N. F. A. van der Vegt, K. Kremer Macromol. **39**, 6708 (2006).
5. H. J. Qian, P. Carbone, X. Y. Chen, H. A. Karimi-Varzaneh, C. C. Liew, F. Müller-Plathe Macromol. **41**, 6708 (2008).

Hybrid Simulations for Studying the Morphology of Organic Semiconductor Materials on the Mesoscale

Patrick Gemünden[†,1,2,3], **Kostas Daoulas**[1,2,3], **and Kurt Kremer**[1,2,3]

[1] Max Planck Institute for Polymer Research
Ackermannweg 10, 55128 Mainz, Germany

[2] InnovationLab GmbH
Speyerer Straße 4, 69115 Heidelberg, Germany

[3] Ruprecht-Karls-University Heidelberg
Institute for Theoretical Physics
Philosophenweg 16, 69120 Heidelberg, Germany

[†] *E-mail:* gemuende@mpip-mainz.mpg.de

Addressing the mesoscale morphology in organic semiconductors present a twofold problem. On the one hand, the models must be sufficiently coarse-grained, to allow for an efficient simulation of systems with dimensions on the order of a few hundred nanometers. On the other hand, those materials are characterized by complex multiphase morphologies created by an intricate balance between molecular structure, interactions and processing protocols. Thus, albeit coarse grained, the models must account for the above interplay.

For this purpose, we develop here a strategy based on the concept of hybrid simulations,[1,2] which invoke a particle-based description while defining some interactions via collective variables. For polymeric, liquid-crystalline materials, those collective variables can be the scalar local liquid density, as well as tensorial quantities which express the local liquid-crystalline order and which are related to the local orientation of the polymer segments.[3,4]

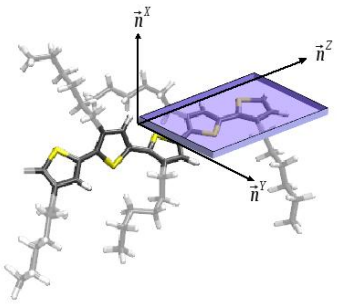


Figure 1. The P3HT molecule can be seen as a chain of connected plate-like segments. In our hybrid simulation scheme, for each segment of the molecule, a set of three orthogonal directions, $\{\vec{n}^X, \vec{n}^Y, \vec{n}^Z\}$, enters the orientation dependent part of the interactions.

A broad class of polymers used in organic semiconducting devices have a rather flat molecular backbone. The P3HT molecules for example consist of linked thiophene rings, which are essentially planar objects. Those highly asymmetric molecules tend to order locally in stacks, due to their molecular shape and the effect of π-π-stacking. Currently, we focus on P3HT melts and describe the polymer chains as flat and semi-flexible ribbons which tend to order along two independent spatial directions. To capture some features of the mesoscale organization of the molecules, a functional has been formulated which depends on the local density and orientation tensors which introduce the behaviour of a biaxial liquid crystal.

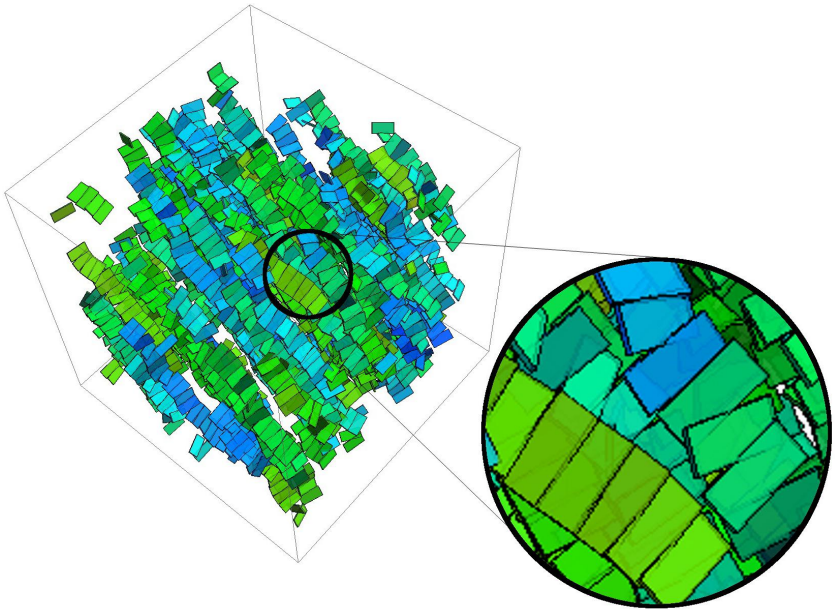


Figure 2. A representative configuration for a system of chains in the biaxial phase obtained in the mean field limit. The bending stiffness of the chains reproduces the persistence length of a P3HT molecule.

The tensorial quantities are related to the local orientation of the plate-like segments of the chain, which is schematically shown in Fig. 1.

For a simple reference system, which is a liquid of biaxial, plate-like particles, we performed order parameter analysis[5,6] in the mean-field limit, setting the interaction to infinite range, and compared our results with similar findings in the literature.[7]

Subsequently we considered the phase behaviour of polymer chains of plate-like particles in the mean field limit. A representative configuration of a system in a biaxial phase is shown in Fig. 2. We currently investigate the proposed method by applying it to systems with finite range of interactions, to study its behaviour beyond the mean-field approximation.

References

1. M. Laradji, H. Guo and M. J. Zuckermann, Phys. Rev. E **49**, 4 (1994).
2. K. Daoulas and M. Müller, J. Chem. Phys. **125**, 18 (2006).
3. R. Holyst and T. A. Vilgis, Macromol. Theory Simul. **5**, 573 (1996).
4. R. Holyst and P. Oswald Macromol. Theory Simul. **10**, 1 (2001).
5. M. P. Allen, Liquid Cryst. **8**, 4 (1990).
6. R. J. Low, Eur. J. Phys. **23**, 111 (2002).
7. J. P. Straley, Phys. Rev. A **10**, 5 (1973).

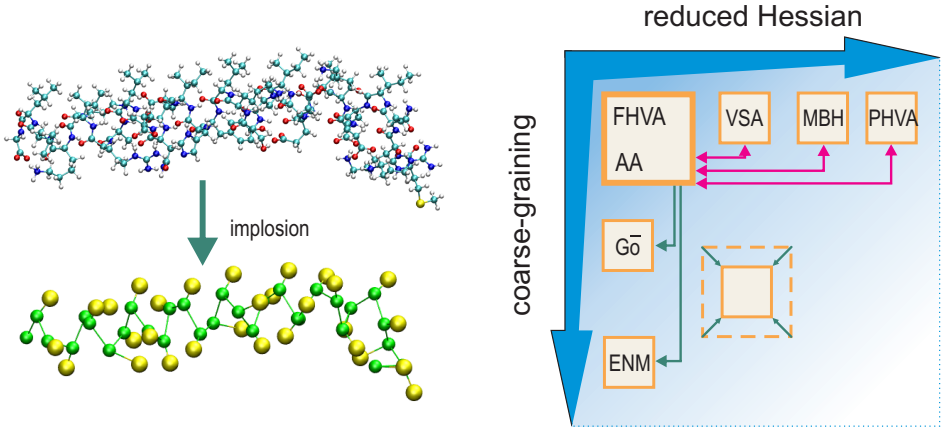
Implosion-Based Mapping Procedure between All-Atom and Coarse-Grained Normal Modes

An Ghysels, Frank C. Pickard IV, Benjamin T. Miller, and Bernard R. Brooks

Center for Molecular Modeling, Ghent University, Ghent, Belgium
Laboratory of Computational Biology, National Institutes of Health, Bethesda, Maryland, USA

E-mail: an.ghysels@ugent.be

Dimension reduction is often necessary when attempting to reach longer length and time scales in molecular simulations. It is realized by constraining degrees of freedom or by course-graining the system. When evaluating the accuracy of the dimensional reduction, one encounters a practical challenge: models that have a different number of degrees of freedom yield displacement vectors of different lengths. Thus direct comparison between the two models is challenging, if not impossible. We have investigated mapping procedures for normal mode analysis, a technique that allows vibrational characterization of a molecule by diagonalizing its mass-weighted Hessian[1]. We review a *horizontal* mapping procedure for the reduced Hessian techniques, which project out degrees of freedom[2]. We then design a *vertical* mapping procedure for the *implosion* of the all-atom (AA) Hessian to a coarse-grained (CG) scale that is based upon Vibrational Subsystem Analysis[3]. This latter method derives both effective force constants and an effective kinetic tensor.



The normal mode matrices have different sizes because of reduced Hessian techniques or coarse-graining. Comparison of normal modes thus requires horizontal or vertical mapping, respectively. An *implosion* procedure between the AA and CG scale transforms the vectors to equal length.

Next, a series of metrics is developed for comparing frequencies and normal modes across different scales, where special attention is given to proper mass-weighting. These metrics can be categorized as dimension dependent and dimension independent. The frequencies, the normal mode vectors, the Hessian similarity, and the thermal fluctuations all belong to the former group, and require prior mapping for proper evaluation, whereas the elastic modulus, the shape derivatives, the vibrational free energy differences and projection, are all techniques belonging to the latter group. The power of these metrics to distinguish between reasonable and unreasonable models is tested on a toy alpha-helix system represented at several scales: the all-atom scale, a Gō-like model, a canonical Elastic Network Model, and a network model with intentionally unphysical force couplings.

From the set of metrics, the following successfully discriminate between the good and bad models: frequencies, overlap plots, fluctuation profiles, total thermal fluctuations, normalized Hessian similarity, locality of modes, lack of globality of modes, total (frequency-weighted) shape derivatives, elastic modulus, and difference in vibrational free energy. In contrast, the density of states profile, entropy of modes, difference in shape derivative, and projection on a spherical harmonics basis set metrics are hardly able or unable to differentiate the unphysical model.

References

1. A. Ghysels, F.C. Pickard IV, B.T. Miller, B.R. Brooks, J. Comp. Chem. , In revision, 2011.
2. A. Ghysels, V. Van Speybroeck, E. Pauwels, S. Catak, B.R. Brooks, D. Van Neck, M. Waroquier, J. Comp. Chem. **31**, 994-1007, 2010.
3. H. Lee Woodcock III, W. Zheng, A. Ghysels, Y. Shao, J. Kong, B.R. Brooks, J. Chem. Phys. **129**, 214109, 2008.

Simulation of Peptide - Ion Interactions During the Early Stages of Biomineralisation

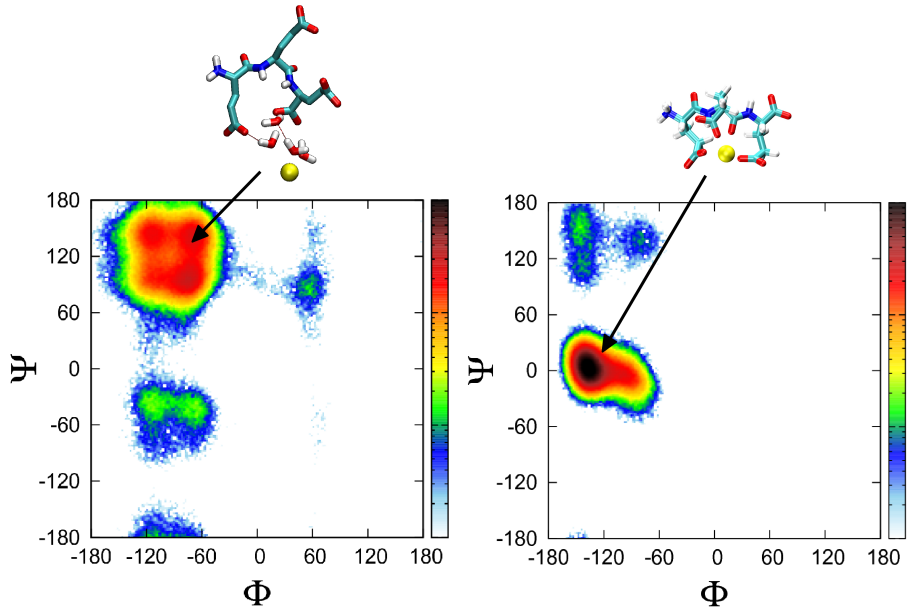
Jens Kahlen, Christine Peter, and Davide Donadio

Max Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

E-mail: kahlen@mpip-mainz.mpg.de

The crystallisation of inorganic compounds such as calcium oxalate, zinc oxide or calcium carbonate is of great academic and industrial relevance. Biomacromolecules such as proteins can have a tremendous influence on the kinetics of crystal growth and resulting morphologies of the crystals formed in solution. This complex process is governed by many physical and chemical phenomena that occur on different time and length scales. Understanding these phenomena and their interplay would provide a great contribution towards the design of new materials.

