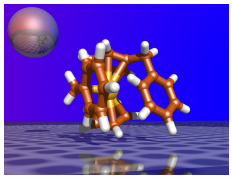
University of Strathclyde



Demystifying Molecular Modelling

List of Participants and Book of Abstracts

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I Workshop Program

- 9.00 Registration in the Mccance Building (MCC3)
- 9.30 Welcome and announcements

Session 1

- 9.40 Prof. Des Higham
- 10.25 Prof. Mikhail Osipov
- 11.10 Break
- 11.30 Dr. Hans Martin Senn
- 12.15 Prof. Nick Stone

- 13.00 Lunch

Session 2

- 14.00 Prof. Rainer Breitling
- 14.45 Break
- 15.10 Prof. Ernesto Estrada

- 15.55 Poster session/Discussion to be followed by Wine/Cheese

II Oral presentations

Popular Approaches to Modelling and Simulating Chemical Reactions

Des Higham

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I will give a very gentle introduction to three different mathematical modelling regimes for chemical kinetics: the master equation (Gillespie), diffusion (Langevin) and deterministic (mass action) frameworks. I will explain how they are related and discuss their relative pros and cons.

Molecular theory of biaxial nematics composed of flat molecules with four mesogenic groups

Mikhail Osipov[1] and Maxim Gorkunov[2]

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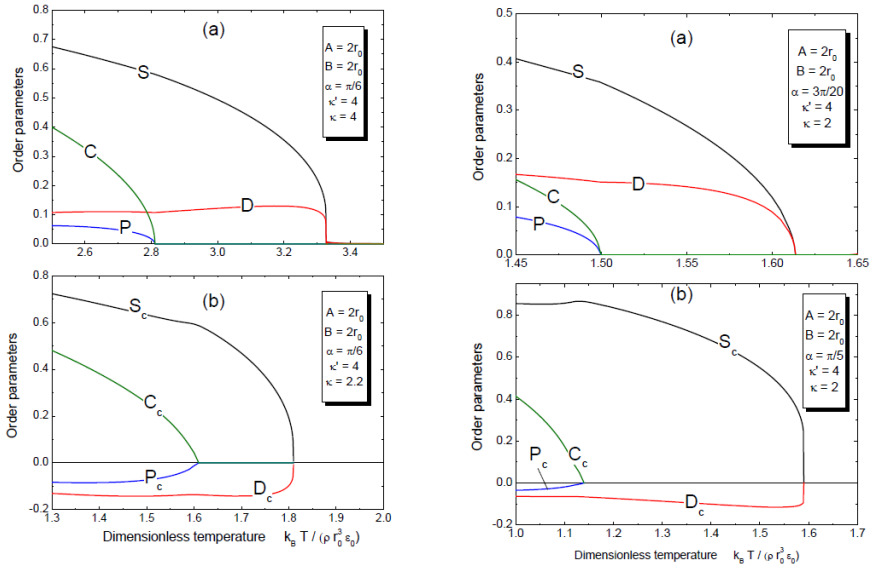
Biaxial nematic phases are expected to be stable in materials with maximum molecular biaxiality. However, several attempts to tailor real plate-like molecules with strong biaxiality have not lead to a biaxial phase. Biaxial ordering has been found in mesogens of lower symmetry including bent-core molecules [1] and tetrapodes with four mesogenic groups [2]. Exisitng molecular theory has made a number of predictions including the shape of the phase diagram [3] but it did not establish a correlation between model molecular structure and parameters of the mean-field potential.

A mean-field theory of phase transitions in biaxial nematics is developed using the molecular model composed of four mesogenic groups rigidly linked to the same centre and interacting via a Gay-Berne potential. Biaxial interactions between such molecules are effectively controlled by the tilt angle between mesogenic groups and the rectangular molecular frame. The coefficients of the mean-field potential are calculated numerically as functions of the tilt angle and elongation of mesogenic groups by expansion of the total interaction potential. Phase diagrams are obtained which enables one to study the dependence of the stability regions of uniaxial and biaxial phases on the molecular model parameters Order parameters of the uniaxial and biaxial nematic phases are evaluated by direct minimization of the free energy for representative points in the phase diagrams. Relative strength of the biaxial intermolecular interaction is increasing with increasing tilt angle of the mesogenic groups which enables one to discuss the origin of the stability of the biaxial ordering in the nematic phase composed of terapode molecules.