Atomistic simulations can be a valuable tool to analyse the dependence of resulting



Ramachandran plots of the dihedral angles ϕ and ψ of a trimer of glutamic acid in the presence of one calcium ion. Left: GROMOS 53 A6 force field with SPC/E water model. Right: OPLS-AA force field with TIP4P-Ew water model.

material properties of these crystals from processes on a molecular scale. Our current research activities are concerned with molecular modeling of the crystallisation of calcium-containing minerals in the presence of peptides such as oligoglutamates. The early stages of this biomineralisation process are controlled by interactions of single ions and peptide molecules in solution. Therefore, we perform classical atomistic Molecular Dynamics calculations to analyse the mutual influence of the adhesion of calcium ions to oligoglutamates and the conformations of the peptides. The dynamics of such molecular processes are assumed to strongly influence phenomena that occur on larger time scales such as nucleation and crystal growth processes.

As the dynamics of the system critically depend on some few interatomic potentials the choice of force field is of major importance. This is demonstrated by our simulations in which we applied two different well-established biomolecular force fields. Due to differences in the interactions between water, calcium ions and carboxylate groups of oligoglutamates, the conformational phase space and dynamics that are observed differ significantly for both cases (figure).

Apart from an accurate description of interatomic potentials it is necessary to ensure a sufficient sampling of conformational phase space. As some of the dynamic processes of interest proceed on large time scales, advanced sampling techniques are required. First results of Temperature Replica Exchange Molecular Dynamics Simulations reveal that the saltbridges that are observed in the system under investigation are stable over a wide range of temperatures, thus illustrating the need for different advanced sampling techniques.

With the information obtained through these studies it will be possible to investigate the adhesion of peptides to the crystal surface which presumably alters crystal growth. In order to validate the applied methods and forcefields through comparison between simulation results and experimental data, cooperation with experimentalists has been initiated.

Amorphous $Ge_{15}Te_{85}$: Density Functional, High-Energy X-Ray and Neutron Diffraction Study

Janne Kalikka[1], Jaakko Akola[1,2,3], Robert O. Jones[3,4], Shinji Kohara[5], and Takeshi Usuki[6]

[1] Nanoscience Center, Department of Physics, University of Jyväskylä, P.O. Box 35, FI-40014 University of Jyväskylä, Finland

[2] Department of Physics, Tampere University of Technology, P.O. Box 692, FI-33101 Tampere, Finland

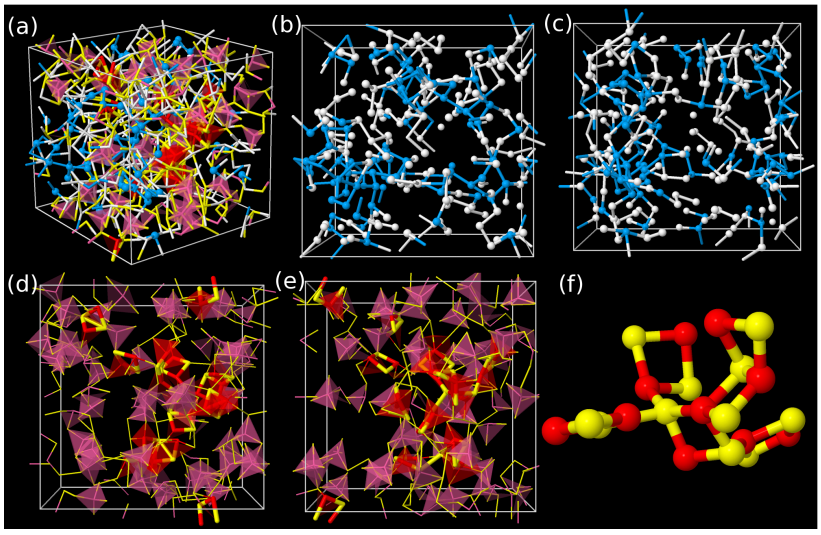
[3] Institut für Festkörperforschung, Forschungszentrum Jülich, D-52425 Jülich, Germany

[4] German Research School for Simulation Studies
Forschungszentrum Jülich and RWTH Aachen University, D-52425 Jülich, Germany

[5] Research & Utilization Division, JASRI/SPring-8, 1-1-1 Kouto, Sayo-cho, Sayo-gun, Hyogo 679-5198, Japan

[6] Graduate School of Science and Engineering, Yamagata University, 1-4-12 Kojirakawa, Yamagata, 990-8560, Japan

E-mail: janne.kalikka@jyu.fi, jaakko.akola@tut.fi



DF-optimized sample: (a) overview, (b-c) Te-atoms not bonded to Ge from front and right, (d-e) Ge atoms and Te atoms bonded to them from front and right, (f) the largest cluster of $ABAB$ rings. Red (thick): Ge atoms in $ABAB$ rings, magenta: other Ge, yellow: Te bonded to germanium, white: Te with nearest germanium as a second nearest neighbour, blue: other Te

Introduction and Methods

The amorphous structure and electronic properties of $Ge_{15}Te_{85}$ have been studied by combining the results of density functional (DF) simulations and high-energy x-ray diffraction (XRD) and neutron scattering (NS) measurements. Three different atomic models of 560 atoms have been constructed with the aid of reverse Monte Carlo method to satisfy several criterions: Good agreement with the experimental structure factors $S(Q)$, low total energy according to DF, and correct electronic properties (with band gap). Two of the models were based on a DF structure which was heated up to viscous regime at 500K and cooled in 5 subsequent simulation steps at 500, 450, 400, 350 and 300 K (simulated annealing) for 20 ps each and optimized. One of the models was based on a hard-sphere RMC run and geometry optimization. The base structures were refined with RMC to produce a close fit to the experimental NS and XRD structure factors, $S(Q)$, while requesting that the DF potential energy of the RMC models had to remain close to (100 ± 5 meV/atom above) the DF-optimized base energy.

Results and Conclusions

All the structures display semiconductor properties close to the Fermi energy, and the electronic spectra are consistent with the base structures.The best structure model is based on the melt-quenched DF structure and has a small number of Ge-Ge bonds. The agreement of $S(Q)$ is good for *both* XRD and NS. The atomic structure can be characterized as two interlocked networks of GeTe and pure Te with a considerable amount (22-24%) of free space, cavities. Approximately one half of Te atoms are in direct contact with Ge, and forms a GeTe network throughout the sample. This network is interlocked with Te domains (Te which are not in direct contact with Ge) which form a similar network and are not able to grow spatially large locally. The Ge coordination displays an interesting co-existence between tetrahedral fourfold coordination and defective octahedral 3+3 coordination as observed for the GeTe and $Ge_2Sb_2Te_5$ alloys previously[1–4], and both situations are equally likely to occur. The obtained bond orders confirm that there is a difference in chemical bonding between the two types of Ge and illustrate the variation of bond strength as a function of distance. Te is slightly overcoordinated in comparison with the $8 - N$ model. Clusters of $ABAB$ squares (A=Ge, B=Te) can be observed in the GeTe network. The nearly-covalent bonding of the material is characterized in terms of chemical bond orders.
This finding suggests that Ge-Ge bonds, albeit their small number, should not be excluded from the amorphous structure.

References

1. Akola J. and Jones R. O., Phys. Rev. B **76**, 235201, 2007.
2. Akola J. and Jones R. O., J. Physics: Condens. Matt. **20**, 465103, 2008.
3. Caravati S., Bernasconi M., Kühne T. D., Krack M., and Parrinello M., Appl. Phys. Lett. **91**, 171906, 2007.
4. Caravati S., Bernasconi M., Kühne T. D., Krack M., and Parrinello M., J. Physics: Condens. Matt. **21**, 255501, 2009.

Phase Behavior of Anisotropic Particles

Carina Karner and Christoph Dellago

Faculty of Physics, University of Vienna Bolzmanngasse 5, 1090 Vienna, Austria

E-mail: {Carina.Karner, Christoph.Dellago}@univie.ac.at

Recent advancements in the synthesis of particles with anisotropic shape open up new possibilities in material design. Nanocrystals and anisotropic colloids then act as building blocks for novel materials with interesting and useful properties. Experiments have demonstrated that the electronic, optical and dynamic properties of those assembled materials are highly dependent on the size and shape of their building blocks. Hence, an important aim of this field of research is to establish a conceptual relationship between the physical properties of the materials and the anisotropy of the particle shape or interaction strength between the particles. In this context, computer simulations offer the possibility to study the underlying physics in a controlled environment.

In our recent project we study the order and disorder transition of hard particles of convex polyhedral shape like cubes, hexagonal prisms and truncated octahedra. By the means of pseudo-dynamic Monte Carlo simulations we explore the phase behavior and transition dynamics of those convex shapes. The phase behavior is determined by various order parameters as bond-order parameters, translational mobility coefficients and rotational auto-correlation functions.

Modulation of Voltage-Gated Potassium Channel Kv1.2 by Lipid Composition

Marina A. Kasimova[1,2], Lucie Delemotte[1,3], Mounir Tarek[1], Alexey K. Shaytan[2], and Konstantin V. Shaitan[2]

[1] Centre National de la Recherche Scientifique, UMR 7565 SRSMC
Nancy Universite, B.P. 70239, 54506 Vandoeuvre les Nancy, France

[2] Department of Biophysics, Faculty of Biology, M.V. Lomonosov Moscow State University
1-12 Leninskie Gory, 119991 Moscow, Russia

[3] Institute of Computational and Molecular Science, Temple University
Philadelphia, PA 19122, USA

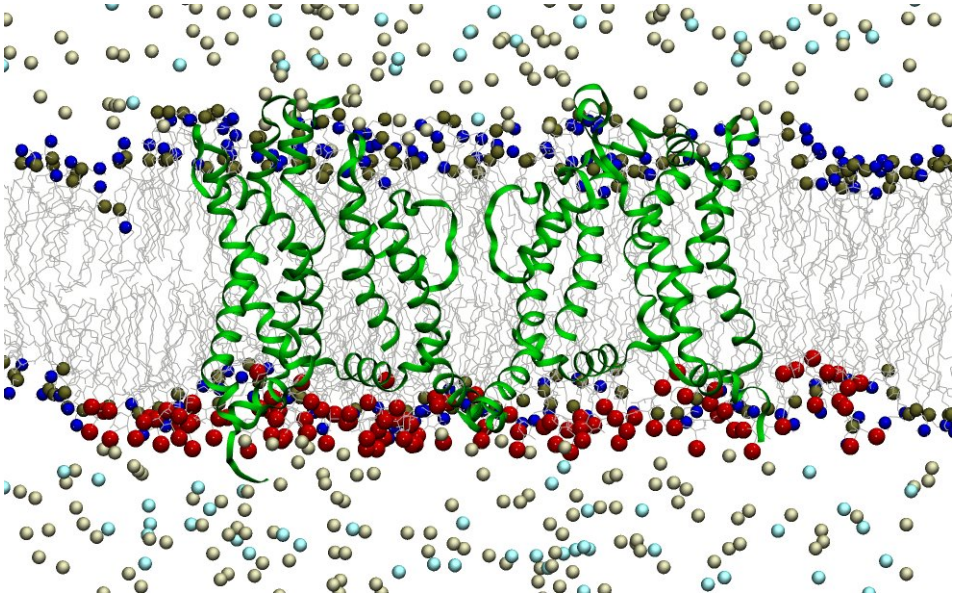
E-mail: marina.kasimova@gmail.com

Voltage-gated ion channels (VGCs) are transmembrane proteins involved in electrical signaling in excitable cells. They enable rapid and coordinated passage of selected inorganic ions along their pore and therefore across the cell membrane. During their working cycle voltage-gated ion channels can be in their closed or open states. The transition between two states called channel gating is regulated by the value of the transmembrane potential and involves movement of S4 a specific helices of the peripheral voltage sensor domains.

The process of VCGs gating appears to strongly depend on the lipid composition surrounding the channel. One of the known channel modulators as was previously shown is phosphatidylinositol-(4,5)-bisphosphate (PIP2), a negatively charged phospholipid of the inner leaflet of the plasma membrane that plays key roles in a variety of cellular processes. Functional and later structural studies have indeed revealed that PIP2 has major impact on the stabilization of the open state of several potassium VGCs. Application of PIP2 to patch-clamp cells increases the ionic current. On the contrary, depletion of PIP2 leads to a decrease of the ionic current. More recently, it was also shown that in addition to open state stabilization PIP2 has an opposite effect involving putatively action on the voltage sensor movement. When applied to patch-clamp cells PIP2 slows down indeed the process of activation.

Despite the importance of PIP2 modulation in a variety of biological processes, the molecular mechanism involved remains elusive. In order to shed light on these effects, we resort here to atomistic molecular dynamics simulations: We studied the structural properties of the voltage-dependent potassium channel Kv1.2. We considered both the crystal structure of Kv1.2 open state and a model of the closed state channel previously obtained in our group[1]. Both structures were studied in their membrane environment (a lipid bilayer) considering a presence of PIP2 in an inner leaflet of membrane.

We have found that PIP2 molecules interact with positively charged residues of the



Voltage-gated potassium channel Kv1.2 embedded in the membrane (for clarity only two of four subunits are presented here). In the inner leaflet of the membrane, there is a ring of PIP2 lipids surrounding the channel (red spheres represent phosphorus atoms of the head groups).

Kv1.2 channel in a state-dependent manner. In particular, we show that PIP2 interact with two different sites in the channel that bear an excess amount of positive charges: Site (1) composed by the basic residues of VSDs and Site (2) located at the end of the transmembrane helices forming the channel pore (the gate). In the closed state PIP2 is shown to interact with residues of Site (1) stabilizing thereby the closed state of the channel. In the open the transmembrane helices surrounding the pore, come closer to the membrane allowing direct interaction of their positive residues with PIP2 which in turn stabilizes the open state of the channel. Hence, our model seems to agree well with the experimental data and provides a further an insight into the molecular mechanisms involved in the modulation of VGCs by PIP2.

References

1. Delemotte L, Tarek M, Klein M L, Amaral C, and Treptow W, *Intermediate states of the Kv1.2 voltage sensor from atomistic molecular dynamics simulations.*, Proc. Natl. Acad. Sci. U.S.A, **108**, 6109–6114, 2011.

Long-Lived and Unstable Modes of Brownian Suspensions in Microchannels

Atefeh Khoshnood and Mir Abbas Jalali

Department of Mechanical Engineering
Sharif University of Technology, Azadi Avenue, Tehran, Iran.
E-mail: atefeh_khoshnood@mech.sharif.edu

The Poiseuille flow is stable under the perturbations of the velocity field for the channel Reynolds numbers < 5780[1]. Microfluidic devices like T-sensors and H-filters operate in such overwhelming laminar conditions where particles migrate across streamlines either through Brownian motion or shear-induced diffusion (SID). Particle-particle and particle-fluid interactions can significantly affect the efficiency of SID.

Despite the apparent stability of low-Renolds flows, some transient substructures like ripples and sharp near-wall features on concentration profiles[2,3] are observed in experimental data. Substructures can be long-lived or unstable modes. They are most likely excited by particle concentration anomalies, wall roughness, particle-particle and particle-wall interactions, and influence both the velocity field and the spatial distribution of particles. On the other hand, the anomalies of velocity profile or particle volume fraction induced by interfaces[4], massive sedimentation[5,6], or the influence of gravity[7] can trigger instabilities so that neither viscous forces nor particle migrations can regulate/suppress growing velocity fluctuations.

We investigate the stability of the pressure-driven flow of Brownian suspensions with spherical particles in microchannels. We adopt the constitutive model of Phillips et al.[8]. We find two general families of modes in the spectrum of suspension flows: (i) low-frequency modes that appear as degenerate pairs with symmetric and anti-symmetric patterns; (ii) high-frequency modes that are either symmetric or anti-symmetric. Both families can be stable or unstable depending on the characteristics of the fully developed steady-state solutions. Once excited, stable modes with the least decay rates can live for about ~ 60 seconds, and are detectable through high-speed imaging. Flows with cuspy concentrations near the channel center are generally stable. Unstable modes occur in highly concentrated suspensions whose velocity profiles are sufficiently flattened near the channel centerline. The patterns of rapidly growing unstable modes suggest that they are Kelvin-Helmholtz instabilities emerged between the central bulk that moves with an almost constant velocity, and highly sheared region near the wall.

References

1. L. H. Thomas, Phys. Rev. **91**, 812, 1953.
2. M. Frank et al., J. Fluid Mech. **493**, 363, 2003.
3. D. Semwogerere et al., J. Fluid Mech. **581**, 437, 2007.
4. K. L. Helton and P. Yager, Lab Chip **7**, 1581, 2007.
5. S. G. Yiantsios, Phys. of Fluids **18**, 054103, 2006.
6. R. R. Rao et al., Int. J. Numer. Meth. Fluids **55**, 723, 2007.
7. R. Govindarajan et al., Phys. Fluids **13**, 3517, 2001.
8. R. J. Phillips, Phys. Fluids **4**, 30, 1992.

Adsorption Behavior of Fibrinogen

Stephan Köhler[1,2], **Giovanni Settanni**[1], **and Friedericke Schmid**[1]

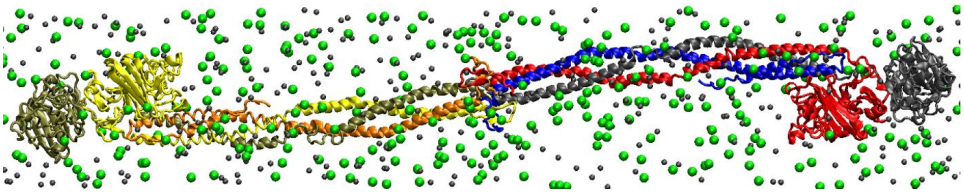
[1] KOMET 331, Institut für Physik,
Johannes Gutenberg-Universität Mainz,
Staudinger Weg 7, D-55128 Mainz, Germany

[2] Graduate School Materials Science in Mainz,
Staudinger Weg 9, D-55128 Mainz, Germany

E-mail: koehlst@uni-mainz.de

Fibrinogen is a large, dimeric glycoprotein in the vertebrate blood. When activated due to, i.e. a wound or blood coming into contact with external bodies, fibrinogen is converted to fibrin, a net-shaped moecular formation to which blood cells attach, resulting in blood clotting[1] and/or immune response. A precise understanding of the adsorption on material surfaces and aggregation properties of human fibrinogen is therefore crucial in a number of circumstances in the clinics, i.e. the choice of materials for implants.

To address this problem, we are using a multi-scale simulation approach where atomistic molecular dynamics simulation are being used to determine with high accuracy the dynamics of single fibrinogen monomers or dimers and the early stages of adsorption of the macromolecules on specific material surfaces, while coarse grained models will be developed based on the atomistic simulation results to describe multimolecular dynamics and aggregation. The simulations are being benchmarked with the experimental data on adsorption of fibrinogen on material surfaces made available by our collaborators[2,3].



Simulation box with a fibrinogen dimer and salt solution. The water molecules are not shown for clarity.

References

1. J. W. Weisel, J. Biophys. Chem. **112**, 267, 2004.
2. N. P. Podolnikova, I. S. Yermolenko, A. Fuhrmann, V. K. Lishko, S. Magonov, B. Bowen, J. Enderlein, A. V. Podolnikov, R. Ros and T. P. Ugarova, Biochemistry **49**, 68, 2010.
3. I. S. Yermolenko, V. K. Lishko, T. P. Ugarova and S. N. Magonov, Biomacromolecules **12**, 370, 2011.

Non-Equilibrium Molecular Dynamics of Crystal Growth

Konstantin Koschke[1], **Davide Donadio**[1], **Kurt Kremer**[1], **and Hans-Jörg Limbach**[2]

[1] Max Planck Institute for Polymer Research, Mainz

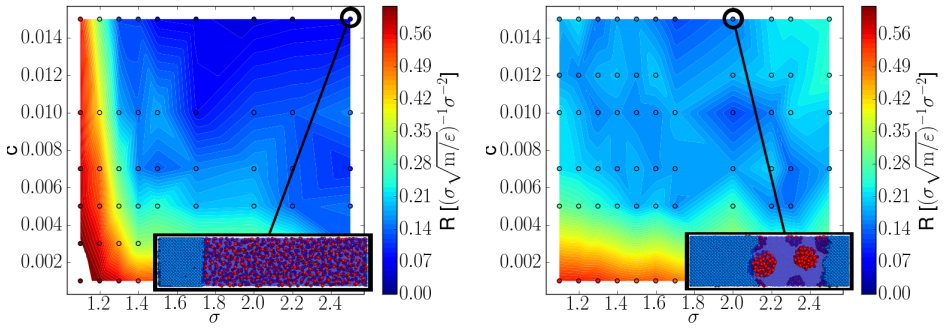
[2] Nestlé Research Center, Lausanne

E-mail: koschke@mpip-mainz.mpg.de

Crystal growth is of uttermost interest for many disciplines, including material, atmospheric and food science. Theoretical approaches complement experiments in the understanding of underlying processes involved in crystal growth. This knowledge not only yields insights into structures and kinetics, but also aid the design of strategies to control and optimize of crystal growth.

We investigate crystal growth in Lennard-Jones systems and in explicit water models by means of non-equilibrium molecular dynamics simulations. MD simulations provide an insight to processes at time and length scales that experiments cannot reach.

Using Lennard-Jones as a model system we established a reliable protocol to compute crystal growth rates that exploits the two-phase approach. We set up a simulation cell made of a crystalline and liquid block in contact and equilibrate it at coexistence conditions. We then perform non-equilibrium simulations supercooling or superheating the system, so to probe the dynamics of the crystallization front. By an effective use of a thermostat we managed to disentangle the effect of mass and heat transport on the kinetics of crystallization/melting.



Crystal growth rate R of a binary Lennard-Jones system as a function of impurity size σ, concentration c and interaction. **Left:** Hydrophilic interaction. The example snapshot shows dispersed impurities causing a reduced growth rate. **Right:** Hydrophobic interaction: The impurities segregate in clusters (visualized in snapshot).

Furthermore, we have considered the effect of additives at low concentration ($< 2\%$) in the crystallization of a Lennard-Jones fluid. Size, concentration and interaction parameters with the solvent of the additives have been varied, so that they affect the dynamics of crystallization in different ways. We can resolve cases in which additives are incorporated in the growing crystal or they accumulate at the crystallization front hindering crystal growth and we have quantified their effect on growth rates.

The general concept can then be readily applied to models with more specific chemical details, such as the rigid TIP4P water model and we are specifically considering the case of small hydrophobic molecules (methane) modifying the crystallization of hexagonal ice.

Molecular Simulation Studies of the Insulin Family

Olga Ksenofontova and Vasily Stefanov

Saint Petersburg State University
Department of Biochemistry, Russia

E-mail: jabiata@yandex.ru

Molecular Simulation Studies is an approach to understand the macroscopic properties of a molecular system in terms of interactions among its constituting atoms with the help of model building and computation[1]. The previous computional research in the insulin family has been limited to the studies of hormone insulin[2], and no theoretical or computional investigations have been reported on the insulin family to date. Experimental structures of the ligand-bound receptors are also elusive, due likely to which the atomic picture of ligand-recognition in the family is yet emerge[3].

We have taken a computional strategy to gain a better understanding of the mechanisms underlying hormone-recognition by IR and IGF1R. We have extensively studied the dynamics of ligands and receptors of the insulin family using molecular simulations. The central goal of our work was to develop an understanding of the structure-function relationships in the insulin family. Using the crystal structure of the IR ectodomain (IR$\Delta\beta$), and a homology model of the IGF1R ectodomain with the help of molecular dynamics simulations, we have extensively studied the flexibility mechanisms of these proteins that can allow binding of their cognate ligands. We observe that the apo ectodomains of both receptors display asymmetric flexibility mechanisms that are consistent with previously proposed notion of a see-saw mechanism of receptor activation[4].

The present work presents detailed molecular simulation studies on insulin monomer, insulin hexamer, type 1 insulin like growth factor (IGF1), type 2 insulin like growth factor (IGF2), insulin receptor (IR), and insulin-like growth factor 1 receptor (IGF1R), which provide new insights into the ligand-recognition in the insulin family, and can also be useful for the treatment of Type I diabetes.

References

1. M. Karplus and A. McCammon, *Molecular dynamics simulations of biomolecules*, Nature Structural Biology **9**, 646 652, 2002.
2. A.E. Mark, H.J.C. Berendsen, W.F. van Gunsteren, *Conformational flexibility of aqueous monomeric and dimeric insulin: a molecular dynamics study*, Biochemistry **30**, 1086610872, 1991.
3. H. Vashisth and C.F. Abrams, *All-Atom Structural Models for Complexes of Insulin-Like Growth Factors IGF1 and IGF2 with Their Cognate Receptor*, J. Mol. Biol. **400**, 645658, 2010.
4. H. Vashisth and C.F. Abrams, *Docking of insulin to a structurally equilibrated insulin receptor ectodomain*, Proteins **9**, 646 652, 2002. J. Comp. Phys. **78**, 1531-1543, 2010.