Temperature variation of four order parameters at the uniaxial calamitic – biaxial nematic (a,b) and uniaxial discotic – biaxial nematic (c,d) transitions calculated numerically along four lines in the phase diagrams.

References

[1] L.A.Maidsen et.al Phys.Rev.Lett. 92,145506 (2004), B.R.Acharya et.al.,Phys.Rev.Lett. 93, 237801 (2004)
[2] K. Merkel, A. Kocot, J.K. Vij, R Korlacki, G.H. Mehl and T. Meyer, Phys. Rev. Lett. 93, 237801 (2004)
[3] F.Bisi, E.G.Virga, E.C.Garland, G. De Matteis, A.Sonnet and G.E.Durand., Phys.Rev.E. 73, 051709 (2006)

Insights into Enzymatic Reactivity from QM and QM/MM Calculations

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In order to model chemical reactions, i.e., bond-making and bond-breaking processes, quantum-mechanical (QM) methods are required. However, QM methods are restricted to systems of up to a few hundred atoms. The size and conformational complexity of biopolymers, on the other hand, calls for methods capable of treating up to several 100 000 atoms and allowing for simulations over time scales of tens of nanoseconds. This is achieved by highly efficient, force-field-based molecular mechanics (MM) methods. To model large biomolecules the logical approach is therefore to combine the two techniques and to use a QM method for the chemically active region (e.g., substrates and co-factors in an enzymatic reaction) and an MM treatment for the surroundings (e.g., protein and solvent). The resulting schemes are commonly referred to as combined or hybrid QM/MM methods. They enable the modeling of reactive biomolecular systems at a reasonable computational effort while providing the necessary accuracy.
I will give an overview of QM/MM approaches and techniques, illustrated with examples from our research on enzymatic reaction mechanisms.

Molecular specific disease diagnosis using vibrational spectroscopy coupled to multivariate analysis

Nick Stone

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BioModel Engineering for metabolomic systems biology

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Abstract: Metabolomics is a late-comer among postgenomic technologies, but it occupies a central position in systems biology. This presentation will illustrate the challenges of metabolomic modelling using examples from trypanosome parasite biology. BioModel Engineering will be introduced as a conceptual framework to connect the worlds of constraint-based stochiometric modelling and quantitative dynamic differential-equation modelling when dealing with sparse and uncertain experimental data.

Graph/network theory and molecular design. Examples from the real world

Ernesto Etsrada

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I will start by introducing the necessity for a 'universal' language for molecular modelling at different size scales. Then, I will propose the use of graph and network theory as a unifier of molecular representations at small, medium and gigantic size scales, which cover from single molecules and biomacromolecules to molecule-molecule interaction networks. I will show some examples based first in the Topological-Substructural-Molecular Design (TOPS-MODE) approach for the rational design of pharmacologically active chemicals as well as in predicting their toxicological and ADME properties.Then, I will show how to use network theory for studying biomacromolecules making emphasis on protein structures. As an example I will illustrate theidentification of possible binding sites in proteins. Finally, I will cover the topic of identifying possible pharmacological targets by studying protein-protein interaction networks. A general approach on how integrate all these tools will be provided.

III Poster Contribution

Maximin and Bayesian Robust Experimental Design for Modeling Signaling Pathways

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Experimental design is an important part of any system identification process, especially when the models are complex and measurement data are sparse and noisy, as occurs in biochemical regulatory pathway identification studies. The quality of conventional optimal experimental design largely depends on the accuracy of model parameter estimates, which are often either unavailable at the stage of design or poorly estimated. Therefore, robust experimental design algorithms have been proposed when model parametric uncertainties need to be addressed during the design process. In this work, two robust design strategies are investigated. The first method is a maximin experimental design approach which is a worst-case design strategy, and the second method is the Bayesian experimental design that “takes an average” of the parametric uncertainty effects. The limitations of maximin design which describe the structural uncertainty using a local Taylor representation are identified and quantitatively assessed. The differences between the maximin and the Bayesian robust experimental designs are also explicitly revealed based on the assessment of parametric uncertainty and the concept of effective design.