Molecular Dynamics and Structure Prediction in Biosciences

Javier Lechuga

Institut für Mathematik, Universität Würzburg
Campus Hubland Nord, Emil-Fischer-Str. 30, 97074 Würzburg, Germany
E-mail: javier.lechuga@mathematik.uni-wuerzburg.de

This poster presents results of Molecular Dynamics in the study of mass transport through biological membranes and of global optimization in the prediction of protein structures.

A biological cell membrane is considered, which is modelled as a phospholipid bilayer, as described as a *fluid mosaic*. This is a two dimensional fluid, along the cell surface, composed of freely diffusing phospholipids with embedded proteins and other complex molecules such as cholesterol, glycolipids, carbohydrates and filaments of cytoskeleton. The behavior of this biological structure is studied using Molecular Dynamics methods[5].

Regarding to the first topic, it is known that the lipids which conform the cell membrane can freely diffuse. This behavior of the lipids, called *lateral diffusion*, can be increased by the introduction of a shock wave into the system[2]. The purpose of the work is to model and understand this diffusion of the lipids and the affection of different shock waves. We recall that the main ingredient of the Molecular Dynamics simulation is the definition of the potential function which provides the internal forces driving the system.

The interaction among the atoms which conform a molecular model can be non-bonded (Electrostatical and van der Walls) and bonded (Bonds, Urey Bradley, Angles, Dihedrals, Impropers). And therefore, the potential function, which has a term for each one of these interactions, can be formulated as the sum of non-bond energy and bond energy using the potential energy function Chemistry at HARvard Macromolecular Mechanics (CHARMM)[3].

The second part of the poster is devoted to our work on Protein Structure Prediction (PSP), which can be formulated as a mathematical optimization problem where the non-bond and bond energies of the molecule become the objectives of a Multi-Objective Optimization Problem (MOOP)[1].

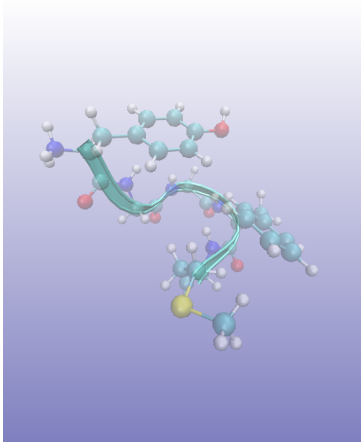
It is known that molecules make transitions to a lower state of energy and this is the reason why most experts expect that the geometry defined by its global minimum is the correct geometry to describe the conformation observed in folded proteins. The PSP problem consists of predicting the folded, native, tertiary structure of a protein from a given sequence of amino acids, correspoding to the minimal conformation energy[4].

For this purpose, the http://www.mathematik.uni-wuerzburg.de/ lechugaAminoas (Aminoacid assembler) code has been developed to sequentially search for the minimum energy of the chosen protein. This PSP algorithm iterates through different conformations and choses the one which satisfies the objectives of the optimization process better. The chosen conformation is called *Dominant* and it becomes the current solution for the next iteration.

The results for protein 1PLW (Met-Enkephalin) are presented in the following table:

Algorithm	Energy ($\frac{kcal}{mol}$)	RMSD (Å)
Aminoas	-48.84±12.36	1.598±0.266
I-PAES	-20.47±1.54	2.835
REGAL	-23.55±1.69	3.230
Lamarkian	-28.35±1.29	3.330
Baldwinian	-22.57±1.62	3.960

The results calculated with Aminoas present lesser minimum energy as the Random Mean Square Displacement (RMSD) indicates that the obtained solution is closer to the native structure that the ones presented by other authors.



Met-Enkephalin

References

1. Cutello, V., Narzisi, G. and Nicosia, G. A multi-objective evolutionary approach to the protein structure prediction problem. Journal of the Royal Society Interface, 3:139-1516, 2006.
2. Kodama, T. and Hamblin, M.R. and Doukas, A.G. Cytoplasmic molecular delivery with shock waves: Importance of impulse. Biophysical Journal, 4:1821-1832, 2000.
3. MacKerell Jr, A. D., Brooks, B., Brooks III, C. L., Nilsson, L., Roux, B., Won, Y. & Karplus, M. 1998 CHARMM: the energy function and its parameterization with an overview of the program. In The encyclopedia of computational chemistry (ed. P. v. R. Schleyer et al.), vol. 1, pp. 271-277. Chichester: Wiley.
4. Neumaier, A.. Molecular modeling of proteins and mathematical prediction of protein structure. Society for Industrial and Applied Mathematics. 39:407-460, 1997.
5. Singer, S.J. and Nicolson, G.L. The fluid mosaic model of the structure of cell membranes. Science, 4023:720-731, 1972.

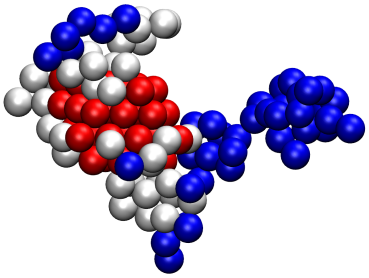
Coil-to-Crystal Transition of a Homopolymer Chain with Square-Well Interactions: A Transition Path Sampling Study

Christian Leitold and Christoph Dellago

Faculty of Physics, University of Vienna, Boltzmanngasse 5, 1090 Wien, Austria

E-mail: {christian.leitold,christoph.dellago}@univie.ac.at

The crystallization of a single, flexible homopolymer chain is investigated using transition path sampling (TPS). The chain consists of N identical spherical monomers evolving according to Metropolis Monte Carlo dynamics. While neighboring monomers have a fixed distance, the non-neighboring monomers interact via a square-well potential. For a sufficiently small interaction range λ, the system undergoes a first order freezing transition from an expanded, unordered phase to a compact crystalline state[1,2]. It can therefore serve as a model for small chain-like proteins with a similar structural transition.

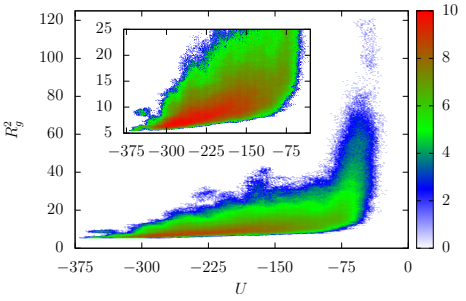


Typical transition state for the $N = 128$ system with $\lambda = 1.04$. Crystalline particles are colored in red and chain-like particles in blue.

Transition path sampling and committor analysis[3,4] are used to study the transition state ensemble of the chain. Earlier observations by Taylor et al.[1] concerning the structural properties of the transition states are confirmed by our calculations: The typical transition states indeed consist of a crystalline nucleus attached to one or more chain fragments.

Furthermore, we calculate $p(r|\mathrm{TP})$, the probability to find the configuration r in a transition pathway. This probability is calculated as a function of the potential energy U and the radius of gyration R_g^2.

We use the final results of our simulations to search for possible reaction coordinates of the transition. For that task, we also experiment with applying machine learning algorithms such as neural networks and support vector machines.



$\ln[p(r|\mathrm{TP})+1]$ as a function of U and R_g^2 with arbitrary normalization. Inset: Zoom into the most interesting region.

References

1. Mark P. Taylor, Wolfgang Paul, and Kurt Binder, *Phase transitions of a single polymer chain: A Wang-Landau simulation study*, J. Chem. Phys., **131**, 114907, 2009.
2. Mark P. Taylor, Wolfgang Paul, and Kurt Binder, *Two-state protein-like folding of a homopolymer chain*, in: Recent developments in computer simulation studies in condensed matter physics, D. P. Landau, S. P. Lewis, and H. B. Schuttler, (Eds.), vol. 4 of *Physics Procedia*, pp. 151–160, Elsevier, Amsterdam, 2010.
3. Christoph Dellago, Peter G. Bolhuis, and Philip L. Geissler, "Transition path sampling", in: Advances in Chemical Physics, vol. 123 of *Advances in Chemical Physics*, pp. 1–78. John Wiley & Sons, New York, 2002.
4. Michael Grünwald and Christoph Dellago, *Nucleation and growth in structural transformations of nanocrystals*, Nano Letters, **9(5)**, 2099, 2009.

Regulation Mechanism of Human SIRT2, A Promising Pharmaceutical Target Protein for Age-Related Diseases

Jinyu Li[1,2], Giulia Rossetti[1], Bernhard Lüscher[2], and Paolo Carloni[1]

[1]German Research School for Simulation Sciences
Forschungszentrum Jülich/RWTH Aachen University, 52425 Jülich, Germany
Institute for Advanced Simulation, Forschungszentrum Jülich, 52425 Jülich, Germany

[2]Institut fur Biochemie und Molekularbiologie, Medizinische Fakultät
RWTH Aachen University, 52057 Aachen, Germany

E-mail: {j.li, p.carloni}@grs-sim.de

SIRT2 protein is a NAD^+-dependent deacetylase that has recently emerged for its high therapeutic potentials in several age-related diseases[1]. These includes diabetes[2], cardiovascular disease[3], neurodegeneration[4] and cancer[5]. However, up to now, the complete understanding of its mechanism was hampered by the lack of its full-length structure. Only the catalytic core of SIRT2 (residue 57-356) is indeed crystallized (PDB ID: 1J8F[6]). The N- and C- terminal regions, whose role has been recently linked to SIRT2 catalytic activity[7], are so far missing. This extremely limits the understanding of the regulatory mechanism of SIRT2 activity. We provide the first full-length molecular structure of SIRT2 (the catalytic core along with the N- and C-terminal regions) using computational methods. We (i) apply bioinformatics tools to assign secondary structure elements of N- and C-terminal regions. (ii) Use homology and *ab initio* modeling to construct models of SIRT2. (iii) Perform molecular dynamics simulations of the full-length protein in aqueous solution. Our calculations allow to identify key residues on the catalytic core surface involved in the interaction with C-terminal region. This may provide a rationale for a variety of experimental facts including regulation of SIRT2. It might also have important implications for SIRT2 target-specific drug design. Our findings are currently being validated or disproved site-directed mutagenesis experiments performed by us at the RWTH-clinics.

References

1. B.D. Sanders, et al., Biochim. Biophys. Acta **1804**, 1604, 2010.
2. R. Luthi-Carter, et al., Pro. Natl. Acad. Sci. USA **107**, 7927, 2010.
3. T.F. Outeiro, et al., Science **317**, 516, 2007.
4. B. Peck, et al., Mol. Cancer Ther. **9**, 844, 2010.
5. H.S. Kim, et al., Cancer Cell **20**, 487, 2011.
6. M. Finnin, et al., Nat. Struct. Bio. **8**, 621, 2001.
7. R. Pardithage, et al., J. Cell Biol. **180**, 915, 2008.

Mechanisms of Crazing in Glassy Polymers Revealed by Molecular Dynamics Simulations

Dhiraj K. Mahajan and Alexander Hartmaier

Interdisciplinary Center for Advances Materials Simulation,
Department of Micromechanical and Macroscopic Modelling,
Ruhr Universität Bochum, Germany

E-mail: dhiraj.mahajan@icams.rub.de

Crazing and shear-yielding are two complementary types of failure of glassy polymers[1]. While the former leads to localization of deformation in form of cavitation induced fibrillated zones, the later causes concentrated deformation in shear zones with negligible volume change. In contrast to shear yielding[2,3], the atomic-scale mechanisms leading to initiation of crazing[4,5] are currently not understood. Here we show that local heterogeneous deformation leads to craze initiation in glassy polymers. Using molecular dynamics simulations of crazing failure in glassy polymers, we found that the zones of high plastic activity are constrained by low plastic activity zones and become unstable under local negative bulk modulus thus initiating crazing from these zones. These conditions are similar to cavitation instabilities observed in ductile metals under highly constrained plastic flow[6]. Furthermore, based on the constant shear stresses we found that micro-cavitation is the essential local deformation mode for crazing to happen in glassy polymers. Our results demonstrate the basic difference in the local deformation mode as well as the conditions that leads to either shear yielding or crazing type failure in glassy polymers. We anticipate our assay to help devise new criterion for craze initiation that not only considers stress state but also local deformation heterogeneities that forms the necessary conditions for crazing in glassy polymers.

References

1. R. N. Haward and R. J. Young, The Physics of Glassy Polymers (1997).
2. A. S. Argon, Phil. Mag. **28**, 839, 1973.
3. N. Brown, J. Mater. Science. **48**, 2241, 1983.
4. C. B. Bucknall, Polymer **48**, 1030, 2007.
5. A. S. Argon, Polymer **52**, 2319, 2011.
6. Y. Huang, J. W. Hutchinson, and V. Tvergaard J. Mech. Phy. Solids **39**, 223, 1991.

Collective Behavior of Single-File Water Chains in Nanopore Membranes

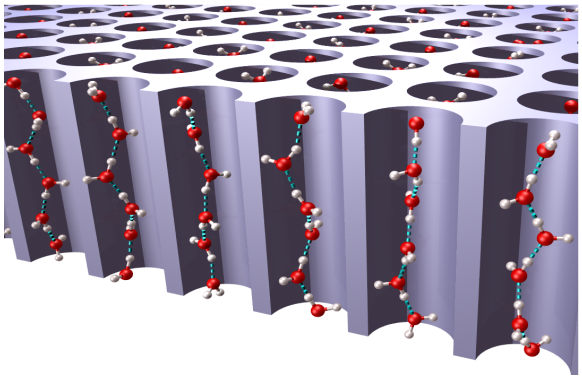
Georg Menzl[1], Jürgen Köfinger[2], and Christoph Dellago[1]

[1] Faculty of Physics and Center for Computational Materials Science
University of Vienna, Boltzmanngasse 5, 1090 Vienna, Austria
E-mail: {georg.menzl, christoph.dellago}@univie.ac.at

[2] Laboratory of Chemical Physics, Building 5, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland, 20892-0520 USA

When a membrane of narrow carbon nanotubes is immersed in water, its pores are filled and the spatial confinement within the tubes leads to the formation of single-file water chains. These hydrogen bonded chains show ordering at room temperature such that the average dipole moment of the water molecules in the pores points along the tube axis. This order causes unique properties in comparison to bulk water, such as rapid proton transport along the water wires[1].

We study membranes of parallel water wires by use of a dipole lattice model which accurately captures the energetics of single-file water. This model allows the investigation of large systems and can be mapped onto a 2D spin model. We show that this model is equivalent to a system of effective charges located at opposite sides of the membrane which provides a physically transparent picture of the system since the coupling switches from dipolar to Coulombic with increasing membrane thickness.



Schematic representation of a membrane of parallel water-filled pores arranged in a square geometry. All hydrogen bonds within a chain point into the same direction and chains in adjacent pores are oriented in opposite directions, representing the low-temperature ordered state.

Our simulations show a continous order-disorder transition on square membranes to an anti-ferroelectrically ordered low-temperature-phase, in which water wires in adjacent pores are oriented in opposite directions. The critical temperatures for various pore lengths and pore spacings are obtained and we derive an analytic expression for corresponding states of a lattice of ordered chains which makes our simulation results applicable to a wide range of parameters.

Analysis of the susceptibilities of square and triangular lattices shows the strong influence of inter-chain coupling on the dielectric response of the system, effectively lowering the dielectric constant even for temperatures far above the critical regime. This unexpected behavior could also significantly affect proton transfer rates across such membranes.

References

1. J. Köfinger, G. Hummer and C. Dellago, PNAS **105**, 13218, 2008.

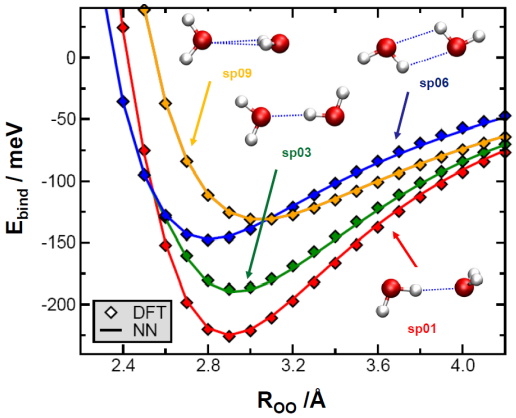
A High-Dimensional Neural Network Potential for Water: First Applications to Water Clusters

Tobias Morawietz, Vikas Sharma, and Jörg Behler

Lehrstuhl für Theoretische Chemie
Ruhr-Universität Bochum, D-44780 Bochum, Germany
E-mail: tobias.morawietz@theochem.ruhr-uni-bochum.de

Understanding the unique properties of water still represents a significant challenge for theory and experiment. Molecular dynamics (MD) simulations are a valuable tool to study water at the atomic level but realistic MD simulations of large systems require efficient and reliable potentials to describe the atomic interactions. To date, numerous water potentials have been developed, but most of them have a very simple functional form and keep the water monomers frozen.

In recent years, artificial neural networks (NNs) have become a promising method for the development of accurate potential-energy surfaces (PESs) for a wide range of systems[1]. Due to their flexible functional form NNs are able to represent even most complicated PESs using a set of energies and forces obtained from electronic structure calculations. Once constructed, they can be evaluated several orders of magnitude faster than the underlying electronic structure data.



Binding energy as a function of the oxygen-oxygen distance R_{OO} for four stationary points (sp) of the water dimer potential-energy surface. The solid diamonds represent DFT energies while the lines correspond to the neural network (NN) potential-energy surface.

Using a generalized NN scheme for multicomponent systems[2,3], we present a full-dimensional NN potential for water clusters[4]. This potential is based on environment-dependent atomic energy contributions and incorporates long-range electrostatic interactions employing environment dependent atomic charges. We show that properties like binding energies and vibrational frequencies are in excellent agreement with the underlying reference density-functional theory data.

References

1. J. Behler, Phys. Chem. Chem. Phys. **13**, 17930, 2011.
2. J. Behler and M. Parrinello, Phys. Rev. Lett. **98**, 146401, 2007.
3. N. Artrith, T. Morawietz and J. Behler, Phys. Rev. B **83**, 153101, 2011.
4. T. Morawietz, V. Sharma and J. Behler, submitted, 2011.

Carbon-Like Structures of DNA Tethered Particles

Ulf R. Pedersen[1,2], **Panagiotis Theodorakis**[1,2], **Gerhard Kahl**[1], **and Christoph Dellago**[2]

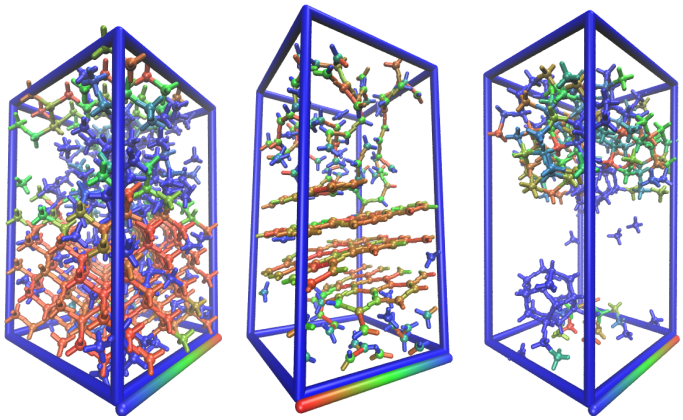
[1] Institute of Theoretical Physics and CMS, Vienna University of Technology, Austria
E-mail: {ulf.pedersen, gerhard.kahl}@tuwien.ac.at

[2] Faculty of Physics, University of Vienna, Austria
E-mail: {panagiotis.theodorakis, christoph.dellago}@univie.ac.at

Attaching DNA strands to colloidal particles is a possible way to novel matrials. Here, we investigate a coarse-grained model motivated by effective potentials of a detailed model. Inspired by the structural diversity of water and carbon we focus on colloids with four DNA strands located in a tetrahedral symmetry.

We find that the colloidal systems share structural features with their atomic analogue. This includes: i) hexagonal and cubic diamond phases, ii) amorphous structures iii) fullerenes (exemplified by clusters of dodecahedra), and iv) graphene sheets (when attaching three DNA strands in a plane). These structure form spontaneous in Monte Carlo simulations, and in some cases without being the thermodynamical stable state. Selected configurations are shown in the figure below.

Interestingly, the colloidal systems also exhibit features quite different from their atomic counterpart due to more specific and short-range interactions. This allow additional particles in the structures of carbon. As an example, crystal structures are penetrated by gas particles (see figure). Also, the symmetry of the cubic diamond structure allow several interpenetrating lattices (when increasing pressure).



Structures formed in a model of DNA tethered colloidal particles. (left) A cubic diamond structure in coexistence with a fluid phase. Unlike the cubic diamond of carbon, gas particles penetrate the crystal lattice. (middle) Spontaneously formed graphene sheet. (right) Particles in an amorphous rigid state. Particles in the lower part of the box have formed a dodecahedron. Colors indicate local orientational order.

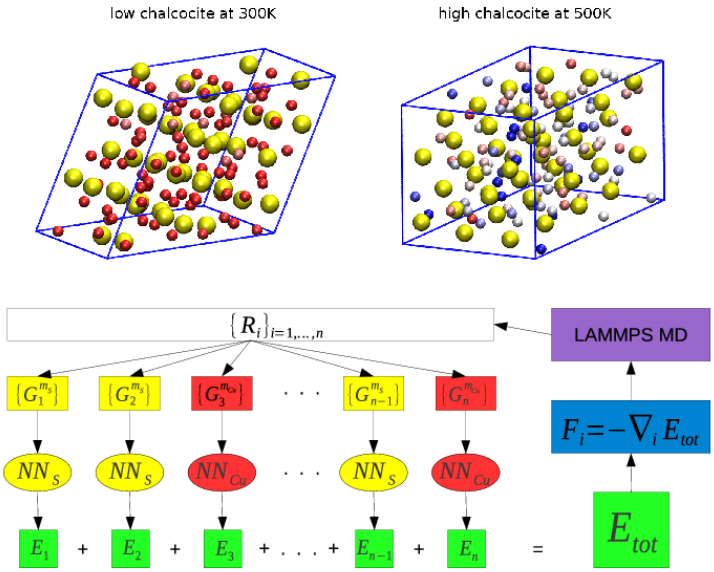
A Neural Network Potential for Copper Sulfide

Andreas Singraber[1], **Jörg Behler**[2], **and Christoph Dellago**[1]

[1] Faculty of Physics, University of Vienna
Boltzmanngasse 5, 1090 Wien, Austria
E-mail: andreas.singraber@univie.ac.at
E-mail: christoph.dellago@univie.ac.at

[2] Lehrstuhl für Theoretische Chemie
Ruhr-Universität Bochum, 44780 Bochum, Germany
E-mail: joerg.behler@theochem.ruhr-uni-bochum.de

The choice of an appropriate potential for a given system is a crucial part of any molecular dynamics (MD) simulation and determines if critical parts of the true dynamics are correctly reproduced or missed. While the combination of *ab initio* methods and MD provides high accuracy its application is restricted to small system sizes due to computational cost. Empirical potentials available for lots of systems are much faster but their fixed functional form inevitably introduces inaccuracies. The recently developed neural network potential method[1] combines several positive aspects of both worlds. Here we present a neural



Typical low- and high-chalcocite configurations from MD simulation, with copper atoms colored according to mean square displacement (top). Flow chart for the implementation of the neural network potential method into LAMMPS (bottom).

network potential for the multi-component system copper sulfide. Depending on temperature one finds two possible Cu_2S phases commonly named low- and high-chalcocite. For both cases we compare trajectories and radial distribution functions from a neural network potential energy surface with data obtained from VASP reference calculations and an empirical EAM potential. In addition we present a MPI/OpenMP implementation of the neural network potential method into the MD software LAMMPS[2] and test its scalability on a typical cluster setup.

References

1. J. Behler and M. Parrinello, *Generalized Neural-Network Representation of High-Dimensional Potential-Energy Surfaces*, Phys. Rev. Lett. **98**, 146401 (2007).
2. S. J. Plimpton, *Fast Parallel Algorithms for Short-Range Molecular Dynamics*, J. Comp. Phys. **117**, 1-19 (1995).

Polymer Mechanics at Interfaces: Molecular Dynamics Simulations and Mapping to Continuum Approaches

Mathieu Solar

Theoretical Polymer Science in Department of Physics (Prof. Wolfgang Paul)
Martin-Luther-University Halle-Wittenberg
Naturwissenschaftliche Fakultät II, 06099 Halle (Saale) Germany
E-mail: mathieu.solar@physik.uni-halle.de

The appropriate modeling of matter is becoming an increasingly unavoidable step in the predictive numerical simulations of phenomena like adhesion/adherence taking part of indentation (or scratch) tests and cracking or damage of polymers. In such modeling, the matter is considered from two points of view: (1) from a continuum point of view, i.e. as a homogeneous or heterogeneous continuous medium with the assumption of mean values for the material behavior and (2) from a discrete point of view in relation to the fact that microscopically the medium consists of particles. These points of view are related to two familiar simulation techniques: (1) the finite element method (FE simulations, for large systems) based on continuum mechanics (CM) and (2) the molecular dynamics method (MD simulations, for small systems) based on the forces acting between the particles at a molecular level. For example, Fig. 1 recapitulates the scale transition from the macroscopic to the microscopic point of view.