Nanomaterials theory at Strathclyde

Ben Hourahine

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I will briefly outline the main themes, topics and tools of my research. I\'m the resident theorist in the Semiconductor Spectroscopy and Devices group at Strathclyde. The group remit is the less developed semiconductors, with a recent focus on the III-nitride materials. My primary research areas are based around defects and impurities in the Al/Ga/In-N family of materials and Si/Ge, but I also work with other materials including transition metal nanoclusters and strongly correlated and magnetic systems containing lanthanides.
I'm also active in developing new theoretical methodologies, in particular I'm a co-author of the DFTB+ semi-empirical tight-binding code (http://www.dftb-plus.info). I also use large scale density fuctional modelling (AIMPRO) and assorted home-brewed Monte Carlo codes.
Additionally I'm involved in a collaboration with my colleague Francesco Papoff to develop new efficient and accurate methods for calculation of the optical fields of nano-particles and structures.
For more details visit http://ssd.phys.strath.ac.uk

Mechanisms and dynamics of protein clustering on a solid surface

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In this poster we explore protein clustering mechanisms on a solid surface using Atomic Force Microscopy, Monte Carlo simulation and atomistic molecular dynamics (MD). Lysozyme-on-mica is used as a model system. We show that as the protein aggregates on the surface, clusters are formed that possess significant mobility on the surface. The cluster mobility follows a powerlaw dependence on size, which implies a specific diffusion mechanism. The MD work illustrates the key features of the protein adsorption process and helps to provide a more complete picture of the structural evolution of the protein film, and in particular how protein immobilisation is achieved.

Modeling Metabolic Switching in Differentiating Bacterium Streptomyces coelicolor

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SIPBS, University of Strath

Ms Leena Nieminen: leena.nieminen@strath.ac.uk

Streptomyces are filamentous bacteria that are commonly found in soil ecosystems. Through their complex life cycle Streptomyces produce secondary metabolites some with antibiotic activities. The filamentous, multicellular growth of Streptomyces presents challenges for industrial scale fermentations. When growing in liquid cultures the individual hyphae of the S. coelicolor tangle together forming hyphal aggregates and eventually dense pellets. The morphology and metabolism of hyphae are influenced by depleting external oxygen and nutrient profiles within a pellet. To understand the heterogeneous nature of hyphal growth, we developed a discrete, mathematical model for filamentous growth and pellet formation. The model was parameterised with experimental results from early hyphal growth, and it predicts hyphal density and external substrate profiles within a pellet. To test the model, we have constructed enhanced green fluorescent protein constructs to study the spatio-temporal localization of enzymes in key metabolic pathways inside pellets. Based on the model simulations and experimental results, we are addressing the issues concerning the development of single pellets.

From DFT to spectroscopy and back: The use of both techniques to unearth active compounds in homogeneous catalysis

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For some time now we are using the combination of DFT calculations and spectroscopy, in particular NMR and IR, as a work horse for the investigation of active species in homogeneous catalysis. This combination has proved to be very fruitful. The poster will present selected examples. For the combination of DFT and NMR, we present work in the area of group 4 metallocene catalysts. The area of DFT and IR will be represented by a Fe pincer compound.

Equilibrium behaviour of a novel gas separation process, with application to carbon capture

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A novel gas separation process is described and analysed in the context of carbon capture. It involves a highly selective absorbent fluid below its saturation pressure adsorbed into a porous solid. This fluid simultaneously forms gas-like and liquid-like regions within the porous solid depending on the pore size. When a gas mixture is passed through this modified material it is selectively absorbed by the liquid-like regions, leading to separation of the gas components. A novel 'pressure-swing wetting layer absorption' process is used to recover the absorbed gas. This work examines the equilibrium behaviour of this process in the context of carbon capture using the density functional theory (DFT) of classical fluids. The DFT model employed represents the porous solid in terms of ideal graphitic slit-pores, and a ternary fluid model is calibrated to represent mixtures of tetrahydrofuran (the absorbent fluid), carbon dioxide and nitrogen. Under the conditions investigated here we find that the equilibrium behaviour of this system is superior to the analogous pressure-swing adsorption process without solvent. However, further experimental and process modelling work is needed to confirm this.

A self-interacting random walk model for polymer chains

F. Comets, M.V. Menshikov, S. Volkov, and A.R. Wade

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Random walks are often used to model polymer molecules in solution. The classical self-avoiding walk model has some disadvantages. We introduce a new model that is a genuine stochastic process, in which the walk interacts with its previous path. The self-interaction is mediated by the centre of mass of the previous trajectory. The model can be tuned to model polymers in extended or collapsed phases. In the extended phase, we present rigorous results on the scaling of the model.

Layer Undulations in Planar Layered Smectic C Liquid Crystals

A. J. Walker and I. W. Stewart

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A compressible dynamic theory for smectic C (SmC) liquid crystals is presented and then used with a constructed bulk elastic energy to describe a system of planar layered SmC liquid crystal undergoing various undulation modes. We show that we can expand and verify previous results on smectic A liquid crystals. Novel and confirming estimate for SmC material parameter values are produced by considering the dependence of the system on said variables.

Monte-Carlo Simulations of Organically Modified Clays in Organic Solvents

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Suspensions of organically modified clays on a monomer solvent are one of the main routes to the formation of polymer-clay nano-composites. These materials exhibit remarkable improvements in thermal and mechanical properties, when compared to pure polymer based ones, and have applications in, for example, the automotive, microelectronics and plastics industries. The key issue for improvement of these properties is control over the dispersion state of the clay platelets that will be crucial for the morphology of the final polymerized compound.

The clay platelets (e.g. Laponite, Montmorillonite) are usually very hydrophilic due to their distribution of surface charge. This charge distribution is balanced by a layer of adsorbed counter-ions. These counter-ions can be substituted with a range of ionic surfactants, leading to modification of effective clay-clay interactions and hence more stable dispersions.

The aim of our work is to better understand these effective clay-clay interactions to achieve better dispersions and hence polymer-clay materials. Previous theoretical and simulation work has focused on the description of aqueous suspensions with added salt. These models are not adequate for describing our suspensions in a monomer solvent (e.g. styrene) as the dielectric constant of the medium is significantly weaker and there is almost no screening of electrostatic interactions. Furthermore, the role of the surfactant-surfactant and surfactant-monomer interactions should be investigated to capture the main features of these complex systems.

Here we present the results for Monte Carlo simulations of a model of organically modified Laponite dispersed in styrene. Results are presented in terms of snapshots of the obtained structures and comparison of simulated radial distribution functions (RDF) with the Small Angle X-Ray Scattering (SAXS) and Static Light Scattering (SLS) experiment results for real systems. The simulations were set up to approximately match the density of the experimental systems. We find that above a critical temperature the platelets are fully dispersed showing a gas-like RDF. For lower temperatures the system is non-ergodic and gets trapped in meta-stable/unstable configurations where the platelets are arranged in networked structures. The RDFs of these structures show long range correlations and partially match the experimental results.

IV List of Participants

Dr Yu Chen
Dr Rachel Clark
Mr Diego Cortizo
Miss Jennifer Dougan
Dr Abdunaser El Ayeb
Mr Saadeldin Elmasly
Dr Rui Fartaria
Mr Neil Findlay
Professor David Flint
Miss Kirsty Gibson
Prof Peter Halling
Dr. Fei He: "*Maximin and Bayesian Robust Experimental Design for Modeling Signaling Pathways"*
Dr Aaron Hernandez-Santana
Dr Paul Hoskisson
Dr Ben Hourahine: "*Nanomaterials theory at Strathclyde"*
Mr Lirong Huang
Mr. Somkid Intep
Dr Blair Johnston
Mr. Martin Keating
Miss Stacey Laing
Dr Iain Larmour
Mr Danny van Lierop
Miss Audrey Loudon
Prof Xuerong Mao
Dr Antonio Martinez
Mr Greg McEntee
Mr Niaz McGuire
Ms Rajni Miglani
Prof Nigel Mottram
Dr Paul Mulheran: "*Mechanisms and dynamics of protein clustering on a solid surface"*
Ms Leena Nieminen: "*Modeling Metabolic Switching in Differentiating Bacterium Streptomyces coelicolor"*
Mr Mikael Olsson Robbie
Prof. Gian-Luca Oppo
Miss Clara Orofino
Dr Ben Pickard
Prof Robin Plevin
Mr Rajeev Rajasekharan Nair
Dr. Qinghua Ren
Dr Gordon Robb
Dr. Jörg Saßmannshausen: "*From DFT to spectroscopy and back: The use of both techniques to unearth active compounds in homogeneous catalysis"*
Mr Fraser Scott
Dr Andre Sonnet
Dr Ross Stevenson
Dr Martin Sweatman: "*Equilibrium behaviour of a novel gas separation process, with application to carbon capture"*
Miss Katherine Trotter
Dr Shashank Virmani
Ms. Zuzana Vobecka
Dr Andrew Wade: "*A self-interacting random walk model for polymer chains"*
Dr Alan Walker: "*Layer Undulations in Planar Layered Smectic C Liquid Crystals"*
Dr Jim Wood
Mr Iain Wright
Dr Alison Yao
Mr. Yinan Zhang