First, this poster presentation illustrates former works[1–4] on the rheology of polymer melts and films in the glassy and near the rubbery domain using two different methods: molecular dynamics (MD) and finite element (FE) simulations. In a first step, the uniaxial mechanical behavior of a bulk polymer sample was studied by means of particle based MD simulations. The results were in good agreement with experimental data and mechanical properties may be computed from the simulations. This uniaxial mechanical behavior was then implemented in FE simulations using an elasto-viscoelasto-viscoplastic constitutive law in a continuum mechanics (CM) approach. In a second step, the mechanical response of a polymer film during an indentation test was modeled with the MD method and with the FE simulations using the same constitutive law. Good agreement was found between the MD and CM results (see Fig. 2, left).

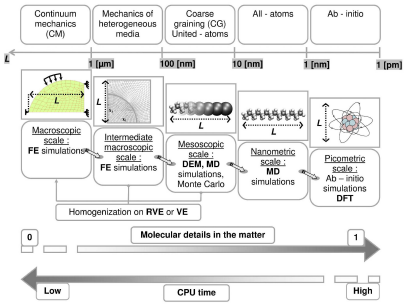


Figure 1. Various techniques for the numerical simulation of matter with their corresponding characteristic length scales L (VE = volume element; RVE = representative volume element; DEM = discrete element method; DFT = density functional theory).

These previous works[1–4] provided evidence in favor of using MD simulations to investigate the local physics of contact mechanics, since the volume elements studied were representative and thus contained enough information about the microstructure of the polymer model, while surface phenomena (adhesion, surface tension) were naturally included in

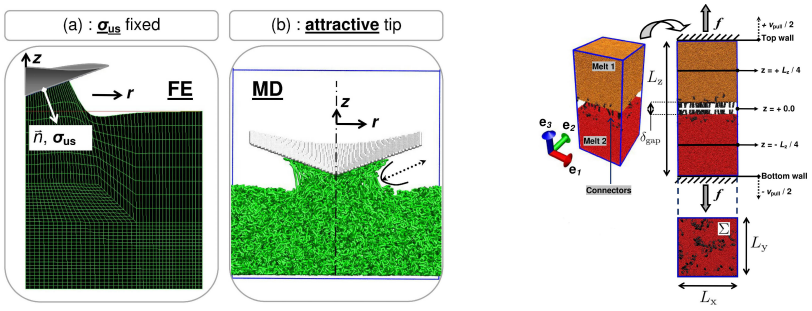


Figure 2. Left: panel (a), modeling of adherence during unloading with FE simulations. Panel (b), modeling of an indentation test with an attractive tip in MD simulations. In both cases, the temperature was $T = 0.2$ ($< T_g$). Strong similarities are observed, although surface tension was not accounted for in the FE simulations. Right: straining of a coarse-grained system with two melts linked together by connectors. The system is pulled at both sides with a velocity $v_{\text{pull}}/2$, the corresponding response is the force f on each wall.

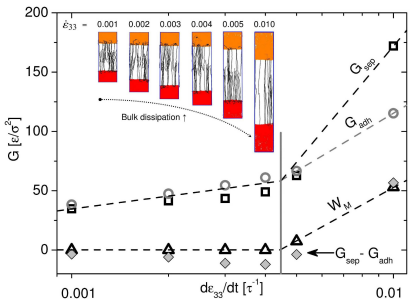


Figure 3. The separation energy $G_{\text{sep}} = W_{\text{sep}}$ (squares), the adhesion energy $G_{\text{adh}} = W_{\text{adh}}$ (circles), the energy dissipated in the melts W_{M} (triangles) and the difference '$G_{\text{sep}} - G_{\text{adh}}$' (filled rhombs) as a function of the strain rate $\dot{\varepsilon}_{33}$. The snapshots of debonding MD simulations are taken at the failure of adhesion and illustrate the increase of the bulk dissipation with strain rate.

the MD approach. Thus, this poster presentation illustrates then MD simulations of the failure of adhesion (complex phenomenon involving bulk dissipation, i.e., shear yielding, cavitation and crazing, surface adhesion through Van der Waals interactions and connector chain pull-out) between two polymer melts stitched together with connector chains[5] (see Fig. 2, right). The contributions to the separation energy from the dissipation in the bulk and at the surface were studied, in dependence of the separation rate at constant temperature and at fixed basic molecular parameters (see Fig. 3). The results will be key to future developments of continuum cohesive models for adhesion on polymer surfaces.

References

1. M. Solar *et al.*, J. Phys. D **43**, 455406
2. M. Solar *et al.*, Wear **271**, 2751 (2011).
3. M. Solar *et al.*, P. R. E., to be published (2012).
4. M. Solar *et al.*, (unpublished).
5. M. Solar *et al.*, submitted to Comp. Mat. Sci., (2012).
6. L. Lamport, *LaTeX* (Addison-Wesley, Reading, 1994).

Modelling of Non-Adiabatic Dynamics of Rare-Gas Clusters

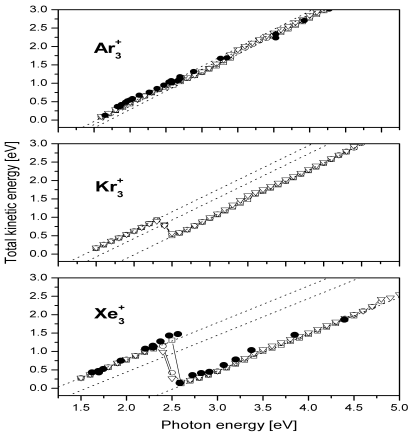
Martin Stachoň[1], Ivan Janeček[2,3], Florent Xavier Gadéa[4], and René Kalus[1]

[1] Centre of Excellence IT4Innovations and Department of Applied Mathematics
Faculty of Electrical Engineering and Computer Science
VŠB - Technical University of Ostrava, 17. listopadu 15, 708 33 Ostrava, Czech Republic
E-mail: {martin.stachon,rene.kalus}@vsb.cz

[2] Institute of Geonics of the AS CR, v.v.i. and Institute of Clean Technologies for Mining and Utilization of Raw Materials for Energy, VSB - Technical University of Ostrava, Czech Republic

[3] LCPQ, IRSAMC and UMR5626 du CNRS, Université de Toulouse
118 route de Narbonne, 31062 Toulouse Cedex, France

Ionic rare-gas clusters present various interesting particularities. As clusters, they are aimed to improve the understanding of the transition between the gas and the condensed phases of matter. The charge is localized on a small chromophoric subunit, mainly trimer, but also tetramer or dimer, while the surrounding atoms are almost neutral. Therefore, the ionic rare-gas clusters are bound by heterogeneous interactions, with strong chemical interactions between the core atoms and loosely bound neutrals. However, the charge may migrate, particularly after the clusters are excited. Reflecting their heterogeneity, when excited by photons or impacting electrons, they undergo nonadiabatic dynamics, which is imprinted by a competition between the fission of the core, evaporation of neutrals, internal conversion, and relaxation over various electronic or nuclear degrees of freedom. Consequently a variety of fragment types is produced. Moreover, the ionic rare-gas clusters can be easily produced and analyzed in experiments. Therefore, they have been intensively studied for more than 20 years, both in experiment and in theory.



Temperature dependence of the total kinetic energy deposited in the photodissociation fragments of $Rg_3^+ \rightarrow Rg^+ + 2\,Rg$ obtained for the DIM+SO model: Ar_3^+ - $\square$ $T = 50\,\mathrm{K}$, $\bigcirc$ $T = 150\,\mathrm{K}$, ∇ $T = 225\,\mathrm{K}$; Kr_3^+ - $\square$ $T = 100\,\mathrm{K}$, $\bigcirc$ $T = 150\,\mathrm{K}$, ∇ $T = 200\,\mathrm{K}$; Xe_3^+ - $\square$ $T = 100\,\mathrm{K}$, $\bigcirc$ $T = 200\,\mathrm{K}$, ∇ $T = 250\,\mathrm{K}$. Experimental points by Haberland *et al.* ($\bullet$) and theoretical estimates for $Rg^+(^2P_{3/2})$ (upper $\cdots$), $Rg^+(^2P_{1/2})$ fragments (lower $\cdots$), as well as for the fragments of the DIM model without inclusion of the spin-orbit coupling (middle $\cdots$) are also included for comparison.

In our work, we focus on the modeling of ionized Rg_n^+ clusters because a reliable and computationally cheap interaction model with a sufficient number of excited states is available.

This allows us to study various non-adiabatic phenomena like post-ionization fragmentation, photodissociation, and atom-cluster collisions.

Initial conditions (nuclear coordinates and velocities and electronic amplitudes) for the dynamics are generated using microcanonical Monte Carlo sampling. Because the initial conditions are independent, computation of their time evolution can be done in parallel.

The equations of motion for a system of classical nuclei surrounded by a cloud of electrons can be written within the mean-field approximation as coupled classical Hamilton equations for the nuclei, and the time dependent Schrödinger equation for electrons.

For solving the equations we need a reliable and computationally feasible electronic Hamiltonian. We use the DIM (*diatomics-in-molecules*) approach, where the electronic hamiltonian is written as a sum of diatomic and atomic contributions,

$$\hat{\mathrm{H}} = \sum_{p=1}^{n-1} \sum_{q=p+1}^{n} \hat{\mathrm{H}}_{pq} - (n-2) \sum_{p=1}^{n} \hat{\mathrm{H}}_{p}, \tag{1}$$

where n denotes the number of atoms. The wavefunction basis set consists of $3n$ valence-bond Slater determinants and represents states with the positive charge localized on a particular atom in a valence p_m-orbital.

The model has been further extend by including the spin-orbit coupling using a semiempirical *atoms-in-molecules* scheme, which doubles the basis set, and the inclusion of three-body polarization forces of the induced dipole-induced dipole type. Recently a new approach for hybrid quantum-classical dynamics has been developed, which includes quantum decoherence by introducing periodic collapse of the electronic wave function. This is called the MFQ (mean field with quenching) method.

The implementation is written in FORTRAN 90 and parallelized using MPI. Integration of trajectories is distributed using task management, where trajectories are distributed among CPU cores by a single master process. Scalability has been tested for up to 16384 CPU cores, on PRACE Tier-0 supercomputers JUGENE and HERMIT.

Financial support by IT4Innovations Centre of Excellence project, reg.no. CZ.1.05/1.1.00/02.0070 supported by Operational Programme 'Research and Development for Innovations' funded by Structural Funds of the European Union and state budget of the Czech Republic.

References

1. D. Hrivnak, R. Kalus and F. X. Gadea, Europhys. Lett., 71 (1), pp. 4248 (2005).
2. I. Janecek, D. Hrivnak and R. Kalus, THE JOURNAL OF CHEMICAL PHYSICS, 125, 104315 (2006).
3. I. Janecek, S. Cintava, D. Hrivnak, R. Kalus, M. Farnik, and F. X. Gadea, THE JOURNAL OF CHEMICAL PHYSICS 131, 114306 (2009).
4. P. Pukowiecova, F. X. Gadea and R. Kalus, THE JOURNAL OF CHEMICAL PHYSICS 133, 214302 (2010).

Multiple Histogram Methods for the Isothermal Isobaric Ensemble

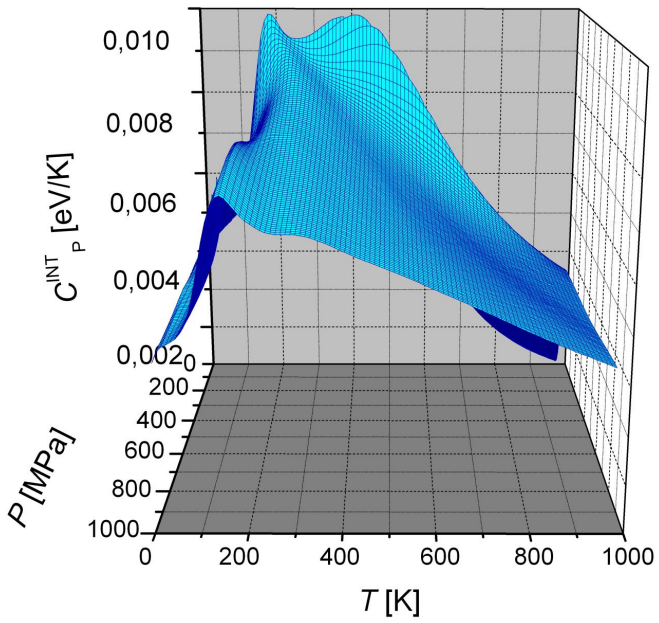
Aleš Vítek[1] **and René Kalus**[2]

[1] Centre of Excellence IT4Innovations,
VŠB - Technical University of Ostrava, 17. listopadu 15, 708 33 Ostrava, Czech Republic
E-mail: ales.vitek@vsb.cz

[2] Centre of Excellence IT4Innovations & Department of Applied Mathematics
VŠB - Technical University of Ostrava, 17. listopadu 15, 708 33 Ostrava, Czech Republic
E-mail: rene.kalus@vsb.cz

In classical constant-temperature (NVT) thermodynamic simulations of physical systems using both Monte Carlo or molecular dynamics approaches, mean values of thermodynamic quantities (internal energy, heat capacity, etc.) are obtained only for temperatures for witch simulations are carried out. If the complete temperature dependence of the measured quantity is needed, an appropriate interpolation and/or extrapolation technique has to be used. Of course, schemes based on physical assumption should be preferred to those purely mathematical. In 1988, Ferrenberg showed how to calculate the classical density of states of the system, $\Omega(E)$, from a single temperature Monte Carlo simulation (carried out at specific temperature T_{S}) and how to determine the mean value of any variable $\langle X\rangle_T$ which depends on system coordinates and momenta only through the instanteous energy, $X(q,p) = X(E(q,p))$, for an arbitrary temperature T close to T_{S} (*the single histogram method*[1]). Later on, Ferrenberg derived a more general scheme, *the multiple histogram method*[2], within which the classical density of states $\Omega(E)$ is calculated from energy histograms $h_I(E)$ obtained from simulations at several different temperatures T_I covering the temperature range of interest and mean values are calculated at essentially any temperature from this range by means of the 1D numerical integration.

In the present work, we introduce a modification of the multiple histogram methods for the isothermal - isobaric (NPT) ensemble. Two-dimensional classical density of states, $\Omega(E,V)$, is calculated from energy - volume histograms, $h_{IJ}(E,V)$ drawn from simulations performed at temperatures T_I and pressures P_J and using an isothermal - isobaric parallel tempering Monte Carlo method[3]. The value of a variable dependent only on the system energy and volume, $X(E,V)$, can be then easily determined for any temperature and pressure from density of states $\Omega(E,V)$ by means of the computationally still very cheap 2D integration. Nevertheless, compared with the multiple histograms method for the NVT ensemble, the two-dimensional histograms used in the present approach impose high demands on the computer memory, in particular, at low temperatures and high pressures. This is because energy and volume fluctuations are very small in this case and very fine grids of energy and volume are needed. In this work, we show that non-uniform grids of energy and volume used in histograms can reduce these demands to an acceptable level. This is mainly because regions of the system phase space corresponding to low energies and small volumes are sampled at low temperatures and high pressures, respectively, and, consequently, denser grids are needed exactly near the minimum of the energy and near the minimum of the volume while sparse grids are sufficient elsewhere.



Interaction part of constant pressure heat capacity $C_{\mathrm{P}}^{\mathrm{INT}}$ of $(\mathrm{H_2O})_{15}$ cluster as a function of temperature T and pressure P.

We have performed this method to study thermal properties of water clusters exposed to high pressures. After isobaric isothermal parallel tempering Monte Carlo simulations we have used multiple histogram methods for calculations of constant pressure heat capacity and Pearson correlation coefficient for energy and volume. Local maximum of heat capacity on the temperature axes correspond to the temperature intervals of cluster phase changes (phase coexistence regions). As an example, constant pressure heat capacity of $(\mathrm{H_2O})_{15}$ cluster is illustrated in the figure. Pressure conditioned structural changes occurred at pressure intervals, where PV therm of enthalpy is high enough to become comparable with cluster interaction energy and structures with smaller volume may by favored over those with low interaction energy. It can be expected that in the structural transformation region on the pressure axis energy and volume will be strongly anti-correlated and hence the correlation coefficient approaches the value -1. Both, heat capacity and Pearson coefficient has been used to figure phase diagram of water clusters.

References

1. New Monte Carlo technique for studying phase transitions: A. M. Ferrneberg, R. H. Swendsen, Phys. Rew. **61**, 31, 1988.
2. Optimized Monte Carlo data analysis: A. M. Ferrneberg and R. H. Swendsen, Phys. Rew. Lett **63**, 12, 1989.
3. Replica-exchange Monte Carlo method for the isobaric-isothermal ensemble: T. Okabe, M. Kawata, Y. Okamoto, et al., Chem. Phys. Lett **335**, 5-6, 2001.

Atomistic Study of the Influence of Lattice Defects on Thermal Conductivity

Tao Wang and Alexander Hartmaier

Interdisciplinary Centre for Advanced Materials Simulation (ICAMS)
Ruhr-Universität Bochum, Germany

E-mail: tao.wang@ruhr-uni-bochum.de, Alexander.Hartmaier@ruhr-uni-bochum.de

Lattice defects such as vacancies, grain boundaries and cracks are inevitably present in technical materials. We conduct non-equilibrium molecular dynamics simulations to calculate the thermal conductivity of different materials and to study the influence of lattice defects. In order to test the microstructural effects on thermal conductivity for a broad range of interatomic bond types, we chose several model materials: silicon with covalent bonds, calcium-fluoride with ionic bonds and copper with metallic bonds. The results show that there is a strongly non-linear response of the thermal conductivity with respect to vacancy concentration. Concerning grain boundaries and micro cracks a sharp drop of the thermal conductivity at the interface is observed, which leads to the definition of a effective interfacial thermal conductivity. The results of this study can be used to estimate the influence of lattice defects on the thermal conductivity of technical materials.

”Stress Relief” via Embedding of Cyclopropane Derivatives in Polymers

Miriam Wollenhaupt

Ruhr-Universität Bochum, Lehrstuhl für Theoretische Chemie, 44780 Bochum, Germany

E-mail: miriam.wollenhaupt@theochem.ruhr-uni-bochum.de

The conventional way of starting chemical reactions is to use thermal, photochemical, or electrochemical activation. Recently developed atomic force microscopy and sonochemical processes in an ultrasonic bath provide the possibility of applying mechanical forces to molecules while monitoring the change in the molecules' structure and reaction behaviour. Therefore, it is now well appreciated that external mechanical forces can be applied to specific covalent bonds within molecular systems, defining the field of covalent mechanochemistry.

Under mechanical forces, gem-dichlorocyclopropanes incorporated along the backbone of cis-polybutadiene exhibit an electrocyclic ring opening accompanied with a chlorine migration[1].

Besides the practical results, theoretical investigations on cis- and trans-1,1-dichloro-2,3-dimethylcyclopropane have revealed some striking features, such as a lack of selectivity at high forces or unexpected branching ratios[2]. We used static calculations to investigate changes in electronic properties along the reaction pathways under a variety of forces. The analysis of wavefunction and electron density was performed using Natural Bond Orbitals and Quantum Theory of Atoms In Molecules.

References

1. J. M. Lenhardt, A. L. Black, S. L. Craig, J. Am. Chem. Soc. **131**, 10818-10819, 2009.
2. P. Dopieralski, J. Ribas-Arino, D. Marx, Angew. Chem. Int. Ed. **50**, 7105-7108, 2011.

Computational Molecular Systems Biology

Samira Yazdi and Matthias Stein

Molecular Simulations and Design
Max Planck Institute for Dynamics of Complex Technical Systems Magdeburg, Germany

E-mail: yazdi@mpi-magdeburg.mpg.de

Systems biology is the study of the dynamic interactions of molecular components of biological systems. Through integration of computational and experimental approaches a model of the structure and dynamics of a biological system is generated, shedding light on inter- and intra-cellular behavior. When high-resolution crystal structures of biological molecules are not available, computational molecular modeling techniques are used to generate a structural model based on homologous molecules with existent crystal structures. The dynamic interactions of a system is studied with simulation techniques that sample the conformational flexibility of molecules. Over the past decades molecular modeling/simulation has emerged as a very powerful tool to analyze features of biomolecular structures that are difficult or impossible to capture experimentally, ranging from ranking of interaction strengths and affinity calculations to the mapping of transition states and pathways involved in conformational changes.

The focus of a current study involves studying the ubiquitination of the transcription factor NF-κB inhibitor, IκBα; a process catalyzed by the ubiquitin-protein ligase known as SCF. The SCF is a four-subunit RING-type ligase which is active at the last of a three step ubiquitination process. SCF complexes are composed of the scaffold protein Cul1, the RING-domain protein Rbx1/Roc1, the adaptor protein Skp1, and an F-box protein that binds a substrate. The F-box protein β-TrCP recognizes a doubly phosphorylated DpSGφXpS destruction motif, present in IκBα, which is followed by ubiquitination of these proteins at specific lysines by the SCF complex. Cytokines induce the phosphorylation of the two serine residues in the IκBα destruction motif, essential for β-TrCP binding, signaling for its ubiquitination and destruction by the proteasome and ultimately activation of NF-κB. To better understand the mechanisms of recognition of doubly phosphorylated IκBα by β-TrCP and the influence of phosphorylation on rates of association, we are modeling the interaction between β-TrCP and phosphorylated IκBα by employing Brownian and molecular dynamics.

In another study, we are investigating the molecular basis for antigenic shift and antigenic drift in haemagglutinin (HA), the glycoprotein in the membrane of type A influenza viruses which binds to sialic acid attached to host cell-surface glycoproteins thereby mediating receptor binding and membrane fusion in influenza. We will also design an anti-viral drug for treatment of influenza in a process where identification of a peptidic ligand will ultimately act as an HA inhibitor. A thorough investigation of the structure and receptor binding properties of HA together with a structural mapping of mutations in the HA binding pocket is a crucial initial step in this process. Through generation of homology models of influenza HA proteins, a detailed analysis is then carried out of the properties of salic acid binding site in different influenza viruses in human, identifying mutations and key residues taking part in binding. Only then can the design and docking of peptides to the HA binding pocket take place.

Simulation of Nonlinear Spectra with Classical Response Functions

Tobias Zentel, Sergei Ivanov, and Oliver Kühn

Institut of Physics, University of Rostock, Germany
Molecular Quantum Dynamics Group

E-mail: tobias.zentel@uni-rostock.de

To calculate nonlinear spectra from equilibrium simulations response functions are needed. In the classical limit the quantum commutator is replaced by Poisson brackets and the third order response function obeys:

$$R_{cl}^{(3)}(t,t_3,t_2;t_1) = -\langle\{\{\{\mu(t),\mu(t_3)\},\mu(t_2)\},\mu(t_1)\}\rho_{eq}\rangle\,,$$

where $\langle\,\rangle$ indicates averaging over the phase space. The key element to calculate these classical response functions are stability (monodromy) matrices. They measure how chaotic a system behaves. The stability matrix $\mathbf{M}$ is definded as

$$\mathbf{M}(\mathbf{t},\mathbf{t}') = \begin{pmatrix} \frac{\partial q_t}{\partial q_{t'}} & \frac{\partial q_t}{\partial p_{t'}} \\ \frac{\partial p_t}{\partial q_{t'}} & \frac{\partial p_t}{\partial p_{t'}} \end{pmatrix},$$

with q and p being position and conjugate momenta. The elements show how each coordinate of the system responds at a time t to small initial offsets at an earlier time t'. For deterministic, quasi-periodic systems, like a 1D harmonic oscillator or Morse potential, the elements stay finite and small. But for chaotic systems the elements diverge in $t - t'$. It was proposed by van Kampen that this is a fundamental limitation arising from the perturbative ansatz, which should not be valid in chaotic systems for long times[1]. This would make the computation of response functions unstable for longer times and hence limits the resolution in the frequency domain. On the contrary it is argued that upon calculating the response functions from the stability matrices and averaging over the phase space the divergence is lost, and the response functions behave nicely[2].

In the present contribution this issue is studied for simple model systems. In a 1D Morse potential, as expected, the linear classical response decays upon averaging. But, even so the stability matrix stays finite, the third order response functions for two pulse echo measurements diverge linearly. This divergence is also reported for other 1D anharmonic oscillator systems[4] . In contrast, dissipative and chaotic systems do not show a divergence of response functions.[3]

References

1. N.G. van Kampen Phys. Norv. **5**, 279, 1971
2. S. Mukamel, V. Khidekel, V. Chernyak Phys. Rev. E **53**, 4, 1996.
3. M. Kryvohuz, J. Cao PRL **108**, 21, 2006.
4. W. Noid, G. Ezra, R. Loring J. Phys. Chem. **19**, 21, 2004.

Index of Authors

List of Participants

Ahmadi, Amirhossein
Universidad Nacional de Educación a Distancia (UNED)
Departamento de Ciencias y Técnicas Fisicoquímicas, Madrid, Spain
aahmadi@bec.uned.es

Balasubramanian, Ganesh
Technische Universität Darmstadt
Eduard-Zintl-Institut für Anorganische und Physikalische Chemie, Darmstadt, Germany
bganesh@theo.chemie.tu-darmstadt.de

Beckmann, Nils
Fraunhofer-Institut für Werkstoffmechanik IWM, Freiburg, Germany
nils.beckmann@iwm.fhg.de

Bastian, Peter
Universität Heidelberg
Interdisciplinary Center for Scientific Computing (IWR), Heidelberg, Germany
peter.bastian@iwr.uni-heidelberg.de

Behler, Jörg
Ruhr-Universität Bochum, Lehrstuhl für Theoretische Chemie, Bochum, Germany
joerg.behler@theochem.ruhr-uni-bochum.d

Bravo-Rodríguez, Kenny
Max-Planck-Institut für Kohlenforschung
Theory Department, Mülheim an der Ruhr, Germany
kenny@mpi-muelheim.mpg.de

Bücker, Oliver
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
o.buecker@fz-juelich.de

Carloni, Paolo
German Research School for Simulation Sciences
Computational Biophysics, Jülich, Germany
p.carloni@grs-sim.de

Chiodo, Letizia
Università degli Studi di Roma ”La Sapienza”
Center for Life - NanoScience, Physics Department, Roma, Italy
letizia.chiodo@iit.it

Costanzo, Andrea
Forschungszentrum Jülich GmbH, Institute for Advanced Simulation (IAS)
Institute of Complex Systems (ICS), Theoretical Soft Matter and Biophysics, Germany
a.costanzo@fz-juelich.de

Crawford, Luke
University of St. Andrews, School of Chemistry, St. Andrews, Scotland
lc437@st-andrews.ac.uk

Curioni, Alessandro
IBM Zurich Research Laboratory
Computational Science Group, Rüschlikon, Switzerland
cur@zurich.ibm.com

de la Torre, Jaime Arturo
Universidad Nacional de Educación a Distancia (UNED)
Departamento de Física Fundamental, Madrid, Spain
jatorre@bec.uned.es

Dellago, Christoph
University of Vienna, Faculty of Physics, Vienna, Austria
Christoph.Dellago@univie.ac.at

Delle Site, Luigi
Freie Universität Berlin, Institute for Mathematics, Berlin, Germany
luigi.dellesite@fu-berlin.de

De Nicola, Antonio
Université di Salerno, Dipartimento di Chimica e Biologia, Fisciano (SA), Italy
adenicola@unisa.it

Derevyanko, George
Forschungszentrum Jülich GmbH
Institute of Complex Systems (ICS), Molecular Biophysics, Jülich, Germany
g.derevyanko@fz-juelich.de

Devadoss V., Fredrick Robin
Universität Konstanz, Konstanz Research School Chemical Biology, Konstanz, Germany
Fredrick.Devadoss@uni-konstanz.de

Di Pasquale, Nicodemo
Politecnico di Torino, Institute of Chemical Engineering
Department of Applied Science and Technology, Torino, Italy
nicodemo.dipasquale@polito.it

Doltsinis, Nikos. L.
Universität Münster, Institut für Festkörpertheorie, Münster, Germany
nikos.doltsinis@wwu.de

Dünweg, Burkhard
Max Planck Institute for Polymer Research, Polymer Theory, Mainz, Germany
duenweg@mpip-mainz.mpg.de

Eckhardt, Wolfgang
Technische Universität München, Institut für Informatik, 85748 Garching, Germany
eckhardw@in.tum.de

Eisbein, Emanuel
Technische Universität Dresden, Physikalische Chemie, Dresden, Germany
emanuel.eisbein@chemie.tu-dresden.de

Español, Pep
Universidad Nacional de Educación a Distancia (UNED)
Departamento de Física Fundamental, Madrid, Spain
pep@fisfun.uned.es

Fedosov, Dmitry A.
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Institute of Complex Systems (ICS), Theoretical Soft Matter and Biophysics, Germany
d.fedosov@fz-juelich.de

Fekete, Ádám
Pázmány Péter Catholic University
Interdisciplinary Technical Sciences Doctoral School, Budapest, Hungary
fekete.adam@itk.ppke.hu

Gemünden, Patrick
Max Planck Institute for Polymer Research, Polymer Theory, Mainz, Germany
gemuende@mpip-mainz.mpg.de

Ghysels, An
Ghent University, Center for Molecular Modeling, Ghent, Belgium
an.ghysels@ugent.be

Goez, Albrecht
Technical University Braunschweig
Institute for Physical and Theoretical Chemistry, Braunschweig, Germany
a.goez@tu-bs.de

Gompper, Gerhard
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Institute of Complex Systems (ICS), Theoretical Soft Matter and Biophysics, Germany
g.gompper@fz-juelich.de

Gräter, Frauke
Heidelberg Institute for Theoretical Studies (HITS)
Molecular Biomechanics, Heidelberg, Germany
frauke.graeter@h-its.org

Grotendorst, Johannes
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
j.grotendorst@fz-juelich.de

Gutheil, Inge
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
i.gutheil@fz-juelich.de

Halver, René
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
r.halver@fz-juelich.de

Hartmaier, Alexander
Ruhr-Universität Bochum, Interdisciplinary Center for Advances Materials Simulation (ICAMS), Department of Micromechanical and Macroscopic Modelling, Germany
alexander.hartmaier@rub.de

Helms, Volkhard
Universität des Saarlandes, Computational Biology
Center for Bioinformatics, Saarbrücken, Germany
volkhard.helms@bioinformatik.uni-saarland.de

Hummer, Gerhard
Laboratory of Chemical Physics, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
National Institutes of Health (NIH), Bethesda, Maryland, USA
hummer@helix.nih.gov

Kaffel, Ahmed
ICERM Brown University, School of Engineering, Providence RI, USA
kaffel@vt.edu

Kahlen, Jens
Max Planck Institute for Polymer Research, Polymer Theory, Mainz, Germany
kahlen@mpip-mainz.mpg.de

Kalikka, Janne
University of Jyväskylä, Department of Physics, Jyväskylä, Finland
janne.kalikka@jyu.fi

Karner, Carina
University of Vienna, Faculty of Physics, Vienna, Austria
carina.karner@univie.ac.at

Kasimova, Marina A.
Lomonosov Moscow State University
Department of Biophysics, Faculty of Biology, Moscow, Russia
marina.kasimova@gmail.com

Khoshnood, Atefeh
Sharif University of Technology, Department of Mechanical Engineering, Teheran, Iran
atefeh_khoshnood@mech.sharif.ir

Köhler, Stephan
Johannes Gutenberg Universität Mainz, Institut für Physik, Mainz, Germany
koehlst@uni-mainz.de

Körfgen, Bernd
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
b.koerfgen@fz-juelich.de

Koschke, Konstantin
Max Planck Institute for Polymer Research, Polymer Theory, Mainz, Germany
koschke@mpip-mainz.mpg.de

Ksenofontova, Olga
Saint Petersburg State University, Department of Biochemistry, Petersburg, Russia
jabiata@yandex.ru

Laino, Teodoro
IBM Zurich Research Laboratory, Mathematical and Computational Sciences Department
Rüschlikon, Switzerland
teo@zurich.ibm.com

Lechuga García, Javier
Universität Würzburg, Institut für Mathematik. Würzburg, Germany
javier.lechuga@mathematik.uni-wuerzburg.de

Leitold, Christian
University of Vienna, Faculty of Physics, Vienna, Austria
christian.leitold@univie.ac.at

Li, Jinyu
German Research School for Simulation Sciences
Computational Biophysics, Jülich, Germany
j.li@grs-sim.de

Lippert, Thomas
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
th.lippert@fz-juelich.de

Mahajan, Dhiraj K.
Ruhr-Universität Bochum, Interdisciplinary Center for Advances Materials Simulation (ICAMS), Department of Micromechanical and Macroscopic Modelling, Germany
dhiraj.mahajan@rub.de

Marx, Dominik
Ruhr-Universität Bochum, Lehrstuhl für Theoretische Chemie, Bochum, Germany
dominik.marx@theochem.ruhr-uni-bochum.de

Melchionna, Simone
Università degli Studi di Roma "La Sapienza"
Dipartimento di Fisica, Roma, Italy
simone.melchionna@roma1.infn.it

Meléndez Schofield, Marc
Universidad Nacional de Educación a Distancia (UNED)
Departamento de Física Fundamental, Madrid, Spain
mmelendez@fisfun.uned.es

Menzl, Georg
University of Vienna, Faculty of Physics, Vienna, Austria
georg.menzl@univie.ac.at

Mohr, Bernd
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
b.mohr@fz-juelich.de

Morawietz, Tobias
Ruhr-Universität Bochum, Lehrstuhl für Theoretische Chemie, Bochum, Germany
tobias.morawietz@theochem.rub.de

Müller, Kathrin
Forschungszentrum Jülich GmbH, Institute of Complex Systems (ICS)
Theoretical Soft Matter and Biophysics, Jülich, Germany
k.mueller@fz-juelich.de

Neogi, Sanghamitra
Max Planck Institute for Polymer Research, Polymer Theory, Mainz, Germany
neogi@mpip-mainz.mpg.de

Ozmaeian, Masoumeh
Max Planck Institute for Polymer Research, Polymer Theory, Mainz, Germany
ozmaeian@mpip-mainz.mpg.de

Pedersen, Ulf R.
Vienna University of Technology, Institute of Theoretical Physics and CMS, Austria
ulf@urp.dk

Perez, Danny
Los Alamos National Laboratory, Theoretical Division, Los Alamos, USA
danny_perez@lanl.gov

Peter, Christine
Max Planck Institute for Polymer Research, Polymer Theory, Mainz, Germany
peter@mpip-mainz.mpg.de

Podewitz, Nils
Forschungszentrum Jülich GmbH, Institute of Complex Systems (ICS)
Theoretical Soft Matter and Biophysics, Jülich, Germany
n.podewitz@fz-juelich.de

Rüde, Ulrich
Universität Erlangen-Nürnberg
Department of Computer Science, Erlangen, Germany
Ulrich.Ruede@informatik.uni-erlangen.de

Saggiorato, Guglielmo
Forschungszentrum Jülich GmbH, Institute of Complex Systems (ICS)
Theoretical Soft Matter and Biophysics, Jülich, Germany
g.saggiorato@fz-juelich.de

Salimi Parvaneh, Leila
Max Planck Institute for Polymer Research, Polymer Theory, Mainz, Germany
salimi@mpip-mainz.mpg.de

Schiller, Annika
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
a.schiller@fz-juelich.de

Singraber, Andreas
University of Vienna, Faculty of Physics, Vienna, Austria
andreas.singraber@univie.ac.at

Solar, Mathieu
Martin Luther Universität, Theoretical Polymer Physics, Halle, Germany
mathieu.solar@physik.uni-halle.de

Spallanzani, Nicola
CINECA, SuperComputing, Applications and Innovation Department
Casalecchio di Reno (Bologna), Italy
n.spallanzani@cineca.it

Stachoň, Martin
VŠB - Technical University of Ostrava
Department of Applied Mathematics, Ostrava-Poruba, Czech Republic
martin.stachon@vsb.cz

Sutmann, Godehard
Forschungszentrum Jülich, Institute for Advanced Simulation (IAS)
Jülich Supercomputing Centre (JSC), Jülich, Germany
g.sutmann@fz-juelich.de

Tavernelli, Ivano
Laboratory of Computational Chemistry and Biochemistry, Institute of Chemical Sciences and Engineering, Swiss Federal Institute of Technology EPF Lausanne, Switzerland
ivano.tavernelli@epfl.ch

Theodorou, Doros N.
National Technical University of Athens, Department of Materials Science and Engineering, School of Chemical Engineering, Athens, Greece
doros@central.ntua.gr

Thome, Christian
Universität des Saarlandes, Theoretische Physik, Saarbrücken, Germany
thome@lusi.uni-sb.de

Tuckerman, Mark E.
New York University, Department of Chemistry and Courant Institute of Mathematical Sciences, New York, USA
mark.tuckerman@nyu.edu

Vítek, Aleš
VŠB - Technical University of Ostrava, Centre of Excellence IT4Innovations, Ostrava, Czech Republic
ales.vitek@vsb.cz

Wang, Tao
Ruhr-Universität Bochum, Interdisciplinary Centre for Advanced Materials Simulation (ICAMS), Bochum, Germany
tao.wang@icams.ruhr-uni-bochum.de

Winkler, Roland G.
Forschungszentrum Jülich GmbH, Institute of Complex Systems (ICS)
Theoretical Soft Matter and Biophysics, Jülich, Germany
r.winkler@fz-juelich.de

Wollenhaupt, Miriam
Ruhr-Universität Bochum, Lehrstuhl für Theoretische Chemie, Bochum, Germany
Miriam.Wollenhaupt@ruhr-uni-bochum.de

Yazdi, Sammy
Max Planck Institute for Dynamics of Complex Technical Systems
Molecular Simulations and Design, Magdeburg, Germany
yazdi@mpi-magdeburg.mpg.de

Zentel, Tobias
Universität Rostock, Institut für Physik, Rostock, Germany
tobias.zentel@uni-rostock.de